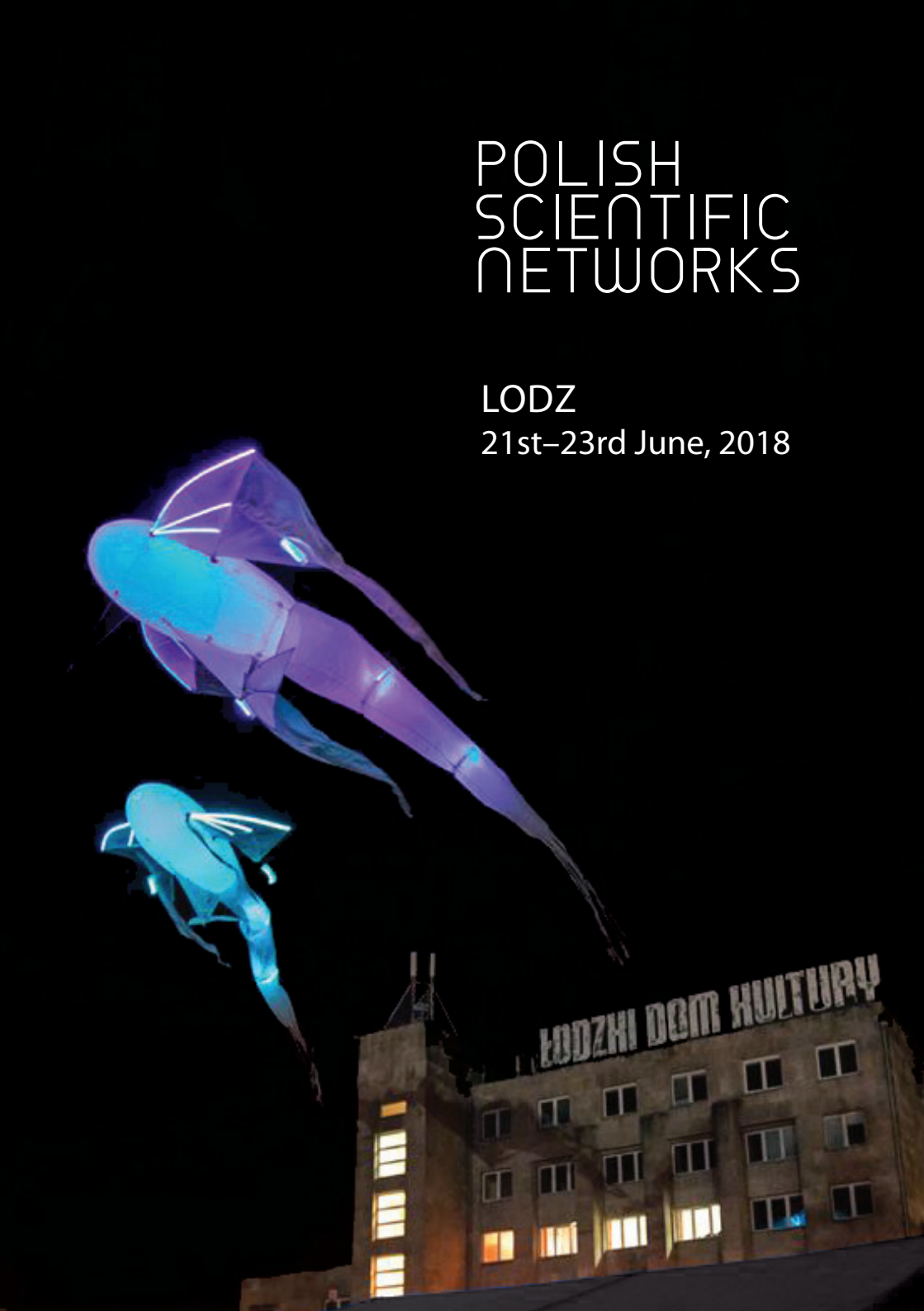
POLISH SCIENTIFIC NETWORKS

LODZ
21st–23rd June, 2018



POLISH SCIENTIFIC NETWORKS

ORGANIZERS:

AMU Akademia Młodych Uczonych

Ministry of Science and Higher Education Republic of Poland

FNP Association of the Foundation for Polish Science Scholars

STRATEGIC PARTNERS:

PAN

FNP Foundation for Polish Science

UM Medical University of Lodz

MEDIA PATRONAGE:

Naukaonline.pl

Teraz Polska

ISBN: 978-83-63305-51-2

'SYMMETRY' DUET

EWA FORTUNA-WOSZCZYŃSKA – VIOLINIST

Graduate of 2nd degree Władysław Żeleński State Secondary School of Music in Kraków, Faculty of Fine Arts and Music of University of Silesia (specialization: violin), and the Pontifical University of John Paul II in Kraków (philosophy). As a member of a string quartet she has given concerts, among others, in Japan, and with orchestras in Germany and France. She currently plays in a string orchestra Unplugged Orchestra.

ANNA BROŻEK – PIANIST

Currently Professor of the Institute of Philosophy, University of Warsaw, she studied piano and philosophy in Kraków. She has published many books in the field of philosophy and music theory (among others: "Symmetry in Music", "Principia musica", "Obraz duszy polskiej w mazurkach Romana Maciejewskiego"); she has also recorded a double album with Roman Maciejewski's mazurkas.

PROGRAMME

1. John Williams, "Theme from Schindler's List" from the movie "Schindler's List"
2. Trevor Jones, "Promontory" from the movie "The Last of the Mohicans"
3. James Horner, "For the Love of Princess" from the movie "Braveheart"
4. Michał Lorenc, "Elena's Dance" from the movie "Bandit"
5. Alan Silvestri, "Feather Theme" from the movie „Forrest Gump"
6. Hans Zimmer & Lisa Gerrard, "Now We Are Free" from the movie "Gladiator"
7. Justin Hurwitz, "Mia and Sebastian Theme / Another Day of Sun / City of Stars" from the movie "La La Land"
8. John Williams, "Devil's Dance" from the movie "The Witches of Eastwick"

PLAN CENTRUM DYDAKTYCZNEGO
UNIWERSYTETU MEDYCZNEGO W ŁODZI
PIĘTRO II - poziom I

WJAZD
NA PARKING

LEGENDA:

UCZELNIANE LABORATORIA
DOSTĘPNE NA TYM PIĘTRZE:

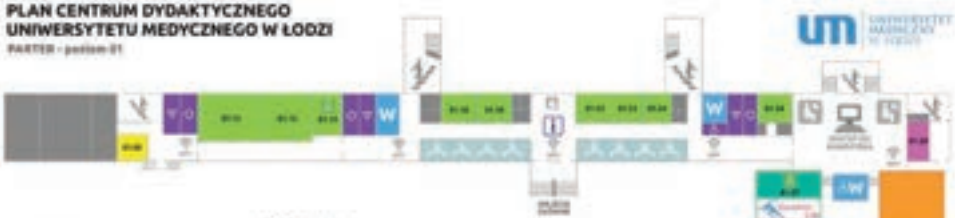
1.36 LABORATORIUM REGULACJI UKŁADU
1.37 LABORATORIUM FUNKCJI
1.38 LABORATORIUM FUNKCJI
1.39 LABORATORIUM ANTROPOMETRII
1.40 LABORATORIUM ANTROPOMETRII

58A

ULICA POMORSKA

15, 15A, 43

PLAN CENTRUM DYDAKTYCZNEGO
UNIWERSYTETU MEDYCZNEGO W ŁODZI
PARTER - poziom 01



WJAZD
NA PARKING

LEGENDA:

58A

ULICA POMORSKA

15, 15A, 43

LETTER TO PARTICIPANTS

Ladies and Gentlemen,

The Polish Scientific Networks: Science & Medicine conference is organized by the Ministry of Science and Higher Education, the Polish Young Academy, and the Association of the Foundation for Polish Science Scholars, in cooperation with the Medical University of Lodz.

The conference is dedicated primarily to non-clinical researchers and clinicians, as well as to all institutions and companies interested in supporting innovation by collaborating with medical doctors and scientists.

The main purpose of the conference is to establish favourable conditions:

- for interaction between scientists and physicians focused on translating the most recent research results into clinical practice,
- for researchers to present the currently most interesting projects, among others, in the field of epigenetics, cancer, biological chemistry, neuroscience, developmental biology, bioinformatics, systems biology, and biomodelling,
- for clinicians to point out the emerging possibilities for the application of the latest scientific achievements in patient care.

We hope that this year's Polish Scientific Networks conference will outgrow the success of previous editions and become an opportunity to exchange thoughts, establish new collaborations and inspire the participants to undertake new challenges.

We wish you fruitful discussions and a memorable stay in Lodz.

On behalf of the Organizing Committee
Anna Bielec

On behalf of the Scientific Committee
Wojciech Fendler
Krzysztof Jóźwiak

ORGANIZERS

THE POLISH YOUNG ACADEMY (PYA) was constituted under the Polish Academy of Sciences (PAS) Parliamentary Act of April 30, 2010. It is a part of the PAS corporation and was established thanks to the effort of the PAS authorities inspired by the activity of similar bodies in other countries.

One of the PYA's tasks is to promote the activity of the young scientific community, in particular:

- participating in the formation of science policy
- promoting scientific excellence
- disseminating scientific results.

Selection procedure of the PYA members is based on the election procedures for the PAS members, main criterion being the candidate's outstanding scientific achievements. PYA members are nominated for a period of 5 years, without a possibility of re-election. Each PYA member can contribute to the work of the PAS by participating in the work of divisions, branches, scientific committees and task force committees.

PYA is formed by leaders in respective scientific domains – scientists that have typically already been honoured with other prestigious awards and distinctions, including recipients of the European Research Council grants, the Ministry of Science and Higher Education Scholarships or the Foundation for Polish Science programmes. Despite their young age, many of them have already been appointed or awarded a professor title.

PYA is actively involved in consultations regarding science and higher education policy, including "Law 2.0". PYA was represented in the Council of the National Congress of Science (NCS) and participated in the NCS

conferences. Members of PYA were also involved in consultations conducted by the Policy Support Facility, a group assigned by the Ministry of Science and Higher Education with a peer review of Poland's higher education and science system, and in consultations regarding programmes supporting internationalization of Polish science, proposed by the newly founded National Agency for Academic Exchange.

In an effort to promote scientific excellence, PYA supports the mobility of Polish scientists. This activity is illustrated e.g. by the report on national and foreign mobility of scientists, published in 2015 in cooperation with „Nauka Ludzka Rzecz" Initiative. Cooperation and mobility of scientists was also the main topic of the 1st edition of Polish Scientific Networks conference (PSN, Warsaw, June 16 -18 2015), organized, as well as the next editions, in cooperation with the Ministry of Science and Higher Education and the Association of the Foundation for Polish Science Scholars. Intersectorial mobility was, in turn, the topic of the PSN: Science and Business, meeting held in Wrocław a year later (June 30 – July 1, 2016). PYA also cares about building competence of young scientists. For that purpose, PYA organizes annually summer schools Forge of Young Talents (Kuźnia Młodych Talentów) addressed to PhD students specializing in life and exact sciences and developing so called soft skills.

In order to encourage new generations to practice science, PYA actively supports its popularization. For many years, PYA members have been taking part in Science Festivals in different Polish cities, in Warsaw Science Picnic, in European Researchers' Night in Olsztyn, etc. PYA has also initiated Flying Scientific Cafes (Latające Kawiarenki Naukowe), popular science meetings that are mainly addressed to children and school youths.

Since May 2017, PYA numbers only 15 members. This situation is, however, only temporary: in 2019, new members will join. The call for applications will be open since autumn of 2018.

More information: http://www.amu.pan.pl/

ASSOCIATION OF THE FOUNDATION FOR POLISH SCIENCE (FNP) SCHOLARS unifies laureates of postdoctoral scholarship programmes of the Foundation for Polish Science. Among the Association's aims are the interdisciplinary and intergenerational integration of FNP Scholars, actions aimed at supporting science and popularizing the ethos of a scientist and teacher, promoting of good scientific practice and improving qualifications, as well as supporting scholars in critical situations.

The Association, initially named Association of the Foundation for Polish Science Foreign Scholars, was founded in 2000, during a meeting organized by the Foundation for Polish Science attended by laureates of the Foundation postdoctoral scholarship programme KOLUMB. Initially, the Association was established as an informal group of young scientists, whose postdoctoral training in foreign research centres was financed by the Foundation. In April 2003, the Association was officially registered as an association. In December 2009, the Association, following the establishment of different postdoctoral scholarship programmes of FNP, was joined by laureates of several other Foundation programmes, such as Homing (later replaced by Homing-Plus), Focus, Ideas, Team, Master, Welcome, and – in May 2014 – by the laureates of the programme Bridge, who have completed at least 6 months long fellowship in a foreign research centre. Since May 2016, laureates of all types of TEAM programmes are also welcomed among FNP scholars. At the same time, in 2009, the association was renamed as the Association of FNP scholars.

The Association's activity manifests mainly in the organization of meetings and conferences, both informal and formal, that support scientific cooperation – interdisciplinar, international and intersectorial, including the series of Polish Interdisciplinary Symposia Inter-Mix and the Polish Scientific Networks conference, that addresses scholars interested in applying research in practice. Every year, in May members of the Association meet during the Annual Alumni Congress, organized in different academic centres in Poland.

The Congresses are an excellent occasion for the presentation of most recent research results, scientific discussions, as well as to maintain contacts and friendships. Additionally, members of the Association have been engaged in the debate about the reorganization of science in Poland for many years, as part of advisory bodies or as experts in panels and conferences dedicated to specific subjects.

The history of the Association has been marked with a painful event – a tragic death of dr Artur Rojszczak, founder and animator of the Association. In his memory, the Association has established an award named after dr Rojszczak. The award is granted to young doctors who stand out not only with prominent scientific achievements, but also with a humanistic attitude towards the world, broad horizons and the ability to break down barriers and to surpass the framework of narrow scientific specializations. The awarding ceremony of Artur Rojszczak Award takes place every year during the Annual Congress of the Association.

More information: klub-fnp.pl

THE MINISTRY OF SCIENCE AND HIGHER EDUCATION supports the development of Polish universities, research institutes and the Polish Academy of Sciences science institutes. Pursuing policy in the area of science and higher education, the Ministry prepares strategic solutions and oversees the implementation of EU programs and the use of European funds.

At present, over 400 public and private universities operate in Poland. The Ministry of Science and Higher Education supervises most of them. The Ministry handles the affairs of students, universities and scientists. The scope of cooperation between the Ministry and the universities is regulated by the Law on Higher Education act, and the relations between the Ministry and research institutes are regulated by the Law on Research Institutes act.

The Ministry of Science and Higher Education also has at its disposal the budget allocated to science and higher education, established annually by the Council of Ministers. The rules for financing higher schools and research institutes are regulated by the act on Principles of Financing Science. The ministerial funds are used to finance, among others, statutory activities, science scholarships and material aid.

| **PRIORITIES** OF THE MINISTRY OF SCIENCE AND HIGHER EDUCATION

Ministry's priority is to improve the functioning of Polish universities and scientific units and, ultimately, to make Polish science and higher education modern and competitive on international level.

Despite the Ministry's surveillance and broadly defined cooperation, Polish universities are granted extensive autonomy. To further improve their functioning, and to take action to resolve existing problems of higher education and science, the Ministry, in close cooperation with academic community, created the Constitution for Science – project aimed at radical, but gradual reform of Polish higher education system. The new law introduces changes designed to strengthen the position of Poland in

the global race, to improve the quality of Polish academic and vocational studies, to stop the exodus of Polish scientists and students, to allow for a balanced development of universities in Poland, and to improve the working conditions of university employees and deliver innovations and research necessary for the implementation of Strategy for Responsible Development. The law will enter into force on October 1, 2018.

The Constitution for Science introduces new, consistent and clear regulations concerning the entire existing science and higher education system. It offers, for instance, a new model of obtaining a doctoral degree for PhD students, who soon will constitute the Polish intellectual elite. The model is based on two possible modes of procedures – PhD studies in doctoral schools or an external mode. The law introduces a universal scholarship system for PhD students. Optimal conditions for scientific research for PhD students are also created by the "introductory doctorate" programme, which aids the development of PhD theses that improve the operation of the companies hiring participants of doctoral studies. Additionally, the graduate will receive double salary: one – for the work in the company, and the other - as a scholarship funded by the Ministry.

A key objective of the Ministry is an increase in the innovativeness of the Polish economy by enabling a more efficient cooperation between the sectors of science and business. The efforts are, at one hand, made to encourage scientists to participate in the industrial processes, and, on the other, to facilitate scientific research for the companies – by, among others, favourable fiscal policies, offered by two laws on innovativeness already implemented by the Ministry of Science and Higher Education.

Aside from the deregulation and innovativeness, the Ministry concentrates on supporting development of the liberal arts in Poland. Polish scientists may apply for funding for research in two new modules: National Heritage and Universals. This way, scholars have the opportunity to focus on problems important for Polish culture, on popularizing achievements of Polish liberal arts outside of the country, and on gaining access to yet untranslated foreign works. In the process of supporting human sciences, the role of National Science Centre has been enhanced, and its actions gained integrity and complementarity with actions of the Ministry.

National Programme for the Developments of Humanities is a grant programme unique on European scale, addressed solely to humanists. Grants are awarded for traditional research and translatory works.

In October 2017, National Agency for Academic Exchange initiated its activity for internationalization of Polish science by supporting international scientific cooperation and academic exchange. Students, PhD students, young scientists, science institutions and non-governmental organizations can benefit from scholarships and grant programmes. Another pillar of the Agency's activity is the popularization of Polish language abroad and the enforcement of its position as a foreign language.

EXECUTIVE AGENCIES OF THE MINISTRY

As a public administration authority, the Ministry holds only a fraction of funds allocated to Polish science. Some funds are also governed by two executive agencies. Polish grant system favours interdisciplinary cooperation and undertaking novel and innovative activities. Competitions allow for the selection of projects and research with the greatest scientific and implementation potential.

The National Centre for Research and Development implements actions regarding scientific, technical and innovative national policy. Competitions announced by the Centre focus mainly on applied research, research and development studies and implementation actions. The competitions are very often highly specialized, pertaining to specific domains (Innochem, Innomed), and force the participants to cooperate with corporations and business (Lider).

The National Science Centre is a government executive agency set up to fund basic research. Among a wide variety of competitions, offers can be found both for PhD students (Etiuda programme) and for young scientists and experienced researchers (Maestro programme). With Polonez programme, the Centre encourages also foreign researchers to carry out research in Poland.

Both agencies cooperate, implementing projects that fully utilize both basic and applied research (Tango programme).

MINISTERIAL **ADVISORY BODIES** AND **INSTITUTION**

One of the fundamental rules of the Ministry of Science and Higher Education is maintaining constant connection with academic environment and using the rich experience of scholars and administrative employees of specific units. Therefore, numerous advisory bodies exist alongside the Ministry, supporting the creation of development strategies and the day to day business.

The General Council for Science and Higher Education is an elective body representative of the environment of science and higher education. The Council delivers opinions on matters of higher education, science, culture and education; it also evaluates laws proposed by the Ministry.

The major task of the Scientific Policy Committee is to assist the minister in the preparation of documents pertaining to the development of science, science policy and innovation policy, state budget drafts and financial plans that establish financial resources for science, national and foreign investment priorities, and to give advisory opinions on draft laws regarding science development and innovation, National Science Centre and National Centre for Research and Development establishment plans, and to prepare the assessment of their activity reports.

Evaluation of the quality of research conducted in Poland is performed by the Committee for Evaluation of Scientific Units. The parametric assessment performed by the Committee allows to assign units to appropriate categories in order to determine, among others, the level of financial support granted by the Ministry of Science and Higher Education.

The Polish Accreditation Committee is watching over the quality of education at the universities. Members of the Committee are elected from the employees of universities and employers' organizations. PAC is independent from the Ministry and, apart from the evaluation, it issues decisions on the establishment of new courses of studies.

The Ministry improves the quality of Polish science and higher education by creating ministerial programmes and competitions. We reward the best, support good practices and create good standards. We help

promising students accelerate their scientific career and support research teams.

For instance: every year, 100 best students can be awarded the Diamond Grant. Award-winning students receive up to PLN 220 000 for their scientific research projects. Laureates can also cut short their career path and undertake doctoral study programmes even though they do not yet have a master title. The EU operational programme Knowledge-Education-Development, disposed of by the Ministry, allowed, among others, for the organization of competitions preparing students to enter the job market. In the Studiujesz? Praktykuj! Programme, universities can prearrange high quality, paid internships for students. As a result of the competition of September 2017, 196 projects for a total of PLN 268 000 000 were accepted for implementation. Competence Development Programme allows universities to implement specific courses that will aid the development of soft skills, useful in the professional career. In 2017, universities were implementing 207 projects selected in two editions of the competition (total amount PLN 230 700 000). Expanding professional and soft skills of the students will also be part of the implementation of Integrated University Programmes (in May 2017 competition, 138 projects were selected, for a total of PLN 1 300 000 000). In the Dual studies competition, announced in December 2017 with allocated PLN 100 000 000, the students will also receive financial resources for internships in the companies. The Ministry also carries out, outside of the competition, a vocational practice programme in Higher Vocational Schools. Students are given opportunity to participate in extended, 6-month long vocational practice (targeted number of students in the programme is 7000). Another non-competitive project, in the framework of POWER – Best of the best!, is a continuation of Generation of the Future programme. From the obtained funds, the students may cover the costs of participation in international championships, competitions and conferences. In the second, 2017 edition of the programme, the maximum funds was PLN 290 000 for a team and PLN 79 000 for an individual participant.

More information at: nauka.gov.pl

STRATEGIC PARTNERS

POLISH ACADEMY OF SCIENCES (PAS), as the leading scientific institution in Poland, carries out comprehensive research activity aimed at the development, promotion, integration and popularization of science and the development of education, and also the enrichment of national culture. The Academy achieves these goals by carrying out advanced research of strategic importance for the development of science and economy, by organizing interdisciplinary research teams involved in the concentration of modern research apparatus, integrating Polish scientific community, educating academic staff, and by innovatively utilizing the results of scientific research, also in cooperation with economic entities, and by organizing scientific conferences and participating in science popularization events.

Structure of PAS unites traditional functions of autonomic scientific corporation with an academia that directly realizes research goals. This combination provides the possibility to create science by personal research involvement of PAS members affiliated in different research facilities. The corporation of scholars of the Academy includes:

- scientific committees, that on the grounds of their composition constitute the most representative scientific circle in the given discipline;
- task force committees, that are appropriately selected groups of experts, established to accomplish certain research tasks
- national committees, established in order to maintain and develop the cooperation with international scientific organizations,
- divisions, participating in the performance of tasks of the Academy within the scientific fields included in its scope, by the involvement of its members in the works of branches of the Academy, scientific committees, task force committees, and the boards of experts of the research institutions,

- territorial branches, established in order to perform the tasks of the Academy in a particular region of Poland, that above all integrate the academic life in the region of Poland in question,
- Scientific institutes, that are the basic organizational units of the corporation.

Gathered around departments, the institutes conduce international and internal research, both basic and applied, organize conferences, symposia and scientific lectures, provide financial services and perform the transfer of technology.

Recently, Polish Young Academy functions in the structure of PAS. Its tasks are centred around stimulating the activity of the young scientific community, by, among others, presentation of opinions and programmes related to the scientific issues, the organization of debates, discussions and scientific conferences, and the dissemination of scientific results.

Polish Academy of Sciences is also engaged in the publishing and expertise, provides access to the library, museum and archival stocks, organizes conferences, exhibitions and popular science lectures.

As a publishing body, PAS ensures the continuity in the publishing of the scientific publications and journals most important in given specializations, a part of which are available in open access on the Academy's web page. Science popularization tasks involve, above all, open popular science lectures "Wszechnica", participation in picnics and science festivals, nights of museums or book fairs; concerts and exhibitions are also organized periodically. PAS research units are actively involved in the preservation and restoration of material culture heritage and natural resources in Poland and abroad. The Academy's institutions possess in their collections, among others, printed literary treasures, dating back to 15th century, that include early editions of Hevelius' and Copernicus' works and Marie Skłodowska Curie's or Albert Einsteins' letters. Biological collections, comprising unique plants and seed banks, are also not without significance.

For outstanding achievements, the Polish Academy of Sciences grants: Medal of the Polish Academy of Sciences, Nikolas Copernicus Medal, Stefan Banach Medal of the Polish Academy of Sciences and the Polish Academy of Sciences Statuette.

More information at: pan.pl

FOUNDATION FOR POLISH SCIENCE (FNP) has been in operation since 1991. It is a non-governmental, non-political, non-profit institution and the largest source of science funding in Poland outside of the state budget.

Foundation's mission is to support outstanding scholars and research groups and to back innovative projects and the commercialization of research results.

The Foundation is offering prizes, scholarships and subsidies for scientists of any age, at all career stages, irrespective of the represented field of science.

Operating rules of FNP:

- to offer support directly to scholars and research groups
- all subventions, prizes and scholarships are awarded on the basis of a competition
- scientific excellence is the most important criterion in awarding of support
- assessment of the achievements of participants in the Foundation's competitions is made by Polish and foreign scientists recognized in their field (peer-review method)
- the support is awarded according to the "Hard money" principle (strict accounting procedures for funding awarded)

The Foundation actively supports and promotes scientific mobility and international research cooperation, and many FNP laureates achieve international success. FNP collaborates with over 45 foreign scientific institutions and organizations. We are a member of European Foundation Centre (EFC) and Science Europe.

Foundation's statutory activities are funded from its own resources, including donations of 1% of income taxes, private donations and European funds. In 2008, the Foundation began the realization of programmes founded by the European Regional Development Fund under the Operational Programme Innovative Economy, and in 2011 it started the SKILLS project, financed from

the Operational Programme Human Capital funds. At the end of 2015 and at the beginning of 2016, the Foundation launched new projects financed from the Operational Programme Smart Growth: International Research Agendas, TEAM, TEAM-TECH, FIRST TEAM, HOMING and POWROTY. At the end of 2015 and at the beginning of 2016, the Foundation launched new programmes financed from the Operational Programme Smart Growth: International Research Agendas, TEAM, TEAM-TECH, FIRST TEAM, HOMING and POWROTY/REINTEGRATION. Also in August 2018 FNP plans to open a new programme TEAM-NET.

Detailed information on the programmes can be found on www.fnp.org.pl

THE MEDICAL UNIVERSITY OF LODZ is one of Poland's largest medical universities, its tradition dating back to the 1940s. Nowadays, with five faculties and sixteen programmes, its student body consists of over 9 500 students. The education offer comprises also programmes with English as lecturing language, with 750 foreign students enrolled in the programmes of medicine, dentistry and postgraduate studies. The University's clinical facilities include three renowned hospitals, all of them highly rated in national rankings.

The Medical University of Lodz is heavily involved in the academic life of the city of Lodz and the whole country. The University provides education to future doctors and specialists in medical and paramedical fields, carries out research and development studies, and provides research services. In order to accommodate to the job market shifts, the University's educational offer is constantly adjusted and broadened.

The University's research and development activities also show dynamic growth.

As reflected by top positions in rankings that evaluate both the publication and citation impact, the research conducted at the University is met with high interest and esteem.

The Medical University of Lodz has extensive experience in project management based on PRINCE2 methodology.

At present, the college is carrying out:

- 13 projects under structural funding for a total amount of PLN 48 000 000
- 85 scientific grants for a total amount of PLN 46 000 000
- 8 projects under the Strategmed Project
- 21 international projects (H2020, COST, 3 Program Zdrowia, KIC – EIT Health)
- 8 grand infrastructural projects for a total amount of over PLN 84 000 000

Scientific projects conducted in accordance with the principles of the knowledge triangle (education, research, innovation) are continued both in new, integrated curricula and in the cooperation with business. The University actively seeks and develops new schemes of cooperation with the external environment by, among others, mapping out and testing potential solutions which can then be applied in clinical practice or public healthcare.

The Medical University of Lodz is a renowned, attractive scientific and educational centre in the European research area, focused on promoting research and developing innovative health-promoting solutions for the epidemiological and socio-demographic challenges faced by our society. Healthy aging and active lifestyle are strategic areas of development of the University. 2011 marks the foundation of the Healthy Aging Research Centre (HARC), and since 2015 the University is a member of the international EIT health consortium (www.eithealth.eu) with aim to support entrepreneurship and create innovations in the areas of healthy lifestyle and active aging, as well as seeking ways to improve the quality of life in Europe.

More information at: umed.lodz.pl

ORGANIZING COMMITEE

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ANNA BIELEC

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POLISH YOUNG ACADEMY

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INSTITUTE OF PHARMACOLOGY
POLISH ACADEMY OF SCIENCE

ASSOCIATION OF THE FOUNDATION FOR POLISH SCIENCE SCHOLARS

PIOTR TRZONKOWSKI

MEDICAL UNIVERSITY OF GDAŃSK

PROGRAMME

THURSDAY, 21.06.2018 [Auditorium 1000]

16.00–17.00	Registration of participants
17.00–17.30	Opening ceremony
17.30–18.30	Plenary lecture Prof. Piotr Trzonkowski, Prof. Piotr Witkowski „Therapy of type 1 diabetes of the XXI century – surgery meets molecular medicine"
18.30–19.30	Discussion panel "Role of scientists and physicians in the era of post-truth" with representatives of: • Polish Academy of Science – Prof. Stanisław Jerzy Czuczwar • Foundation for Polish Science – Prof. Maciej Żylicz • Medical University of Lodz – Prof. Lucyna Woźniak • The University of Chicago Medicine – Prof. Piotr Witkowski Moderator: Dr. ANNA AJDUK
19.30–20.00	Coffee break
20.00	Film music concert *Performed by a duet "Symetria": Ewa Fortuna-Woszczyńska (violin) and Prof. Anna Brożek (piano)*

The first day of the event is not part of the main event program. Coffee break and concert are financed by the organizer's own funds and are not financed from the funds of innovative companies associated in INFARMA.

FRIDAY, 22.06.2018

7.30–9.00 Registration of participants [Reception desk]

9.00–10.30 **SCIENTIFIC SESSION 1**

Bioinformatics and Big Data analysis [Room 1.17]

Chairman: Prof. JANUSZ BUJNICKI

Plenary lectures:

- Dr. Gosia Trynka "Functional fine-mapping of GWAS variants for complex immune traits"
- Prof. Tomasz Burzykowski "Statistical bioinformatics: when statistics helps in "omics" data analyses"
- Konrad Pagacz "Novel approach to normalization of human serum and plasma microRNA qPCR quantification data"
- Dr. Ireneusz Grulkowski "Volumetric macro- and micro-scale assessment of crystalline lens opacities in cataract patients using long-depth-range swept source optical cohrence tomography"

Molecular Biology [Room 1.27]

Chairman: Prof. KRZYSZTOF GIANNOPOULOS

Plenary lectures:

- Prof. Wojciech Młynarski "Search for molecular targets in the therapy of acute lymphoblastic leukemia in children: from lab bench to bedside"
- Prof. Przemysław Juszczyński "Immune evasion mechanisms in classical Hodgkin lymphoma: towards new immunotherapies"
- Artur Wnorowski "Development of (r,s')-4'-methoxy-1-naphthylfenoterol (mnf) as an inhibitor of pancreatic tumor growth"
- Dr. Aleksandra Markiewicz "Clinical significance of mesenchymal phenotype of breast cancer cells at different stages of metastatic cascade"

Translational Neuroscience [Room 1.20]

Chairman: Dr. KATARZYNA STAROWICZ-BUBAK

Plenary lectures:

- Dr. Franziska Denk "Pain Vulnerability: Why Do Only Some of Us Have to Suffer?"
- Prof. Jacek Kuźnicki "Zebrafish as a model to study human diseases"
- Prof. Sylwia Rodziewicz-Motowidło "Novel technologies for pharmacological stimulation of regeneration"
- Dr. Emilia Witkowska Nery "Machine learning techniques for neurobiological data analysis – studies on simultaneous neurotransmitter detection and evaluation of mice stress model"

10.30–11.00 Coffee break [Breakfast room]

11.00–12.30 Scientific speed dating [Rooms: 1.17, 1.02, 1.03]

12.30–14.00 Lunch [Breakfast room] / Industry session (concurrent)

14.00–15.30 Keynote lectures and discussion [Room 1.27]

- Prof. Piotr Siciński "Targeting Cell Cycle Machinery for Cancer Treatment"
- Prof. Dipanjan Chowdhury "Harnessing the translational potential of DNA damage repair machinery"

15.30–17.00 SCIENTIFIC SESSION 2

Bioinformatics and Big Data analysis [Room 1.17]

Chairman: Prof. MARCIN DRĄG

Plenary lectures:

- Prof. Krystian Jażdżewski "BadamyGeny.pl – national cancer risk assessment program – BIG picture"
- Prof. Rafał Płoski "Whole exome sequencing for discovery of novel human diseases"
- Dr. Lech Mankiewicz "Social media and Making health and medicine understandable for patients"
- Marta Sobalska-Kwapis "Metagenomics as a complex analysis in biobank lab"

Molecular Biology [Room 1.27]

Chairman: Prof. DOMINIKA NOWIS

Plenary lectures:

- Dr. Tomasz Stokłosa "From genetics to targeted therapy and back – studies on the molecular mechanisms of drug resistance and disease progression in chronic myeloid leukemia and other myeloproliferative neoplasms"
- Dr. Jarosław Baran "Human TRAIL-producing Lactobacillus lactis bacteria as potential immunotherapy of colon cancer?"
- Prof. Marta Miączyńska "Synthetic lethality between Vps4A and Vps4B in colorectal cancer"
- Dr. Anna Grabowska "Translational regulation contributes to biological adaptation in the human pathogen mycobacterium tuberculosis"

Translational Neuroscience [Room 1.20]

Chairman: Prof. KRZYSZTOF JÓŹWIAK

Plenary lecture:

- Prof. Krzysztof Selmaj "Translational research and multiple sclerosis – basic science meets clinical application"

Discussion panel "From bench to bedside and beyond" with Dr. Michał Korostynski, Dr. Dorota Frydecka and Dr. Klaudia Szklarczyk-Smolana

Moderator: Prof. KRZYSZTOF JÓŹWIAK

17.00–17.30 Coffee break [Breakfast room]

17.30–19.00 Discussion panel [Room 1.27]

"Mentoring and interdisciplinary collaboration" with Dr. Wojciech Fendler and Prof. Dipanjan Chowdhury, Prof. Krzysztof Jóźwiak and Prof. Krzysztof Palczewski

19.00 Dinner & networking session

SATURDAY, 23.06.2018

8.00–9.00 Science breakfast [Breakfast room]

Dr. Gosia Trynka, Dr. Bogna Ignatowska-Jankowska, Prof. Agnieszka Chacińska, Prof. Leszek Kaczmarek, Prof. Krzysztof Palczewski, Prof. Sergiusz Jóźwiak

9.00–11.00 Poster tour [Staircase hall]

11.00–11.30 Coffee break [Breakfast room]

11.30–13.00 Discussion panel [West Auditorium]

"How to break the glass ceiling and not hurt oneself?" with Prof. Maria Ciemerych-Litwinienko, Dr. Anna Czarnecka, Dr. Anna Fabijańska and Dr. Joanna Sułkowska

Moderator: Dr. KATARZYNA STAROWICZ

13.00–14.30 Lunch [Breakfast room]

Industry session (concurrent)

14.30–16.00 **SCIENTIFIC SESSION 3**

Bioinformatics and Big Data analysis [Room 01.11]

Chairman: Dr. WOJCIECH FENDLER

Plenary lectures:

- Prof. Marcin Drąg "In quest of optimal technology to investigate activity of proteolytic enzymes in health and disease"
- Prof. Andrzej Bojarski "Academic in silico platform for new drug discovery"
- Prof. Nuno Sepulveda "Global analysis of Plasmodium falciparum histidine-rich protein-2 (pfhrp2) and pfhrp3 gene deletions using whole-genome sequencing data and meta-analysis"
- Dr. Filip Stefaniak "Modeling of ribonucleic acid-ligand interactions"

Molecular Biology [West Auditorium]

Chairman: Prof. WOJCIECH MŁYNARSKI

Plenary lectures:

- Prof. Dominika Nowis "The role of arginase-1 in the development of antitumor immune response"
- Prof. Marcin Moniuszko "MOBIT study – in search of 'omic' markers for the personalized diagnosis and treatment of non-small cell lung cancer"
- Anita Helińska "Myogenic differentiation of Pax7-/- pluripotent stem cells in teratomas"
- Joanna Jurek "An investigation of how a single nucleotide polymorphism (SNP) may impact post-translational modification of retinoid x receptor alpha (rxr) through sumoylation"

Translational Neuroscience [Room 01.12]

Chairman: Prof. SERGIUSZ JÓŹWIAK

Plenary lectures:

- Dr. Bogna Ignatowska-Jankowska "Emerging behavioral models: from 3D motion capture to behavioral transcriptomics"
- Dr. Justyna Totoń-Żurańska "Next generation sequencing in searching for causal variants of rare neurological disorders"
- Dr. Emilia Zgorzyńska "Omega-3 fatty acids affect the release of pro- and anti-inflammatory mediators in activated astrocytes"
- Tomasz Wichur "Search for multifunctional ligands aiming at symptoms and causes of Alzheimer`s disease"
- Dr. Michał Fiedorowicz "Magnetic resonance imaging and spectroscopy in preclinical studies of neurodegenerative ocular diseases"

16.00–17.00 Coffee break [Breakfast room]

17.00–17.45 Flash Talks – short lectures selected from abstracts [West Auditorium]

17.45–18.45 Closing lectures [West Auditorium]

- Prof. Leszek Kaczmarek "Matrix metalloproteinase, MMP-9 unties brain-mind knot"
- Prof. Agnieszka Chacińska "Reporting on the status of mitochondria"
- Prof. Krzysztof Palczewski "Chemistry and Biology of Vision"

18.45–19.00 Closing ceremony [West Auditorium]

During the second and third days of the Polish Scientific Networks conference, the participants will have the option to meet with:

- Representatives of the Foundation for Polish Science and their current offer for scientists regarding individual scholarships and funding research projects
- The team of the Bureau of Scientific Excellence of the Polish Academy of Sciences which will share their know-how on applying for European Research Council grants,
- Representatives of the National Center for Research and Development who will present their latest initiative – the TANGO3 programme, which is a joint undertaking with the National Science Center and focuses on bridging the gap between basic and applied research and introducing the latest in technologies, services and products to the market.

The PSN conference is also supported by two industry sessions organized by the Foundation of the Medical University of Lodz.

Prof. **PIOTR TRZONKOWSKI**
Clinical Immunology and Transplantology,
Medical University of Gdańsk

Prof. **PIOTR WITKOWSKI**
Department of Surgery, University of Chicago,
Chicago, IL, USA

Therapy of type 1 diabetes of the XXI century – surgery meets molecular medicine"

While insulin treatment was discovered over a century ago, it is still the only effective routine treatment for type 1 diabetes. In this talk we will describe our attempts to stop the progression of this disease with T regulatory cells (Tregs) and to restore insulin secretion with the transplantations of pancreatic islets. We will present long-term results of our trials discussing clinical, metabolic and immune background of the patients, which, in our opinion, influenced the efficacy of this treatment. These strategies pave a way towards better treatment for diabetic patients in the near future.

KEYNOTE SPEAKERS

PIOTR TRZONKOWSKI is actively involved in the clinical research with T regulatory cells for over 20 years. His group developed and applied first-in-man protocols of the treatment with expanded T regulatory cells. The trials have covered graft versus host disease, type 1 diabetes, multiple sclerosis and pancreatic islets allotransplantation. Other research of the group is focused on novel approaches to cellular therapy in autoimmune and malignant diseases in man, synthesis of immunosuppressive small-particle drug candidates and posttransplant laboratory diagnostics in allograft recipients. For these studies, he has been awarded with the Foundation for Polish Science Prize in the life and earth sciences in 2017.

PIOTR WITKOWSKI, MD, PhD, is a leading expert in islet transplantation. He is also highly skilled in kidney, pancreatic, and liver transplantation, including laparoscopic techniques used to procure organs from living kidney donors. Dr. Witkowski also performs islet autotransplantation for patients who need a pancreatectomy.

A widely published researcher, Dr. Witkowski has an impressive record of success in both basic science and clinical research pertaining to islet cell and abdominal organ transplants. Among other accomplishments, he was instrumental in developing an optimized islet isolation technique that greatly improved success in clinical transplants. Under Dr. Witkowski's leadership, multidisciplinary research teams at the University of Chicago are currently conducting several studies skillfully designed to improve quality and outcomes in islet cell transplantation in patients with type 1 diabetes.

PETER SICINSKI
Department of Genetics, Harvard Medical School,
Department of Cancer Biology, Dana-Farber Cancer
Institute, Boston, Massachusetts, USA

Targeting Cell Cycle Machinery for Cancer Treatment

Cyclins and their catalytic partners, the cyclin-dependent kinases (CDKs), represent components of the core cell cycle machinery that drives cell proliferation. Abnormal activation of these cell cycle proteins is seen very frequently in essentially all human tumor types. In my talk, I will discuss our mouse genetic experiments that delineated the requirement for different cell cycle proteins in specific tumor types. Our work has validated the cyclin D-CDK4/6 kinase as a therapeutic target for breast cancer treatment, and paved the way for clinical trials. Currently, inhibitors of CDK4/6 are in clinical trials for breast cancer patients, with very promising results. I will also discuss our studies, which revealed that CDK4/6 kinase plays important roles in controlling tumor cell metabolism as well as anti-tumor immune response. Lastly, I will discuss our ongoing work implicating other cell cycle proteins as potential therapeutic targets.

PETER (PIOTR) SICINSKI received his M.D. and Ph.D. degrees from the Warsaw Medical School in Warsaw Poland. He was a visiting scientist at MRC Molecular Neurobiology Unit in Cambridge, UK, prior to becoming a postdoctoral fellow in the laboratory of Dr. Robert A. Weinberg at the Whitehead Institute, MIT, in Cambridge, Massachusetts. Peter joined Harvard Medical School faculty as an assistant Professor in 1997, where he is currently a Professor with tenure at the Department of Genetics at the Harvard Medical School. Peter's laboratory, located at the Dana-Farber Cancer Institute Investigates cell cycle machinery in development and in cancer.

KEYNOTE SPEAKERS

Prof. **DIPANJAN CHOWDHURY**
Department of Radiation Oncology, Division of Radiation and Genome Stability, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Both environmental sources and metabolic by-products in our body constantly damage cellular DNA. To survive DNA damage, cells have to rapidly sense the DNA break and repair it in an error free manner. One of the primary causes of cancer is the incorrect repair of damaged DNA. Therefore an efficient and accurate DNA repair system needs to be in place to prevent the transformation of a normal cell to a tumor. However the converse is also true, the DNA repair machinery can be hijacked by cancer cells to negate the effects of therapy. Radiotherapy and most chemotherapeutic agents are directed to kill cancer cells by inducing irreparable DNA damage. The cancer cells counter this treatment with changes in their DNA repair machinery, promptly repairing the damaged DNA. These cells become resistant to chemo and radio therapy. Therefore we need to have an in-depth understanding of DNA repair and the factors involved, both for gaining insight into the cause of cancer and for enhancing the efficacy of cancer therapy. Major focus of our research is to decipher the molecular mechanism of the cellular response to DNA damage, particularly DNA double strand breaks.

DIPANJAN CHOWDHURY, PhD, is an Associate Professor of Medicine at Harvard Medical School, and Chief of the Division of Radiation and Genomic Stability in the Department of Radiation Oncology at Dana-Farber Cancer Institute and Associate Member of Broad Institute of Harvard a MIT. He is the Brigham &Women's Hospital Distinguished Chair in Radiation Oncology. He is also an Affiliate Faculty Member of the Department of Biochemistry and Molecular Pharmacology and the Department of Immunology at Harvard Medical School. Dr. Chowdhury's research focuses on deciphering cellular

response to DNA damage, particularly DNA double strand breaks, with the goals of generating strategies for personalized radio and chemotherapy, and countering accidental radiation exposure. His work is supported by the NIH and several foundations, including the American Cancer Society, Ann-Fuller Foundation, Tina Brozman Foundation, Claudia Adams Barr program for Innovative Cancer Research and the Leukemia Lymphoma Society.

Dr. Chowdhury received his Bachelor of Science in Chemistry from St. Xavier's College, Kolkata; his Master of Science in Biochemistry from Calcutta University, and his Doctor of Philosophy in Molecular Biology from Brandeis University.

KEYNOTE SPEAKERS

Prof. **LESZEK KACZMAREK**
Laboratory of Neurobiology, Nencki Institute
of Experimental Biology Polish Academy
of Sciences, Warsaw

Matrix metalloproteinase, MMP-9 unties brain-mind knot

Matrix metalloproteinase 9, MMP-9 is an extracellularly operating enzyme that has been demonstrated as important regulatory molecule in control of synaptic plasticity, learning and memory. We have shown that either genetic or pharmacological inhibition of MMP-9 impairs late phase of long-term potentiation at various pathways, as well as appetitive and spatial memory formation, although aversive learning remains apparently intact in MMP-9 KO mice. MMP-9 is locally translated and released from the excitatory synapses in response to neuronal activity. Extrasynaptic MMP-9 is required for growth and maturation of the dendritic spines to accumulate and immobilize AMPA receptors, making the excitatory synapses more efficacious. Our studies on animal models have implicated MMP-9 in such neuropsychiatric conditions, as e.g., epileptogenesis, autism spectrum disorders, development of addiction, and depression. We have also reported that in humans MMP-9 appears to contribute to epilepsy, alcohol addiction, Fragile X Syndrome, schizophrenia and bipolar disorder. In aggregate, all those conditions may be considered as relying on alterations of dendritic spines/excitatory synapses and thus understanding the role played by MMP-9 in the synaptic plasticity may allow to elucidate the underpinnings of major neuropsychiatric disorders.

LESZEK KACZMAREK (b. 1957) is a professor of neurobiology and head of the Laboratory of Neurobiology at the Nencki Institute of Experimental Biology, the Polish Academy of Sciences (PAS). He is an elected member of PAN (Chair of the Division of Biological Sciences, 2003–2007, and since 2015, a Dean of the Division of Biological and Agriculture Sciences), Academia Europaea

(Physiology and Medicine Section Committee member, 2006–2014), European Molecular Biology Organization (EMBO, 2010–2015: member of the Council). He served on the Council of the International Society for Neurochemistry (ISN, 1995–1999), and the Executive Committee of International Brain Research Organization and Chair of the Central and Eastern Europe Regional Committee (CEERC, 2003–2005). He is a Polish representative to the European Molecular Biology Conference (EMBC, Vice-President, 2012–2014) and European Molecular Biology Laboratory Council (EMBL). He was a member of the Council of the National Science Centre (NCN), where he chaired the Life Sciences Committee, 2010–2016. He chaired Joint Selection Committee of the Polish-Swiss Research Programme (2011–2016) and was a member of the Joint Programming on the Neurodegenerative Disorders (JPND), as well as Horizon 2020 Advisory Group for the Societal Challenge 1 "Health, demographic change and wellbeing" (2013–2015) and Horizon 2020 Future and Emerging Technologies (FET) Advisory Group (since 2018). He has served on numerous program and organization committees of international scientific meetings and congresses. He has been invited to deliver more than 130 plenary/symposia lectures and almost 300 seminars and other talks worldwide. He was visiting professor at the University of Catania (Italy), McGill University (Montreal, Canada), University of California, Los Angeles (USA). He promoted 41 PhDs, and 21 his former lab members obtained Dr. hab. degree. He published over 240 research papers in renowned journals, cited over 9 000 times. Among his most important scientific discoveries are (i) defining the role of c-Myc protein in the control of the cell cycle (ii) demonstration of gene expression in the brain in mammalian learning; (iii) revealing neuronal apoptosis in the adult brain; (iv) describing the role of matrix metalloproteinases in neuronal plasticity, learning and memory; (v) demonstrating specific role of the central nucleus of the amygdala plasticity in appetitive learning and addiction. He has received several awards for his research achievements, including a prize from the Foundation for Polish Science (2000) and Prime Minister of Poland Award for Life Time Achievements in Science. He was nominated by the Ministry of Science and Higher Education among the top 25 most important events and achievements of Polish science during 1989–2014.

KEYNOTE SPEAKERS

Prof. **AGNIESZKA CHACIŃSKA**
The Centre of New Technologies, University of Warsaw

Reporting on the status of mitochondria

Mitochondria must import the large majority of their proteome. We aim to understand cellular consequences of defects in the mitochondrial protein import. Two main arms of he cellular response to protein import dysfunction include the inhibition of cytosolic translation and activation of the major protein degradation machinery, the proteasome. The stimulation of the proteasome is driven by its more efficient assembly as a direct response to the amount of mistargeted proteins. The mechanism is beneficial for cells. Interestingly, activation of the proteasome could be uncoupled from translational inhibition by mistargeting of mitochondrial proteins and in the presence of healthy mitochondria. Under these conditions only proteasomal activity, and not the cellular protein synthesis, was modulated. The synthesis of cellular proteins is regulated by the signals, which come directly from the dysfunctional mitochondria. To understand translational inhibition, a site-specific redox proteomic analysis to delineate the yeast redoxome was performed. Increased levels of intracellular reactive oxygen species (ROSO caused by the mitochondria serve as a signal to attenuate global protein synthesis. Mapping of redox-active thiols in proteins revealed ROS-sensitive sites in several components of the translation apparatus. Thus, the increased levels of intracellular ROS caused by dysfunctional mitochondria serve as a signal to attenuate global protein synthesis.

AGNIESZKA CHACINSKA has graduated in Biology, University of Warsaw. In 2000 she has received the doctoral degree in biochemistry at Institute of Biochemistry and Biophysics of Polish Academy of Sciences. From 2001–2009 she has worked at the University of Freiburg as a postdoc and head of a research group. Since 2009 she has been based at the International Institute of Molecular and Cell Biology in Warsaw, Poland, where she was the group leader of the Laboratory of Mitochondrial Biogenesis. In 2014 she was awarded the title of full professor by the President of Republic of Poland. In 2017 Agnieszka Chacinska and her group has moved to the Centre of New Technologies, University of Warsaw, where she is holding the position of Director and a research group leader. Prof. Chacinska is the recipient of multiple awards and prestigious grants, including International Research Agendas programme and Welcome grant of the Foundation for Polish Science as well as Maestro grant of the National Science Center. She is member of The Polish Academy of Sciences and The European Molecular Biology Organization (EMBO).

Professor Chacinska's interests focus on biogenesis, transport and degradation of mitochondrial proteins and their failure resulting in pathologies. Her research explores links between transport of mitochondrial proteins and cellular protein homeostasis.

KEYNOTE SPEAKERS

Prof. **KRZYSZTOF PALCZEWSKI**
Department of Pharmacology at Case Western Reserve University, Cleveland, Ohio, USA

Chemistry and Biology of Vision

Retinal photoreceptor cells can respond to light throughout our lives because they continuously regenerate a light-sensitive chromophore and certain essential structures. This series of reactions takes place in photoreceptor and the retinal pigment epithelium (RPE) cells. Defects in many proteins involved in these processes cause photoreceptor degeneration. For example, mutations in the rhodopsin gene may cause human diseases like retinitis pigmentosa (RP) that usually result in late-onset blindness. Our long-term goal is to elucidate the molecular mechanisms of phototransduction and retinal degeneration to discover therapeutics for inherited human blinding diseases caused by mutations in phototransduction genes. This is a necessary prerequisite for developing evidence-based therapeutic approaches for treatment of these pathological conditions. Combining disciplines such as state-of-the art imaging, bioinformatics, genomics, and structural biology with classical histopathological, physiological, and biochemical methods can dramatically increase understanding of causes of inherited human retinopathies.

KRZYSZTOF PALCZEWSKI laboratory made a historic contribution by solving the crystal structure of rhodopsin, which has been cited over 6,000 times. His laboratory employs classical biochemical methods, crystallography, cryo-electron microscopy, cellular cryo-electron tomography, and two-photon microscopy to study phototransduction and visual retinoid cycle to obtain a comprehensive view of the visual system in health and during disease. His recent studies in two-photon functional imaging in the eye, advanced the discovery and validation of treatments that can prevent retinal degenerative

diseases. He developed visual chromophore supplementation, detoxification of harmful retinoids, and systems pharmacology toward the treatments of common retinal diseases. His next goal is to move pharmacological approaches beyond preclinical studies in animal models.

Dr. Palczewski's contributions to the chemistry and biology of vision and development of new therapies were recognized with numerous awards, including the ARVO Cogan Award in 1996, the ARVO Friedenwald Award in 2014, Beckman-Argyros Award in Vision Research in 2014, and Distinguished University Professor at CWRU in 2016. His publications (>560) were cited more than 39,000 times.

He received M.Sc. in Organic Chemistry from the University of Wroclaw, PhD in Biochemistry from the Wroclaw University of Science and Technology, and then trained in Dr. Paul Hargrave's laboratory. Dr. Palczewski established his first laboratory in 1992 in Portland, Oregon. He was promoted to a full professor at the University of Washington in 1997. After moving to Cleveland in 2005 to become the Chair of the Department of Pharmacology at Case Western Reserve University he continued productive vision research.

DISCUSSION PANEL I

ROLE OF SCIENTISTS AND PHYSICIANS IN THE ERA OF POST-TRUTH

An increasingly digital environment we live in gives us many new ways of finding and accessing diverse information and views. It also enables an increase in the volume of various kinds of disinformation in circulation. In the 21st century the numbers of supporters of anti-vaccine, flat Earth, or creationism movements are increasing at astonishing rate. This panel will address questions why science and evidence-based medicine are losing the battle for the public trust and how scientists and physicians can counteract the flood of disinformation.

MODERATOR

Dr. **ANNA AJDUK**
Polish Young Academy

Dr. Anna Ajduk specializes in mammalian developmental and reproductive biology and works in the Department of Embryology, Faculty of Biology, University of Warsaw. She completed her MSc (2003) and PhD (2007) studies in the same faculty. She also worked abroad in Cardiff University and University of Cambridge (UK) and in the Institute for Biogenesis Research, University of Hawaii (US).

For over 15 years Dr. Ajduk has worked on fertilization and early embryonic development in mammals, including research aiming at optimization of the assisted reproduction protocols. Recently, she focuses mostly on various aspects of oocyte aging and, in collaboration with physicists, on application of optical coherence microscopy in reproductive biology and medicine.

In 2013 her research was awarded Prof. Stefan Pieńkowski Prize for the outstanding achievements in science. She is also a beneficiary of fellowships and grants funded by the Foundation for Polish Science, National Science Centre, National Centre for Research and Development, Schering Foundation and FEBS.

Apart from conducting scientific research, Dr. Ajduk also participates in outreach initiatives and is an active member of various organisations federating scientists. Since 2012 she has been a member of the Association of the Foundation for Polish Science Scholars (she presided the Association in 2013–2017) and since 2016 – of the Polish Young Academy (chair of the PYA 2017–2019).

Prof. **STANISŁAW JERZY CZUCZWAR**
Polish Academy of Science

Head of Department of Pathophysiology (Lublin Medical University) and Department of Physiopathology (Institute of Rural Medicine in Lublin). Corresponding member of the Polish Academy of Arts and Sciences (Cracow) since 2012 and Polish Academy of Science (Warsaw) since 2013. Member of the Editorial Board of Pharmacology Biochemistry and Behavior (Elsevier) since 1998 and Associate Editor of Neurochemical Research (Springer) since 2015. Past President of the Polish Pharmacological Society.

His research is focused on the interactions between antiepileptic drugs for the search of the rational drug combinations for the treatment of drug-resistant epilepsy. He is also involved in studies concerning the effects of ligands affecting various neurotransmitter systems upon the anticonvulsant and neurotoxic activities of antiepileptic drugs.

He is an author/co-author of 376 scientific papers (according to PubMed) which so far have been cited 7562 times. His H-index is 42 (citations and H-index according to Web of Science).

He was a chairmen of the Scientific Committee of the International Congress of the Polish Pharmacological Society (held in 2010 in Krynica) and is a main organizer of the yearly Lublin conferences "Progress in Research on Epilepsy and Antiepileptic Drugs". In 2008, he was awarded a prestigious professor grant "Master" by the Polish Science Foundation.

Up till present, under his supervision 40 people received their Ph.D. degrees. Four of them were habilitated and two were awarded professorships. In the Department of Pathophysiology, there are, apart from him, 3 professors and 2 habilitated scientists.

PANELISTS

Prof. **MACIEJ ŻYLICZ**
Foundation for Polish Science

Professor Maciej Zylicz was born in 1953 in Gdansk. Studied experimental physics and biology at the University of Gdańsk. In 1980 he completed his doctorate in biochemistry, in 1986 he was awarded his habilitation degree in molecular biology, and in 1992 he was made professor. In 1980–1999 he worked at the University of Gdańsk, where he was vice-rector for science (1990–1993). In 1993–1994 he was a visiting professor at the Institute of Oncology of the University of Utah. In 1999–2016 he was head of the Molecular Biology Department of the International Institute of Molecular and Cell Biology in Warsaw.

Among Prof. Żylicz's interests are the molecular biology of heat shock proteins. He isolated the first heat shock proteins and recognised their role in DNA replication. With colleagues, he has demonstrated that these proteins are also involved in the protection of proteins of other types, dissociation of oligomers and protein aggregates, and proteolysis. Since 2000, he has been investigating the role of heat shock proteins in cell transformation, showing that tumour suppressor protein p53 requires heat shock proteins to work, and that the MDM2 oncogene possesses activity of a chaperone protein. The author of almost 90 scientific works cited in global literature (over 6000 citations), he has supervised 15 doctorates in Poland, while six of his closest colleagues (doctoral and habilitation candidates) have been appointed as professors.

Prof. Żylicz is a full member of the Polish Academy of Sciences, member of the German National Academy of Sciences Leopoldina, Academia Europae and the European Cancer Research Academy, and corresponding member of the Polish Academy of Arts and Sciences.

In 1997–2000 he was a member of the council of the Polish State Committee for Scientific Research, in 2001–2004 Chairman of the Group for Biological Sciences, Earth and Environment Protection and member of the State Committee for Scientific Research, and in 2001–2002 Chairman of the Base Research Committee there. Currently he is a member of the Senate of the Max Planck Society.

He is also a member of the European Molecular Biology Organization (EMBO), and was a member of its Council in 2003–2007, as well as of the Polish Biotechnology Society, Polish Genetics Society, and American Society of Biochemistry and Molecular Biology. In 2008–2010 he chaired the Molecular and Structural Biology and Biochemistry Panel (LS1) of the European Research Council. He also served as the Polish delegate to the European Molecular Biology Conference (2000–2004) and the European Science Foundation (2003–2005). He was a member of the ERC Identification Committee (2010–2013). He was a Voluntary Advisor to the President of the Republic of Poland (2010–2015). Since 2014 is a member of Max Planck Senat.

The recipient of the Foundation for Polish Science Prize (1999), the Prime Minister of the Republic of Poland's Award for Scientific Achievements (2002), as well as honorary doctorates from the University of Wrocław (2007), University of Gdańsk (2011) and Jagiellonian University (2013).

Prof. Żylicz was appointed President of the Foundation for Polish Science Executive Board by the Foundation Advisory Board on 20 May 2005.

PANELISTS

Prof. **LUCYNA WOŹNIAK**
Medical University of Lodz

Professor Lucyna Woźniak, PhD, DSc, graduated from the Technical University of Łódź. After PhD from the Polish Academy of Sciences and a post-doc in Kings College London, she received habilitation (DSc.) from The Centre of Molecular and Macromolecular Studies Polish Academy of Sciences. Professor at the Medical University of Lodz (MUL) working in the field of medical chemistry and molecular biology. Interested in diabetes in context of pregnancy induced diabetes (GDM) as an early predictor of type two diabetes in women population. She serves as a Deputy Director of the Healthy Ageing Research Centre (HARC), Medical University of Lodz since 2012. Vice Rector for Science and International Affairs and Head of Department of Structural Biology at Medical University of Lodz, coordinator of EITHEALTH INNOSTARS, LODZ POLAND and Supervisory Board Member of EIT HEALTH. Member of High Level Group on maximising impact of EU Research and Innovation Programmes (Pascal Lamy Group).

Department of Structural Biology, Faculty of Biomedical Sciences and Postgraduate Education, Medical University, Lodz, Poland

Prof. **PIOTR WITKOWSKI**
The University of Chicago Medicine

Associate Professor of Surgery.

Director, Pancreatic and Islet Transplant Program.

Piotr Witkowski, MD, PhD, is a leading expert in islet transplantation. He is also highly skilled in kidney, pancreatic, and liver transplantation, including laparoscopic techniques used to procure organs from living kidney donors. Dr. Witkowski also performs islet autotransplantation for patients who need a pancreatectomy.

A widely published researcher, Dr. Witkowski has an impressive record of success in both basic science and clinical research pertaining to islet cell and abdominal organ transplants. Among other accomplishments, he was instrumental in developing an optimized islet isolation technique that greatly improved success in clinical transplants. Under Dr. Witkowski's leadership, multidisciplinary research teams at the University of Chicago are currently conducting several studies skillfully designed to improve quality and outcomes in islet cell transplantation in patients with type 1 diabetes.

DISCUSSION PANEL II

MENTORING AND INTERDISCIPLINARY COLLABORATION

Effective motivation of the research team and the ability to inspire junior team members are what defines a good Leader. In this panel, two established team leaders will share their thoughts on mentoring junior team members, directing them towards new research areas and motivating them to take upon themselves high-risk ventures and succeed. Once the group grows and the scientific interests of team members diverge, the question arises how can one coordinate projects that bridge several disciplines? Such interdisciplinary projects require a broad scientific perspective and the ability of the Leader to effectively manage specialists from different fields. This panel's aim will be to present how such interdisciplinary projects can be effectively coordinated, what are the potential gains of such efforts and what difficulties arise when basic research meets application-driven science. Whether the results to undertake such endeavors are worth it or not will be discussed with the audience during this panel.

MODERATOR

Dr. **WOJCIECH FENDLER**

Department of Biostatistics and Translational Medicine, Medical University of Lodz

Department of Radiation Oncology, Dana-Farber Cancer Institute , Harvard Medical School

Dr. Wojciech Fendler was born in 1982 in Lodz. His research interests expanded during medical studies and culminated in the Primus inter Pares award for the best medical student in Poland. After finishing his medical internship (2008) he devoted fully to his scientific pursuits working in Professor's Mlynarski group on monogenic diabetes. Dr. Fendler's PhD thesis (2011) concerned neonatal diabetes caused by mutations of the proinsulin gene. Expanded, nationwide epidemiological study on the matter resulted in the assembly of the most numerous group of patients with monogenic diabetes worldwide, spurring several publications in top diabetological journals and allowing dr. Fendler to obtain his habilitation degree in 2013.

After setting up his independent scientific group, through the actions of the Mentoring programme of the FNP dr. Fendler started a collaboration with the Dana-Farber Cancer Institute in Boston and expanded on his interest in circulating microRNAs. This collaboration resulted in publications in several high ranking journals: Science Translational Medicine (2015, 2017), Nature Communications (2017) and eLife (2017).

Right now dr. Fendler leads his own research group at the Department of Biostatistics and Translational Medicine funded by the FNP's First TEAM programme "Predictive biomarkers of radiation toxicity (PBRTox)".

During his scientific career he obtained several prestigious awards for young researchers including two START scholarships, Medtronic-ISPAD Young Investigator Award and the Wierzuchowski's lecture-award of Diabetes Poland – the highest award for scientific merit granted by this society.

Prof. **DIPANJAN CHOWDHURY**
Department of Radiation Oncology, Division of Radiation and Genome Stability, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA

Dipanjan Chowdhury, PhD, is an Associate Professor of Medicine at Harvard Medical School, and Chief of the Division of Radiation and Genomic Stability in the Department of Radiation Oncology at Dana-Farber Cancer Institute and Associate Member of Broad Institute of Harvard a MIT. He is the Brigham &Women's Hospital Distinguished Chair in Radiation Oncology. He is also an Affiliate Faculty Member of the Department of Biochemistry and Molecular Pharmacology and the Department of Immunology at Harvard Medical School. Dr. Chowdhury's research focuses on deciphering cellular response to DNA damage, particularly DNA double strand breaks, with the goals of generating strategies for personalized radio- and chemotherapy, and countering accidental radiation exposure. His work is supported by the NIH and several foundations, including the American Cancer Society, Ann-Fuller Foundation, Tina Brozman Foundation, Claudia Adams Barr program for Innovative Cancer Research and the Leukemia Lymphoma Society.

Dr. Chowdhury received his Bachelor of Science in Chemistry from St. Xavier's College, Kolkata; his Master of Science in Biochemistry from Calcutta University, and his Doctor of Philosophy in Molecular Biology from Brandeis University.

PANELISTS

Prof. **KRZYSZTOF JÓŹWIAK**
Department of Biopharmacy at the Medical University of Lublin

Krzysztof Jóźwiak, head of the Department of Biopharmacy at the Medical University of Lublin, Poland, conducts medicinal chemistry projects by combining computational modeling with experimental (affinity and functional efficacy) studies on drugs targeting neuronal receptors. The aim is to develop substances with selective action on a specific subtype of a receptor and/or on a specific intracellular signaling event. Co-author of over 90 research articles, editor and co-author of the book: Drug Stereochemistry: Analytical Methods and Pharmacology (New York, 2012). The Laureate of the 2012 edition of the UCB-Ehrlich Award for Excellence in Medicinal Chemistry granted by the European Federation for Medicinal Chemistry in Berlin, Germany.

Prof. **KRZYSZTOF PALCZEWSKI**
Department of Pharmacology at Case Western Reserve University, Cleveland, Ohio, USA

Krzysztof Palczewski's laboratory made a historic contribution by solving the crystal structure of rhodopsin, which has been cited over 6,000 times. His laboratory employs classical biochemical methods, crystallography, cryo-electron microscopy, cellular cryo-electron tomography, and two-photon microscopy to study phototransduction and visual retinoid cycle to obtain a comprehensive view of the visual system in health and during disease. His recent studies in two-photon functional imaging in the eye advanced the discovery and validation of treatments that can prevent retinal degenerative diseases. He developed visual chromophore supplementation, detoxification of harmful retinoids, and systems pharmacology toward the treatments of common retinal diseases. His next goal is to move pharmacological approaches beyond preclinical studies in animal models.

Dr. Palczewski's contributions to the chemistry and biology of vision and development of new therapies were recognized with numerous awards, including the ARVO Cogan Award in 1996, the ARVO Friedenwald Award in 2014, Beckman-Argyros Award in Vision Research in 2014, and Distinguished University Professor at CWRU in 2016. His publications (>560) were cited more than 39,000 times.

He received M.Sc. in Organic Chemistry from the University of Wroclaw, PhD in Biochemistry from the Wroclaw University of Science and Technology, and then trained in Dr. Paul Hargrave's laboratory. Dr. Palczewski established his first laboratory in 1992 in Portland, Oregon. He was promoted to a full professor at the University of Washington in 1997. After moving to Cleveland in 2005 to become the Chair of the Department of Pharmacology at Case Western Reserve University he continued productive vision research.

DISCUSSION
PANEL
III

HOW TO BREAK THE GLASS CEILING AND NOT HURT ONESELF?

Diversity is essential in science. It fosters new ideas, enables different perspectives, and fresh approaches to problem-solving – the elements necessary for creativity and innovation. In recent years, women are getting increasingly involved in scientific fields previously dominated by male researchers, like physics or engineering. Nevertheless, an equal number of men and women in senior academic positions remains an unfulfilled dream. How should we approach gender equality in science? Female panelists: leading experts in the fields of oncology, biology, chemistry, physics and computer sciences, will address the issue of how to counteract the gender discrimination.

MODERATOR

Dr. **KATARZYNA STAROWICZ**
Institute of Pharmacology Polish Academy of Sciences, Kraków

Katarzyna Starowicz-Bubak (PhD) is a neuropharmacologist leading a research group based at the Institute of Pharmacology Polish Academy of Sciences (www.if-pan.krakow.pl).

Her education includes M.Sc. degree in Biotechnology from the Jagiellonian University (2000), PhD in Pharmacology at the Medical Sciences at the Utrecht University (2005) and Habilitation in Medical Biology at the Faculty of Medicine of the Jagiellonian University Medical College (2013). After receiving a PhD degree, she started a postdoctoral fellowship in Endocannabinoid Research Group under the supervision of prof. Vincenzo Di Marzo. After completing the postdoctoral fellowship, she returned to Poland where she established and maintained a laboratory focused on understanding of the mechanisms of chronic pain and on the characteristics of endogenous system involved in the transmission of pain stimuli with particular attention to endocannabinoid system. Subsequently, her research interests expanded to include the issue of degenerative joint disease (particularly osteoarthritis, OA) and more recently towards reward and motivation in pain and pain relief.

Please visit http://www.painlab.pl for more details and full description of current research interests.

Prof. **MARIA ANNA CIEMERYCH-LITWINIENKO**
Faculty of Biology, University of Warsaw

Maria Anna Ciemerych-Litwinienko graduated from Faculty of Biology University of Warsaw. Both her MSc (1991) and PhD (1998) projects focused on the regulation of meiotic maturation of oocytes as well as early development of mouse embryos and were supervised by prof. Andrzej K. Tarkowski. During her PhD thesis she participated in many collaborations which allowed her to work at the School of Biological Sciences University of Manchester, Insitut Jacques Monod in Paris, Wellcome/CRC Institute University of Cambridge. Between 1999 and 2002 she was a postdoctoral fellow at Dana Farber Cancer Institute, Harvard Medical School in Boston. Working with Piotr Sicinski she was analyzing the role of cell cycle regulators in mouse development and cancer. In 2006 she received DSc diploma, in 2012 – full professorship nomination. Currently she is the head of the Department of Cytology Faculty and also deputy Dean of Biology University of Warsaw. Her interests focus at the mechanisms of stem cells differentiation and skeletal muscle regeneration. She was the recipient of START fellowship of Foundation for Polish Science (1995), "Stay with Us" fellowship of POLITYKA foundation (2003), and L'Oreal-UNESCO for Woman in Science fellowship (2005).

PANELISTS

Dr. **ANNA MAŁGORZATA CZARNECKA**
Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology in Warsaw
Mossakowski Medical Research Centre Polish Academy of Sciences

Anna Malgorzata Czarnecka M.D, Ph.D. – graduate of the Ist Medical Faculty of the Medical University of Warsaw and the Inter-Faculty Individual Studies in Mathematics and Natural Sciences. Currently a specialist of clinical oncology in the Department of soft tissue tumors, bone tumors and melanomas of the M. Sklodowska-Curie Memorial Institute of Oncology. She got her Ph.D. degree at the Institute of Oncology for her work during the Studies in Molecular Medicine – "Mitochondrial aberrations in carcinogenesis" (Promoter: Professor Ewa Bartnik). Her habilitation was granted in oncology at the Medical Faculty of the Medical University of Gdansk for a series of publications collected under the title "Clinical and molecular markers of renal cell carcinoma with tyrosine kinase inhibitors". She has also finished studies "Innovations Management in Healthcare" at the Leon Kozminski Academy in Warsaw and "Innovations Management" at the SGH Warsaw School of Economics. Her research experience includes residencies at the Department of Genetics of the Medical University of Warsaw, Department of Urology Emory School of Medicine (Atlanta, USA), Dipartimento di Medicina Sperimentale Universite degli Studi di Palermo (Palermo, Italy) Universitätsklinik für Kinder- und Jugendheilkunde, Paracelsus Medizinische Privatuniversität (Salzburg, Austria), Gene Function Research Center National Institute of Advanced Industrial Science and Technology (Ibaraki, Japan). She is the recipient of several awards including the TOP500 programme, Junior Faculty Merit Award of the International Society of Oncology and Biomarkers, Mentoring and START programmes of the Foundation for Polish Science, L'Oreal scholarship for Women in Science and the Warsaw scientific society as well as the Goldman Sachs, Kosciuszko and Fulbright Foundations.

Dr. **ANNA FABIJAŃSKA**
Institute of Applied Computer Science of the Lodz University of Technology

Dr. Anna Fabijańska, Ph.D., D.Sc. (born in 1982) is an Associate Professor in computer science at the Institute of Applied Computer Science of the Lodz University of Technology, Poland where she is also holding the position of the Institute's vice director for the development. She received her master of engineering degree (2006), doctoral degree (2007) and habilitation degree (2013) in computer science from the Faculty of Electrical, Electronic, Computer and Control Engineering of the Lodz University of Technology. She also gained her scientific experience abroad at the University of Kent (UK), Claude Bernard University Lyon 1 (France) and University of Clermont Auvergne (France).

Her scientific interests focus on digital image processing and analysis, machine vision and artificial intelligence (especially deep learning). In particular, they concern the development of the dedicated image processing pipelines for computer-aided diagnosis systems and applications of computer vision in various fields of science and industry. She has authored or co-authored over 100 scientific papers which have been cited over 700 times.

She was a beneficiary of the Ministry of Science and Higher Education fellowship for outstanding young scientists in the years 2013–2015, a beneficiary of the Foundation for Polish Science (FNP) START fellowship in 2011 and the leader of scientific grants including the project within the framework of the Iuventus Plus programme in the years 2013–2015. Since 2016 she has been the member of The Polish Young Academy of the Polish Academy of Sciences and the member of the Committee on Informatics of the Polish Academy of Sciences. She has also served as an independent reviewer for the Polish National Science Center (NCN), The National Centre for Research and Development (NCBR) and the Netherlands Organisation for Scientific Research (NWO-WOTRO). Recently, she has been supervising 3 Ph.D. students in computer science.

PANELISTS

Dr. **JOANNA SUŁKOWSKA**
Centre of New Technologies, University of Warsaw

Dr hab. Joanna Sułkowska is the head of the "Interdisciplinary laboratory for modeling biological systems" at the Centre of New Technologies at the University of Warsaw. Her M.Sc. thesis, carried out at the Vrije Universiteit in Amsterdam and defended at the Faculty of Physics at the University of Warsaw in 2003, was devoted to properties of viscoelastic polymers. In 2007 she defended with distinction her doctoral dissertation in the field of biophysics, devoted to the characteristics of mechanical properties of proteins, which was awarded as the best PhD thesis at the Institute of Physics of the Polish Academy of Sciences. In 2016 she obtained her habilitation at the Faculty of Chemistry of the University of Warsaw. For several years, as part of a postdoctoral internship, she worked at the University of California, San Diego. She is an author of over 50 scientific publications, including articles in Nature Structure & MB, JACS, PNAS, PRL. Joanna Sułkowska has been awarded many times for her scientific achievements. She received both Installation Grant and Young Investigator title from the European Molecular Biology Organization (EMBO), as well as grants from the National Science Centre, the Foundation for Polish Science, and the Ministry of Science and Higher Education (currently she conducts research under the Ideas Plus grant). She received the habilitation scholarship L'Oreal scholarship for Women in Science and the international prize Unesco-L'Oreal "Rising talent". She was chosen as a person of the year "MocArty – człowiek roku 2017" by Radio RMF Classic. She was also ranked among the group of 50 brave people and in the initiative Jutronauci by Gazeta Wyborcza in 2017.

For her greatest scientific achievement so far, she considers the discovery and characterization of non-trivial topology in proteins, the determination of mechanisms of their formation and relationships with biological function. The results of her work contribute to understanding of Alzheimer's and Parkinson's diseases and obesity.

FLASH TALKS

The Scientific Committee has decided to honour the highest-rated abstracts by offering to their authors an opportunity to present during flash talks session proceeding the closing of the conference. These three minute-long presentations will briefly showcase the main finding or research focus of the honoured participants. We believe that this form of presentation will provide an interesting opportunity to demonstrate the range of topics discussed during PSN 2018 to the general public.

HOSTS:

Dr. **WOJCIECH FENDLER**

Prof. **KRZYSZTOF JÓŹWIAK**


RAINBOW
HOTEL GRAND

BIOINFORMATICS AND BIG DATA ANALYSIS

SPEAKERS

GOSIA TRYNKA
Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Cambridge, UK

Functional fine-mapping of GWAS variants for complex immune traits

Thousands of genetic variants have been linked to common diseases that affect the immune system, such as type 1 diabetes, rheumatoid arthritis, celiac disease and inflammatory bowel disease. However, the molecular mechanisms by which genetic variants predispose an individual to the development of immune diseases are largely unknown. Many of these variants localise in non-coding parts of the genome, indicating that they may function through regulation of gene expression. As gene expression can be highly cell type specific it is important that functional follow-up studies are carried out in disease most relevant cell types. We have developed methods that integrate disease associated variants with histone marks to pinpoint critical disease cell types. One of the identified cell types is the CD4 regulatory T cell (Tregs). Using Tregs from 100 healthy blood donors we generated detailed map of gene expression regulation by mapping quantitative trait loci (QTL) for RNA-seq (gene transcripts), ATAC-seq (chromatin accessibility) and ChIP-seq (promoter and enhancer histone modifications). This approach allowed us to refine immune disease signals to functional variants and prioritise candidate causal genes.

Dr GOSIA TRYNKA leads the immune genomics group that studies how human genetic variation impacts immune system and predisposes to development of autoimmune diseases.

I strongly believe that interdisciplinary approaches are essential to achieve meaningful insights into biological processes. The combination of molecular techniques, genomic assays, and computational methods that we develop

and apply to study the immune system is a reflection of my own career path through several disciplines within biology and genetics.

With a backround in molecular biology, I became interested in medical and population genetic approaches to study genetic determinants for immune related diseases. I joined Prof. Cisca Wijmenga's group where I was a co-lead analyst for the genome-wide association study (GWAS) and an Immunochip study for coeliac disease (an immune disease of the small intestine resulting from intolerance to gluten). These studies resulted in identification of tens of disease risk loci and pointed to strong shared genetic backround between celiac disease and a range of other common immune conditions, including type 1 diabetes, rheumatoid arthritis, and inflammatory bowel disease.

Despite our great success in mapping disease risk variants, I was disappointed by the limited insights that we gained in understanding biology of complex immune diseases. I therefore carried out my postdoctoral research at Brigham and Women's Hospital, Harvard Medical School and Broad Institute where I joined Dr. Soumya Raychaudhuri's and Dr. Robert Plenge's groups. I invested my time in developing statistical methods that allow translation of GWAS associations into biological functions. By integrating disease-associated variants with functional genomics data, these approaches pointed to specific cell types being relevant in the pathogenesis of numerous complex traits, including immune diseases. My group at the Sanger Institute continuous with experimental and computational efforts to further map and translate immune disease genetic variants to function.

Apart from science, I am enthusiastic about photography, and you might frequently find me on my road bicycle or playing volleyball.

SPEAKERS

TOMASZ BURZYKOWSKI
Hasselt University (Belgium), International Drug Development Institute (Belgium)

Statistical bioinformatics: when statistics help in "omics" data analyses

In 2007, Ransohoff (Journal of Clinical Epidemiology) stated that "The search for molecular markers for cancer (…) many promising initial results have been found to be unreliable or not reproducible, and the larger process of discovery can seem slow and inefficient." In 2017, Ioannidis and Bossuyt (Clinical Chemistry) wrote: "The current biomarker pipeline is too prone to failures." These two quotations suggest that, in the decade separating the two publications, not much has changed regarding the quality of the process of discovering and validating markers obtained by using advanced 'omics' technologies. Yet, the concept of precision cancer medicine is very much linked to the use of such markers. In this presentation, we review some common errors related to the design and analysis of (bio)marker studies. Avoiding those (and similar) errors might speed the search for molecular markers up and make it more efficient.

Prof. TOMASZ BURZYKOWSKI received a master's degree in applied mathematics (1990) from Warsaw University (Poland), and master's (1991) and PhD (2001) degrees in biostatistics from Hasselt University (Belgium). He works as Full Professor of Biostatistics & Statistical Bioinformatics at Hasselt University (Belgium) and as Vice-President of Research at the International Drug Development Institute (Belgium). His main areas of expertise include methodology of clinical trials, meta-analysis of clinical trials, validation of surrogate endpoints, survival analysis, and analysis of "omic" data. He is a co-author of numerous papers applying statistical methods to clinical data

in different disease areas (oncology, Alzheimer's disease, ophthalmology, cardiovascular diseases, orthodontics). Tomasz teaches introductory and advanced courses on statistical methodology in various educational programs at the graduate and post-graduate level. He also serves as a statistical consultant for the biotech- and pharmaceutical industry as well as academia.

SPEAKERS

KRYSTIAN JAŻDŻEWSKI
Department of Genomic Medicine, Medical University of Warsaw

BadamyGeny.pl – national cancer risk assessment program – BIG picture

We developed Cancer Risk Assessment Method, which predicts the risk of getting cancer, based on the clinical data provided by the patient, and genomic data obtained by next-generation sequencing of all the genes associated with familial cancers. Our goal is to identify all people with high risk of cancer in whole Polish population of 38 million. We just started the population screening program on the scale unheard of mainly due to high costs of genomic sequencing. To make the screening program possible, we developed a novel method of genomic sequencing and analysis, which decreased 20-fold the price of the multigene test i.e. below a hundred Euros. The method has been designed and tested by the interdisciplinary research team at the University of Warsaw, and after validation immediately translated into clinical practice. It is estimated that there is at least a million women with high risk of getting breast cancer and equal number of men with high risk of getting prostate cancer in Poland. We target at finding them all with the aim of introducing them into personalized prophylactic program. The patient's prophylactic plan is personalized based on his or her medical history and genetic mutations found in any of the 70 cancer-related genes screened. During the presentation we shall provide the preliminary results, including the prevalence and spectrum of gene mutations, based on first 15 000 patients.

Prof. KRYSTIAN JAZDZEWSKI, M.D., Ph.D. is the head of interdisciplinary group comprising medical doctors, molecular biologists, and geneticists from Genomic Medicine (Medical University of Warsaw) and the Laboratory of Human Cancer Genetics (Centre of New Technologies, University of

Warsaw) in Poland. The group focuses on identifying the molecular changes underlying heritability and pathogenesis of human malignancies. Using the most innovative methods of molecular and genetic analysis, including next-generation sequencing, we seek for mutations that predispose to carcinogenesis. Recently, we started the National Screening Program with the aim to identify all the people predisposed to inherited cancers in whole Polish population.

Prof. Jazdzewski has published several papers in peer-reviewed journals, including PNAS, Cell Cycle, JCEM, Thyroid, Human Genetics, Endocrine-Related Cancers, and Clinical Cancer Research with more than 3000 citations.

SPEAKERS

RAFAŁ PŁOSKI
Medical Genetics Department of Warsaw Medical University, Warsaw

Whole exome sequencing for discovery of novel human diseases

In 2012 Department of Medical Genetics (Warsaw Medical University) has acquired Illumina HiSeq 1500 which allowed to establish whole exome sequencing (WES) as method for both research and diagnostic purposes. Since then we have performed >1000 WES analyses, most of which aimed at finding diagnosis in patients suspected to suffer from rare disorders with a genetic basis. During the lecture selected findings will be presented illustrating how this approach enables discovery of novel diseases (i.e. those caused by mutations in genes not yet associated with known human disorder). (MPNs), especially triple-negative MPNs, in respect to canonical mutations in JAK2, calreticulin (CALR), and myeloproliferative leukemia virus oncogene (MPL) and atypical myeloid leukemia. New discoveries in our understanding of genomic landscape of CML and MPNs help not only in routine diagnostics but may help to find a cure for these malignancies and will give again new inspiration in cancer research.

Prof. RAFAŁ PŁOSKI – Professor of genetics, the Head of Medical Genetics Department of Warsaw Medical University. Graduated Warsaw Medical Academy (1990) and got his PhD at the University of Oslo (1995). Since then prof Płoski worked in HLA Lab of Institute of Rheumatology (Warsaw) and subsequently Genetics Lab of Department of Forensic Medicine of Warsaw Medical Academy. In 2005 he started the Department of Medical Genetics at the Warsaw Medical University and has been its head till now. The main current focus of his activity is whole exome/genome sequencing on Illumina HiSeq 1500 platform for the diagnosis of human monogenic disorders.

Apart from diagnostic activity specific research projects involve studies of disease discordant monozygotic twins and search for novel gene-disease associations by mapping of break point regions in symptomatic balanced chromosomal translocations as well as development of novel bioinformatic tools for the analysis of whole exome/genome sequencing data. Prof. Płoski is a specialist in laboratory medical genetics and laboratory forensic genetics; he also serves as an expert witness in human genetics at Regional Court of Justice in Warsaw. Prof Płoski has published >250 research papers from the area of human genetics which have been cited 4000 times (Hirsch Index 33).

SPEAKERS

MARCIN DRĄG
Department of Chemistry, Wroclaw University of Science and Technology, Wrocław

In quest of optimal technology to investigate activity of proteolytic enzymes in health and disease

Proteolysis is one of the most important and ancient reactions in biology. Enzymes that catalyze this reaction are called proteases. Proteases as "good guys" perform many significant biological processes like cellular quality control, apoptosis, blood coagulation or signal transduction. However they can be also "bad guys" contributing to pathological events like cancer, diabetes, coagulopathies, inflammation, infectious or degenerative diseases. It is estimated that 5–10% of all pharmaceutical targets being pursued for drug development are proteases.

Despite significant progress in recent years, one of the biggest problems in the investigation of proteases is their similar activity and location. Due to the overlapping substrate specificity (preference in the recognition of natural amino acids) it is very hard to distinguish many major proteolytic enzymes families using chemical tools developed using classic screening technologies. This also very often limits the discovery of selective drug or marker for specific activity monitoring.

Our group has recently developed technology to obtain new types of ultrasensitive chemical tools (substrates, inhibitors, activity-based probes) for major families of medically important proteases. Using this novel, unique and very efficient technology called Hybrid Combinatorial Substrate Library (HyCoSuL) we have demonstrated that protease substrate specificity can be significantly enlarged by the use of unnatural amino acids in peptide sequence. An overview of major strategies to develop very active and selective chemical

tools, which can be used for reliable investigation of activity and location of proteases in health and disease will be presented.

1. Drag & Salvesen, Nature Reviews Drug Discovery 2010, 9, 690; 2. Kasperkiewicz et al. Proc. Natl. Acad. Sci. U S A. 2014, 111, 2518; 3. Poręba et al. Cell Death & Differentiation 2014, 9, 1482; 4. Poręba et al. Cell Chemical Biology 2016, 23, 1023; 5. Poręba et al, Scientific Reports 2017, 7, 43135; 6. Rut et al, Antiviral Research 2017, 139, 88; 7. Kasperkiewicz et al., FEBS Journal 2017, 284, 1518; 8. Kasperkiewicz et al., Journal of the American Chemical Society 2017, 139, 10115

Prof. MARCIN DRĄG was born in Świdnica (Poland) in 1975. He earned his M.Sc. degree from Department of Chemistry at University of Wroclaw in 1999. Next, he moved to Department of Chemistry at Wroclaw University of Science and Technology, where he earned his Ph.D. in organic and bioorganic chemistry working on new inhibitors of metallo- and cysteine proteases under supervision of prof. Pawel Kafarski. His Ph.D. thesis was awarded the best thesis in organic chemistry by Polish Chemical Society and Sigma-Aldrich (2004). In 2003 he was appointed Assistant Professor at Wroclaw University of Science and Technology and shortly after (2004) adjunct position. In years 2005–2008 he conducted postdoctoral research at The Burnham Institute for Medical Research (currently SBP Medical Discovery Institute) in La Jolla, CA (USA) in prof. Guy Salvesen laboratory. In 2011 he received Doctor of Sciences Degree in chemistry (habilitation) for his work on new types of combinatorial libraries to investigate proteolytic enzymes. In 2016 he received Professor title in chemistry from President of Poland. Prof. Drąg supervised four Ph.D. students (all cum laude) and 4 post-docs. He is an author of more than 100 publications in peer-reviewed scientific journals. His research interests in chemical biology include the design and synthesis of substrates, inhibitors and activity-based probes to decipher the mechanism of action and the function of proteases in health and disease with particular focus on use of unnatural amino acids.

SPEAKERS

ANDRZEJ J. BOJARSKI
Department of Medicinal Chemistry Institute of Pharmacology Polish Academy of Sciences, Kraków

Academic *in silico* platform for new drug discovery

GPCRs (G-protein coupled receptors) are a key part of the cell interface between its external and internal environments. As GPCRs are involved in etiology of many diseases, despite that they are targets of many existing drugs, a lot of efforts are still focused on development of new medicines acting selectively on a given receptor subtype, having a specific receptors profile or operating through other than orthosteric mechanism of action (like e.g. allosteric modulation).

Since the first application of our multistep virtual screening (VS) protocol to search for new serotonergic 5-HT7 receptor ligands, similar VS procedures were used in search of agents acting on many different targets (e.g., 5-HT6, 5-HT2B, GABA-B, metabotropic glutamate receptors). All the VS filters are constantly upgraded using the most recent data of ligands of a given target (for the ligand-based stage) as well as available crystal structures for homology model development and docking (for the structure-based stage). The evolution of the VS protocol, the development of different tools for docking results analysis and several applications of the in silico platform will be presented.

Prof. ANDRZEJ BOJARSKI, head of the Department of Medicinal Chemistry at the Institute of Pharmacology of the Polish Academy of Sciences. His research interests are focused on the design and synthesis of ligands of metabotropic G-Protein Coupled Receptors (in particular serotonergic and glutamatergic) and application of different molecular modeling techniques in ligands design, simulation of ligand-receptor interactions and dynamics of L-R complexes. Besides the development of methods and tools supporting drug design,

his lab is also one of the most efficient in vitro screening centers for CNS-oriented compounds in Poland. Being involved in a number of national and international projects (e.g. www.platformex.eu, www.cns-platform.eu) and collaborations with both academia and Polish pharmaceutical companies, he has successfully developed a number of innovative drug candidates for the treatment of schizophrenia and depression.

Andrzej Bojarski has graduated in Chemistry (Jagiellonian University, Kraków, 1990), obtained PhD (1996), habilitation (2005) and profesorship (2013) in Pharmaceutical Sciences (Faculty of Pharmacy, Jagiellonian University Medical College). Since 2006 he is a Member of the Board of the Polish Society of Medicinal Chemistry.

NOVEL APPROACH TO NORMALIZATION OF HUMAN SERUM AND PLASMA MICRORNA QPCR QUANTIFICATION DATA

Pagacz Konrad[1], Kucharski Przemysław[1,2], Smyczyńska Urszula[1], Fendler Wojciech[1]

[1] Departament of Biostatistics and Translational Medicine, Medical University of Lodz (Mazowiecka 15, 92-215 Łódź, Poland)

[2] Institute of Computer Science Lodz Univeristy of Technology (Stefanowskiego 18/22, 90-537 Łódź, Poland)"

Presenting author: Konrad Pagacz, M.D. (*konradpagacz@gmail.com*)

INTRODUCTION: Researchers have not agreed on a single data normalization strategy for microRNA molecules quantification in serum or plasma using RT-qPCR method. In contrast to mRNA quantification in specific types of tissues, a search for a stable, endogenous reference microRNA or a set of microRNAs did not bring a success – plentiful of candidates did not pass validation. In this work, we presented an ensemble approach to normalization, which aimed to find the most stable, endogenous housekeeping microRNA or set of microRNAs.

METHODS: We conducted a literature search to gather available datasets of microRNA qPCR profiling from serum or plasma. We applied three different normalization algorithms (GeNorm, BestKeeper, NormFinder) to each dataset to calculate the most stable single microRNA. Then we repeated the analysis for all possible pairs in each dataset to find the most stable pair of microRNAs? We calculated a ranking showing the position of single microRNAs and pairs determined by stability value.

RESULTS: We downloaded 11 datasets, which followed our inclusion criteria, found in Gene Expression Omnibus database. The median fractional ranking value was higher for single than combination of microRNAs (0.49 vs. 0.26, $p = 0.0159$). The 10 most stable pairs derived on average from 48.62% percent of single microRNAs (48.62 95%CI34.62–62.62%).

CONCLUSIONS: We outlined a new normalization scheme and performed the analysis on 11 available datasets, which showed that pairs of microRNAs are a better fit for a reference factor than a single microRNA. We also proved that the most stable pairs are derived from the most stable single microRNAs.

VOLUMETRIC MACRO- AND MICRO-SCALE ASSESSMENT OF CRYSTALLINE LENS OPACITIES IN CATARACT PATIENTS USING LONG-DEPTH-RANGE SWEPT SOURCE OPTICAL COHERENCE TOMOGRAPHY

Grulkowski Ireneusz[1], Manzanera Silvestre[2], Cwiklinski Lukasz[1], Mompean Juan[2], de Castro Alberto[2], Marín José María[3], Artal Pablo[2]

[1] Institute of Physics, Nicolaus Copernicus University (ul. Grudziadzka 5, 87-100 Toruń, Poland)
[2] Laboratorio de Óptica, Universidad de Murcia (Campus de Espinardo, E-30100 Murcia, Spain)
[3] Servicio de Oftalmología, Hospital Virgen de la Arrixaca (Ctra. Madrid-Cartagena, El Palmar, E-30100 Murcia, Spain)

Presenting author: Ireneusz Grulkowski, Ph.D. (*igrulkowski@fizyka.umk.pl*)

INTRODUCTION: Cataract is developed by the formation of opacifications of the crystalline lens, which becomes less transparent. Age-related cataracts are leading causes of blindness nowadays affecting more than half population of 75+ yo. The methods for detection and objective evaluation of cataract *in vivo* are crucial for a proper management of cataractous eyes. In this paper, we demonstrate comprehensive visualization of crystalline lens opacities *in vivo* in patients with different types of cataracts.

METHODS: We also present visualization strategies to enhance image contrast related to lens opacifications, and to identify features of lenticular macro- and micro-morphology in different types of cataracts.

RESULTS: We developed and optimized an OCT-based optical platform enabling imaging the entire anterior segment of the eye with micrometer resolution. We imaged 50 eyes of 30 participants (mean age: 60±18 yo; age range: 26–91 yo). The access to volumetric data allowed for generating virtually any cross-section as well as *en-face* and/or side projection maps contrasted with different parameters. We visualized and identified different features characteristic for cataract formation such as cortical spokes, water clefts, vacuoles and enhanced scattering in the nucleus. Finally, the OCT projection maps have been used for a quantitative analysis of opacification at different grades of cataracts.

CONCLUSIONS: We demonstrated that 3-D SS-OCT technology enables volumetric visualization of *in vivo* macro- and microstructural changes in the crystalline lens related to opacification. Access to volumetric data allows for contrast enhancement due to the increased scattering inside the lens. Quantification of opacities may help in diagnosing and grading cataract eyes.

SOCIAL MEDIA AND MAKING HEALTH AND MEDICINE UNDERSTANDABLE FOR PATIENTS

Mankiewicz Lech

Science and Society, Center for Theoretical Physics PAS (Al. Lotników 32/46, 02-668 Warsaw, Poland)

Presenting author: Lech Mankiewicz, Ph.D. (*lech@cft.edu.pl*)

INTRODUCTION: A patient condition is often compromised by a lack of understanding of the disease and proposed therapy. It is a particular problem in Poland where the majority of medical personnel is convinced that it is not necessary to discuss with a patient about his or her conditions.

METHODS: Social media and educational platforms similar to Khan Academy offer unique opportunity to present solid knowledge and valid interpretations of conditions and functioning of organs in a human body in an accessible and understandable manner.

RESULTS: I present results of localization of Health and Medicine chapter of Khan Academy in the Polish language together with its usage statistics.

CONCLUSIONS: Knowledgeable citizens and knowledgeable patients mean a better understanding of treatments and stricter following of rules. Social media and educational platforms are natural tools for building a better understanding of therapies. A prerequisite is, however, that the healthcare community accepts the need and understands the advantages of dealing with better-informed patients.

METAGENOMICS AS A COMPLEX ANALYSIS IN BIOBANK LAB

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Metagenomics is one of the widest developed area in Next Generation Sequencing. This method of nucleic acids analysis finds wide application in environmental, medical and industrial researches. The metagenomic profiling through sequencing enables both complex environmental and host associated samples analysis.

DNA for metagenomics analysis is isolated from different materials e.g. from salt, water, soil, saliva, stool or buccal, nasal and ear swabs. To identify and compare complex communities present within a given sample, 16S ribosomal RNA (rRNA) sequencing (Illumina) is used in our laboratory. For studying phylogeny and taxonomy of samples, amplicons of variable regions V3 and V4 of the 16S rRNA are amplified. Cause of its length, ~550bp, preferred sequencing platform is Illumina MiSeq in 2 x 300bp mode.

In data analysis, we use OpenSource ools like Qiime2 platform for bacterial and fungal metagenomics analysis and other tools like ViromeScan or FastViromeExplorer for virome analysis. The use of these tools allows us to analyse community richness, dissimilarity, taxonomic assignment and difference abundance.

Our basic metagenomic analysis pipeline is based on Qiime2. This platform lets us perform all steps of data pre-processing and analysis in one environment. Based on our hypothesis we can chose the best metrics of α and β diversity. Taxonomic assignment is performed with reference sequence databases which are specially prepared for Qiime2.

In summary, metagenomics is a powerful tool which provides information about all prokaryotic organisms living in the environment of interest. Advanced bioinformatics tools give us chance to easily and effectively analyse the metagenomic data.

GLOBAL ANALYSIS OF PLASMODIUM FALCIPARUM HISTIDINE-RICH PROTEIN-2 (PFHRP2) AND PFHRP3 GENE DELETIONS USING WHOLE-GENOME SEQUENCING DATA AND META-ANALYSIS

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Many rapid diagnostic tests (RDT) used on suspected malaria cases are based on the detection of the protein encoded by *Plasmodium falciparum* histidine-rich protein-2 (*pfhrp2*) gene. Parasite samples lacking *pfhrp2* and*pfhrp3* genes have recently emerged, but a compre-hensive genetic analysis of these variants is lacking. With this purpose, genomic data from experimental *P. falciparum* genetic crosses between different laboratory lines were first analysed. The data provided insights into the segregation pattern of these deletions and the fitness of the parental genotypes in each mating experiment. The frequency of *pfhrp2* deletions was consistent with a Mendelian prediction in HB3 x DD2. The *pfhrp2* and *pfhrp3* deletions also appear to segregate independently of each other. Analysis of 3D7 x HB3 and 7G8 x GB4 estimated the probability of spontaneously generating a *pfhrp2* deletion during sexual recombination to be less than 6.2%. Next, whole genome sequence data from 1,970 *P. falciparum* isolates collected globally were analysed. Nine samples displayed evidence of *pfhrp2* deletions whereas twenty-eight isolates had evidence of *pfhrp3* deletions, which are widespread in Southeast Asia. Finally, a meta-analysis of six studies from South America and four studies from Africa revealed a positive

mean association between the frequencies of *pfhrp2* and *pfhrp3* deletions in each continent. This may reflect a selective pressure jointly acting upon both loci. In conclusion, evidence of genetic selection on both *pfhrp2* and *pfhrp3* gene deletions is presented, but experimental crosses do not provide evidence of a fitness cost of these variants.

MODELING OF RIBONUCLEIC ACID-LIGAND INTERACTIONS

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Computational methods play a pivotal role in the early stages of small molecule drug discovery, and are widely applied in virtual screening, structure optimization, and compound activity profiling. Over the last decades in medicinal chemistry, almost all the attention has been directed to protein-ligand binding and computational tools were created with such targets in mind. However, with growing discoveries of functional RNAs and their possible applications, RNA macromolecules have gained considerable attention as possible drug targets. This flow of discovery was followed by adapting existing computational tools for RNA applications, as well as active development of new RNA-tailored methods. However, due to the different nature of RNA, especially its tendency to use morphological plasticity (conformational change in ligand binding), the modeling of RNA still remains a challenging task ([1], Figure 1).

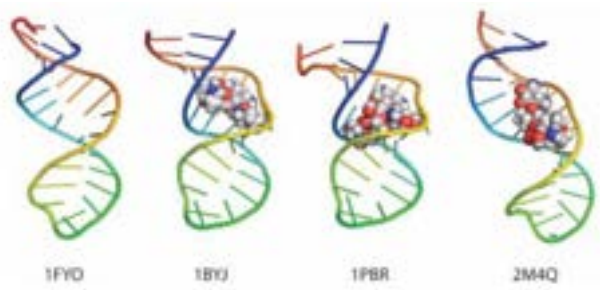

Figure 1. RNA flexibility in response to ligand-binding: NMR structures of decoding region A-Site.

The evolution of 'protein-based' drug discovery, and related computational methods, offers some clues on possible future directions and developments in modeling RNA interactions with small molecule ligands. We will present a new computational tool for predicting RNA-ligand interactions, which uses a coarse grained representation of both interacting partners. We will also present the plans for the future development of a predicting method which takes into account the full flexibility of the RNA and ligand.

[1] Stefaniak F., Chudyk E., Bodkin M., Dawson WK., Bujnicki J.M., Wiley Interdiscip Rev Comput Mol Sci 2015 Sep 14, doi: 10.1002/wcms.1226

1 SIMILARITIES IN MOLECULAR STRUCTURE DETERMINED BY DYNAMIC COMBINATORIAL LIBRARIES

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NTRODUCTION: The activity of common drugs relies on the capability of given molecules to form specific supramolecular complexes. These properties depend on the adopted spatial arrangement of functional groups, which define the molecular geometry. Experimental determination or theoretical prediction of molecular geometry is a highly challenging task. Our aim is to employ a dynamic combinatorial libriary to act as a sensor array to determine certain aspects of molecular structure and evaluate geometrical and functional similarity between different chemical compounds.

METHODS: In the initial studies a set of molecules (templates) – carboxylates that vary in number of functional groups, size, shape and flexibility – was used to interact with dynamic combinatorial libraries of macrocyclic disulphides. The composition of the library, influenced by introduction of a template was evaluated by HPLC. Concentrations of the library members were in the next step analysed by principal component analysis (PCA) and artificial neural networks (ANN).

RESULTS: The dynamic combinatorial library is able to distinguish all of the used templates. After PCA certain clusters are easily recognised, which correspond to templates of similar length of bearing the same structural feature. After training, the ANN can be used to determine the number of functional groups in an unknown template with approx. 70% efficiency.

CONCLUSIONS: These results indicate that dynamic combinatorial library in combination with PCA or ANN can recognise specific structural features and assess structural similarity between chemical compounds. This property may be particularly useful in analysis of potential action and side effects of novel drugs.

2 A SERVER FOR GENOMIC STRUCTURES

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INTRODUCTION: KnotGenom server enables to analyze entanglement of a single chromosome and links between chromosomes in the entire cell. All types of entanglement can be determined by different deterministic and probabilistic methods. The knotting complexity of the chromosome is presented in the form of a matrix diagram that shows users the knot type of the entire polypeptide chain and of each of its subchains. Entanglement of links is also computed by Gaussian linking integral. Entangled chromosomes are presented graphically in an intuitive way. The stability of entanglement can be studied based on the relaxation method.

METHODS: Knot theory

RESULTS: The topological analysis of chromosomes has shown that single chromosome can be knotted and this knowledge is used to improve current data, 3D chromosome structure. However, according to our knowledge, a pair of chromosomes has never been analyzed from the point of view of links. A link is formed from at least two chains – e.g. a pair of chromosomes. Our review of available data shows that a significant number of stable links between chromosome pairs exist. Some links are even conserved between cells. In the paper we also present methods used to determine types of links and their locations along chromosomes.

CONCLUSIONS: Identified links might suggest that a small fraction of chromosomes are entangled not only locally. Presented methods should be used also as a quantitative assessment – descriptor – to distinguish the quality of modeled data.

3 SIMRNA: A COARSE-GRAINED METHOD FOR RNA FOLDING SIMULATIONS AND 3D STRUCTURE PREDICTION

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INTRODUCTION: The molecules of the ribonucleic acid (RNA) perform a variety of vital roles in all living cells. Their biological function depends on their structure and dynamics, both of which are difficult to experimentally determine, but can be theoretically inferred based on the RNA sequence. We have developed a computational method for molecular simulations of RNA, named SimRNA.

METHODS: SimRNA is based on a coarse-grained representation of a nucleotide chain, a statistically derived energy function, and Monte Carlo methods for sampling of the conformational space. The backbone of RNA chain is represented by two atomsper nucleotide, whereas nucleotide bases are represented by three atoms. All terms of the energy function were derived from a database of crystal RNA structures, as a statistical potential. Sampling of the conformational space was accomplished by the use of the asymmetric Metropolis algorithm coupled with a dedicated set of moves.

RESULTS: Recent tests demonstrated that SimRNA is able to predict basic topologies of RNA molecules with sizes up to about 50 nucleotides, based on their sequences only, and larger molecules if supplied with appropriate distance restraints. The user can specify various types of restraints, including restraints on secondary structure, distance and position.

CONCLUSIONS: SimRNA can be used for RNA folding and RNA 3D structure prediction. It is also able to fold/refine structures with irregular (non-helical) geometry of the backbone (RNA pseudoknots, ulges etc.). SimRNA is a folding simulations method, thus it allows for examining folding pathways, getting approximate view of the energy landscapes.

4 BIG DATA LAB MANAGEMENT SYSTEMS

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We work on a huge amount of data. We still collect and process thou-sands of genotypic and phenotypic information about one patient for the use in extensive genetic and medical research. We are helped by the biobanking system, which we are currently improving in Poland as a part of the European Consortium European Research Infrastructure Consortium BBMRI-ERIC. All procedures for collecting material, recruitment of volunteers and patients, data anonymization, entering declarative data and medical history into the system, storage procedures for a given biological and DNA samples must be subject to inspection and registration. For this we need platforms edited only by authorized administrators. Since 2010 such a system has been created in Biobank Lodz of University of Lodz. As part of the TESTOPLEK project, we have created the Sample Management System (SMS) to collect and manage biological samples and phenotype data. We collected samples from over 10 000 Polish adults including children, people suffering from cancers, endometriosis etc.

We created unique questionnaires, in which personal data were irreversibly anonymized, contained very detailed questions about appearance pheno-type, ethnicity, addictions, diseases and treatment. As a member of BBMRI.pl consortium, we comprehensively tested freeware software BBMS for management of Biobanks, available online on the manufacturer's website (LabMind). The purpose of BBMS is to manage sample storage and track all the experimental procedures. This homogeneous system makes possibilities to unify data collection and management procedures for broad sharing and learning others, cooperation and information exchange between other scientific units and medical centers.

5 ANALYSIS OF MODERN DNA AS A PART OF PLATFORM E-CZLOWIEK.PL

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Within project "Digital sharing of biomolecular and descriptive resources of Biobank and Department of Anthropology, University of Lodz – characteristics of populations living in present-day Poland through the ages. Information platform e-Czlowiek.pl (e-Human.pl)" we obtain data of Polish individuals and after analysis we will publish it on platform e-Czlowiek.pl. This is long and difficult way but results are invaluable.

The platform will contain anthropological and genetic information of human populations living in the central Poland in the period from the Piasts to the beginning of the 19th century and also genetic data of contemporary Poles from the whole country. Analysis of modern and ancient DNA differ from each other.

First step of modern DNA analysis is acquisition of the data about over 0.5 million SNPs digitized on microarrays. After this stage we have to compare our data to databases such as tools delivered by NCBI, GWAS Catalog, PredictSNP and others. We check SNP location, description of occurrence SNP in world populations and functional consequences of SNP. We get results by PLINK 1.07 using case-control association analysis, covariative with environmental factors and we also build logistic and linear models. Important stage of analysis is to visualise our results by HaploView software where we obtain Manhattan plots and linkage disequilibrium blocks. For visualisation we also use LocusZoom to depict the location of genetic markers and its correlation with the reference SNP.

The objectives of present study is genetic characterization of Polish population living in present-day Poland through the ages.

6 NEEDLE IN A HAYSTACK – USING "BIG DATA" TO FIND NOVEL ONCOGENIC DRIVERS

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Despite recent revolutionary progress in the understanding of the mechanisms of oncogenic transformation, personalized cancer therapy remains largely elusive. Instead, to eradicate the tumor we still rely on surgery, broad-spectrum chemotherapeutics, and radiation therapy, all of which severely reduce the patient's quality of life. And yet, cells in each tumor rely on just a handful of deregulated signaling pathways to maintain their growth. In principle, if we were able to precisely identify these pathways, we could target them therapeutically and eliminate the tumor with minimal side effects. Finding such pathways has become feasible in recent years due to progress in automation, DNA sequencing, and data analysis methods, which enabled screening of potential targets on an unprecedented scale. Recently, two large-scale loss-of-function screens yielded a trove of data regarding the sensitivity of cancer cells to the loss of different genes. We searched the data generated in these screens to identify previously unknown cancer type-specific factors that determine the growth capacity of cancer cells. We hope that these factors will serve as targets for personalized therapy or as biomarkers to stratify cancers for different therapeutic interventions.

This work was supported by the SONATA BIS grant 2014/14/E/NZ3/00033 from the National Science Centre.

7 CLUSTERING – "A USEFUL TOOL" USED IN POPULATION STUDIES

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In population studies, getting the right population division can be difficult. Administrative regions are useful however they do not reflect the structure of specific population. When sample size increases and samples start to come in from different places this problem occurs. The solution could be clustering, the machine learning method of sample grouping, based on their spatial coordinates and creating new intermediate division that are best suited to data. The aim of the present study was to find the method to visualize trait distribution in Polish population. We had at our disposal two types of data: genetic, based on single nucleotide polymorphism in DNA and survey, based on information from questionnaire. The experimental group included samples taken from 5852 individuals representing administrative units of both levels of local administration in Poland. Many different methods for clustering were tested with scikit-learn package in Python including Ward, Birch but K-Means turned out to be the simplest way to obtain reliable results. K-means can give cluster centres or cluster's borders which can be further used in analysis for example to interpolate trait distribution in population on maps using GIS software.

Funding: *"Biobank network in Poland, within the BBMRI-ERIC Research Infrastructure of Biobanks and Biomolecular Resources" no. DIR/WK/2017/01 and POPC.02.03.01-00-0012/17: „Digital sharing of biomolecular and descriptive resources of Biobank and Department of Anthropology, University of Lodz – characteristics of populations living in present-day Poland through the ages. Information platform e-Czlowiek.pl" (Operational Programme Digital Poland for 2014–2020).*

8 MODELING INTERACTIONS BETWEEN TRANSCRIPTION FACTORS AND GENETIC VARIANTS IN MITOCHONDRIAL D-LOOP IN THE CONTEXT OF BMI

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INTRODUCTION: Mitochondrial RNA synthesis is a proces which originates from the D loop – a regulatory region of the mitogenome. This study is aimed to detect significant interactions between the level of heteroplasmy in the D-loop region of the mitochondrial genome and the expression of mitochondrial transcription factors encoded in the nuclear genome in the context of the body mass index (BMI).

METHODS: The analysis of genetic variants was performed using Whole Genome Sequencing and RNA-seq data from the Genotype-Tissue Expression (GTEx) project. Two tissues were selected for analysis – subcutaneous adipose tissue (89 individuals) and skeletal muscle tissue (107 individuals).

RESULTS: The analysis revealed a statistically significant association between the expression level of the transcription factor TFAM in the skeletal muscle tissue and the levels of heteroplasmy at position 16293 of the mitochondrial DNA in the context of BMI. This site is a variable locus exhibiting an A to G or T nucleotide change (rs878890610) and an AC to GT or TT (rs386828867). The increased expression of the TFAM gene and elevated levels of heteroplasmy correlate with BMI values [p(nuc) = 0.01 i p(mito)0.003]. Their interaction leads to a compensatory effect and correlates with lower BMI (p = 0.001). In the subcutaneous adipose tissue an association was identified between: (1) TFB2M expression and a variant at position 493 of the mitochondrial genome in the context of BMI (p = 0.03); (2) expression of TFB1M andavariant at position 302 in the context of BMI (p = 0.02) and (3) TFAM expression and a variant at position 16189 in the context of BMI (p = 0.05).

CONCLUSIONS: The presented results indicate the existence of statistically significant interactions between expression of mitochondrial transcription factors and polymorphic variants in the D loop of the mitogenome in the context of BMI.

9 USING ARTIFICIAL NEURAL NETWORKS TO PREDICT CHANGES IN CATARACT PROGRESSION AFTER PARS PLANA VITRECTOMY

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INTRODUCTION: Our purpose was to evaluate the effectiveness of artificial neural networks (ANN) in predicting cataract development after pars plana vitrectomy in phakic patients.

METHODS: Thirty-seven patients were included in the study group. The examinations were performed before vitrectomy, one month and three months after. Visual acuity and the grade of opacity of the lens based on the LOCS III scale (N, C, P) were analyzed. The results were used in the ANN learning process. Input parameters included the patient's age and stage of cataract before and one month after the surgery. The stage of cataract 3 months after the operation was the output parameter. For each patient, 2 000 MLP networks of the different structure with distinct activation functions were used. The network with the highest learning, validation, and testing rates was selected for analysis.

RESULTS: The accuracy of prediction the stage of cataract advancement 3 months after the pars plana vitrectomy was checked both for the combined

grade of cataract (N + C + P) and for each variable separately. At the learning stage, the ANN has achieved high rates of learning, validation, and testing for combined N + C + P (over 90%). For the N - ANN produced poor learning, validation, and testing parameters, while the P and C were good and very good respectively.

CONCLUSIONS: Our results indicate the possibility of prediction with ANN the combined grade of cataract and the grade of posterior subcapsular cataract and cortical cataract. The patient's age and the stage of cataract before and one month after vitrectomy were sufficient input parameters.

10 A NEW APPROACH TO SHARING DATA

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Obtaining of biomedical data is essential for science and constitutes the most expensive and time consuming part of scientific projects. Publishing data as a scientific paper attachments does not resolve the problem of the lack of available data in public resources, which could be used for additional analyses. Main question is: is it the right way? The answer is not so simple and explicit. We think, that one of the reasons of this situation can be Legal Property issue. Therefore, we would proudly announce new approach in data sharing. Project "Digital sharing of biomolecular and descriptive resources of Biobank and Department of Anthropology, University of Lodz – characteristics of populations living in present-day Poland through the ages. Information

platform e-Czlowiek.pl (e-Human.pl)" gained European Union founding in "Digital Poland Operational Program". The idea is to share as many data as we can, but what makes us different from other already existing repositories is that usage of data is under licensing embargo. Our web platform will provide advanced search capabilities, we are planning to enable searching even at the level of individual sample details. The designed platform will be open for all scientists to upload and share theirs data on conditions that they define (MTA/DTA licensing, co-authorship, citation of resources, etc.)

Launch of platform is planned on 3rd quarter of 2020. Initial data set: 10000 individuals with phenotype data collected by a questionnaire and DNA Microarray results (over 550K SNPs/Donor); 3D scans of 200 skeletons dated from XI to XIX century, isolated DNA, genomes.

11 A CHALLENGE OF NEXT GENERATION SEQUENCING DATA ANALYSES

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INTRODUCTION: The Next Generation Sequencing (NGS) technology has revolutionized the biological sciences. With its ultra-high throughput, scalability, and speed, NGS enables researchers to perform a wide variety of applications and study biological systems at a level never before possible. Due to the increasing popularity and lower price we get more and more data to analyze.

METHODS: The most important analysis we are interested in is identification of differentially expressed genes (DEGs) between specific conditions. High-throughput transcriptome sequencing (RNA-Seq) has become the main

technique for these studies. Thus, the number of methods and softwares for differential expression analysis from RNA-Seq data also increased rapidly.

RESULTS AND CONCLUSIONS: There are several different approaches to analyzing such data, each consisting of several steps. Each step of the analysis can be carried out by many different tools. Most of them give slightly different results for the same input. The question is which approach and tools we should use, since there is no consensus about the most appropriate pipeline or protocol. In our research we use data from bacteria and yeasts to find the optimal pipeline for this type of analysis, by comparing the results obtained from different tools.

12 OLIGOMETASTATIC DISEASE – THE ROLE OF STEREOTACTIC RADIOTHERAPY

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INTRODUCTION The aim of the study is to evaluate stereotactic body radiotherapy (SBRT) results of cancer patients with small number of metastases (so called oligometastases). Evaluation of prognostic and predictive factors.

METHODS: Inclusion criteria were: histological confirmation of cancer, 1 to 3 metastases, except brain metastases, SBRT as local treatment of metastatic lesion.

RESULTS: Group consisted of 542 consecutive cancer patients (186 female, 356 male; age 21–85) treated in with SBRT due to 698 metastases, (241 lung, 227 lymph node, 106 bone, 105 liver and 19 adrenal/soft tissue metastases). Among them 120 metastases were synchronous and 422 metachronous. In 91% of them primary radical treatment of tumor was employed. SBRT

total dose was 6–60 Gy (median 36). Median follow-up was 5.6 years and 5-year overall survival was 54%. Patients with synchronous metastases had worse OS compared to patients with metachronous metastases (37% vs 58%, p = 0.0003). Factors that statistically significantly affected OS in multivariate analysis were: the type of primary tumor treatment (radical vs. palliative, p = 0.0075), age (p = 0.0047), SBRT treatment year (p = 0.000) and location of metastatic lesions (p = 0.0009). The percentage of patients who had local response to SBRT was 91%, and 1-, 2-, and 5-year local control rates were: 88%, 74% and 65%. Metastases, outside irradiated area, occurred in 51% of patients after completion of SBRT, and 1-, 2-, and 5-year progression-free survival was 62%, 37% and 27%.

CONCLUSIONS: Radical treatment of the primary tumor in patients with oligo-metastases is associated with better overall survival. Patients with metastases diagnosed synchronously with the primary tumor have worse prognosis compared to patients with metachronous metastases.

13 POTENTIAL INVOLVEMENT OF EXTRINSIC NEURAL PATHWAY IN THE COLO-ANAL REFLEX PHYSIOLOGY

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BACKGROUND: The colo-anal reflex is a distinct reflex whereby the internal anal sphincter (IAS) relaxes in association with colonic high amplitude propagating contractions (HAPCs) in contrast to the recto-anal inhibitory reflex (RAIR),

which is characterized by IAS relaxation upon rectal distension. The RAIR is mediated by the myenteric plexus and therefore absent in Hirschsprung disease. In the present study, we retrospectively assessed the presence and the characteristics of the colo-anal reflex in children in whom large bowel continuity had been surgically disrupted.

METHODS: High-resolution (HR) colonic manometry and HR-anorectal manometry were used to evaluate both colonic and anal motor activity in ten children with treatment-unresponsive slow transit constipation (STC), who had previously undergone left sided colostomy formation with consequent disruption of the bowel continuity, and in two children with Hirschsprung's disease (HSCR), who had previously undergone distal colon resection followed by Duhamel pull-through. Eight children with STC, normal colonic motor activity and preserved large bowel continuity served as a control group. The presence and characteristics of colo-anal reflex were analysed.

KEY RESULTS: In the study group, all patients showed the presence of both the normal HAPCs and the colo-anal reflex. In two cases of HSCR, RAIR was absent; however both patients demonstrated a colo-anal reflex.

CONCLUSIONS: In children with disrupted continuity of the colon and/or abnormal anal myenteric reflex, the colo-anal reflex is still preserved suggesting that it is mediated by a different pathway from the RAIR, possibly an extrinsic neural pathway.

MOLECULAR BIOLOGY

SPEAKERS

WOJCIECH MŁYNARSKI

Department of Pediatrics, Oncology, Hematology and Diabetology, Medical University of Lodz

Search for molecular targets in the therapy of acute lymphoblastic leukemia in children: from lab bench to bedside

Acute lymphoblastic leukemia (ALL) is the most common cancer type among children and adolescents. Overall survival in this disease in pediatric population reaches 90–95%, however, ALL relapse might occur in approximately 10–20% of patients with probability of long-term survival of 60%. Recent advances in understanding of molecular background of pediatric ALL revealed that this disease is very heterogeneous and some of the genetic lesion could be targetable by specific drugs. The most common high-risk subtype of B-cell precursor ALL (15–20%), which could be identified by genomic screening is BCR-ABL1-like leukemia. In this group of ALL, multicolor flow cytometry, RNA NGS-sequencing and dense SNP-arrays might show molecular defect for targeted therapy with tyrosine kinase inhibitors (TKI) in 60–70%. BCR-ABL1-like BCP-ALL is also heterozygous disease and many different genomic aberration might lead to activation of a few common targetable signaling pathways like JAK-STAT, MAP-ERK and ABL1/ABL2. This knowledge would be transferable into therapeutic strategies for pediatric ALL, which may further improve clinical outcome of the patients in near future.

WOJCIECH MŁYNARSKI is a Professor in the Department of Pediatrics, Oncology, Hematology and Diabetology at the Medical University of Lodz, Poland. His primary field of expertise is pediatric oncology and hematology together with some aspects of the monogenic form of diabetes and new technology in medicine. He has also contributed to the description of the genetic background of novel genetic syndromes in paediatrics, including

monogenic forms of diabetes and SHAM (severe hemophilia and moyamoya) syndrome.

Professor Młynarski completed his medical training at the Medical University of Lodz in 1996 (MD), and training in molecular biology at the University of Lodz in 1995 (MSc) and followed this with a PhD in biostatistics and genetics in 2000. Between 2002 and 2004 he held a post-doctoral position at the Department of Genetics and Epidemiology, Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA. In 2004–2008 he continued his scientific experience as a visiting researcher at the Harvard Medical School. He is a full professor of pediatric oncology and hematology at the Medical University of Lodz, Poland since 2011.

Professor Młynarski is a member of the Polish Society of Pediatric Oncology and Hematology (treasurer since 2016), the Polish Society of Hematology and Transfusiology (Member of Hemostatic Group since 2016), the European Association for the Study of Diabetes, the Steering Committee of the Polish Diabetes Association and the International Society for Pediatric and Adolescent Diabetes, of which he is also a former advisory board member. He has contributed to over 280 scientific papers (IF>610), mainly focusing on pediatric oncohematology, monogenic disorders and diabetes care, in journals such as the Lancet, Nature Clinical Practice Neurology, Blood, Leukemia, Clincal Cancer Research, Haematologica, Diabetes, Diabetes Care and Diabetologia.

SPEAKERS

PRZEMYSŁAW JUSZCZYŃSKI
Department of Experimental Hematology, Institute of Hematology and Transfusion Medicine, Warsaw

Immune evasion mechanisms in classical Hodgkin lymphoma: towards new immunotherapies

Classical Hodgkin lymphoma (cHL) is a B-cell malignancy diagnosed in ~20,000 new patients in North America and Europe each year. Classical HLs include small numbers of malignant Reed–Sternberg (RS) cells within an extensive inflammatory infiltrate. RS cells secrete a variety of chemokines and cytokines that attract immune system cells.

However, despite the prominent inflammatory infiltrate in cHL, there is little evidence for effective immune response against tumor cells. We found that RS cells selectively overexpressed the immunoregulatory glycan-binding protein, galectin-1 (LGALS1), thus suppressing anti-tumor Th1 responses and favoring expansion of Treg cells. More recently, we have demonstrated that RS cells overexpress PD-L1 and PD-L2 ligands as key targets at the 9p24.1 amplification peak in cHL lines and in primary RS cells. Since the NFkB and JAK/STATs pathways control the expression of multiple immunoregulatory proteins, therapeutic targeting of NFkB and STATs might decrease their expression, increasing immunogenicity of RS cells. We found that PIM1/2/3 inhibition blocked JAKSTAT signaling and markedly attenuated NFkB-dependent gene expression. PIM inhibitor decreased the expression of multiple molecules engaged in developing the immunosuppressive microenvironment, including galectin-1 and PD-L1/2. These findings indicate that PIM kinases in cHL exhibit pleiotropic effects, orchestrating tumor immune escape and supporting RS cell survival. Inhibition of PIM kinases decreases RS cell viability and disrupts signaling circuits that link RS cells.

Taken together, RS cell are genetically and functionally programmed to blunt host anti-tumor responses.

Importantly, detailed understanding of these mechanisms can be effectively translated to game-changing therapies for cHL patients.

Prof. PRZEMYSŁAW JUSZCZYŃSKI, MD PhD was born in Łódź, Poland. He graduated from Medical University of Lodz in 2000 with an MD degree. In 2001 he trained at the Department of Hematology and Hematologic Malignancies Diagnostic Services, Leeds General Infirmary, Leeds, UK. In 2002 he defended his dissertation and obtained PhD degree. His work was recognized and awarded by the START fellowship from Foundation for Polish Science. Right afterwards, he received ICRETT fellowship from International Union Against Cancer (Geneva, Switzerland) and KOLUMB fellowship from Foundation for Polish Science and in August 2003 began his postdoctoral training at the Dana Farber Cancer Institute, Harvard Medical School, Boston, MA in prof. Margaret Shipp laboratory. He completed multiple bioinformatic courses at the Whitehead Institute for Biomedical Research, Massachusetts Institute of Technology, Cambridge, MA. In 2006 he joined Harvard Medical School junior faculty as an Instructor in Medicine. In 2010, he joined the Institute of Hematology and Transfusion Medicine, where he obtained DSc (habilitation) degree and was appointed as associate professor. Since 2011 he is the Scientific Director of the Institute. Przemek's studies are focused on the pathogenesis and targeted therapies of lymphoid malignancies. He has supervised numerous grants, including Polish National Science Center, Foundation for Polish Science, Leukemia & Lymphoma Society of America and mentored several PhD students, who are now succesfull postdocs at best universities. In 2017, he received full professor nomination. In his spare time he enjoys motorcycle journeys, photography and conversations with his daughters.

SPEAKERS

TOMASZ STOKŁOSA
Department of Immunology, Medical University of Warsaw, Warsaw

From genetics to targeted therapy and back – studies on the molecular mechanisms of drug resistance and disease progression in chronic myeloid leukemia and other myeloproliferative neoplasms

Since the discovery of Philadelphia chromosome by Nowell and Hungerford in 1960, chronic myeloid leukemia (CML) became a model neoplastic disease, not only for the studies on leukemogenesis, but also in the search for an effective cancer therapy. This myeloproliferative disease is characterized by almost uniform genetic aberration, the presence of Philadelphia chromosome, a result of reciprocal translocation t(9;22) (q34;q11) and formation of fusion BCR-ABL1 gene, encoding chimeric protein – BCR-ABL1. BCR-ABL1 is a constitutively active oncogenic tyrosine kinase that phosphorylates a number of downstream target proteins, and in effect facilitates expansion of leukemic cells. Introduction of imatinib, tyrosine kinase inhibitor (TKI), almost two decades ago, change dramatically the landscape of the CML therapy and outcome for the majority of patients. However, despite unquestionable success of TKIs in the treatment of CML, drug resistance remains a serious problem for a significant number of patients and progression to incurable acute phase (aka blastic phase or blast crisis) still occurs. Current treatment also cannot eradicate the disease, because of the persistence of the leukemic stem cells (LSCs) and although patients are "operationally" cured, therapy must be continued indefinitely, except for a minority of patients, who can safely stop therapy. LSCs are intrinsically resistant to TKIs, since their survival and proliferative capabilities are not solely dependent on BCR-ABL1 oncogenic kinase.

Recently, advances in genetics, especially next-generation sequencing (NGS), allowed us to look with high resolution at the clonal architecture of leukemia,

including LSCs and find additional genetic and epigenetic aberrations responsible for drug resistance. We employed a custom-designed panel of more than a thousand genes involved in human cancer followed by targeted NGS and focus on patients with unfavorable course of CML. Additionally, we studied other Philadelphia-negative myeloproliferative neoplasms.

TOMASZ STOKLOSA was born in 1970 in Puławy. He graduated in medicine at the Medical University of Warsaw (MUW) and received his doctoral degree in 2000. He works as an assistant professor in the Department of Immunology at MUW. He completed his postdoctoral research at Temple University in Philadelphia – he was awarded with Oncology Research Faculty Development Program Fellowship from the National Cancer Institute. He received several awards of Ministry of Health and Social Welfare in Poland and of the Rector of MUW. In 2008 he received The Tomasz Jakub Michalski Foundation award for young scientific researchers whose work helps advance the fight against cancer and in 2009 UICC Yamagiwa-Yoshida Memorial International Cancer Study Grant for a short-term project related to hematology and drug resistance in leukemia. Currently, he is a team leader and principal investigator in two NCN-funded grants (HARMONIA and OPUS) focused on molecular mechanisms of progression and genomic instability in leukemia. His publication track includes original publications in such journals as Blood, Cancer Research, Journal of Clinical Investigation, Leukemia and others with more than 2000 citations. He actively collaborates with several genetical laboratories and clinical hematology departments in Poland and abroad. He is a member of the Polish Society of Hematology and Blood Transfusion, American Society of Hematology and the European Hematology Association. He has served as an independent reviewer and panel expert for the Ministry of Science and Higher Education, Polish National Science Center and foreign grant agencies. His research is focused on hematooncology and pharmacogenetics, employing modern genetic tools.

JAROSŁAW BARAN
Department of Clinical Immunology, Institute of Paediatrics, Faculty of Medicine, Jagiellonian University Medical College, Kraków

Human TRAIL-producing *Lactobacillus lactis* bacteria as potential immunotherapy of colon cancer?

Introduction: One of the main problems in the current treatment of colon cancer is the resistance of tumor cells to chemotherapy. TRAIL is a natural protein that effectively eliminates many types of tumor cells and potentially may act synergistically with some chemotherapeutics. However, the biological half-life of TRAIL in mammalian organisms is very short, significantly affecting its therapeutic effectiveness. The aim of the study was to investigate, if genetically engineered *Lactococcus lactis* bacteria can be used as a safe carrier of the TRAIL protein, enabling both, the control of long-term TRAIL secrection and elimination of tumor cells.

Methods: Recombinant plasmid with codon optimized for hsTRAIL-cDNA was constructed and transformed via electroporation into *L. lactis* NZ9000 cells. Synthesis and secretion of hsTRAIL was determined in broth supernatants by PCR, ELISA and western blot. Cytotoxic activity of hsTRAIL against tumor cells was determined *in vitro* after incubation of human colon cancer cell lines HCT116 and SW480 with broth supernatants from *L. lactis* culture or by co-culture of tumor cells with selected *L. lactis* clones alone or in combination with chemotherapeutics (5-Fluorouracil, irinotecan, puromycin). Apoptosis of cancer cells was confirmed by Annexin V binding and flow cytometry analysis.

Results: *L. lactis*(hsTRAIL+) bacteria effectively kill HCT116 and SW480 cells and acts synergistically with cytostatics, enhancing elimination of colon cancer cells.

Conclusion: *L. lactis*(hsTRAIL+) bacteria produce biologically active hsTRAIL with potential application in colon cancer immunotherapy.

Supported by the National Science Centre in Poland (UMO2014/15/B/NZ5/03484) and H2020-MSCA-RISE-2017 action no.777682 "CANCER".

Dr. JAROSŁAW BARAN, Ph.D., D.Sc. is an Associate Professor at the Department of Clinical Immunology, Institute of Paediatrics, Faculty of Medicine, Jagiellonian University Medical College in Krakow and is the head of the Laboratory of Immunological Diagnostics at the University Children's Hospital in Krakow. He majored in Laboratory Medicine and received his MSc degree from the Jagiellonian University Medical College. He started his research career under the mentorship of Prof. Juliusz Pryjma and in 1994 obtained his Ph.D. in immunology. At that time, Dr. Baran was one of the pioneers of FACS analysis and sorting in Poland. He was trained and gained his research experience at Forschungszentrum Borstel, Germany and Brown Cancer Center, University of Louisville, Kentucky. In 2010 he obtained his D.Sc. (habilitation) degree in medical sciences. He is an author/co-author of 72 publications, including papers in Blood, Cancer Research, Journal of Immunology and Cancer Immunology Immunotherapy, among others (H index = 18, citations number >1700). His research interests focus on tumor immunology with special emphases on tumor derived extracellular vesicles, tumor immunotherapy and role of monocytes/macrophages in tumor development and tumor eradication. Currently, Dr. Baran is working on the use of genetically modified lactic acid bacteria and their potential use in colon cancer immunotherapy. Dr. Baran is supervising 4 Ph.D. students and is involved in several ongoing international collaborations, including those supported by EU H2020 Programmes – COST ("Mye-EUNITER") and RISE ("CHARMED", CANCER") actions. He acts as an expert for National Science Centre in Poland, European Commission (FP7 and H2020) and Foundation for Science and Technology (FCT) in Portugal.

SPEAKERS

DOMINIKA NOWIS
Center of New Technologies, University of Warsaw,
Medical University of Warsaw

The role of arginase-1 in the development of antitumor immune response

Depletion of essential (L-tryptophan) or semi-essential (L-arginine) amino acids has been shown to suppress antitumor immune responses. Arginase-1 (Arg-1) is a cytosolic enzyme catalyzing degradation of L-arginine to L-ornithine and urea, depleting tumor microenvironment of this compound. T cells need arginine to support their proliferation in the lymph nodes and to promote their ability to kill tumor cells. Arginine deprivation is associated with decreased proliferation potential of activated T cells as well as with down-regulation of CD3 zeta, a major signal transducer from the T cell receptor (TCR). Thus, arginine deprivation due to increased Arg-1 activity is a very efficient strategy of the tumor to avoid T cell-mediated effector mechanisms and, at the same time, one of the potential targets of anti-tumor therapy. Arg-1 is overexpressed not only by cancer-associated fibroblasts (CAFs), myeloid-derived suppressory cells (MDSCs) but also numerous cancer cells such as renal cell carcinoma, breast carcinoma, prostate cancer and colorectal cancer. We have recently discovered that exosomes, a double-layered small vesicles produced by ovarian cancer cells, contain enzymatically active Arg-1. Exosome-derived Arg-1 suppresses proliferation of CD4 and CD8-positive T cells activated with anti-CD3/anti-CD28 antibodies as well as T cells activated in the antigen-specific manner. All these *in vitro* effects are reversed by addition of an arginase inhibitor. Arg-1 containing tumor-derived exosomes are efficiently being engulfed by the dendritic cells and transported to the draining lymph nodes to create immunosuppressive environment at the site of the development of the immune response. Moreover, tumor-derived Arg-1 is detectable in the ascites of ovarian cancer-bearing animals. Arg-1-expressing ovarian cancer grows faster *in vivo* and its growth is slowed

down by the treatment of animals with the arginase inhibitor. *In vivo*, in Arg-1-expressing ovarian cancer cells arginase inhibition results in maturation of the peritoneal dendritic cells and their enhanced ability to engulf and present tumor-derived proteins. Altogether, our findings provide the first evidence for the role of Arg-1 in the formation of an immunosuppressive microenvironment in ovarian cancer. We identify a novel mechanism of exosomal Arg-1 distribution from the tumor cells to antigen presenting cells. Moreover, inhibition of Arg-1 activity may be an attractive novel anti-cancer strategy. The latter idea will be further discussed in this presentation. Funding: National Science Center – OPUS 6 Program 2013/11/B/NZ6/02790, National Science Center – OPUS 12 Program 2016/23/B/NZ6/03463, National Center for Research and Development – STRATEGMED2/265503/3/NCBIR/15, and European Commission Horizon 2020 Programme 692180-STREAMH2020-TWINN-2015.

Prof. DOMINIKA NOWIS, M.D., Ph.D. works at the Department of Genomic Medicine, Medical University of Warsaw and runs her own research group in the Laboratory of Experimental Medicine, Center of New Technologies, University of Warsaw, Poland. She graduated with honors from the 2nd Medical Faculty of the Medical University of Warsaw in 2003. In 2005 she defended with honors her Ph.D. thesis on targeting cytoprotective mechanisms induced in cancer cells exposed to the photodynamic therapy. From 2005 till 2014 she worked at the Department of Immunology, Medical University of Warsaw, first under the supervision on Prof. Marek Jakobisiak, next – Prof. Jakub Golab. In 2011 she obtained her D.Sc. (habilitation) for the cycle of publications on the mechanisms of intracellular protein degradation and their role in the development of human pathologies. In 2016 she got the professor title from the President of the Republic of Poland. Prof. Nowis gained her research experience at Dana-Farber Cancer Institute, Boston, USA, MRC Weatherall Institute of Molecular Medicine, Oxford University, Oxford, UK, University College Dublin, Ireland, Indiana University School of Medicine, USA and University of Verona, Italy. She is an author or co-author of over 70 publications published in internationally

recognized scientific journals such as Nature Comm, PLoS Medicine, Am J Pathol, Blood, Oncogene, Cancer Res, CA: Cancer Journal for Clinicians, Clin Cancer Res. Her publications have already been cited over 2500 times, her H-index equals 22. For her scientific achievements Prof. Nowis has been awarded with the Prime Minister of the Republic of Poland habilitation award, Ministry of Science and Higher Education 3-year fellowship for outstanding young researchers, L'Oreal Poland for Women and Science Ph.D. fellowship, Foundation for Polish Science START fellowship, and POLITYKA weekly journal "Zostańcie z nami" scientific award among many others. In 2012 Prof. Nowis was awarded with 3rd place in the first „Super-talents in medicine" contest. She was a member of the first Young Researcher Council in the Ministry of Science and Higher Education. Prof. Nowis considers as her major scientific achievements the discovery of the cardiotoxic effects of the proteasome inhibitors. For the past few years she has been working on the development of research techniques to study antitumor immune responses and finally settled in the field of oncoimmunology. Prof. Nowis finds passion in teaching. Till 2018 Prof. Nowis has supervised 7 successfully defended Ph.D. theses. For over 15 years she teaches the complete course of immunology to the medical.

MARCIN MONIUSZKO
Department of Regenerative Medicine and Immune Regulation, Medical University of Bialystok, Poland

MOBIT study – in search of 'omic' markers for the personalized diagnosis and treatment of non-small cell lung cancer

The aim of the MOBIT project is to create a novel integrated system of Personalized Tumor Diagnostics based on high quality biobanking and integrated analysis of 'omics' analysis of the patients with the most common tumors, mostly non-small cell lung cancer. The integrated analysis of genomic, transcriptomic, proteomic and metabolomic biomarkers (including analysis of tumor heterogeneity) and PET/MRI imaging as a tool for the invidualized therapy has been performed on model group of patients with non-small cell lung cancer. MOBIT team is using the most advanced research equipment for high-throughput studies and it has an experience in analysis of large-scale data, access to the know-how in the field of biobanking and the hybrid PET/MRI system. The result of the development phase of the project will be the reference model of personalized tumor diagnosis (the creation of commercial services ONCOSup) and the creation of a unique software platform for the collection, integration and analysis of omics and clinical data (SmartBioBase) for use in the implementation of individualized therapy.

Prof. MARCIN MONIUSZKO, MD, PhD – Following graduation from medical faculty, prof. Moniuszko has been extensively trained abroad (e.g. at National Cancer Institute, NIH, Bethesda, MD, USA). He has been awarded with numerous prizes (e.g. "Polityka" Award, Foundation for Polish Science). Since 2004 he has been working at Department of Allergology and Internal Medicine. In 2012 he became a head of newly created Department of Regenerative Medicine and Immune Regulation. He is a Vice-Rector for Science at Medical University

of Bialystok wherein the studies on development of personalized diagnostics and therapy have been conducted for last couple of years (e.g. first-in-world study on personalized diagnostics and therapy of lung cancer patients). It has been achieved (among others) by innovative international PhD studies in biomedicine and biostatistics created by prof. Moniuszko that are funded by grants from H2020 program and Ministry of Science and Higher Education.

DEVELOPMENT OF (R,S')-4'-METHOXY-1-NAPHTHYLFENOTEROL (MNF) AS AN INHIBITOR OF PANCREATIC TUMOR GROWTH

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(*R*,*R'*)-4'-methoxy-1-naphthylfenoterol, (*R*,*R'*)-MNF, is an antitumorigenic GPR55 antagonist and β_2-adrenoceptor (β_2-AR) agonist. Incubation of human pancreatic carcinoma PANC-1 cells with (*R*,*R'*)-MNF attenuated AKT and ERK signaling, with subsequent decrease in the expression of cancer biomarkers. These effects were coupled with reduced survival and motility of PANC-1 cells. Encouraged by these *in vitro* results, we carried out an *in vivo* experiment in mice bearing PANC-1-derived tumor xenografts. Unexpectedly, (*R*,*R'*)-MNF failed to produce any significant reduction in *in vivo* tumor growth. As β_2-AR activation results in increased proliferation of PANC-1, we hypothesized that the β_2-AR agonistic property of (*R*,*R'*)-MNF may cancel the compound's antitumor effects associated with GPR55. To test this hypothesis we employed the bitopic (*R*,*S'*)-MNF, a diastereoisomer of (*R*,*R'*)-MNF that displays β_2-AR agonism biased towards β-arrestin over G protein-coupling. We assayed (*R*,*S'*)-MNF activity in PANC-1 mice xenograft study, which was followed by metabolomic, transcriptomic and cell signaling analysis. (*R*,*S'*)-MNF produced 70% inhibition in PANC-1 xenograft growth. Altered lipid metabolism and metabolic reprogramming accompanied this effect. Our transcriptomic data indicated that (*R*,*S'*)-MNF interfered with the activation of the pro-oncogenic

Hippo/YAP and Wnt/β-catenin signaling pathways, which is consistent with the observed reduction in expression of YAP, β-catenin, HIF-1α, and c-Myc. Observed activity pattern of (*R*,*S*')-MNF is consistent with its dual properties as GPR55 antagonist/β_2-AR-biased agonist and represents a novel bi-functional approach to the treatment of pancreatic adenocarcinoma. Our new aim is to identify specific differences in signaling pattern between (*R*,*R*') and (*R*,*S*')-MNF that shape varying activity of the compounds.

CLINICAL SIGNIFICANCE OF MESENCHYMAL PHENOTYPE OF BREAST CANCER CELLS AT DIFFERENT STAGES OF METASTATIC CASCADE

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Presenting author: Aleksandra Markiewicz, Ph.D. (*aleksandra.markiewicz@biotech.ug.edu.pl*)

INTRODUCTION: Development of cancer metastases is related to dismal prognosis, still the mechanism behind is not well understood. Recently, reactivation of epithelial-mesenchymal transition (EMT) program was linked with increased metastatic abilities of cancer cells, also those which have already disseminated to blood – circulating tumor cells (CTCs). The aim of our research was to isolate and molecularly characterize breast cancer tumor cells from different stages of metastatic cascade – primary tumors (PT), CTCs and lymph nodes metastases (LNM).

METHODS: Analyses were performed on PT (N = 107), matched LNM (N = 52) and CTCs-enriched blood fractions (N = 85) from 107 early breast cancer (BC) patients. We have developed a method for isolation of epithelial (before EMT), and mesenchymal CTCs (after EMT). Levels of markers related to EMT, cancer stem cell (CSCs) (ALDH1, CD44, CD133, OCT-4, NANOG) and invasion and metastasis (uPAR, CXCR4) were tested in the collected samples. Additionally, heterogeneity of CSCs markers expression was tested in PT and LNM.

RESULTS: Mesenchymal phenotype was consistently showing increased expression of CSCs markers in PT, LNM and CTCs. Mesenchymal CTCs displayed especially malignant phenotype, with increased CXCR4, uPAR, ALDH1, OCT-4, NANOG, CD44 in comparison to epithelial CTCs. Mesenchymal CTCs were also related to poor clinico-pathological characteristics (larger tumors, lymph node involvement) and 5.4-higher risk of death ALDH1, CD133, OCT-4 and CD44 heterogeneity was decreased in LNM in comparison to PT, indicating enrichment of malignant clones at the metastatic site.

CONCLUSIONS: Molecular profiling of cancer cells disseminated from PT can deliver additional clinically important information for BC patients.

SYNTHETIC LETHALITY BETWEEN VPS4A AND VPS4B IN COLORECTAL CANCER

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Presenting author: Marta Miączyńska, Ph.D., Prof. (*miaczynska@iimcb.gov.pl*)

Vps4A and Vps4B, members of the AAA ATPase family, are the only enzymes of the ESCRT machinery, which mediate membrane remodeling events, such as endosomal cargo sorting, exosome secretion, autophagy, and cytokinesis. Recent studies have shown that expression of ESCRT proteins is changed in human pathologies, including cancer.

The *VPS4B* locus is localized to the chromosome 18q which undergoes frequent deletions in colorectal cancer (CRC). Our analysis of The Cancer Genome Atlas dataset revealed mono- and bi-allelic deletions of *VPS4B* at a frequency of 67% and 2% in CRC, respectively. Consequently, by testing clinical samples of CRC, we observed a significant downregulation of both mRNA and protein levels of Vps4B. Based on this data, we hypothesized that loss or decreased levels of Vps4B make CRC cells more dependent on the Vps4A activity. We confirmed that concomitant depletion of Vps4A and Vps4B generates a synthetic lethal phenotype in CRC cell lines grown *in vitro* and as xenografts in immunodeficient mice. Our transcriptomics analysis indicated a number of processes affected by lack of both Vps4 paralogs. Specifically, we confirmed that cell death induced by Vps4 depletion is accompanied by a strong induction of inflammatory response involving NF-κB activation.

Cumulatively, our data demonstrate a synthetic lethality between Vps4 paralogs. We believe that vulnerability of CRC cells to Vps4 inhibition may serve as a potential target for precision CRC therapy. This may further provide a rationale for the development of specific Vps4 inhibitors.

TRANSLATIONAL REGULATION CONTRIBUTES TO BIOLOGICAL ADAPTATION IN THE HUMAN PATHOGEN MYCOBACTERIUM TUBERCULOSIS

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Particularity of *Mycobacterium tuberculosis* (MTB) as a pathogen lies in a small percentage of infected people developing active disease, whereas in most of them the bacteria remain in an asymptomatic 'latent' state even for decades. It is hypothesized that in latent infection bacteria re-programme their metabolism and enter a 'persister' state, thus avoiding immune response and antibiotics.

Molecular mechanisms of persistence, and metabolic switching between replicating and non-replicating state, are so far poorly understood. They constitute though a potential target for new improved treatments, especially where antibiotic therapy is unsuccessful.

Recent identification of leaderless transcripts (lacking SD sequence) in MTB in significantly higher proportion than in other bacteria, and discovery of 'specialised' ribosomes preferentially translating leaderless mRNAs in *Escherichia coli* in response to antibiotic stress, suggest that metabolic re-programming could occur at the translational level.

Leaderless transcripts in MTB encode proteins with secondary adaptive functions, like toxin-antitoxin systems, known to be activated in 'persistence' models. We observed efficient translation of MTB leaderless mRNAs in stress

conditions, i.e. in starvation model of growth arrest. Leaderless translation was preferentially enhanced in these conditions comparing to SD transcripts. This indicates that phenotypic adaptation of MTB relies on translational regulation and raises the questions of ribosome specialization.

Here we present recent advances in the work of our team on identification of trigger factors and mechanisms of canonical *versus* leaderless translation in MTB by means of translational fusions with reporter genes, of nascent chain purification and of ribosome profiling.

MYOGENIC DIFFERENTIATION OF PAX7-/- PLURIPOTENT STEM CELLS IN TERATOMAS

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NTRODUCTION: In muscular dystrophies endogenous pool of myogenic precursors, i.e. satellite cells, declines and is insufficient to effectively repair damaged tissue. Transplantation of stem cells, like embryonic stem cells (ESCs), that could replenish satellite cells population and support muscle regeneration could be considered as possible therapy of such diseases. Understanding the molecular mechanisms that drive the differentiation of ESCs is crucial to make foundation and strengthen the basis for the therapeutic use of these cells in the future. Pax7 is the key factor that drives the specification of skeletal muscle precursor cells, controls embryonic and fetal muscle differentiation in the developing embryo, and is responsible for maintaining satellite cells in adult muscle.

METHODS: The aim of our research was to determine the role of Pax7 at the early and advanced stages of *in vivo* myogenic differentiation of ESCs. Two types of ESCs: control (Pax7+/+) and lacking functional Pax7 (Pax7-/-) were

transplanted under the skin of mice to generate teratomas. Such model allowed us to analyze terminal myogenic differentiation, including the formation of myoblasts, myotubes, and innervated mature muscle fibers.

RESULTS: Skeletal muscle tissue was formed in all teratomas. However, teratomas arising from Pax7-/- ESCs differed from the control ones in the expression of certain mesodermal and myogenic markers. Interestingly, in Pax7-/- teratomas smaller area was occupied by cells/fibers expressing skeletal myosin.

CONCLUSIONS: In the absence of functional Pax7 initiation of myogenic differentiation of ESCs is modulated. Pax7 role in the advanced myogenesis stages was also revealed by using teratoma model.

AN INVESTIGATION OF HOW A SINGLE NUCLEOTIDE POLYMORPHISM (SNP) MAY IMPACT POST-TRANSLATIONAL MODIFICATION OF RETINOID X RECEPTOR ALPHA (RXR) THROUGH SUMOYLATION

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The Retinoid X Receptor alpha (RXRa) is a nuclear receptor (NR), with an ability to control gene expression, therefore maintain diverse biological processes. That capability is regulated by post-translational modifications, SUMOylation, which involves Small Ubiquitin-Like Modifiers (SUMO) binding to the sequences within the NR. The SUMO-acceptor site is created by lysine (K) residue, surrounded by consensus motif: Ψ-K-x-E/D, where Ψ is a hydrophobic amino acid, and x any amino acid.

The methodology included protein sequences files for RXR (a,b,g) homo sapiens and applying online tools to perform multiple protein sequence alignment to assess conservation patterns in RXR family. The SUMOylation

sites predictors indicated candidates for lysine modification in isoforms. Potent sites in RXRs were evaluated, in terms of polymorphisms reported in Exome Variant Server.

The identified mutant, RXRa E247K, was assessed by site-directed mutagenesis Polymer Chain Reaction (PCR). Then, the sequence was confirmed by Sanger Sequencing. Furthermore, the cell-based SUMOylation assays *in vitro* will explore SNP effect on RXR ability to undergo SUMOylation.

The findings indicated high degree of similarity and identity between RXRs. The verified SUMOylation sites present in RXRa, K245 and K108, are conserved in isoform RXRb and RXRg. The use of SUMO-predictors discovered new sites in RXRb, K435; and in RXRg, K205.

Outcome from EVS searching indicated the missense mutation was present in African population for K245 in RXRa, which caused protein change: p.(E247K), and might have damaging effect on its function.

14 EVALUATION OF ANTICANCER POTENTIAL OF GLUTAMINE METABOLISM MODULATION AND ER STRESS UPREGULATION IN PLASMA CELL MYELOMA CELL LINES

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Plasma cell myeloma (PCM), with the 5-year survival rate of 50%, remains still an incurable disease. Although the therapeutics such as proteasome inhibitors, including bortezomib, show initial strong antimyeloma effects, the disease frequently relapse due to acquired resistance.

Recently, the role of glutamine metabolism in response to chemotherapy has been identified as an emerging topic in tumor biology. It has been shown by Jeon et al., that in breast cancer, degradation of glutamine transporter ASCT2 by ubiquitin ligase RNF5 in response to endoplasmic reticulum (ER) stress is crucial for paclitaxel anticancer effects. It suggests that the treatment of glutamine – dependent tumors with ER stress inducing chemotherapy may be enhanced by modulation of glutamine metabolism. Indeed, the combination of ER stress inducing agents with glutaminase (GLS) inhibitors demonstrated strong antitumor potential *in vitro* and *in vivo*. Within our project, we investigate the role of glutamine metabolism in response to ER stress in PCM cell lines. Moreover, we aim to evaluate the potential of glutamine metabolism inhibition to sensitize PCM cells to ER stress-inducing agents.

Our results show that PCM cell lines rely on glutamine metabolism for their growth and survival. These cell lines are characterized by upregulated basal levels of ER stress markers such as BIP, p-eIF2a or XBP1s. Moreover, in these cells, the ER stress – related mechanism of ASCT2 degradation is also observed. Finally, the inhibition of glutamine metabolism combined with ER stress induction decreased proliferation and survival of PCM cell lines.

15 TARGETING THIOREDOXIN SYSTEM AS A NOVEL STRATEGY AGAINST B CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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B cell precursor acute lymphoblastic leukemia (BCP-ALL) is a genetically heterogeneous disease characterized by abnormal expansion of B cell precursors. Although treatment regimens and hence cure rates have improved significantly over past years (>90% for pediatric patients), some genetic subtypes, e.g. breakpoint cluster region-abelson kinase (BCR-ABL1) ALL, or mixed lineage leukemia (MLL)-rearranged ALL, are still associated with poor prognosis. The therapy of patients with unfavorable outcome and BCP-ALL relapses are still challenging, therefore novel targeted treatments with possibly low side effects are needed. In this study we aimed to validate antioxidant enzymes of the thioredoxin (TXN) system as potential targets in BCP-ALL. We observed elevated oxidative stress in serum of BCP-ALL patients as compared to age-related healthy subjects (HS), accompanied by upregulation of antioxidant enzymes of TXN system in BCP-ALL blasts. Subsequently, targeting TXN enzymes with small molecule inhibitors, auranofin (AUR) and adenanthin (ADE) resulted in BCP-ALL cells death. Primary leukemic cells

were effectively killed not only in monoculture but also in the co-culture with bone marrow mesenchymal stem cells (BM-MSC), which were shown to provide chemoprotection for ALL. Finally, we observed that AUR delayed the progression of the disease *in vivo* in patient-derived xenograft model of MLL-rearranged ALL. In summary, our results show that targeting TXN system may be a novel strategy for the treatment of BCP-ALL and encourage further studies evaluating the efficacy of therapy combining TXN system inhibitors with other anti-leukemic drugs.

This work was supported by the National Science Centre grant 2015/18/E/NZ5/00723

16 ROLE OF ACTBL2 IN PROCESSES UNDERLYING THE CHANGES IN THE CYTOSKELETON DURING MELANOMA PROGRESSION

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INTRODUCTION: The majority of deaths due to the skin neoplastic changes is caused by melanoma, which is one of the most invasive type of tumours. Metastasis of melanoma is based on alterations in cells' adhesion and motility, in which actin is one of key players. The data on actbl2 – newly discovered actin isoform in tumorigenesis is limited, thus our studies focused on the role of actbl2 in melanoma cells' motility and invasiveness.

METHODS: In our studies we derived stable clones from a melanoma cell line (A375) deprived of ACTBL2 (actbl2) expression by the means of CRISPR/Cas9(D10A) technique. Further we analyzed clones' motility in 2D and 3D conditions and proliferation ratio using BrdU assay, as all of those may influence melanoma progression. We also analyzed formation of stress fibers and motility structures, i.e. lamelipodia and invadopodia.

RESULTS: We observed changes in morphology and behavior of cells when deprived of expression of actbl2. Lack of ACTBL2 expression increased proliferation potential of tested cells. Additionally knock-out of ACTBL2 resulted in higher number of stress fibers. Affected 3D-migration pararelled with differences in invadopodia formation and may indicated that actbl2 has a role in invasive propagation of melanoma cells.

CONCLUSIONS: Summarizing, presented data shed new light on the functional role of actbl2 in melanoma cells. Studies may contribute to better understanding of the processes underlying the changes in the cytoskeleton during metastasis. Presented data is a result of an ongoing project.

Supported by the National Center for Science (2015/17/B/NZ3/03604) and statutory funds.

17 THE ROLE OF MECP2 TRANSCRIPTION FACTOR IN THE RESPONSE TO ANTIDEPRESSANTS TREATMENT IN THE CHRONIC MILD STRESS (CMS) MODEL OF DEPRESSION

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INTRODUCTION: Recent studies indicate that the methyl-CpG-binding protein 2 (MeCP2) plays significant role in the activity-dependent neuronal plasticity and regulation of depressive-like behavior. Moreover, the role of MeCP2 phosphorylation at serine 421 (p-S421-MeCP2) in the regulation of antidepressants activity has been shown [1]. This study investigated the impact

of chronic mild stress (CMS), as well as chronic antidepressant treatment on the p-S421-MeCP2 protein level in frontal cortex (FCx) and hippocampus (Hp) of rats.

METHODS: Rats were subjected to CMS procedure according to Pochwat et al [2]. The following drugs: imipramine (10mg/kg), escitalopram (10mg/kg), venlafaxine (10mg/kg) or olanzapine (2mg/kg) were given *(i.p.)* for 35 days. 24 h after the last dosage, animals were perfused transcardially with 4% paraphormaldehyde in 0.1M PBS. p-S421-MeCP2 protein levels was determined using immunofluorescence staining in paraffin-embedded brain sections.

RESULTS: CMS procedure induced a significantly decreased p-S421-MeCP2 protein level (by 22%) in FCx (but not in Hp). In FCx, chronic treatment of imipramine and escitalopram (but not venlafaxine and olanzapine) reversed CMS-induce changes. In Hp, imipramine, escitalopram and olanzapine (but not venlafaxine) normalized p-S421-MeCP2 level.

CONCLUSIONS: Obtained results, confirm the role of MeCP2 in development of CMS-induced depressive-like behavior. p-S421-MeCP2 protein level, seems to be important in the regulation of response to antidepressants treatment, however observed effects can vary depending on the brain structure or pharmacological profile of antidepressants.

This study was supported by National Science Centre grant No: 2013/09/D/NZ7/02520.

[1] JNeurosci. 2012; 32(41): 14355–1436.
[2] Int JNeuropsychopharmacol. 2014; 17(3): 393–405.

18 ASSOCIATION OF NUCLEAR – MITOCHONDRIAL EPISTASIS WITH BMI IN T1DM PATIENTS

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INTRODUCTION: Obesity results from an imbalance between energy intake and its expenditure. Since it was shown that interaction and communication between nuclear and mitochondrial genome are indispensable for normal cell function we have looked for epistatic interactions between the two genomes to find their correlation with BMI.

METHODS: The analysis was performed on 366 T1DM patients using Illumina Infinium OmniExpressExome-8 chip. Gene expression analysis was performed on GTex data. Association analysis between genetic variants and BMI was performed with the use of Linear Mixed. Analysis of association between mRNA expression and BMI was performed with the use of linear models and standard significance tests in R.

RESULTS: Among genes involved in epistasis we have identified mitochondrial transcription factor TFB2M. It interacted with mitochondrial variants localized to MT-RNR1, MT-ND2 and MT-ND4. Analysis of the interaction between nuclear variant rs6701836 localized to TFB2M and rs3021088 localized to MT-ND2 has shown that the combination of the two led to BMI decrease ($p = 0.02411025$). Each of the variants on its own does not correlate with higher BMI. Although rs6701836 is intronic it influences gene expression in thyroid ($p = 0.000037$). rs3021088 is a missense variant that leads to Alanine to Threonine substitution

in the MT-ND2 gene. The analysis of the influence of genetic variant on gene expression has confirmed the trend explained above.

CONCLUSIONS: Our results show that nuclear-mitochondrial epistasis can influence BMI in T1DM patients. The correlation between transcription factor expression and existence of genetic variants will be subject of further analysis.

This study was supported by the grant from National Science Centre (NCN) no. UMO-2013/11/D/NZ5/03219.

19 ROLE OF T REGULATORY CELLS INDUCED BY NEMATODES IN EAE REMISSION

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Epidemiological data suggests the negative correlation between occurrence of autoimmune diseases and helminth infections. Nematode infection sometimes can have beneficial effect on patients with Multiple Sclerosis (MS). *Heligmosomoides polygyrus* infection is an established model of immunomodulation, reduces experimental autoimmune encephalomyelitis (EAE) symptoms, T regulator cells number is increased significantly in cerebrospinal fluid of EAE mice in 6th day post infection. In this study we tested and compared if nematode induced $CD4^+$ or $CD8^+$ Tregs were able to inhibit autoimmune induced CNS inflammation and reduce demyelisation of neurons.

We sensitized C57BL/6 female mice with MOG_{35-55} (myelin oligodendrocyte glycoprotein)peptide in CFA with *Mycobacterium tuberculosis* H37RA and *Bordetella pertussis* toxin. On the 21st day after sensitization animals received adoptive transfer of CD8+CD25hi lymphocytes from two donors: (i) uninfected $MOGp_{35-55}$-immunized mice for 27 days and (ii) $MOGp_{35-55}$-immunized mice

and infected with 300 L3 *H. polygyrus* for six days at 21 days post immunization. After 10 days post transfer changes in EAE clinical score and the nervous tissue structure were evaluated. The number of fluorescent dye-labelled transferred T cells was evaluated in the tissue cross sections of the brain.

$CD8^+CD25^+$ cells transfer leaded to EAE symptoms reduction. In both groups we obtained migration to cerebrospinal fluid and nervous tissue of high percentage of transferred T regulatory cells. $CD8^+$ Treg transferred cells influenced the activity of donors' lymphocytes in cerebrospinal fluid. Structure of the brain tissue improved and recovered to the control level.

This work was supported by National Science Center grant No. 2014/15/N/NZ6/025025.

20 CIRCULATING MICRORNAS AS BIOMARKERS OF IRRADIATION – A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRODUCTION: The hunt for identification of easy to measure biomarkers of irradiation led scientists to the field of microRNA studies. We aimed at identification of evolutionary conserved, radiation-induced circulating miRNAs.

METHODS: The systematic review was registered in the PROSPERO database (ID: 81701). Three databases were searched: MEDLINE , Embase and Cochrane Database of Systematic Reviews. We downloaded the list of studies with usage

of the query: (circulating OR plasma OR serum) AND (miRNA or microRNA) AND (radiat* OR radiotherapy OR irradiati*). We selected 467 studies – 103 from MEDLINE and 364 from EMBASE. After deleting 116 duplicates, remaining 351 abstracts were then reviewed. Inclusion criteria were as followed: experimental study; human, mice, rat or non-human primates study; serum or plasma microRNA expression measured after irradiation exposure. Duplicates were excluded.

RESULTS: Screening procedure yielded 62 research studies. After verification, 31 articles were found to contain data on significant expression change after irradiation. Thus, we obtained database of 82 significant records from 31 articles reporting 350 significant changes (160 up-regulations and 190 down-regulations) of 129 microRNAs. The top 5 most commonly reported changes were: decrease of miR-150 (FC (fold change) = 0.39 (95%CI 0.33–0.45), miR-342 (FC = 0.57 (95%CI 0.38–0.86)) and miR-142 (FC = 0.51 (95%CI 0.41–0.64) and increase of miR-30b (FC = 2.22 (95%CI 1.66–2.98)) and miR-30c (FC = 2.63 (95%CI 1.86–3.72)).

CONCLUSIONS: Circulating microRNAs reflect biological impact of ionizing radiation and this effect remains stable irrespectively of the studied species. This makes circulating microRNAs as promising candidates for biodosimetry.

The study is supported by FNP First TEAM Programme.

21 THE ROLE OF MLK4 UPREGULATION IN TRIPLE-NEGATIVE BREAST CANCER PROGRESSION

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INTRODUCTION: Breast cancer is a highly heterogeneous disease classified into several subgroups varying on molecular subtypes, treatment responses and clinical outcomes. Recent cancer genomic data revealed amplification or mRNA upregulation of Mixed-lineage Kinase 4 (MLK4) at 23% in invasive breast carcinoma. In this study, we examined the impact of MLK4 upregulation on the progression of breast cancer and its contribution to aggressive phenotype of breast cancer cells.

METHODS: To assess the functional role of MLK4, we used several phenotypic assays including proliferation, migration, invasion and 3D assays. We also performed transcryptomics analysis and immunohistochemial staining of samples obtained from breast cancer patients.

RESULTS: We first discovered that MLK4 is highly expressed in triple-negative breast cancer patients comparing to other subtypes. The knock-down of MLK4 in TNBC cell lines with high endogenous expression level of this kinase decreased cell proliferation and anchorage-dependent colony formation. Moreover, MLK4 depletion led to a dramatic reduction of migratory and invasive capacity of cells, reduction of spheroid formation in 3D and slower tumor growth *in vivo*. We also established that MLK4 activates NF-κB pathway and promotes mesenchymal phenotype of breast cancer cells. Furthermore,

immunohistochemical staining of samples obtained from TNBC patients revealed positive correlation between high expression of MLK4 and metastatic potential of primary tumors.

CONCLUSIONS: Our data point out that MLK4 is important for acquisition of invasive phenotype of triple-negative breast cancer cells and it may represent a druggable target for a subset of breast cancer patients.

22 (R,R')-4'-METHOXY-1-NAPHTHYLFENOTEROL AS A MODULATOR OF CANCER CELL KINOME

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(*R*,*R*')-4'-Methoxy-1-naphthylfenoterol, (*R*,*R*')-MNF, inhibits growth of 1321N1 astrocytoma and PANC-1 pancreatic carcinoma cells through different mechanisms. Attenuation of 1321N1 proliferation occurs via activation of β2-adrenergic receptor (β2-AR) whereas suppression of PANC-1 depends on the blockage of oncogenic receptor GPR55. Both β2-AR and GPR55 belong to G protein-coupled receptors (GPCRs), however they differ in respect to the downstream pattern of kinase activity. The first receptor interact predominantly with $G\alpha_s$ and $G\alpha_i$ to modulate the activity of protein kinase A (PKA), the latter acts through Gαq and $G\alpha_{13}$ leading to the activation of protein kinase C (PKC). Moreover, both receptors interact with β-arrestin to elicit additional signaling events, including the activation of mitogen-activated protein kinases (MAPKs). Activation pattern of kinases in 1321N1 and PANC1 cells in response to (*R*,*R*')-MNF remains to be deciphered. Thus, the purpose of this study was to map the activity of key cellular kinases

using SDS-PAGE, western blotting and motif antibodies (i.e. antibodies that recognize phosphorylated epitopes characteristic for substrates of targeted kinase). This approach enabled us to cover a significant part of the human kinome. We identified PKA (EC_{50} = 9.26 nM), MAPK/CDK (IC_{50} = 5.14 nM) and AKT (EC_{50} = 11.39 nM) as main kinases affected by (*R*,*R*')-MNF in PANC-1 cells, whereas ATM/ATR and AMPK were not affected. In 1321N1 cells, PKA and AKT were detected to undergo activation in response to (*R*,*R*')-MNF treatment; however, further studies are needed to obtain a full picture of (*R*,*R*')-MNF-dependent kinome modulation in 1321N1 and PANC 1 cells.

23 ARTIFICIAL MEMBRANE-POLYMER PARTICLES FOR MEMBRANE RECEPTOR STUDIES

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INTRODUCTION: It is estimated that 40% of marketed drugs produce their clinical effects via modulation of G protein-coupled receptors (GPCRs). One of the main obstacles in studying membrane receptors is the inherent difficulty of obtaining a fully functional, structurally stable and water-soluble form of GPCRs to be used for drug binding studies in solution. The advances in membrane protein research allowed to develop new approaches for the solubilization of GPCRs inside fragments of native cell membrane surrounded by an amphiphilic polymer. The most promising polymer for this application is the styrene-maleic acid co-polymer (SMA), which can be used to produce polymer-embedded membrane nanoparticles called SMA lipid particles (SMALPs).

METHODS: Plasmid construct encoding for human β2AR based on pcDNA3.1 vector was created. The receptor was tagged with a peptide FLAG tag at

the N-terminus and at the C-terminus with attachment of oligohistidine tags, containing double oligo histidine sequences separated by a number of amino acids. HEK293T cells were transiently transfected using cationic polymer method. Cells were harvested and membrane fraction isolated. Correct expression of receptor was monitored with immunostaining. Cells were subjected to solution of SMA polymer and purified using immobilized metal ion affinity chromatography.

RESULTS: β2AR receptors were expressed correctly in membranes, exhibiting both aforementioned peptide tags with immunostaining methods. β2AR receptors were solubilized correctly with SMA based on turbidity measurement and size-exclusion chromatography results.

CONCLUSIONS: Embedding membrane particles in a SMALPs proves to be reliable method of obtaining functional, water soluble G-protein coupled receptor for downstream applications.

24 NEW APPROACH IN EVALUATION OF CERAMIC-POLYMER COMPOSITE BIOACTIVITY AND BIOCOMPATIBILITY

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POSTER PRESENTATIONS

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INTRODUCTION: Nowadays the challenge for the Medical engineering technologies is designing bone substitute materials. The increasing number of accidents, injuries and bone tumours along with developments in medical sciences result in growing demand for bone substitute materials.

METHODS: Regeneration of bone defects was promoted by a novel β-glucan/carbonate hydroxyapatite composite and characterized by Raman spectroscopy, microCT and electron microscopy. The elastic biomaterial with an apatite-forming ability was developed for bone tissue engineering and implanted into the critical-size defects of rabbits tibiae. The bone repair process was analyzed on non-decalcified bone/ implant sections during a 6-month regeneration period.

RESULTS: Using spectroscopic methods, we were able to determine the presence of amides, lipids and assign the areas of newly formed bone tissue. Raman spectroscopy was also used to assess the chemical changes in the composite before and after the implantation process. SEM analyses showed the mineralization degree in the defect area and that the gap size decreased significantly. Microscopic images revealed that the implant debris were interconnected to the poorly mineralized inner side of a new bone tissue.

CONCLUSIONS: Our study demonstrated that the composite may serve as a biocompatible background for collagen ingrowth and exhibits the advantages of applying Raman spectroscopy, SEM and microCT in studying these samples.

25 ANTI-TUMOUR ACTIVITY OF GLYCODENDRIMER NANOPARTICLES IN SUBCUTANEOUS MEC-1 XENOGRAFT MODEL OF HUMAN CLL

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INTRODUCTION: Dendrimers are well-defined, monodisperse, three-dimensional structures with bonds emerging radially from a core and functional terminal groups allowing attachment of various molecules. Because of their unique structure and properties, dendrimers have attracted great interest in biomedical applications. Our studies are based on dense shell (80–90% surface modification; DS) and open shell (35–50% surface modification, OS) maltotriose-modified fourth-generation poly(propylene imine) dendrimers as polymeric drugs in chronic lymphocytic leukemia (CLL). They demonstrate higher cytotoxicity to CLL than to normal cells and influence the expression of genes responsible for apoptosis and cancer cell survival.

METHODS: *In vitro* studies are not sufficient to confirm the effectiveness of the dendrimers as anti-leukemic agents that is why the *in vivo* studies were conducted. We used subcutaneous MEC-1 xenograft model of human CLL in NSG™ mice treated with OS, DS, fludarabine (FA) or 0.9% NaCl.

RESULTS: Results provided a preliminary assessment of the clinical value of treating CLL patients with glycodendrimers by proving, that they do have anticancer properties. OS dendrimer not only inhibited the subcutaneous

tumour growth more efficiently than FA (TGI value 88.7% vs. 54.8% for FA and TCR 0.35 vs. 0.59 for FA) but also prevented/inhibited spread of CLL to the brain and its transformation into diffuse large B cell lymphoma (DLBCL) associated with a bad prognosis.

CONCLUSIONS: Although preclinical studies provided only a limited indication of the potential clinical efficacy, the results of our studies have a potential important impact for the design of the future personalized therapies as well as clinical trials.

26 CANINE T LYMPHOCYTES ACTIVATION DEPENDS ON SIGNAL STRENGTH AND TEMPERATURE

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INTRODUCTION: Domestic dog is an attractive model for immunological studies. Major subsets of the dog immune system were characterized with significant homology to humans. However, culture of large amounts of canine T cells for the purpose of adoptive cellular immunotherapy still requires optimization.

METHODS: We used nano-sized beads coated with anti-canine CD3 antibody to trigger the signal mediated by TCR. Moreover we coated beads with anti-canine CD28 antibody to provide co-stimulatory signal ensuring proliferation and cytokine production. We evaluated T cells activation status based on phenotypic features of T cells and expression of CD25 molecule (alpha chain of IL2 receptor), which is upregulated upon activation. In addition, we used bead at different concentrations, at either 1:1, 1:2 or 1:0.5 T cell:magnetic bead ratio. We also determined the impact of temperature range from 37^{0}C to 41^{0}C on T lymphocytes activation and proliferation.

RESULTS: Our research shown that low-strength activation signal (1:0.5 ratio) caused increased expression of CD25 molecule on canine T cells, 24 and 72h post-stimulation. Lower beads concentration made T lymphocytes to create multiple aggregates, which are the sign of cells activation. We found that 38.5^0C is optimal temperature for canine T cell activation and expansion.

CONCLUSIONS: Overall our research revealed the optimal conditions for canine T cells expansion for further immunological assessment and most importantly for adoptive T cell transfer, which is a very promising therapy to treat cancer in humans, as well as, in canine patients.

Research funded by the European Union and the Foundation for Polish Science.

27 EFFECT OF APELIN ON MIGRATION AND INVASION ABILITIES OF COLON CANCER CELLS MARTA

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Apelin belongs to the family of adipokines – hormones released by adipose tissue. It is secreted peptide derived from 77-amino acid precursor – pre-proapelin, that is cleaved and produces a family of apelin-derived fragments, including apelin-36, -17, -13 and its pyroglutamyl form [Pyr-1]apelin-13. Apelin is a ligand for APJ receptor, that belongs to G protein-coupled receptor family. Presence of apelin in different tissues indicates, that it may play crucial role in many physiological processes, including cardiovascular system regulation, angiogenesis and metabolism regulation. Moreover, apelin is connected with several pathologies, such as heart diseases, obesity and cancer. Accumulating evidence suggests that this peptide can enhance migration and invasion of cancer cells.

Our data indicated that apelin-36 may affect migration abilities of colon cancer cells. However, the antagonist of the APJ receptor, ML221, which inhibits apelin-APJ complex formation, could show opposite effect. We observed the increased ability to creating migratory protrusions – blebs – in cells incubated with apelin-36 and opposite effect with ML221, what was confirmed by examination of level of proteins connected with regulation of actin polymerization. Therefore, we checked the migration and invasion abilities of colon cancer cells using TranswellTM assay. Apelin-36 increased ability to migrate and invade, whereas APJ antagonist decreased these facilities. Furthermore, we examined the proteolytic capabilities to degrade the gelatin using fluorescent-substrate degradation assay. The cells incubated with apelin-36 demonstrated increased activity of metalloproteases. Summarizing, our data shows, that apelin-36 stimulates migration, invasion and increases proteolytic abilities, whereas APJ antagonist ML221 acts in opposite way.

28 CHLORAMBUCIL LABELLED WITH THE PHENOSAFRANIN SCAFFOLD AS A NEW CHEMOTHERAPEUTIC FOR IMAGING AND CANCER TREATMENT

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Here we report the first of the phenosafranin-chlorambucil conjugate as a new type of a chemotherapeutic agent suitable for dual detection methods (spectrophotometric and fluorescence) in imaging systems and cancer treatment. The synthetic cationic dye (3,7-diamino-5-phenylphenazinium chloride) is used as a fluorescent light-triggered scaffold that acts as a carrier for an anti-cancer drug. The chlorambucil was attached covalently via amide bonds to the bifunctional fluorophore, which facilitates tracking with visible light. Our studies revealed that the new photosensitive compound exhibits

improved intrinsic activity *in vitro* in HeLa cells culture experiments; thus it could be a potential anti-cancer candidate in theranostic drug-delivery systems. In light of the urgent need for *in vivo* monitoring of the biodistribution of anti-cancer drugs, this strategy for the synthesis of innovative conjugates based on the phenosafranin backbone offers a promising possibility for drug control in anti-cancer therapy and diagnosis. This aspect makes the phenosafranin-chlorambucil conjugate unique among currently available biomarkers.

29 THE ROLE OF PROLINE DEHYDROGENASE/PROLINE OXIDASE (PRODH/POX) IN METFORMIN-INDUCED APOPTOSIS/AUTOPHAGY IN BREAST CANCER MCF-7 CELLS

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Metformin, the first-line drug in the treatment of type II diabetes evokes anti-cancer activity. However, the molecular mechanism of this process is unknown. One of the effects of metformin is activation of AMP kinase (AMPK), which activates PRODH/POX, the mitochondrial enzyme converting proline to pyrroline-5-carboxylate. During this process ATP is produced for survival or ROS for apoptosis. It has been suggested that the proline availability for this process may represent switching mechanism between apoptosis/autophagy. The main process for proline utilization is collagen biosynthesis that limit proline availability to degradation in mitochondria. The aim of the studies was to evaluate the role of PRODH/POX in metformin-induced apoptosis/autophagy in MCF-7 cells.

We found that metformin added to cultured MCF-7 cells contributed to dose-dependent decrease in cell viability. Cell viability and DNA biosynthesis was

decreased to about 60% of control after incubation with metformin. Collagen biosynthesis was similarly decreased to about 40% of control, simultaneously. Inhibition of collagen biosynthesis by metformin suggests inhibition of free proline utilization in cytoplasm and availability of proline to mitochondrial degradation by PRODH/POX. Metformin in dose-dependent manner increased expression of PRODH/POX and AMPKβ in MCF-7 cells, as well as increased expression of beclin-1 (autophagy marker) and cleaved caspase-9 (mitochondrial-dependent apoptosis marker). The data suggests metformin induces PRODH/POX apoptosis/autophagy in MCF-7 cells.

The link between AMPK, PRODH/POX and proline with apoptosis/autophagy in tumor cells and stimulating the effect of metformin on AMPK allows to present a hypothesis on the mechanism of PRODH/POX-dependent apoptosis/autophagy.

30 AUGMENTATION OF THE ANTITUMOR EFFECT OF HISTONE DEACETYLASE INHIBITOR SCRIPTAID BY BORTEZOMIB *IN VITRO* AGAINST OVARIAN CANCER CELLS

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INTRODUCTION: To investigate antitumor activity of histone deacetylase (HDAC) inhibitor scriptaid, used either alone or in combination with standard chemotherapeutics: paclitaxel, doxorubicin, carboplatin or etoposide, as well as, bortezomib, on ovarian cancer cells (SKOV-3, OVP-10, MDAH 274) *in vitro*. Scriptaid can sensitize ovarian cancer cells and can reverse resistance of cancer cells to drugs used in currently established therapeutic protocols. That was the justification for combining the former together with conventional chemotherapeutics or bortezomib.

METHODS: Cytotoxic /cytostatic effect of the agents was tested in a 72-h MTT assay. Apoptosis assay by flow cytometry was performed using annexin V-FITC/PI assay. Apoptotic proteins: caspase-3, caspase-9 and the key marker of cell cycle arrest protein p21 were determined by Western blotting.

RESULTS: Incubation of ovarian cancer cells with scriptaid and bortezomib (or doxorubicin) led to synergistic antitumor effect resulting from both induction of apoptosis and inhibition of proliferation. In contrast, combination of paclitaxel or carboplatin and scriptaid presented additive antitumor effects against ovarian cancer cells. Etoposide did not significantly affect cell viability. Additionally, treatment with scriptaid and bortezomib resulted in a marked increase in p21, suggesting that cell cycle arrest mechanisms significantly contributed to the cytotoxic/cytostatic effects of this combination. Contrary to, did not change expression of caspase 3 and caspase 9.

CONCLUSIONS: Our data suggest that the use of scriptaid may enhance effectiveness of conventional chemotherapy of ovarian cancer and that the new combination: scriptaid and bortezomib could be used as a treatment option of heavily pretreated patients.

31 THE COMBINATION OF L-ASCORBATE WITH INHIBITORS OF THIOREDOXIN SYSTEM TRIGGER A SYNERGISTIC CYTOTOXICITY OF MALIGNANT B-CELLS

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Malignant B-cells have elevated levels of ROS compared with healthy counterparts, and therefore are sensitive to ROS-inducing therapies, such as L-ascorbate (L-ASC), which generates H_20_2. To maintain cellular homeostasis and protect from oxidative damage, malignant B cells upregulate antioxidant systems, mainly the peroxiredoxin (PRDX)-thioredoxin (TXN)-tioredoxin reductase (TXNRD) system and the glutathione (GSH) system, which undermine the efficacy of ROS-inducing therapies.

Our aim was to evaluate the cytotoxic effect of L-ASC in combination with inhibitors of antioxidant enzymes to malignant B cells.

We observed that the inhibition of TXN-TXNRD system with two inhibitors: SK053 and auranofin (AUR) greatly enhanced the cytotoxicity of L-ASC toward malignant B-cell lines. In turn, the treatment with L-ASC and buthionine

sulfoximine, a glutathione system inhibitor, had no effect. Moreover, we showed that the L-ASC+AUR combination triggered massive increase of intracellular ROS level, which was abolished in the presence of catalase (CAT), a known H_2O_2 scavenger. The synergistic cytotoxicity of L-ASC and AUR combination we also observed in primary B-CLL cells cultured *ex vivo*. Importantly, there was almost no toxicity towards normal B-cells. Moreover, the mRNA level of PRDX1, TXN1 and TXNRD1, but not CAT or glutathione peroxidase 1, was upregulated in B-CLL cells treated with L-ASC+AUR, which suggest the key role of TXN-TXNRD system in ROS removal. Altogether, our results indicated that the L-ASC and AUR combination exhibits selective anti-cancer activity and has a potential as therapy for B-cell malignances.

This work was supported by the OPUS grant from National Science Center (2016/21/BNZ7/02041).

32 ISOLATION AND BIOPHYSICAL STUDIES OF PROTEINS FROM IFIT AND FASTKD FAMILIES

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RNA-binding proteins are involved in post-transcriptional regulation of gene expression, for example on translation level, making them a very important group of biomolecules and a hot research topic in the search for new drugs and gene therapy tools. We study proteins of two families, FASTK and IFIT, that contain non-canonical RNA-binding domains. Human proteins of those

families were obtained by heterologous expression and chromatographic purification. The proteins will subsequently be characterized by their secondary structure and protein-protein or protein-ligand interactions, using molecular biophysics techniques like circular dichroism and differential scanning calorimetry. Such information may not only contribute to better understanding of the function of RNA-binding proteins, but also to the search for specific biotechnological applications of investigated proteins.

33 THE INFLUENCE OF RAPAMYCIN AND PREDNISOLONE ON T REGULATORY CELLS

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INTRODUCTION: Regulatory T lymphocytes (Tregs) exert suppressive effects on other immune cells. The aim of the study was to compare the effect of immunomodulators: rapamycin and prednisolone on activity of Tregs. Rapamycin has been recognized as optimal inducer of Tregs, but the effect of prednisolone on Tregs has been less studied.

METHODS: In the first step of the study, drug-induced changes of Treg phenotype was assessed. Isolated $CD4^+$ lymphocytes were cultured in the presence of anti-CD3/CD28 microbeads, TGF-β and different concentrations of immunomodulators for 5 days. Phenotype of Tregs was analysed using flow cytometry. Functionality of Tregs was measured in MLR tests. Following 5-day culture with microbeads, TGF-β, and either drug, Tregs were isolated and incubated with responding $CD4^+$ T cells and allogenic peripheral blood mononuclear cells. Suppression of proliferation was measured using thymidine incorporation assay.

RESULTS: Induction of Foxp3 in $CD4^+$ T cells incubated with rapamycin at a concentration of 2.5 mg/ml, and with prednisolone at a concentration of 25 mg/ml was higher compared to control samples – 2.69 ± 0.2 and 2.68 ± 0.16 fold increase, respectively. Tregs obtained from cultures with immunomodulators were characterized by high suppressive activity against responder cells. This effect was more significant in cultures with prednisolone-stimulated in comparison to rapamycin-stimulated Tregs (suppression of proliferation 30% vs 49%).

CONCLUSIONS: In this study, we showed that rapamycin and prednisolone promote expansion of T regulatory cells from naive $CD4^+$ T cells. Prednisolone-induced Tregs suppressed proliferation of responder lymphocytes to a greater extent than rapamycin-induced Tregs.

34 EVALUATION OF POLYMORPHISMS AT POSITION C3435T OF THE ABCB1 GENE IN THE GROUP OF PATIENTS WITH LUNG CANCER

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INTRODUCTION: *ABCB1* gene encodes MDR1- P-glycoprotein (P-gp). P-qp takes part in the transport of drugs, creates a barrier for xenobiotics, removes them from the inside of the cell preventing their accumulation in various organs. One of the most common polymorphisms present in the *ABCB1* gene is C3435T. The aim of study was to asses C3435T SNPin the *ABCB1* gene in the group of patients with lung cancer.

METHODS: The material for the study consisted of 40 blood samples collected from patients with diagnosed lung cancer; control group accounted for 96 blood samples taken from blood donors. For genotyping C3435T SNP in *ABCB1* gene PCR-RFLP method was used.

RESULTS: Preliminary assessment of the C3435T SNP in the *ABCB1* gene showed that CT genotype was dominant in both groups. However, TT genotype was more common in persons with lung cancer than healthy people ($p = 0.02377$). An analysis was also carried out that studied the connection between genotype and clinical parameters of cancer. It shows that the presence of allele T is associated with histological grading and occurs in G1 or G2 cases; that was statistically significant ($p = 0.01492$).

CONCLUSIONS: Conducted analysis reveal the existence of the relationship between C3435T SNP in the *ABCB1* gene and the occurrence of lung cancer and degree of its malice.

Funds: 502-03/3-015-02/502-34-085, 503/3-015-02/503-31-001-17

35 QUICK RIBOSOME PROFILING IN BACILLUS SUBTILIS

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The ribosome profiling (RIBO-seq) is a powerful method allowing for direct monitoring of the exact position of the ribosome on transcripts – the so-called translatome [1][2]. Unlike RNA-seq (total mRNA sequencing), RIBO-seq not only provides information about the mRNA composition in the cell at a given time, but also tells us about the rate of translation of each mRNA, number of copies of a synthesized protein, unveils ribosome stalling events – regulatory mechanisms, evaluates the character of small-RNAs (coding versus non-coding) or reveals cryptic open reading frames, which may lead to discovery of novel proteins and pathways.

For this project, the original protocol published by the Weissmann lab [1] has been restructured. During translation, approximately 28–30 nucleotides of the mRNA are buried within the ribosomal small subunit. Since upon nuclease treatment

these nucleotides are protected from degradation, such ribosome-protected mRNA fragments can be converted into a DNA library and characterized by deep sequencing (using next generation sequencing methods).

Introduced amendments resulted in a simple, robust, reliable and reproducible protocol generating good quality sequencing data. The protocol has been successfully applied to study translation in various bacteria including *Escherichia coli*, *Bacillus subtilis* and *Streptomyces* spp.

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36 SPORULATION IN BACILLUS SUBTILIS AS A TOOL TO STUDY TRANSLATION

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INTRODUCTION: Sporulation is a way for bacteria to respond to hostile conditions like nutrient deprivation. It's highly organized process were mother cell divides asymmetrically to give a rise to a spore. Unlike vegetative division, where cells divide every 20–40 min, sporulation takes hours and can be divided into highly trackable stages. Sporulation in *Bacillus subtilis* – a non–pathogenic relative of such bacteria like *B. anthraxis* or *B. cereus* – is well described on the level of transcriptional regulation, but almost nothing is known about translation regulation of this process. Intriguingly, as early as 1970s, it was reported that ribosomes isolated from vegetative and sporulating cells translate mRNA differently. We use sporulation as a model to study specialization of ribosomes – a way to regulate gene expression on the translational level.

METHODS: Sporulation can be easily induced and synchronized. We look into translational machinery of *B. subtilis* applying high-throughput approaches,

like ribosome profiling, combined with genetic approaches and microscopy. We expect to find ribosomes carrying different sets of ribosomal proteins (still unexplained role of paralogues of r-proteins) showing selective properties towards specific mRNAs.

RESULTS: Our preliminary data shows huge global rearrangements of the translatome during sporulation. Moreover, we have identified translation of previously unannotated regions and 5'UTRs occupied by ribosomes – indicating translation regulation. Currently, we are selecting and testing factors which may have a role in ribosome specialization and translational remodeling.

37 DISCOVERING THE NEW FACE OF OLD DRUGS: ANGIOTENSIN II TYPE 1 RECEPTOR BLOCKERS AS INHIBITORS OF KYNURENINE AMINOTRANSFERASES

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Overactivity of renin-angiotensin system (RAS) is an essential trigger of cardiovascular disorders. Among antihypertensive agents, angiotensin II type 1 receptor blockers (ARBs) play significant role in improving patients' survival. Beyond hypotensive properties, ARBs were shown to abolish glutamate's toxicity to provide additional level of organ protection, however the exact mechanism of this action is not well understood.

An endogenous ionotropic glutamate receptors antagonist, kynurenic acid (KYNA), is formed from kynurenine (KYN) by kynurenine aminotransferases (KATs). Out of four described KAT isoenzymes, KAT II is the predominant

enzyme found in the brain, whereas in kidney KAT III and KAT IV. High KYNA level has been linked with negative symptoms of schizophrenia and Alzheimer's disease progression. Elevated KYNA serum concentration was reported in end stage kidney failure.

The goal of our study was to analyze the effect of ARBs on KYNA production in rat brain cortex and kidney *in vitro*. All tested ARBs, irbesartan, losartan and telmisartan dose-dependently decreased KYNA production in both organs. Molecular docking suggested that the ARBs interact with residues within the active site of KAT II, mirroring the interactions of native substrate.

This novel mechanism of ARBs action can explain protective effects of the drugs in the context of glutamate toxicity and suggest repurposing ARBs towards application in the management cognitive deficits and in kidney function control.

This study was supported by the grant from National Science Centre (NCN) PRELUDIUM 4, UMO-2012/07/N/NZ4/02088 and grant for young scientists from Ministry of Science and Higher Education MNmb515/2016.

38 CHITOSAN – GRAPHENE OXIDE NANOCOMPOSITES FOR BONE TISSUE ENGINEERING

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INTRODUCTION: Connections of biopolymers with nanostructured carbon materials are recently the subject of intensive research. The nanocomposites containing chitosan and graphene oxide are particularly important. These complexes have many interesting properties, such as biocompatibility, non-toxicity and antibacterial, so can be safely used in medicine. The aim of this study was prepared a new generation of hybrid system for used in bone tissue

engineering. A subject of research were thermosensitive chitosan hydrogels containing graphene oxide prepared from β – sodium glycerophosphate.

METHODS: Chemical structure of CS-GO nanocomposites was analyzed by FTIR spectroscopy. The crystallinity of hydrogel structure was determined by X-ray diffraction analysis. Within biological tests there has been an evaluation of survival of osteoblast cells the Saos-2 line. A cell culture was carried out under aseptic conditions, maintaining constant temperature parameters – 37°C, humidity – 95% and carbon dioxide content – 5%.

RESULTS: The obtained diffraction patterns have shown that the chitosan chloride gels contain crystalline phases due to presence of β – sodium glycerophosphate and precipitation of NaCl during drying, while the lactate gels are partially amorphous. In turn, the biological research has shown that osteoblast cultures on the carrier with GO were characterized by a significantly higher number of viable cells than in the case of a pure hydrogel.

CONCLUSIONS: Based on the results of the study, it was found that chitosan hydrogels with GO can be a potential material used as injectable scaffolds for the regeneration of bone tissue.

39 IDENTIFICATION OF IMPORTANT MISSENSE MUTATION IN KCNK10 GENE IN POLISH INDIVIDUALS WITH MYOCARDIAL INFARCTION INCIDENCE ANALYSED BY SNP MICROARRAYS

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INTRODUCTION: Cardiovascular diseases (CVD) are leading health problem which take the lives of 17.7 million people each year. In the human heart, multiple types of K+ channels contribute to the control of cardiac electrical

and mechanical functioning. In this study we are focusing on the gene *KCNK10* coding potassium channel which belongs to the subfamily of two pore domain K+ channels. The objective of present study is to determine in what manner the polymorphic risk variants in *KCNK10* gene affect susceptibility to occurrence the myocardial infraction in the Polish population.

METHODS: All participants were from Poland and were registered in a POPULOUS collection. 118 adults who have experienced myocardial infraction were consider as a case group. Control group consisted of 150 people over 65 years old without incidents of myocardial infraction. Genomic DNA were genotyped using microarrays and 23 SNPs in gene *KCNK10* were analyzed.

RESULTS: Our results showed statistically significant difference between presence of a heterozygous missense mutation (rs17762463) in the gene *KCNK10*. This genetic variant found on microarrays is significantly related to myocardial infraction in Polish population. Therefore we tried to predict the effect of this variant on structure and function of KCNK10 using a tool PredictSNP. PolyPhen-2 and SIFT indicated that this mutation was likely to damage the structure and function of *KCNK10*.

CONCLUSIONS: Our result suggests that the heterozygous missense mutation (rs17762463) in the gene *KCNK10* may be involved in determining the susceptibility to myocardial infraction in Polish population.

Project No. POPC.02.03.01-00-0012/17

40 CYTOPROTECTIVE ROLE OF KYNURENIC ACID IN EXPERIMENTAL MODEL OF LIVER DAMAGE

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INTRODUCTION: The latest research on the peripheral effect of kynurenic acid (KYNA) show that it reduces the development of oxidative stress and has an anti-inflammatory and cytoprotective effect, so it causes biological actions which may inhibit acute liver failure (ALF) development. The aim of this work was to assess the influence of KYNA on the inflammatory process and oxidative stress in thioacetamide (TAA) induced ALF in rats.

METHODS: The research was conducted on male Wistar rats. The level of liver damage was estimated based on histopathological image analysis as well as alanine and aspartate aminotransferase (ALT, AST) activity. The influence of KYNA on the synthesis of interleukin 10 (IL-10) and cachectin (TNF-α) as immunological activation markers was also investigated. The level of oxidative stress was assessed based on the measurement of concentration of heme oxygenate induced form (HO-1), the level of lipids peroxidation products – malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE) and myeloperoxidase activity (MPO). Additionally, oxygen radical absorbance capacity (ORAC) was quantified based on the decrease in fluorescence of the so-called molecular probe. The level of oxidative protein damage was assessed based on measurement of concentration of thiol groups (-SH) in the liver homogenates. The nitric oxide (NO) synthesis was estimated basing on concentration of nitrates and nitrites in the plasma. The concentration of KYNA in tissue homogenates was assessed with HPLC methods.

RESULTS: KYNA had positive effect on all studied biochemical parameters and decreased level of proinflammatory TNF-α.

CONCLUSIONS: KYNA shows a protective effect, inhibiting development of TAA-induced ALF.

41 UNDERCOVER TRANSLATION. HIDDEN SECRETS OF THE RIBOSOME

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Ribosomes are a centre of every living cell. For decades, they were perceived as homogeneous macromolecules carrying constant set of ribosomal RNAs and proteins. Consequently, they were not considered to actively participate in the regulatory role of gene expression. The hypothesis of specialized ribosomes assumes the existence of a subpopulation of ribosomes carrying unique structural properties allowing fast and precise response to environmental stimuli throughout selectivity for distinct mRNAs.

We use sporulation process in Bacillus subtilis bacteria as a model to study regulation of gene expression on translational level. Using combination of ribosome profiling, genetics, biochemistry and microscopy, we aim to identify factors modulating translation and accounting for ribosomal selectivity towards mRNAs. Initial data shows massive global rearrangements in proteins synthesis profile and unveils interesting events, like expression of previously unannotated genes, occurrence of paralogues of ribosomal proteins or rearrangements in the ribosomal structure – implying a presence of distinct sub-sets of ribosomes.

Spores, widely found in environment, can survive most of the processes used for sterilization of bacteria, including heat, radiation, chemical treatment, high pressure, they are an increasing burden in food processing and in hospitals.

This work will shed more light on how translation contributes to the gene expression regulation during sporulation. Finding specialised ribosomes will add a new level of regulation of gene expression with a ribosome as an active element. Moreover, within the result, we may identify critical elements suitable for the rational design of new drugs, leading to discovery of novel potential targets for antimicrobials.

42 IMMUNOMODULATORY ROLE OF NEMATODE GALECTIN

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In long-lived gastrointestinal nematode infections, immunosuppression is obviously beneficial for the parasite: it prevents parasite killing and expulsion, improves the fitness of the parasite and benefits the host through inhibition of inflammatory reactions and prevention of pathology. Nematodes produce and release factors that may actively modulate immune reactions, mimic host molecules or deactivate/neutralize immune factors and cells directly. There is increasing evidence supporting a role for helminth surface glycoproteins as well as excretory-secretory products which interact with host glycan-binding proteins and shift the host response toward Th2 responses, and possibly regulatory responses. Nematode galectins bind to β-galactosides (such as lactose and N-acetyllactosamine) and can be involved in modulation of host responses *via* an unknown mechanism. As we observed nematode galectin it either binds to or is bound by IgE. This possible antibody neutralization/deactivation during infection could explain incomplete immunity despite the high level of IgE during nematode infection in high responder host.

The study was supported by National Science Center grant No.2016/23/B/NZ6/03464 (ID352771).

43 NANOGOLD COATED MAGNETIC NANOPARTICLES FOR BIOMEDICAL PURPOSES

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Nowadays, application of nanotechnology in many areas is becoming an interesting alternative for scientists. Diversity of potential use of nano-sized materials results in the advanced development of the mentioned scientific discipline. Among nanomaterials magnetic nanoparticles exhibit a wide range of application possibilities. These particles can significantly affect the development of medicine and pharmacy [1][2]. In presented research synthesis of magnetic nanoparticles coated with gold nanoparticles was conducted. First step of the synthesis involved preparation of magnetic nanoparticles by Massart synthesis, i.e. co-precipitation of chlorides in alkaline environment. Subsequently, nanogold shell was formed on obtained nanoparticles by means of gold-containing reagent and suitable reducing agent. The procedure was carried out in the presence of stabilizing agent to prevent agglomeration of received nanoparticles. Prepared nanomaterials were subsequently subjected to the studies using DLS (Dynamic Light Scattering) analysis and microscopic techniques.

The authors would like to thank the Ministry of Science and Higher Education (Grant no: 0489/IP3/2015/73) for providing financial support to this project.

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44 USE OF DENDRITIC CELLS PRE-EXPOSED TO NEMATODES AGAINST AUTOIMMUNE DISEASES

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Autoimmune disorders are an increasing problem especially in developed countries. There is lack of effective therapy against diseases consequent to inflammatory reactions and current treatment based on corticosteroids has many side effects, hence new cure methods are needed. The use of tolerogenic dendritic cells (DC) is a very promising strategy in autoimmunological disorders treatment. DC as the main group of antigen presenting cells plays a crucial role in developing immune response. Exposing DC to immunomodulatory factors can define tolerogenic reaction, subsequently inhibit inflammation accompanying autoimmune problems. One of the immunoregulatory agents can be nematodes. The immunosuppression induced by worms prevents parasite extermination hence support their survival in the host as a result of prolonged immunoregulation. It has been confirmed already that infection by these multicellular parasites limits symptoms of autoimmune disorders such inflammatory bowel disease and multiple sclerosis on animals as well as humans in clinical studies. However, helminth therapy has many disadvantages. Elaboration of DC exposed to nematodes then using them as vaccine against autoimmune disorders is a promising strategy that avoids parasitic infection.

45 ROLE OF C20917T POLYMORPHISM AT SMAD3 GENE IN COLORECTAL CANCER IN POLISH POPULATION – PRELIMINARY RESEARCH

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Presenting author: Katarzyna Niebudek, M.D. (*katarzyna-niebudek@wp.pl*)

INTRODUCTION: The possible interaction between gene polymorphism and cancers is very interesting issue. SMAD3, also known as mothers against decapentaplegic homolog 3, is a member of SMAD family and it is encoded by the *SMAD3*gene located on chromosome 15q21-22. SMAD3 is the one of the most important agent in transforming growth factor-β (TGF-β) pathway. It is supposed that the abnormal function or expression of *SMAD3*gene may be one of the genetic factors affecting colorectal cancer risk. Purpose: Evaluation of C20917T polymorphism in the *SMAD3* gene in patients with colorectal cancer.

METHODS: DNA isolated from frozen tissue from patients diagnosed with colorectal cancer (N = 53) and from healthy people (N = 51). The evaluation of the polymorphism was conducted with applying the PCR-RFLP technique. [Consent of Bioethics Committee of Medical University of Lodz No: RNN/8/08/KE].

RESULTS: The frequency of particular genotypes in both groups was consistent with the Hardy-Wineberg equilibrium. There was no significant statistical difference between colorectal cancer cohort and healthy individuals (p = 0.9310). In the case of the assessment of the relationship between genotypes and age, gender, TNM classification and histological malignancy in the colorectal cancer cohort, also no statistically significant differences were found (p = 0.9155; p = 0.2243; p = 0.0784; p = 0.9678, respectively).

CONCLUSIONS: The examined polymorphism seems not to correlate with the risk of colorectal cancer development. However obtained results require confirmation in further researches on the greatest group of patients.

Acknowledgments: Funded by No. 503/3-015-02/503-31-001and No. 502 -03/3-015-02/502-34-073 of Medical University of Lodz.

46 SMALL PEPTIDES AS POTENTIAL INHIBITORS TARGETING IMMUNE CHECKPOINTS

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The main function of immune system is to protect the organism against disease The central regulators of the immune response are T-lymphocytes. To activate the T-cell against the pathogen, two signals have to occur. The first, an antigen-specific signal appears after the interaction of the T-cell receptor (TCR) with the antigen presented by the major histocompatibility complex (MHC) and the second one is provided by the interaction of the co-receptors

expressed on the T cell with their ligands expressed on the antigen-presenting cell (APC) or tumor cells. Co-receptors (immune checkpoints) expressed on the T cell can lead to activation or inhibition of immune response. PD-1 (*Programmed death-1*) and PD-L1 (*Programmed death-ligand 1*) or HVEM (*Herpes virus entry mediator*) and BTLA (*B- and T-lymphocyte attenuator*) or HVEM and CD160 (*Cluster of differentiation 160*) are one of immune checkpoint molecules responsible for inhibition of the immune system. It was shown that is involved in the negative regulation of T cell responses in cancer patients and can be targeted by immunotherapy.

Based on the 3D structures of checkpoint complexes the series of peptides, potential inhibitors, were designed and synthesized. To study the protein-peptide interactions the immunoenzymatic assay (ELISA), Nuclear Magnetic Resonance (NMR), mass spectrometry (MS) and cellular assay were carried out. Synthesized peptides can be the groundwork for the future design of the anticancer therapies.

47 EXPLOITING THE *IN VITRO* ANTIPARASITIC ACTIVITY OF NEW HYDROXAMIC ACID AND MONONNAPHTHALIMIDES DERIVATIVES

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Neglected tropical diseases (NTD) affect more than one billion people globally, especially in the third world countries. Examples include Leishmaniasis and Human African Trypanosomiasis (HAT). They affect the poorest of population and limit their living capabilities. Currently available treatment options for these diseases involve mostly parenteral administration, can have

a high toxicity with significant side effect and are associated with growing resistance. Therefore, in the absence of vaccines, there is an increasing need for alternative treatment options. A set of new hydroxyamino and mononapthalimido derivatives was tested against the protozoans Leishmania infantumand Trypanosoma bruceithe causative agents of Leishmanisis and HAT, respectively. The toxicity of the tested compounds was determined by growth inhibition of THP-1 cells. The results suggest that chemical changes in the structure of hydroxamic derivatives as well as changes in the carbon chain linking the naphthalamide and substituting groups, affect their anti-parasitic activity. The NA compound proved to be very effective (EC50 equal 3.55 μM) on L. infantumparasites. Although effective in L. infantumpromastigotes itself was less effective in the Leishmaniaintracellular amastigotes. This compound may be used as a reference for the future drug development. In the case of T. bruceiAS1, AS4, APN, NI and NA compounds showed great effectivity and low toxicity at the same time. The results can provide some basis for the further *in vivo* testing of the effectivity and toxicity in mice. This work provides new insights into the design and optimization of more potent and parasite specific drugs.

TRANSLATIONAL
NEUROSCIENCE

SPEAKERS

FRANZISKA DENK
King's College London, London, United Kingdom

Pain Vulnerability: Why Do Only Some of Us Have to Suffer?

This talk will introduce attendees to how epigenetic mechanisms (i.e. alterations in how the DNA sequence is being accessed) might play a role in bringing about persistent nervous system dysfunction. The audience will hear about mechanisms of chronic pain; how we can study epigenetics in chronic pain; the current state of the evidence; and finally a brief introduction to how some of this evidence can be of use to researchers everywhere.

Dr. FANZISKA DENK is a lecturer at King's College London, where she works on the potential link between epigenetic mechanisms and the development of chronic pain. Does epigenetics make certain individuals more vulnerable to pain or prolong their pain? To address these questions, Franziska uses transgenic mouse models and high-throughput molecular analyses, such as RNA-seq and ChIP-seq, on sorted cell populations. Franziska studied Experimental Psychology at the University of Oxford and completed her DPhil there in 2009. She has been the recipient of an IASP Early Career Research Grant in 2014, an EFIC-Grühnenthal Grant in 2015, and an MRC New Investigator Research Grant in 2017. She is also part of an IMI2-funded consortium investigating neuron-glia interactions in chronic pain (NGN-PET).

https://www.franziskadenk.com/

JACEK KUŹNICKI
Laboratory of Neurodegeneration, International Institute of Molecular and Cell Biology, Warsaw

Zebrafish as a model to study human diseases

The number of people with brain diseases (psychiatric and neurodegenerative disorders, traumatic injuries and stroke, and cancer) increases, and there is an urgent need for new or better treatments and drugs. To find them, cellular and animal models are being used in basic and preclinical studies. One of the emerging animal models for studying brain and its pathologies is zebrafish (*Danio rerio*). It has several features, which make it so attractive, such as high homology with human genome (up to 80%), transparent embryos and a small body, efficient breeding (one pair gives 300 embryos per week), no need for permission to work up to 5 days post fertilization, and possibility to perform automatic high throughput chemical and behavioral screenings. During the lecture a zebrafish model of Parkinson's disease will be described to show the benefits of using this animal for understanding mechanisms of neurodegeneration. Also, the *stim2* knockout zebrafish lines, which we generated by CRISPR/Cas9 technology, will be presented as a model to understand some features of sporadic Alzheimer's disease. Although there is no perfect animal model that fully mimics human pathology, the studies using genetic or chemical zebrafish models allow us to understand the molecular and cellular mechanisms of diseases as well as to identify potential drug targets and to find chemicals that rescue particular phenotype.

Prof. JACEK KUŹNICKI (b. 1952); Director of the International Institute of Molecular and Cell Biology (IIMCB) in Warsaw (2001–2018); Head of the Laboratory of Neurodegeneration in IIMCB (2001–present); corresponding member of the Polish Academy of Sciences (since 2004); Awarded with the

SPEAKERS

Officer's and Knight's Crosses of the Order of Polonia Restituta (2008, 1998). Leader of national and international research projects, i.e. in FP7: FishMed, HEALTH-PROT, COMBIOM, ERA-NET NEURON – NeuConnect, ERA-NET RUS – TargetSOCE, in FP6: PROMEMORIA, APOPIS, and in FP5: Director of Centre of Excellence in Molecular Biomedicine. Research interests: zebrafish as a model of neurodegenerative diseases, calcium homeostasis and signaling, Alzheimer's, Parkinson's, and Huntington's diseases, aging and longevity. Author of over 120 publications in journals from JCR list; H-index = 36.

KRZYSZTOF SELMAJ
Department of Neurology,
University of Warmia and Mazury, Olsztyn

Translational research in multiple sclerosis basic – science meets clinical application?

Effective MS therapy depends on targeting a critical pathogenic mechanism of the disease. Several strategists are under development for immunotherapy in MS, monoclonal antibodies (mAbs), agonists of sphingosine receptors, Nrf 2 agonists and cell depleting agents. However, all currently available therapies in MS attenuate global function of immune system without discrimination between antigen specificity. This approach led to moderate success in MS therapy but at the same time exposed patients to undesired side effects, higher risk of infections, induction of opportunistic infections, and increased risk for cancer. In contrast a strategy based on antigen-specific tolerance induction targeting selectively cells specific for a given antigen attempts to disable only a small part of the immune system directly responsible for autoimmune responses against components of the myelin sheath. We have demonstrated that administration of myelin peptides skin patch in MS patients led to immunologic tolerance to myelin antigens. Myelin peptides applied transdermally to MS patients activated dendritic Langerhans cells in the skin at the site of patch application and induced a unique population of regulatory dendritic cells in local lymph nodes. In the periphery, transdermal applica-tion of myelin peptides resulted in the generation of type 1, interleukin-10 dependent regulatory T cells. The results of clinical trial with skin patches of mixture of three myelin peptides, MBP 85–99, MOG 35–55 and PLP139–155, showed significant effect in reducing the MRI and clinical activity in patients with relapsing-remitting multiple sclerosis. These data demonstrates that

induction of immune tolerance with transdermal application of myelin peptides translates into attenuation of disease activity and represents a promising highly immune selective and safe therapy for multiple sclerosis.

Dr. KRZYSZTOF SELMAJ is a Professor of Neurology, Chair of Department of Neurology, University Warmia and Mazury, Director of Neurology Center in Lodz and a Visiting Associate Professor at Albert Einstein College of Medicine, New York. He obtained the Ph.D. degree in neurology in 1983 and habilitation in 1986. Dr. Selmaj received training in neurology and neuroimmunology at the Charing Cross and Westminster Medical School, University of London, and then as an Advanced Postdoctoral Fellow of National Multiple Sclerosis Society at Albert Einstein College of Medicine, New York, where he worked between 1987 and 1993. Dr. Selmaj has been elected to serve as a vice-President of the European Federation of Neurological Societies (EFNS) in 1999–2005 and a member of International Advisory Board of the International Society for Neuroimmunology. He has served as President of the Polish Neurological Society 2008–2011, and was elected to the Executive Boards of European Committee for Treatment and Research into Multiple Sclerosis (ECTRIMS) and European Charcot Foundation. Prof. Selmaj was awarded with numerous research prizes including the research prize of the Polish Science Foundation in 1994. He has served for the editorial boards for European Journal of Neurology, Journal of Neuroimmunology, Multiple Sclerosis and other Demyelinating Disorders, Archivum Immunologiae et Therapiae Experimentalis and Polish Neurology and Neurosurgery. Prof. Selmaj is a neurologist, clinical scientist and researcher. His research activity considers investigations in neurology, neurobiology and neuroimmunology with a particular interest in mechanisms of demyelination and treatment of multiple sclerosis. He published over 250 papers in the field of neurology and immunology with 15381 citations (Hirsch, 53)

BOGNA IGNATOWSKA-JANKOWSKA
Neuronal Rhythms in Movement Unit,
Okinawa Institute of Science and Technology
Graduate University, Okinawa, Japan

Emerging behavioral models: from 3D motion capture to behavioral transcriptomics

Animal behavior is an expression of the central nervous system function, and its importance in providing insight into physiology of neuronal circuits and neurochemistry is still growing. While there are many reliable assays available, some aspects of behavior have been difficult to study. One common limitation of automated behavior quantification is image analysis, since for complex behaviors standard 2D video-tracking methods are not sufficient. Most of current tools either focus on precise limb position and gait analysis within limited movement range or allow for free movement but are limited by low spatiotemporal resolution. We have demonstrated how high-resolution 3D kinematic tracking allows analysis of variety of behaviors without losing spatiotemporal precision. Such tools for assessment of motor function could be extremely useful in research on neurological and pain-related disorders. On the other hand, interoceptive aspects of animal experience can be approached by behavioral transcriptomics, which allows for direct linking recent experiences of an animal with simple transcriptional signatures uniquely characterizing each experience. This tool allows for decoding past experiences and infer about interoceptive state of an animal but also provides a simple method to identify new genes and brain regions involved in particular behaviors and allowing to manipulate them. These tools provide whole spectrum of new possibilities in studying both motor and interoceptive aspects of behavior that could be applied both in basic and translational research and will likely contribute to exciting discoveries in biology and medicine.

SPEAKERS

Dr. BOGNA IGNATOWSKA-JANKOWSKA is a neurobiologist specializing in experimental research with use of animal models. Currently a Research Fellow at the Okinawa Institute of Science and Technology, Japan, supported by The Japan Society for Promotion of Science (JSPS). Dr. Ignatowska-Jankowska received MSc (2006) and PhD (2011) in Animal Physiology from the University of Gdansk, Poland, and conducted postdoctoral research at the Virginia Commonwealth University, USA (2011–2014) and the Hebrew University of Jerusalem, Israel (2014–2017). She specializes in the physiology of the central nervous system, in particular the function of the endocannabinoid system in the brain, neuropsychopharmacology, and function of the brain reward system. Her scientific interests focus on the neurobiological basis of behavior and use of neuropharmacological and genetic tools to modify animal behavior. Dr. Ignatowska-Jankowska is a beneficiary of several fellowships and awards as well as research grants including Shimon Peres Postdoctoral Award (2016), The Lady Davis Fellowship (2016), Foundation for Polish Science Research Grant within Ventures Program (2009), and many others.

DISCUSSION PANEL

FROM BENCH TO BEDSIDE AND BEYOND

Laboratory is not the only environment for a scientist, clinic in not the only environment for a practitioner. The society expects from us active role in innovative economy, in opinion media or in general education, each of the activities are equally important.

Invited panelists will describe how their research interests sparked action in other areas, how they translate science to general public or to specific business models. Moreover, those beyond-science activities may frequently inspire future research ideas.

MODERATOR

Prof. **KRZYSZTOF JÓŹWIAK**
Department of Biopharmacy at the Medical University of Lublin

Krzysztof Jóźwiak, head of the Department of Biopharmacy at the Medical University of Lublin, Poland, conducts medicinal chemistry projects by combining computational modeling with experimental (affinity and functional efficacy) studies on drugs targeting neuronal receptors. The aim is to develop substances with selective action on a specific subtype of a receptor and/or on a specific intracellular signaling event. Co-author of over 90 research articles, editor and co-author of the book: Drug Stereochemistry: Analytical Methods and Pharmacology (New York, 2012). The Laureate of the 2012 edition of the UCB-Ehrlich Award for Excellence in Medicinal Chemistry granted by the European Federation for Medicinal Chemistry in Berlin, Germany.

Dr. **MICHAŁ KOROSTYŃSKI**
Department of Molecular Neuropharmacology,
Institute of Pharmacology
Polish Academy of Sciences, Kraków

Dr. Michal Korostynski specializes in molecular neurobiology and pharmacogenomics and works in the Department of Molecular Neuropharmacology, Institute of Pharmacology PAS. He completed his Ph.D. (2008) studies in the same faculty. His research interests focus on the genomic determinants of psychotropic drugs actions with special emphases on the drug-induced expression of genes in the brain. He was trained and gained his research experience at Max Planck, Munich, Germany and deCODE Genetics, Reykjavík, Iceland. He is an author of 53 publications, including papers in Nature, Genome Biology, Neuropharmacology, Pain, and Glia among others. He is a beneficiary of grants funded by the National Science Centre and National Centre for Research and Development. He is also actively involved in technology transfer and the development of genome informatics startups.

PANELISTS

Dr. **DOROTA FRYDECKA**
Department of Psychiatry, Wroclaw Medical University, Wrocław

Medical doctor with specialization in adult psychiatry, psychologist and computer scientist. She is a PI in several research grants on the genetic basis of psychotic disorders in relation to immune system and cognitive functions (awarded by Ministry of Science and Higher Education, Foundation of Polish Science, National Science Center). She got additional training in the Institute of Psychiatry (King's College London), Department of Psychiatry (Charite Medical University of Berlin) and Departments of Radiology, Neuroscience, and Psychology (Columbia University). She has received numerous national (Wroclaw Medical University Dean's awards, Foundation for Polish Science awards) and international awards (European Psychiatric Association awards, Maudsley Insitute of Psychiatry awards, European College of Neuropsychopha rmacology awards). Currently she is the Editor of the research topic „Cognitive Function in Schizophrenia: Genetic, Psychopharmacological, Computational, Neural, and Behavioral Studies" for Frontiers in Behavioral Neuroscience journal and research topic „Endophenotypes for schizophrenia and mood disorders: implications from genetic, biochemical, cognitive, behavioral and neuroimaging studies" for Frontiers in Psychiatry journal. She is the board member of the Executive Board - Early Career Psychiatrist Council (ECPC) (initiative of the European Psychiatric Association) -Task Force on Research.

Dr. **KLAUDIA SZKLARCZYK-SMOLANA**
Department of Neurobiology and Neuropsychology,
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Klaudia Szklarczyk-Smolana is a psychologist and a doctor of medical sciences specializing in the molecular underpinnings of stress-related disorders. She received her Ph.D. in 2016 from the Institute of Pharmacology PAS and currently works in the Department of Neurobiology and Neuropsychology, Institute of Applied Psychology at the Jagiellonian University. Her scientific interests include neurobiological psychology, mechanisms of stress coping strategies, and susceptibility to psychiatric disorders. She was a laureate of the FENS Young Investigator Training Programme and an educational grant from the World Federation of Biological Psychiatry. Dr. Szklarczyk is also a co-founder of Intelliseq, which provides bioinformatics solutions for genome interpretation and develops software for genetic applications. On a daily basis, she is a big fan of science popularization and an active member of the Spokesmen of Science Society. As a lecturer and creator of educational materials, she cooperated with the Children's University Foundation and a scientific project ADAMED SmartUP.

ORAL PRESENTATIONS

NOVEL TECHNOLOGIES FOR PHARMACOLOGICAL STIMULATION OF REGENERATION

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The aim of the project was to develop pharmacological methods to stimulate tissue and skin regeneration. The essence of this innovative concept of regenerative medicine is the activation of regenerative response without transplanting tissues or cells from the patient's body. Regenerative medicine is an opportunity for people who are waiting for an organ transplant, victims of serious accidents, such as spinal cord injury, patients suffering from civilization diseases such as diabetes, chronic wounds, cardiovascular diseases, pressure ulcers or effects of stroke.

In our project we designed, obtained and examined the pro-regenerative activity of peptides, peptidomimetics, artificial proteins and low molecular weight compounds as well as to develop innovative delivery systems such as composite hydrogels, peptide fibrils and artificial proteins obtained by genetic

engineering methods. As part of the project, experiments were conducted to develop a method for the stimulation of stem cells naturally occurring in the body (endogenous) as well as transplanted (exogenous) in skin wound healing.

The biological activity of substances with pro-regenerative activity has been studied in animals and on various cell types, both immortalized lines as well as primary cells collected from patients. In the investigations of skin wound healing, the *in vitro* tests of proliferation, differentiation and migration of human stem cells were carried out. In the animal studies, a model of dermal lesion and ear pinnae injury in the mouse were used to quantify the regenerative response.

This work was supported by the grant no. STRATEGMED1/235077/9/NCBR/2014.

MACHINE LEARNING TECHNIQUES FOR NEUROBIOLOGICAL DATA ANALYSIS – STUDIES ON SIMULTANEOUS NEUROTRANSMITTER DETECTION AND EVALUATION OF MICE STRESS MODEL

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Multivariate data analysis is necessary in order to take advantage of the interdependence of the signal coming from multiple sensors and/or measurement techniques as well as the information hidden in the background and noise. We would like to present two examples of application of machine learning techniques for the analysis of neurobiological data.

In the first approach chemometric techniques are used for quantitative electrochemical analysis of neurotransmitters in mixtures containing also

interferents such as uric and ascorbic acids. A novel electrochemical setup, namely the Rotating Droplet allows measurements in a very low volume of liquid (dozens of µL) which is applied between surfaces of the working electrode and a rotating rod. Hydrodynamic conditions of the measurement coupled with filtering of the signal from electrochemically irreversible interferents allow quantification of neurotransmitters in the nanomolar range.

The second application shows the potential of multivariate analysis to unambiguously discriminate between resilient, anhedonic and control specimens in a complex mice stress model. Simultaneous analysis of the data from different tests such as: light-dark box, sucrose preference, forced swim tests as well change of weight during the course of the experiment apart from discrimination allow also to choose variables of highest biological importance.

The aforementioned examples picture wide applicability of common machine learning techniques, which can be used to extract additional information from the background and separate overlapping signals, as in case of the neurotransmitter analysis, or confirm proper design of a complex animal model and choice of methods for its evaluation.

NEXT GENERATION SEQUENCING IN SEARCHING FOR CAUSAL VARIANTS OF RARE NEUROLOGICAL DISORDERS

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INTRODUCTION: Large number of disorders which previously where thought to be multifactorial are now supposed to be rare monogenic diseases with unknown genetic background. Next Generation Sequencing (NGS)

technology with advanced data analysis software may bring us closer to answer the question of the genetic cause of rare neurological diseases. We used NGS in attempt to find variants causing neurological disorders in patients from the Clinic of Neurology Jagiellonian University Medical College.

METHODS: First group of patients was diagnosed as suffering from hereditary spastic paraplegia (HSP) – inherited rare brain disorder characterized by lower extremity spasticity and weakness, often accompanied by other systemic or neurologic abnormalities such as ataxia, seizures, cognitive impairment, dementia, amyotrophy, extrapyramidal disturbance, or peripheral neuropathy. Second group manifested more blurred neurological phenotype, making the precise clinical diagnosis challenging.

RESULTS: We have identified potentially pathogenic variants in 9 of 12 patients with HSP. Some of them were previously described as pathogenic with proven pathogenicity and shared between affected family members. Moreover we have made several interesting findings in group of patients without initial precise diagnosis.

CONCLUSIONS: Here we report on our in-house data analysis pipeline and filtering schemes built to boost discovery power and make drawing clinical conclusions easier and variants which are selected as potentially causal in patients with neurological disorders.

OMEGA-3 FATTY ACIDS AFFECT THE RELEASE OF PRO- AND ANTI-INFLAMMATORY MEDIATORS IN ACTIVATED ASTROCYTES

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INTRODUCTION: Omega-3 polyunsaturated fatty acids (ω-3PUFAs) DHA and EPA play an important role in the function of neurons and glial cells. They have

immunomodulatory effects and as a precursors of proresolving mediators also exert neuroprotective effects. Our previous studies revealed that the increase in content of DHA and EPA in astrocyte membranes significantly improves their antioxidant defense and energy metabolism of mitochondria. The aim of the current study was to determine the changes in the protein levels of COX-2 and iNOS and in the profile and amount of cytokines released by astrocytes preincubated with PUFAs after stimulation with IL-1β, LPS and compounds released by activated microglia.

RESULTS: The results showed reduced expression of COX-2 in LPS-treated astrocytes enriched with DHA, but not with EPA and decreased expression of iNOS only in cells incubated with EPA. In IL-1β-stimulated astrocytes preincubated with both PUFAs expression of COX-2 and iNOS was significantly reduced. Moreover incubation of cells with DHA and EPA before stimulation with IL-1β significantly inhibited the release of several proinflammatory mediators, and increased the release of anti-inflammatory cytokines. Similar results were obtained when PUFAs-enriched astrocytes grown in a medium conditioned with microglia previously activated with LPS.

CONCLUSIONS: This results can be a basis for the development of therapy in which w-3PUFA-modified astrocytes could be used as a support for the brain tissue affected by inflammation.

SEARCH FOR MULTIFUNCTIONAL LIGANDS AIMING AT SYMPTOMS AND CAUSES OF ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) is the fifth leading cause of death among patients aged 65 and older. This fatal, neurodegenerative disease has complex nature reflected in many factors involved in its pathogenesis. Among several well-known hallmarks of AD, amyloid-β plaques and neurofibrillary tangles are of great interest to researchers as biological targets for new anti-Alzheimer's agents.[1] In the search for novel therapies for AD, multi-target-directed ligand (MTDL) strategy seems to be very attractive approach as it provides compounds acting on several targets simultaneously.[2]

Our research team deals with design, synthesis and biological evaluation of novel derivatives with multi-target-directed activity. Recently, we reported a series of 1-benzylamino-2-hydroxyalkyl derivatives combining a unique inhibitory activity against butyrylcholinesterase, β-secretase, β-amyloid and tau protein aggregation. The most promising compound from this series was characterized by balanced activity against both disease-modifying as well as symptomatic targets.[3] Successful results of 5-HT6 receptor (5-HT6R) antagonists in Phase II clinical trials prompted us to design molecules aiming at inhibiting cholinesterases and blocking 5-HT6R. One of the recently published compounds was blood-brain barrier permeable antagonist of 5-HT6R with cholinesterases and amyloid β aggregation inhibitory activities.[4]

Several groups of novel MTDLs aiming at symptoms and causes of Alzheimer's disease will be presented.

Acknowledgments: Part of the research was done in co-operation with University of Ljubljana and University of Barcelona. Financial support: NCN Grants 2016/23/D/NZ7/01328 and 2016/21/B/NZ7/01744.

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MAGNETIC RESONANCE IMAGING AND SPECTROSCOPY IN PRECLINICAL STUDIES OF NEURODEGENERATIVE OCULAR DISEASES

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INTRODUCTION: Neurodegenerative ocular pathologies are not limited to the retina but extend to other parts of the brain. It could be crucial for development of new therapeutic strategies to reliably monitor extra-retinal brain neurodegeneration and possible neuroprotective effects. We have developed a MR-based setting for preclinical evaluation of novel therapies in mouse model of glaucoma.

METHODS: DBA/2J mice that develop spontaneous age-dependent glaucoma-like pathology and age-matched controls were scanned with 7T MR scanner. The protocol included high resolution T2-weighted imaging, localized single voxel spectroscopy (MRS) and evaluation of anterograde axonal transport with MEMRI technique.

RESULTS: We observed age-dependent changes in eyeball morphology in DBA/2J mice – deepening of anterior eye chamber. The visual cortex volume was decreasing in 'glaucoma' mice in an age-dependent manner. MRS revealed biochemical changes in the visual cortex of the 'glaucoma' mice: decrease in taurine and glutamine levels and increase in glutamate. Anterograde axonal transport impairment was detected at an early stage of pathology and was dramatic in mice with advanced pathology.

CONCLUSIONS: DBA/2J mouse model of glaucoma develop pathologies that are associated with early changes in the brain that could be revealed by magnetic resonance imaging and spectroscopy. Our approach may serve

for evaluation of new treatment strategies in ocular disorders that involve neurodegeneration.

Acknowledgments: The project was supported by Polish National Science Centre, grant No. DEC-2012/07/D/NZ4/04199. Project carried out with the use of the CePT infrastructure financed by the European Union – the European Regional Development Fund within the Operational Programme "Innovative economy" for 2007–2013.

48 STRUCTURAL STUDY OF INTERACTIONS BETWEEN EPIBATIDINE AND EPIBATIDINE INSENSITIVE VARIANTS OF NICOTINIC ACETYLCHOLINE RECEPTOR

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INTRODUCTION: Epibatidine (EPI), an alkaloid found in many poisonous frogs of South America is highly potent agonist of nicotinic acetylcholine receptor (nAChR) and important tool to study the receptor pharmacology. The fact that the source animals are not sensitive to EPI toxic effects is very intriguing and very recent work identified several SNP modifi cations of genes encoding nAChR subtypes originating from different species of these poisonous frogs. The aim of this student project is to evaluate by molecular simulations how nAChR variants carrying these modifications interact with EPI and other agonists in comparison with the WT receptor.

METHODS: Molecular models of nAChR variants were prepared by homology modeling using 5kxi.pdb template. Docking simulations of EPI, nicotine and acetylcholine were performed by comparison of several different programs and algorithms.

RESULTS: The most important modification is an exchange of Ser108 into Cys of nAChR beta subunit, the residue provides very important interaction with the hydrogen bond acceptor atom of the agonist. Four other modifications seems to play auxiliary effects in diminishing the binding affinity to EPI in relation to other agonists.

CONCLUSIONS: Resolving of molecular mechanism responsible for nAChR relative insensitivity to EPI is an important step in understanding of the receptor chemistry and may result in better strategies for development of new drug candidates with optimized pharmacological profile.

49 AMYLOID BETA Aβ1-42 PEPTIDES ALTER EXPRESSION OF GENES FOR ANTIOXIDATIVE AND MITOCHONDRIA-RELATED PROTEINS DIFFERENTLY IN NEURONAL AND MICROGLIAL CELLS: RELEVANCE TO MOLECULAR MECHANISM OF ALZHEIMER'S DISEASE

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INTRODUCTION: The interaction between neuronal and glial cells is crucial for the pathomechanism of Alzheimer's disease (AD). Microglia activation could be involved in neuroprotection, however, could also enhance amyloid beta (Aβ) neurotoxicity. In this study we focused on the impact of Aβ oligomers (AβO) on transcription of genes for anti-oxidative enzymes, including sirtuins, and other mitochondria-related genes in neuronal SH-SY5Y and microglial BV2 cells. Moreover, we investigated the consequence of pharmacological modification poly(ADP-ribose)polymerase-1 (PARP-1) and Sirtuin-1 in AβO toxicity.

METHODS: In this study the biochemical and molecular biology methods were applied.

RESULTS: Our data indicated significant differences in the effect of AβO on expression of several genes related to antioxidative defence and to mitochondrial function in neuronal and glial cells. In neuronal cells downregulation of Sod2, Sirt5 and Sdha expression by AβO was observed. Moreover, AβO increased transcription of Sod1, Cat and mt-Nd1 in these cells. However, in microglial cells AβO significantly downregulated transcription of Gpx4, Sirt1, Sirt3, mt-Nd1, Sdha, Mfn2 and significantly enhanced expression of Sod2 and Dnm1l. AβO decreased viability of both cell types, but increased oxidative stress and reduced mitochondrial membrane potential only in SH-SY5Y. Activator of Sirtuin 1 (SRT1720) and inhibitor of PARP-1 (Olaparib) efficiently protected neuronal but not microglial cells against AβO toxicity.

CONCLUSIONS: Our results suggested that cell type-specific alterations of gene expression in neurons and microglial cells could play a key role in different susceptibility of these cells to AβO-evoked apoptotic signaling in neurodegenerative disorders.

50 THE INFLUENCE OF PHYSICAL ACTIVITY OVER OCCURRENCE OF DEPRESSIVE DISORDERS

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Physical activity is an important part of a healthy lifestyle. It is relevant how it affects the mood, feeling of self-satisfaction and accepting your own body. The purpose of the study is to estimate how physical activity impacts on occurrence of depressive disorders. The study was conducted with an anonymous questionnaire, sent out electronically via social networking sites. It contained Beck Depression Inventory and questions about physical activity. The questionnaire estimates the correlation between physical activity of questioned people and the occurrence of various degrees of depressive disorders among them. It also focuses on motivation to exercise and how it affects the mood.

Among people declaring themselves as physically inactive we observed a higher percentage of the occurrence of depressive disorders than among people declaring as themselves physically active. It is important, that in the group of physically inactive people the most common disorder was severe depression, while in the group of physically active people it was mild depression. The main motivation of questioned people to physical activity was the desire to improve the appearance and well- being, as well as the positive impact on health.

SCIENCE BREAKFAST

A good breakfast is the perfect way to start a day. And the perfect breakfast is one that spurs creative discussions between researchers. During the PSN conference, we are hosting a science breakfast networking event. In the course of this informal event, small groups of participants will share the table with our keynote lecturers and will be able to ask them anything about their research, careers, problems they overcome or struggle with and to get valuable mentoring advice. Such a way to meet and talk without the pressure and stress of the scientific sessions will be a great opportunity to break the ice and see the „human face" of our esteemed Guests.

HOST:

Prof. **KRZYSZTOF JÓŹWIAK**

dr GOSIA TRYNKA
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Neuronal Rhythms in Movement Unit, Okinawa Institute of Science and Technology Graduate University, Okinawa, Japan

Prof. AGNIESZKA CHACIŃSKA
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Prof. LESZEK KACZMAREK
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Prof. KRZYSZTOF PALCZEWSKI
Department of Pharmacology at Case Western Reserve University

Prof. SERGIUSZ JÓŹWIAK
The Children's Memorial Health Institute

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INTERNATIONAL INSTITUTE OF MOLECULAR AND CELL BIOLOGY IN WARSAW

The International Institute of Molecular and Cell Biology in Warsaw (IIMCB) was founded as an innovative research center, with rules of operation that are similar to leading scientific institutions throughout the world. IIMCB is one of Poland's most modern research institutes in the life sciences, holding the **highest scientific category** (A+) based on parametric evaluation of research entities in Poland by the Ministry of Science and Higher Education.

The main goals of IIMCB are to **perform high-quality research in molecular biomedicine** and to create the best possible conditions for ambitious, motivated group leaders and their staff to implement modern biotechnology and teach and popularize molecular biology and medicine. **Research topics at IIMCB** cover a wide range of topics, including structural biology, molecular and cell biology, neurobiology, cancer biology, bioinformatics, computer modeling, iron homeostasis, developmental genomics (zebrafish model), ageing, and neurodegeneration.

Nine high-profile research groups and **one partner laboratory** comprise the present structure of the Institute:

- Laboratory of Structural Biology (M. Bochtler)
- Laboratory of Bioinformatics and Protein Engineering (J.M. Bujnicki)
- Laboratory of Molecular and Cellular Neurobiology (J. Jaworski)
- Laboratory of Neurodegeneration (J. Kuźnicki)
- Laboratory of Cell Biology (M. Miączyńska)
- Laboratory of Iron Homeostasis (K. Mleczko-Sanecka)
- Laboratory of Protein Structure (M. Nowotny)

- Laboratory of Protein Metabolism in Development and Aging (W. Pokrzywa)
- Laboratory of Zebrafish Developmental Genomics Max Planck/IIMCB Research Group (C.L. Winata)
- (External) Laboratory of Biomolecular Interactions and Transport (J. Brezovsky), located in AMU, Poznań, Poland

The international character of IIMCB is strongly reflected by all aspects of its functioning. All positions of laboratory leaders are filled through open international competitions, and successful candidates are selected by the International Advisory Board (IAB), a body that is unique to Polish research institutions that consists of renowned scientists and science managers. The IAB ensures that the Group Leaders' selection process maintains full objectivity. International Advisory Board members also consult on the steering and functioning of the Institute. Open and highly competitive character of the Group Leader selection process and IIMCB's achievements attract outstanding researchers from all over the world. The coming competition to be announced in November 2018 will address accomplished excellent investigator in molecular and cell biology who will be offered a Senior Group Leader position at IIMCB under the **ERA Chairs Horizon2020 project**. The new laboratory leader will strengthen scientific excellence of the Institute, enhance links between ongoing projects and contribute to the overall development of the Instituter, in a multinational and multicultural environment. Since 2013, the Institute has been a holder of the **HR Excellence in Research Award**. This prestigious recognition acknowledges IIMCB as an attractive place for researchers to work and develop their careers.

IIMCB has **close scientific collaborations** with world-renowned foreign research centers, such as the Max Planck Society (MPS). Under this strategic partnership, four laboratories were established with double MPS and IIMCB affiliations. The Institute also boasts **cooperation with national research centers**, including the Intercollegiate Faculty of Biotechnology at the University of Gdańsk/Medical University of Gdańsk, Museum and Institute of Zoology PAS in Warsaw, and Institute of Molecular Biology and Biotechnology

at Adam Mickiewicz University in Poznań (AMU). Under this framework of cooperation, the Laboratory of Biomolecular Interactions and Transport AMU/IIMCB in Poznań was created. In addition to institutional agreements, IIMCB research groups develop **individual international collaborations** through common grants, regular contacts, exchange visits, and open seminars that are systematically organized to include outstanding invited speakers from all over the world.

IIMCB actively collaborates with pharmaceutical and biotechnology companies, such as OncoArendi Therapeutics, A&A Biotechnology, Adamed, Over Group, CelonPharma, UbiQ Bio, and IONIS, to develop new therapies in oncology and neurology and biotechnological products. Measures that are implemented by IIMCB to commercialize its inventions and serve as a resource for industrial partners are continually adapted to scientific output and the needs and expectations of commercial partners. The IIMCB commercializes its inventions and technologies in the life sciences, biotechnology, biomedicine, and bioinformatics. Numerous national and international grants and initiatives have resulted in several patent applications and license agreements. The patent applications and patents are transferred to **Biotech Innovations Ltd** (biotech-innovations.com), a special-purpose vehicle that is funded by IIMCB and is committed to turning scientific progress into marketable products and technologies and returning income to the inventors and IIMCB to support further research. IIMCB's portfolio of inventions ranges from platforms that are open to the scientific community (e.g., services offered by the Bujnicki Laboratory at genesilico.pl) to inventions that are protected by worldwide patents.

The most advanced implementations of the research results to business practice:

- **Auresine** (auresine.com): a technology for the highly selective elimination of staphylococci bacteria using Auresine enzyme;
- **Futurenzymes** (futurenzymes.com): a technology of potential importance in medical diagnostics and genetic engineering, using restriction enzymes that specifically cut double-stranded RNA molecules;

- **PRO Biostructures** (com): service in the field of crystallography. The team has extensive experience in supporting drug discovery projects and other scientific endeavors with both biotechnology/ pharmaceutical industry and academia. PRO Biostructures offers a complete range of protein crystallography services from gene to structure.

The Institute also **actively supports social initiatives** that serve groups of patients with particular diseases. It fostered two patient support organizations:

- **Polish Association Supporting People with Inflammatory Bowel Disease "J-elita"** (since 2005), which brings together families of patients with Crohn's disease and Colitis;
- **Polish Ciliary Dyskinesia Society** (since 2011), which was initiated and further supported under two FP7 projects: HEALTH-PROT (RegPot) and BESTCILIA (a collaborative project that focused on better experimental screening and treatment for primary ciliary dyskinesia).

IIMCB is also engaged in **science popularization** initiatives to increase awareness and interest in the life sciences among the general public. The **Center for Innovative Bioscience Education** (BioCEN), an initiative that is supported by IIMCB, regularly hosts workshops with hands-on experiments and is engaged in science popularization events (www.biocen.edu.pl). Moreover, IIMCB organizes popularization campaigns, such as ***Be Healthy as a Fish***, involving the education of primary school students about how zebrafish can be used as a model organism to help scientists understand the way the human body works. The program focuses on the field of biology in a way that complements the children's classroom curriculum and encourages them to broaden their interest in biology in the future. IIMCB also holds regular seminars for students and talented youth.

We welcome visitors to the Institute – please come and meet our staff, activities and our technical resources.

More information at: www.iimcb.gov.pl.

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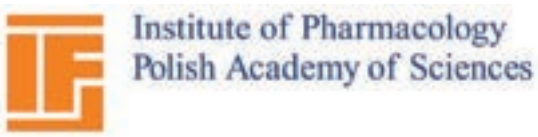

INSTITUTE OF PHARMACOLOGY OF THE POLISH ACADEMY OF SCIENCES

The Institute of Pharmacology of the Polish Academy of Sciences (IF PAN) in Kraków, founded in 1974 (with first organisational structures established in 1954), is currently one of the leading scientific units in Poland, specializing in neuro- and psychopharmacology. Scientific investigations, conducted in 14 departments, laboratories and modern animal house, focus on the nervous system disorders and the search for new biologically active substances that act on the central nervous system and can be used in the treatment of neurological and psychiatric conditions.

The IF PAN research priorities include depression, schizophrenia, chronic pain, drug and natural rewards and addiction. Further, study areas involve anxiety, post-traumatic stress disorder, neurodegenerative and immunoendocrine processes and phytochemistry. The Institute's scientific activity promotes the search for innovative therapeutic strategies and biomarkers of certain pathological processes in the central nervous system using genomics, proteomics and transcriptomics.

Modern infrastructure and broad spectrum of *in vitro* and *ex vivo* methods, such as flow cytometry, mass spectrometry, confocal and fluorescence microscopy, optogenics, microdialysis, chromatography, immunohistochemistry, modern electrophysiological methods, transgenic models and bioinformatics tools, available in the Institute, enable study of brain function at multiple levels. Another significant area of interest is the development of new agents with potential therapeutic properties, using molecular modeling and computational studies of drug-receptor interactions.

IF PAN is equipped with advanced tools and instruments for laboratory behavioral testing in a range of animal models: IntelliCage system, paradigms to test anxiety (e.g. open field, Hole Board), depression and mood disorders (chronic mild stress, prenatal stress), symptoms typical for schizophrenia (sensory-motor gating), learning, memory and attention (e.g. object recognition test, Barnes maze, T-maze, attentional set shifting task) and behavioral effects of addictive substances (e.g. self-administration paradigm).

The Institute is successful in attracting funding for scientific research from national and foreign sources. IF PAN scientists are strongly involved in long-term research projects in collaboration with the world's leading academic units. Good quality of research is reflected in the growing number of publications in high impact journals and a number of patents.

The staff of IF PAN has been also involved in several events aiming at popularization of science, such as the Brain Awareness Week and the Festival of Science and the Arts, as well as in the publishing process of popular science magazine Wszechświat.

The Institute is authorized to award degrees of doctor and habilitated doctor in medical science. Third level education is one of the central tasks of the Institute and the dynamic PhD study held in IF PAN was awarded in the prestigious PROPAN competition in 2016 and 2017. In July 2012 the Institute received the status of the Leading National Research Centre (KNOW) in the field of medicine/health sciences, in consortium with the Faculty of Medicine Collegium Medicum of the Jagiellonian University. In cooperation with Elsevier publishing company, the Institute issues Pharmacological Reports, a scientific bi-monthly journal.

More infotmation at: http://if-pan.krakow.pl/en/

PARTNERS

INSTITUTE OF ANIMAL REPRODUCTION AND FOOD RESEARCH POLISH ACADEMY OF SCIENCES

Established in 1988, the **Institute of Animal Reproduction and Food Research of the Polish Academy of Sciences** in Olsztyn is the highest quality research entity in the Region of Eastern Poland and the best Institute in the domain of agricultural research in the whole country. It holds the status of a Leading National Science Centre (pol. KNOW) "Healthy animal – safe food", Furthermore, the Institute is a member of a prestigious pan-European EIT-Food Knowledge and Innovation Community (KIC) that focuses on entrepreneurship and innovation in the food sector. The members of the EIT Food community are world-class players in the international food domain: over 50 partners from leading businesses, research centers and universities across 13 countries.

The Institute has the mission of carrying out interdisciplinary research investigating the mechanisms of environmental impact on the well-being of humans and animals. Research tasks of the Institute are being accomplished in the Division of Food Sciences and Division of Reproductive Biology, with the main focus put on the three fields of study:

- quality of life with particular emphasis on the influence of environment, including food, on etiology of infertility, prophylaxis of type 2 diabetes, allergies and obesity, as well skin regeneration and development of diagnostic biosensors;
- mutual interactions between food components and the human body; identification, assessment and implementation of strategies for improving nutritive and pro-health values of food, identifying harmful reaction in humans to food ingredients, including intolerances, allergies and pathogenicity;
- identification of reproduction disturbances in animals and humans, introducing new therapeutic techniques and biotechnical methods of infertility prophylaxis and treatment, and designing new tools for protecting biodiversity of animal production and selected species threatened by extinction.

These scientific activities are conducted in 13 research departments which are further supported by highly specialized core facilities of: Molecular Biology, Microbiology, Sensory Analysis, *In Vitro*, Animal Facility and integrated laboratories of: Proteomics, Reproduction Biotechniques and Biotechnology, Bioelectroanalysis, Immunodiagnostics and Metabolomics, all equipped with state-of-the-art infrastructure.

Having incorporated into its structure the Research Station in Popielno, the Institute has considerably extended the scope of its research within the field of animal reproduction and food safety. Current activities of the Station focused on the protection of natural resources and implementation of Polish konik horses and local cattle breeding program, are complemented with research on reproduction of wild animals and conservation biology.

Postgraduate training is an integral part of the Institute's mission, and aims to provide the students with cross-disciplinary knowledge and transferable skills to be used both in commercial and academic centres. Institute is entitled to confer the degree of PhD (doctorate) in agricultural sciences in the field of animal husbandry and food technology and nutrition. Young researchers are actively engaged in research performed in the Institute, being given the opportunity to participate in international studies involving short-term scientific missions and trainings. What is more, they are equipped with tools enabling them to develop and manage their own research endeavours with the access to highly specialized scientific facilities.

In addition, the Institute runs a wide scientific cooperation through partnerships established with world-renowned research centres, stimulation of joint projects, twinning agreements, organization of international conferences and participation in EU-wide actions. At present, it is coordinating or participating in several international programs (FP7, HORIZON 2020 – Joint Programming Initiative, Marie Skłodowska-Curie Actions, COST Actions), fostering its interactions with leading scientific partners and reinforcing integration with the European Research Area.

The Institute transfers its research results to boost industrial effectiveness, keeping the research priorities consistent with the socioeconomic needs of the country and the region. It provides rapid, confidential consultancy and custom-tailored food, health and reproductive biology research services to the sectors of medicine, veterinary, animal breeding, and food processing, offering high quality expertise, training and analysis along with direct access to the Institute's science specialists through a network of science-business partnerships.

More infotmation at: www.pan.olsztyn.pl

MEDICAL UNIVERSITY OF BIALYSTOK

MEDICAL UNIVERSITY OF BIALYSTOK

The Medical University of Bialystok is a modern, dynamically developing university with the mission to provide the best education for a professional, responsible and modern medical staff. University conducts research at the highest international level and implements innovative solutions in cooperation with entities providing medical services and undertakes activities that respond to social needs.

EDUCATION

The number of 127 titular professors and 139 habilitated doctors for 814 academic teachers gives one of the highest rates and places our University in the top tier of all universities in the country.

The development of the University's academic and didactic staff is also constantly strengthened through numerous scholarships, internships, trainings and study visits to the best research and teaching centers in the world. During projects implementation, employees of the University cooperate with partners from domestic and foreign centers within a network of scientific consortia.

For years, the University's development has been oriented towards its internationalization – the development of ever-wider scientific and didactic cooperation with European countries, but also with the USA and Japan. At the same time, the idea of European expert lectures addressed to the entire academic community, with particular emphasis on the role of the so-called 'visiting professors', having to signify outstanding specialists with special scientific achievements. Annually, we host many prominent professors from

such centers as the Mayo Clinic, the National Institute of Health in Bethesda, the Harvard Medical School, the University of Pennsylvania, the University of Heidelberg. Currently, the Medical University of Bialystok has signed agreements on cooperation and scientific exchange with 25 foreign centers.

SCIENCE

The effectiveness of the science policy of the Medical University of Bialystok, carried out consistently for years, was once again confirmed in the results of a comprehensive assessment of scientific activity of over 960 scientific units announced in November 2017 by the Minister of Science and Higher Education. The Faculty of Pharmacy with the Division of Laboratory Medicine was awarded the A category, while the Faculty of Medicine with the Division of Dentistry and the Division of Teaching in English received the category A. Also the third faculty of the University – Faculty of Health Science, received category A and took one of the highest places in the ranking. Thanks to this categorization, our units will be guaranteed a high level of financing statutory activities for the coming years.

Obtaining the status of the National Leading Scientific Center by the Innovation Research Center of the Medical University in Bialystok allowed to prepare and develop valuable projects of the University. As part of the grant, a unique program of interdisciplinary Doctoral Studies in English has been organized and created opportunity to thoroughly learn innovative large-scale research techniques and their application in genomics, proteomics, metabolomics and immunology.

PhD students take part in the implementation of innovative scientific projects carried out with the cooperation of eminent scientists from the Innovation Research Center, including the Medical University of Bialystok; Center for Statistics (CenStat), Hasselt University, Belgium; Center for Metabolomics and Bioanalysis (CEMBIO), University of San Pablo-CEU, Madrid, Spain; The Institute of Experimental and Clinical Medicine of the Polish Academy of Sciences. As part of the studies, there are lectures by eminent specialists from foreign universities, including from: Heidelberg University in Mannheim, Germany,

PARTNERS

Universitätsklinikum Erlangen, Germany, University of Turku, Finland, University of Pensylvania, USA, Rudjer Boskovic Institute in Zagreb, Croatia.

Thanks to the cooperation between clinical and basic science units, intensive scientific activity is carried out on the pathomechanism of civilization diseases, including cancer, cardiovascular diseases, diabetes and obesity, and the search for new, innovative diagnostic and therapeutic methods, using the results of research on molecular points of the potential pharmacotherapy handle, molecular modeling, synthesis and pharmacokinetic evaluation of potential drugs. All this is accompanied by research in the field of practical medicine aimed at improving the quality of life of patients and people with risk factors for the development of civilization diseases.

Scientific research at the Medical University of Bialystok is conducted using the latest research technologies of the 21st century, such as genomic techniques, chromatographic techniques (LCMS, GCMS, ICPMS), cellular imaging and many others. This provides unique knowledge in the field of genomics, transcriptomics, metabolomics, biochemistry, molecular biology, proteomics, and immunology.

The scientific achievements of the University's employees are constantly increasing and in the last decade, the number of works published in journals indexed in the Thomson Scientific Journal Citation Reports (JCR) doubled the total IF value of published works.

The University has a very modern research base and infrastructure to conduct scientific research based, among others, in the Clinical Research Center, Experimental Medicine Center, Euroregional Pharmacy Center, Innovation Research Center, Bioinformatics and Data Analysis Center, Molecular Imaging Laboratory.

- The Clinical Research Center is unique in the country, focused on conducting non-commercial clinical trials in the field of civilization diseases with laboratories enabling research using large-scale techniques in the field of genomics, transcriptomics, proteomics, and metabolomics for all units of the University.

- The Experimental Medicine Center is one of the most modern facilities for breeding and experimental research on laboratory animals in Europe. In 2012, the Center obtained a certificate of compliance with the principles of Good Laboratory Practice in the field of physicochemical properties research, testing of toxic properties and other pharmacokinetic studies.
- The Euroregional Pharmaceutical Center, as a highly specialized research pharmaceutical and analytical unit, introduces modern research techniques to everyday scientific work.
- The Innovation Research Center ensures the cooperation of an interdisciplinary scientific team dealing with issues related to the search for new, innovative diagnostic and therapeutic methods, especially effective pharmacotherapy. This activity was honored with the award of the Marshal of the Podlasie Voivodeship – 'Podlaska Marka Roku' (Brand of the Year) for the contribution to building a positive image of the region.
- The Bioinformatics and Data Analysis Center enables the University's employees to analyze large amounts of data obtained from large-scale techniques and data analysis within the framework of planned population cohort studies.
- The Molecular Imaging Laboratory, equipped with a unique PET/MRI hybrid, enables conducting innovative scientific research in civilization diseases, including Alzheimer's disease, cardiovascular diseases, obesity, and early diagnosis of cancer.

The hitherto activities related to cooperation with the social and economic environment resulted in, inter alia, research projects and intent letters concerning for example creation of unique biobanking system, innovative biotechnology research on healthy food or cooperation with companies in the field of medical technologies.

COOPERATION

The university started cooperation with the University of Greifswald in the implementation of a project unique in Europe, called Bialystok PLUS (Polish Longitudinal University Study), regarding prospective long-term health

examination of city residents. The results of this research project will allow detection of civilization diseases in the early stages of development and risk assessment, which will enable effective prevention or treatment.

The University is actively seeking to expand the scope of Innovation Research Center work in the field of civilization diseases and individualized medicine, as part of the project with a total budget for planned investments exceeding PLN 180 million. It is planned the creation of new scientific units: Center for Preventing the Health Effects of Aging, Biobank, Prevention and Medicine Center, Population Research and Telemedicine Center and the Regenerative Medicine Center.

Considering the above, we encourage everyone to cooperate with our University, where talented and ambitious people will certainly find the right conditions for comprehensive development.

More infotmation at: https://www.umb.edu.pl/en/

NENCKI INSTITUTE OF EXPERIMENTAL BIOLOGY

The **NENCKI INSTITUTE OF EXPERIMENTAL BIOLOGY** (www.nencki.gov.pl) of the Polish Academy of Sciences is the largest non-university biological research center in Poland. High quality research, an excellent publication record and strong international links, place the Nencki Institute among the leading biological research institutions of Central Europe. Research conducted at the Institute focuses on issues directly related to health protection and the improvement of life within society. The main focus relates to novel therapies and diagnostic methods in neurodegenerative diseases, neurological disorders, diabetes, cancer and other diseases of modern civilization. The Nencki Institute also provides a wide range of services, including preclinical trials, dermo-cosmetology studies, genetic engineering, transgenic animals production and biological imaging from electron microscopic to MRI levels (listed below). We appreciate existing collaborations and **we are open to new cooperation with industrial entities to bring novel products to the pharmaceutical, biomedical and biotechnological market**.

The Nencki Institute's infrastructure includes 30 highly-specialized research laboratories and 8 core facilities that provide the following services :

1. Laboratory of Animal Models
    - The production of transgenic mice and rats models together with genotyping and cryopreservation service. Transgenic mice and rats are produced by the standard method of "microinjection" and using lentiviral vectors.

- The production of viral vectors (LV and AAV) and genetic modification by stereotactic injections of LV or AAV into various structures of the brain.
- Long-term metabolic studies. We use metabolic cages which enable continuous, long-term measuring of parameters such as indirect calorimetry, XYZ physical activity, food and water intake, and body weight.
- The set of behavioural tests enabling comprehensive behavioural characterization of an animal. We perform motor skills tests, exploratory tests, learning and memory tests using traditional instrumental conditioning (fear conditioning or operant conditioning), as well as automatic IntelliCages.

2. Laboratory of Brain Imaging
   - Services and expertise in magnetic resonance imaging, magnetic resonance spectroscopy, electroencephalography (including EEG-fMRI simultaneous recordings), as well as transcranial magnetic stimulation.
   - Development of computational approaches for large scale sMRI/fMRI data analyses.
3. Laboratory of Molecular Neurobiology
   - Services in transcriptomics, genomics and data mining.
   - Affymetrix microarray analyses (experiment design, processing of microarrays, quality assessment and filtering, basic exploratory data analysis).
   - RNA and miRNA sequencing, ChIP-sequencing, targeted and whole genome sequencing experiment design, library preparation and sequencing, quality assessment and filtering, data analysis, peak calling, SNVs and CNVs detection.
   - Computational analyses of transcriptomic and genomic data.
4. Laboratory of Imaging Tissue Structure and Function
   - Wide spectrum of advanced light microscopy techniques dedicated to functional and structural studies of biological samples.

- Validation of new fluorescent probes for microscopy-based biological assays.
- Development of algorithms for quantitative microscopy.

5. Laboratory of Preclinical Studies of Higher Standard
   - Comprehensive preclinical *in vitro* and *in vivo* testing of safety and activity of potential new therapeutic substances for diseases of the nervous system, as well as for cancer, in accordance with the principles of Good Laboratory Practice (GLP).
   - Testing of substances activity in cell cultures: cytotoxicity/cell survival (IC50), analysis of apoptosis, proliferation and cell cycle.
   - Analysis of therapeutic substances' mechanism of activity in cell cultures (mRNA, miRNA and protein cellular levels).
   - Maintenance of laboratory mice in experiments.
   - Development and analysis of mouse models of neurodegenerative diseases and cancer.
   - Activity testing of potential neuroprotective or anticancer substances in mouse models of diseases.
   - Toxicological studies: histological preparation and histopathological analysis.
   - Pharmacokinetic assays.
   - Profiling cognitive impairments in memory tasks.
   - Consultations for experimental design and data analysis.
6. Laboratory of Bioinformatics
   - Support of high-throughput methods in genomics, transcriptomics, proteomics (including mass spectrometry data analysis); pre-processing, statistical analysis, functional analysis and visualization.
   - Statistical analysis and visualization of multi-dimensional data combining biochemical, microscopic and functional data.
   - Analysis of gene regulatory regions.
   - Molecular dynamics simulations of proteins with known 3D structure.

7. Laboratory of Electron Microscopy
    - Expertise and assistance in electron microscopic analyses: qualitative and quantitative X-ray microanalysis, mapping of elements, 3D imaging and reconstruction, as well as ultrastructural imaging of various samples (macromolecules, subcellular structures, cells and tissues).
    - Services in the procedure of mild drying of biological samples in liquid CO_2 (critical point drying), coating of the biological samples with neutral metals and specimen grids with carbon.
8. Laboratory of Cytometry
    - Flow cytometry service, as well as high quality expertise and training for external investigators.
    - Expertise in high-tech flow cytometry applications and cell sorting (including rare cell populations and single cells).
    - Assistance in designing and performing experiments, development of protocols and data analysis.

PATENTING AND COMMERCIALIZATION OF SCIENTIFIC RESEARCH

Scientists at the Nencki Institute not only publish high-quality results of basic research, but also deploy the power of research to ensure benefits for society. The way for this, is the patenting and commercialization of research results.

Here is a list of recently granted patents and submitted patent applications:

- "Application of naringenin and a naringenin-containing product and a method of slowing down, counteracting and preventing the process of vitiligo problem", patent number P.416041;
- "Genetically encoded FRET-based MMP-9 activity biosensors and use thereof", patent number P30805USPC;
- "A method for detecting an increased risk of developing skin cancer and a use of a genotype variant of the GRHL3 gene", patent number P.410049;

- "Application of 3-(dodecylsulfanyl)-butanoic acid as a medicine for prevention of insulin resistance and pharmaceutical composition containing 3-(dodecylsulfanyl)-butanoic acid as an active ingredient", patent number P. 414785.
- "Method for the determination of biological age in human beings", patent number EP2976433B1;
- "PreT2D Sensor – early detection of insulin resistance or pre-diabetes in Type 2 Diabetes", application number PCT/IB2016/051087;
- "Prion protein-dendrimer conjugates for use in the treatment of Alzheimer disease", application number PCT/IB2017/052733;
- "Panel of microRNA biomarkers in blood for diagnosis of Alzheimer's disease", application number PCT/EP2017/059800.

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- Zdobądź grant ERC.
  Dołącz do najlepszych.

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- Pomagamy napisać dobry wniosek ERC
- Rozwiązujemy problemy budżetowe i prawne
- Udostępniamy przykładowe wnioski projektowe
- Przygotowujemy do prezentacji projektu w Brukseli
- Organizujemy warsztaty dotyczące ERC

KORZYSTAMY ZE WSPARCIA LAUREATÓW I PANELISTÓW ERC

- Pomagamy napisać dobry wniosek ERC
  Przesłane nam wnioski sprawdzamy pod kontem ich zgodności z zasadami ERC. Analizujemy zarówno ich strukturę, jak i obecność wszystkich elementów merytorycznych wymaganych przez panele oceniające. Pomagamy jak najkorzystniej przedstawić zarówno pomysł na projekt, jak i dorobek naukowy. Dopracowane wnioski, za zgodą kandydata, przesyłamy do specjalistów z poszczególnych dziedzin w celu weryfikacji CV oraz opisu naukowego.

- Rozwiązujemy problemy budżetowe i prawne
  Nasz zespół posiada wiedzę i doświadczenie w zakresie realizacji i rozliczania projektów finansowanych ze środków europejskich. Dzięki temu skutecznie wspieramy osoby piszące wnioski ERC w planowaniu budżetu oraz rozwiązywaniu problemów pojawiających się na styku prawa krajowego i zasad finansowych ERC.

- Udostępniamy przykładowe wnioski projektowe
  Zgromadziliśmy pokaźną bibliotekę wniosków o granty ERC, które możemy udostępniać do wglądu osobom przygotowującym własne projekty. Nasz zbiór obejmuje wnioski reprezentujące wszystkie grupy paneli i stale się powiększa.

- Przygotowujemy do prezentacji projektu w Brukseli
  Osoby, które startują w konkursach Starting ERC Grants oraz Consolidator ERC Grants i przeszły do drugiego etapu oceny proszone są o zaprezentowanie swojego projektu przed panelem oceniającym w Brukseli. Dla takich osób organizujemy próbne prezentacje z udziałem specjalistów z odpowiednich dziedzin, w tym laureatów i panelistów ERC.

- Organizujemy warsztaty dotyczące ERC
  Cyklicznie organizujemy dwa rodzaje warsztatów. Pierwsze to duże spotkania, na których zaproszeni laureaci i paneliści, a także osoby reprezentujące administrację instytucji osiągających znaczne sukcesy w pozyskiwaniu grantów ERC dzielą się swoimi doświadczeniami związanymi z ERC. Drugie to kameralne warsztaty „Wniosek ERC krok po kroku" obejmujące takie zagadnienia jak zespół w projektach ERC, struktura wniosku, profil laureata, proces ewaluacji, kwestie etyczne, budżet.

TANGO is a joint undertaking of the National Science Center and the National Center for Research and Development. The goal of the TANGO program is to bridge the gap between basic and application studies to enable the industry the introduction of modern technologies, products and services to the market. The applicants may thus acquire funds for designing the plan for commercialization of prior scientific work, connecting with partners interested in deploying their products, market research and safeguarding intellectual property rights. The funds may also be used to cover the expenses involved with industrial research and developmental works.

In the 3rd call of the TANGO program, the applicants include: scientific institutions, Institutes of the Polish Academy of Sciences and natural persons. The project may cover 100 of eligible costs of the project with the upper threshold for funding of 200 thousand PLN. The major criterion for eligibility is funding projects which originate from basic studies conducted during projects of the National Science Center: OPUS, PRELUDIUM, SONATINA, SONATA, SONATA BIS, HARMONIA, MAESTRO, SYMFONIA, POLONEZ.

The leader of a TANGO3 project may be an individual who has earlier conducted a basic science project or has a written consent of its leader for acting as one in a project financed by the TANGO 3 competition.

The TANGO3 competition may fund projects in the conceptual or conceptual and research & development phases. The first phase includes: developing a strategy for commercial application of the produced scientific results, securing intellectual property rights for ones results and market research conducted to determine the need for potential solutions resulting from the project. Additionally, this phase includes activities aimed as connecting with a commercial partner interested in deployment of the product and co-funding of the R&D phase. The second phase – research & development – includes industrial studies and developmental work. The project may last for a maximum of 12 months with a total sum of funding of 200 thousand PLN for both its phases.

In the two thus far completed TANGO projects a total sum of 65 million PLN was allocated to 76 projects. The budget of the TANGO3 competition equals 40 million PLN. The competition itself will be conducted in two stages: between the 14th June – 21st September and 21st September – 20th December 2018.

During the prior two TANGO competitions, projects that were funded included:

- development of a system for early detection of hydrologic threats
- designing new technologies of berry fruit production
- devising a system for supervision of stock exchange-listed companies
- creating a system for supporting the communication with sign language in public institutions

SUPPORTING INSTITUTIONS

The Foundation for the Medical University of Lodz was established to support the activity and development of the Medical University of Lodz in the area of education and didactics. It supports students' activity as well. By implementing its projects, it integrates the academic environment and also takes care of the positive image of the University.

The Foundation organizes courses and trainings. It arranges conferences and conventions and many other events of a scientific and cultural nature.

http://fumed.pl

Akademia Młodych Uczonych i Artystów

http://akademia.wroc.pl/

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http://www.terazpolska.pl/

Rada Samorządu Doktorantów UMED

http://doktoranci.umed.lodz.pl/

Studium Medycyny Molekularnej

http://www.smm.wum.edu.pl/

PIOTR WOJDYN – known as **"FU3SKO"**, photographer who for many years has been exploring Lodz, in particular its Bałuty district. Co-author of the "Bałuty Calendar", he has collaborated, among others, with the University of Lodz in the project, University of Lodz – a different perspective' and prepared numerous publications about the University. In 2014–2015 he was awarded twice in the competition 'Lodz at a glance' organized by the municipal companies MPK-Lodz, ZWiK Lodz and MPO Lodz. His photographs were showcased on the city's tramway transportation system and cars – this "mobile gallery" is still on display.

https://www.facebook.com/fu3sko/

SOURCES OF PHOTOGRAPHY:

on pages 11, 15, 42, 50, 56, 64, 185 – Piotr Wojdyn – Fu3sko

on page 17, 205 – Foundation for the Medical University of Lodz

on page 23 – Wojciech Fendler

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