Progress Report 2016–2017

Intercollegiate Faculty of Biotechnology
of University of Gdańsk and Medical University of Gdańsk

UNIWERSYTET GDAŃSKI

IFB

GDAŃSKI UNIWERSYTET MEDYCZNY

Intercollegiate Faculty of Biotechnology
of University of Gdańsk and Medical University of Gdańsk

Antoniego Abrahama 58, 80-307 Gdańsk, Poland

www.biotech.ug.edu.pl

2018

Published by
Intercollegiate Faculty of Biotechnology
of University of Gdańsk and Medical University of Gdańsk

Executive Editor
Prof. Igor Konieczny, PhD

Coordination
Izabela Raszczyk
Marta Dziedzic

Layout & Design
Bartek Truszkowski | Logomotiv Sp.j.

Research Group Profiles & Core Facility Descriptions
Courtesy of the respective Research Groups and Core Facilities

Text and Edition
IFB Staff Members

The project STARBIOS 2 has received funding from the Framework Programme for Research and Innovation Horizon 2020 under Grant Agreement no. 709517

[Contents]

[A Word from the Dean]

I have the pleasure to present the new edition of the Progress Report of the activities of the Intercollegiate Faculty of University of Gdańsk and Medical University of Gdańsk (IFB). This moment is a very special time for us, as we celebrate the 25th Anniversary of the establishing of IFB.

The years 2016-2017 have been marked by an enormous raise in a range of factors positively influencing IFB's research and teaching quality. Our motto to create a unique environment for conducting interdisciplinary research is successfully sustained. I am proud to emphasize that in the recent assessment by Ministry of Science and Higher Education of the R&D activity of research entities, IFB has achieved the highest level A+ category. This remarkable achievement could only be possible thanks to outstanding people being part of this Faculty - investing time, efforts and engagement in their work, and I would like to express my thanks and appreciation for the whole IFB Team.

The years of 2016-2017 were years of significant new openings for IFB. The relocation to our new building at the University Oliwa Campus in 2016 was one of the milestones in our activity. The modern research and teaching complex and new investments in the state of the art research equipment have proved to be an excellent basis for our daily work.

IFB has proven to be an attractive environment for researchers establishing their scientific independence. New excellent researchers from abroad decided to leave UK and USA to continue their careers at IFB. Research projects conducted at IFB have been assessed as the best in the programme for young team leaders funded by the National Centre for Research and Development. A platform for new collaborations for IFB research groups was set up at the end of 2017 by establishing two international research agendas in the field of biotechnology supported by The Foundation for Polish Science. IFB together with international partners is involved in STARBIOS2 the UE Horizon 2020 project considering responsible research. During the last period we have reached the highest level of financial support for research and teaching.

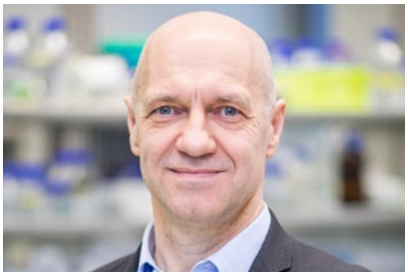
I am convinced that based on the recent achievement and the enormous motivation by our staff, students and partners we will continue to provide an attractive space for excellent research and teaching in the future years and we are looking forward to new collaboration opportunities.

March 2018

Prof. Igor Konieczny
Dean of IFB UG&MUG

Intercollegiate Faculty of Biotechnology of University of Gdańsk and Medical University of Gdańsk (IFB)

IFB Authorities (2016 – 2020)



Dean

Prof. Igor Konieczny

Vice-Dean for Student Affairs & Education

Prof. Sylwia Jafra

Vice-Dean for Science

Prof. Michał Obuchowski

Vice-Dean for Development

Prof. Stanisław Ołdziej

[IFB International Scientific Advisory Board]

Since 2015 IFB has had decided to establish the IFB International Scientific Advisory Board (ISAB). By Polish law, IFB as a research & teaching institution is evaluated every four years by two different governmental committees. An international advisory panel is therefore not an obligation. However, it is a part of IFB's capacity building strategy in order to obtain advice from prominent scientists from different fields covering research topics conducted at IFB. The nominations to the IFB International Scientific Advisory Board were based on the experts' research excellence, management experience and broad research expertise. These aspects are important to cover a broad spectrum of research work and other research-related activities at IFB and provide recommendations for further actions. The International Scientific Advisory Board conduced an on-site meeting in Gdańsk in 2016 and provide evaluation report. ISAB advices IFB continuously on multiple issues including hiring new researchers, equipment investments and expansions on new research areas.

Members of the IFB International Scientific Advisory Board:

- **Prof. Bernd Bukau -** Universität Heidelberg Center for Molecular Biology (ZMBH)
- **Prof. Burkhard Brandt -** Universitätsklinikum Schleswig Holstein, Institut für Klinische Chemie Kiel
- **Prof. Maarten Koornneef -** Max Planck Institute for Plant Breeding Research
- **Prof. Arvind H. Patel -** MRC-University of Glasgow Centre for Virus Research
- **Prof. Dan Tawfik -** Weizmann Institute of Science

[IFB Consulting Board]

IFB Consulting Board supports the planning of the development of the Faculty, in particular the new paths of teaching programmes. Members of the Consulting Board are representatives of companies, institutions from the biotechnology sector and higher schools.
The main goal of cooperation is a continuous increase of the quality of teaching and ensuring a dynamic start at job market for our graduates. The Consulting Board evaluates study courses offered at IFB from a business and employers perspective and gives its recommendations. This practice has already proved to be successful, since IFB has received the award of Best Major and a distinction for the set of learning outcomes prepared for the specialty of Biotechnology as a model set.

Members of IFB Consulting Board are representatives of companies and institutions such as:

- Polpharma Biologics
- The Polpharma Scientific Foundation
- Adamed Group
- The Institute of Biotechnology and Antibiotics
- KAWA.SKA Company
- Pomeranian Special Economic Zone/ Gdańsk Science and Technology Park
- Pomeranian Science and Technology Park in Gdynia
- Innovative and Implementing Company IMPULS
- I Academic High School in Gdynia
- John Paul II Catholic High School in Gdynia

ABOUT IFB

[Structure of IFB]

Dean's Offices and Core Laboratories

Dean's Office for Student Affairs | Head: Ewa Brzana
Dean's Office for Research and Project Management | Head: Patrycja Tucholska
Core Facility Laboratories | Head: Prof. Michał Obuchowski
Core Teaching Laboratories | Head: Prof. Sylwia Jafra

Institute of Biotechnology, University of Gdańsk

Prof. Bogdan Banecki, Director of the Institute of Biotechnology
Wojciech Śledź PhD, Deputy-Director of the Institute of Biotechnology

Department of Biotechnology | Head: Prof. Ewa Łojkowska
Laboratory of Plant Protection and Biotechnology | Head: Prof. Ewa Łojkowska
Laboratory of Molecular Diagnostics | Head: Prof. Krzysztof Bielawski
Laboratory of Plant Biochemistry | Head: Prof. Antoni Banaś
Laboratory of Biological Plant Protection | Head: Prof. Sylwia Jafra
Laboratory of Biologically Active Compounds | Head: Prof. Aleksandra Królicka

Department of Molecular and Cellular Biology

Head: Prof. Krzysztof Liberek
Laboratory of Protein Biochemistry | Head: Prof. Krzysztof Liberek
Laboratory of Molecular Biology | Head: Prof. Igor Konieczny
Laboratory of Evolutionary Biochemistry | Head: Prof. Jarosław Marszałek
Laboratory of Physical Biochemistry | Head: Prof. Bogdan Banecki
Laboratory of Biophysics | Head: Prof. Jacek Piosik

Other laboratories

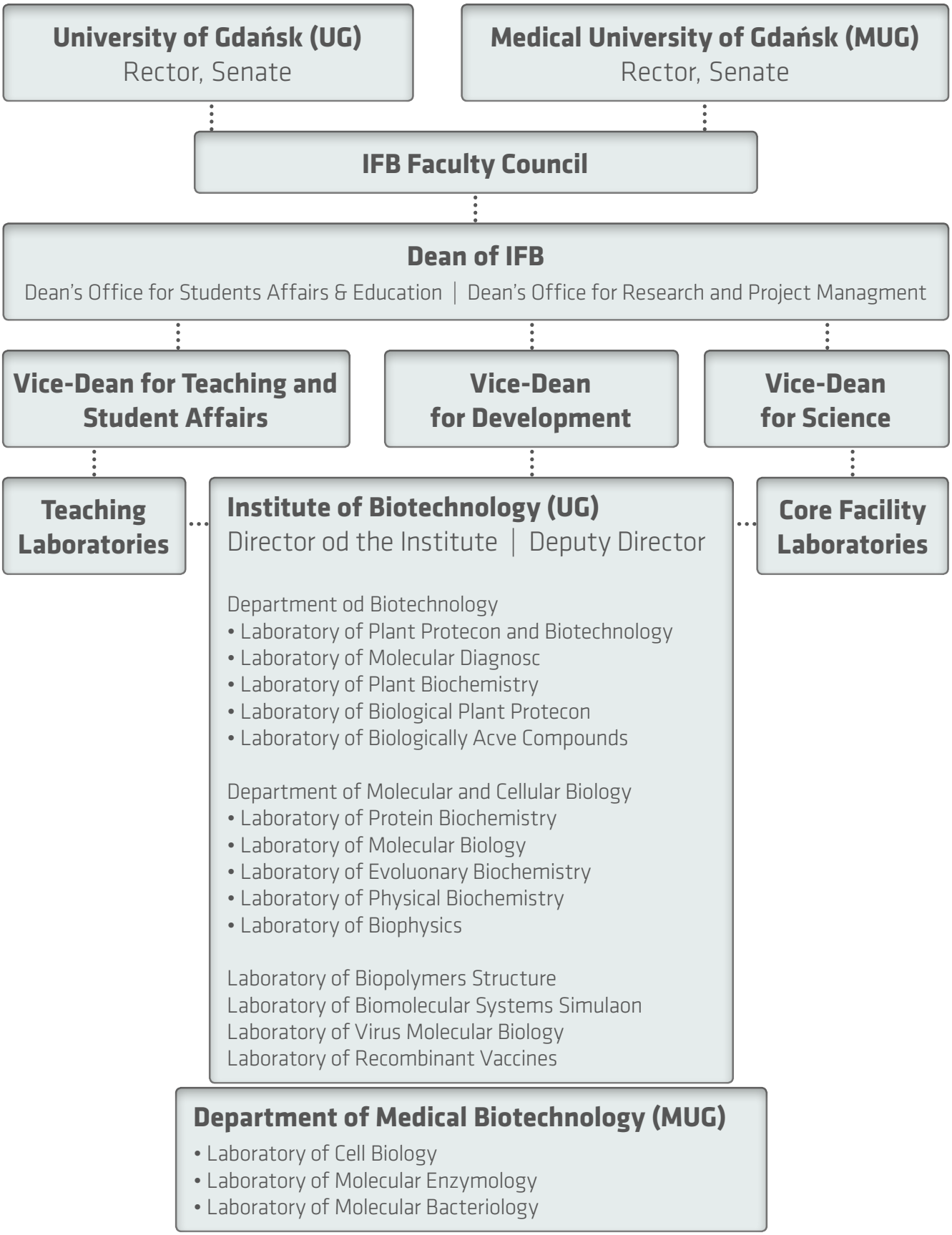
Laboratory of Biopolymers Structure | Head: Prof. Stanisław Ołdziej
Laboratory of Biomolecular Systems Simulation | Head: Prof. Rajmund Kaźmierkiewicz
Laboratory of Virus Molecular Biology | Head: Prof. Krystyna Bieńkowska-Szewczyk
Laboratory of Recombinant Vaccines | Head: Prof. Boguław Szewczyk

Department of Medical Biotechnology, Medical University of Gdańsk

Prof. Jacek Bigda, Head of Department of Medical Biotechnology

Laboratory of Cell Biology | Head: Prof. Jacek Bigda
Laboratory of Molecular Enzymology | Head: Prof. Andrzej C. Składanowski
Laboratory of Molecular Bacteriology | Head: Prof. Michał Obuchowski

Structure of IFB



[Background]

The Intercollegiate Faculty of Biotechnology of the University of Gdańsk and the Medical University of Gdańsk (IFB) has been established in 1993 by the decision of the Senates of the University of Gdańsk (UG) and the Medical University of Gdańsk (MUG). The initiators of the Faculty were Prof. Anna Podhajska, Prof. Wacław Szybalski and Prof. Karol Taylor. The Faculty is a unique institution in Poland created by two universities. This leads to the interdisciplinary character of the conducted research and teaching by combining biomedical and bio-molecular issues and their applications in biotechnology for health and life quality. Since 1999, IFB is authorized to confer the degree of doctor, and since 2010 - the scientific degree of habilitated doctor in the area of biological sciences - discipline of biochemistry. Taking into account PhD students, approximately 190 people take part in research and teaching at IFB.

[Achievements]

IFB is a leading research and teaching institution that since 2002 has had the status of the European Centre of Excellence in Biosafety and Molecular Biomedicine (since EU FP5) and occupies high positions in the rankings of the Ministry of Science and Higher Education (MNiSW) regarding scientific effectiveness. In 2017, in a parametric assessment IFB was granted the highest-level category A+.

The quality of teaching at IFB is evaluated as the highest in Poland. The Polish Accreditation

Committee awarded the Faculty with a distinction for the quality of teaching (2011) and the Ministry of Science and Higher Education granted the specialty of BIOTECHNOLOGY at IFB the title of The Best Major (2012). The Central Council of Science and Higher Education recognised the set of learning outcomes prepared by IFB for the specialty of Biotechnology as a model one. These are the only distinctions of this kind granted in Poland in the area of biological sciences.

Faculty members play important functions in international societies and scientific commissions, for example prof. Krzysztof Liberek is a member of European Molecular Biology Organisation (EMBO), prof. Krzysztof Bielawski – vice-president of ScanBalt and Council Member of the European Society for Translational Antiviral Research (ESAR), prof. Ewa Łojkowska – member of the International Selection Committee of the Award L'OREAL-UNESCO For Women in Science International Rising Talents and prof. Bogusław Szewczyk - member of the Commission of European Food Safety Authority. IFB staff members are also laureates of prestigious programmes and awards (EMBO YIP, HHMI, EUPHRESCO ERANET, InfectEra, STRATEGMED2, Polish-Norwegian Research Programme, Polish-South Africa Programme, Polish-French Polonium Programme) Polish national programmes such as: LIDER, TOP 500 Innovators, MISTRZ, START, HOMING PLUS, TEAM, First TEAM). Publications by IFB staff have received numerous awards and distinctions for the best work conducted in Polish

laboratories, granted by the Committee of Microbiology of Polish Academy of Science, Polish Genetic Society or Polish Biochemical Society. In 2016 the publication from prof. Igor Konieczny research group published in Proceedings of National Academy of Science USA has been awarded by the Polish Academy of Science as the best publication in microbiology published by Polish laboratories. In recent period we successfully increased the quality of publications (Fig. 1). The results of our investigations have been published in high impact journals among

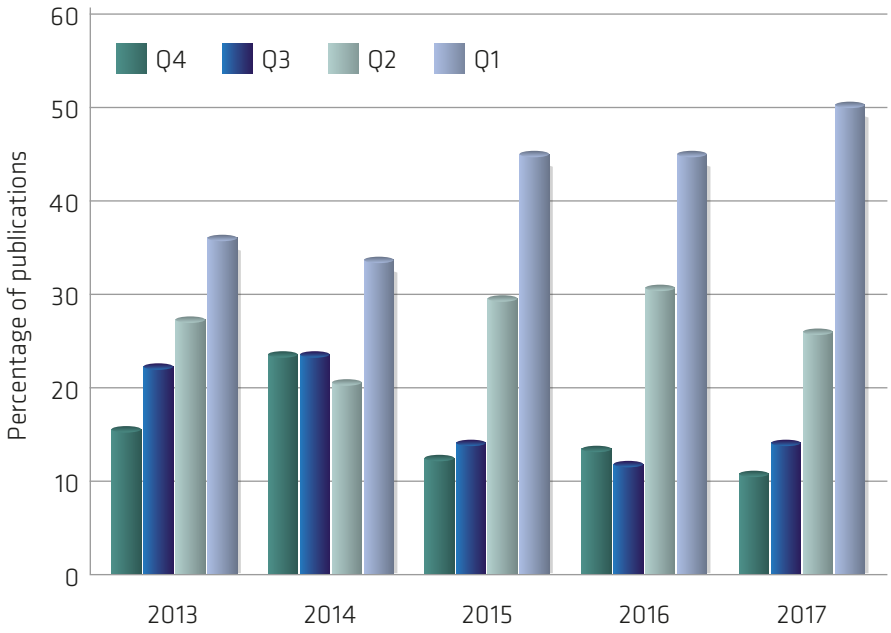


Figure 1. Percentage of publications with IFB affiliation in years 2013-2017 divided into quadrilles. Scientific journals are classified into quadrilles according to the Journal Citation Reports – Clarivate Analytics.

with Nature, The EMBO Journal, Mol. Biol and applied Evolution, NAR, eLife, PNAS, Plant Physiology, New Phytopatology, Journal of Virology. Almost all of our research is published in indexing journals and more than 50% in journals from Q1 from the Web of Science journal list.

The IFB researchers received various awards including Elseviere award for dr. Katarzyna Węgrzyn, Krzysztof Celestyn Mrongowiusz award for the best teacher for dr. Wioletta Żmudzińska or award „Primum Cooperatio" given by the Pracodawcy Pomorza for the best collaboration of research and business, for prof. Bogdan Banecki.

We are constantly increasing our innovation outcome. Large number of our research projects (sixteen in last two years) are directed into R&D. As results the Faculty obtained several national and international patents.

Our position in independent rankings evaluating teaching and research is established. Besides the highest result in the recent evaluation by MNiSW we have also obtained the highest scores in PERSPEKTYWY rankings in 2016 and 2017. IFB got second overall position among all academic units providing programs for teaching biotechnology.

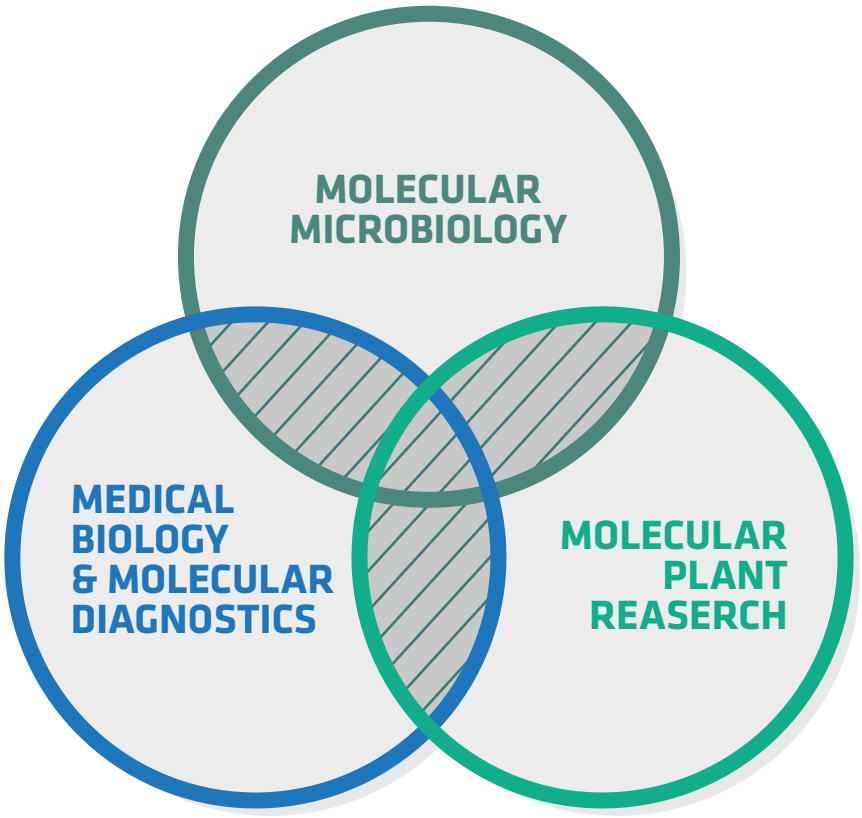
[A+]

We are very proud about the result we have achieved in the recent assessment by Ministry of Science and Higher Education of the R&D activity of research entities in Poland. IFB has achieved the top category A+ indicating the highest effectiveness and quality of research. It must be emphasized that in the assessment IFB got the highest scores in two out of four parameters specified. Those two parameters are also the most valuable and mostly influencing the overall result. We were assessed highest in the parameter 1 indicating the highest outcome quality of research achievements and parameter 3 indicating the highest achievements in research development and applied research activity.

[Research Potential]

IFB comprises 17 teams involved in research activities. Basic as well as applied research areas at IFB cover molecular microbiology, medical biology and molecular diagnostics as well as molecular plant biology. These areas are the basis of biotechnology development. Relationships and synergy between these research areas give an added value in the form of common thematic areas. Maintaining three main research areas increases the number of interactions between research teams, their effectiveness and broadens competence.

At IFB about 88 research pathways supported by external grants are conducted simultaneously. 31 projects concern molecular microbiology. In these projects various microorganisms are used as models for the analysis of basic cell processes. The main research topics include protein aggregation and disaggregation, the role of molecular chaperones, proteolysis, replication of DNA, plant, animal and human pathogens, infection mechanisms, cell response to viral infections and pathogen diagnostics.



36 projects concern the area of medical biology and molecular diagnostics. We conduct work concerning recombinant vaccines, edible vaccines, new immune-modulating substances development, proteases inhibitors in anticancer therapy, tumour markers, neoplasm analysis in in vivo models, markers used in neurodegenerative diseases diagnostics, nanobiotechnology in treating burns as well as diagnostic methods in infectious plant diseases.

Another research area concerning molecular plant research is connected with the already mentioned research projects concerning the diagnostics of plant diseases, projects related to infection mechanisms and identification of genes and lipid metabolic pathways in plant cells. Research is also carried out into identification of plant nutraceutics.

The Faculty employed new researchers from Oxford University and Texas University who are opening new research lines in immunology focused on allergic and inflammatory reaction and structural biology focused on replication of mitochondrial DNA and its impact on health problems. Those, young but already recognised scientist in the community with its research topics are bringing a new value to the research potential of IFB.

In the last two years we also improved our expertise in mass spectrometry and initiated development of state of art technology in the analysis of biomolecule interactions by using atomic force microscopy (AFM). We are developing the AFM microscopy facility for study biological systems.

In 2016 – 2017 we invested approx. EUR 750 000 for upgrade our equipment or obtaining the new one. In such period we obtained for example: Western Blot Near-Infrared Detection System (LI-COR), flow cytometer Guava easyCyte (Merck), Circular Dichroism Spectrophotometer J-1500 (Jasco), plasmon resonance analyser T200 (Biacore), 24 node computation cluster (Intel). Continuously the Faculty increases research potential by obtaining new, modern research equipment.

The IFB continuously increases the budget for research obtained from various external sources. In 2017 over half of the Faculty budget came from competitive grants from national and international agencies (Fig. 3). In 2017 only, two grants obtained from The Foundation for Polish Science for establishing the new groups at IFB secured almost EUR 1.5 M of funding.

The possibilities for new collaborations for IFB research groups were set up at the end of 2017 by establishing two international research agendas in the field of biotechnology. The two research centres in a frame of International Research Agenda Programme from The Foundation for Polish Science were established at University of Gdańsk and Medical University of Gdańsk. First, called The International Centre for Cancer Vaccine Science was established in cooperation with the University of Edinburgh (UK), second named 3P-Medicine – Preventive, Personalized, Precision was established in cooperation with the University of Uppsala (Sweden).

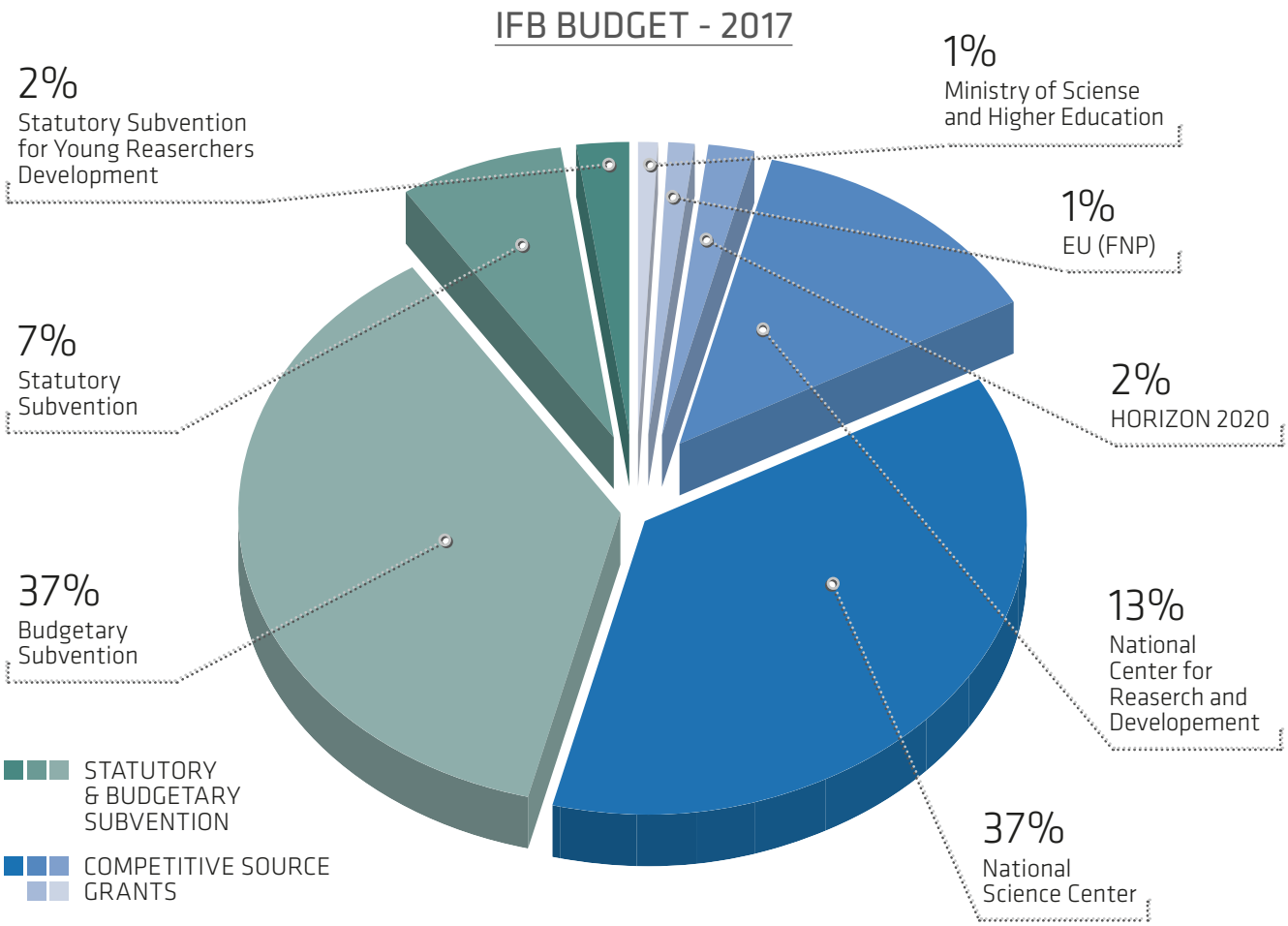


Figure 2. IFB Budget 2017

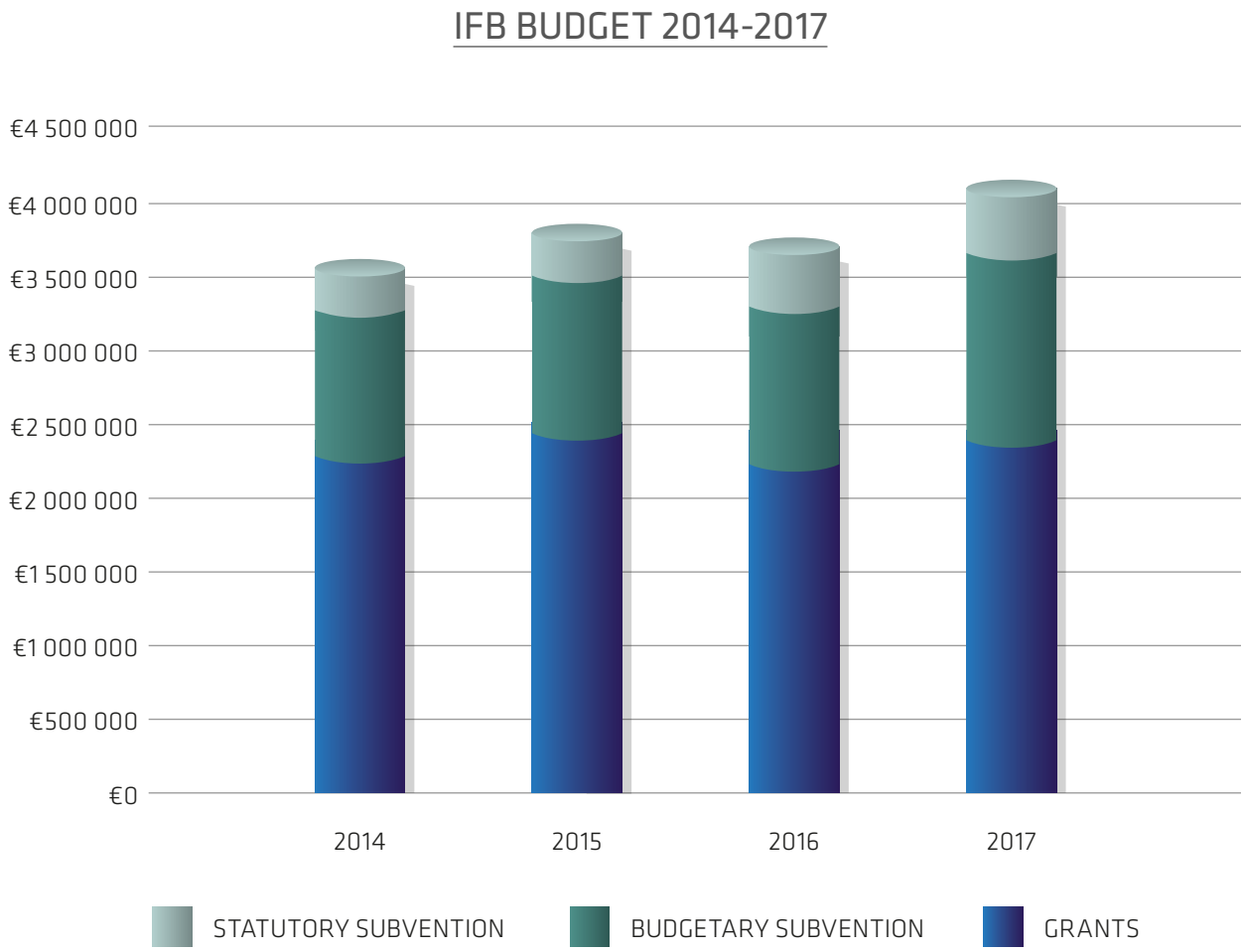


Figure 3. IFB Budget 2014 - 2017

[Research Projects]

Selected granted research projects 2016/2017

Project	Project Leader	Start	Funding Source *	Programme	EUR
Exosomes produced by epidermal cells (keratinocytes) in allergy induction and tolerance to environmental allergens	Gutowska-Owsiak Danuta	2017	FNP	First Team	473 933
Functional characteristics and therapeutic potential of gain-of-function mutations in complement C2 protein	Okrój Marcin	2016	NSC	Harmonia 7	305 971
System NaNoEXpo – as an innovative technology of production process of new generation of vaccinations	Gromadzka Beata Marta	2016	NCBiR	LIDER VI	284 360
Virus-like particles produced in life bioreactors as a vaccine against the most dangerous disease of poultry	Rąbalski Łukasz	2017	NCBiR	LIDER VII	284 360
The combined (synergistic) use of the lytic bacteriophages and antagonistic bacterial isolates in the biological control of pectinolytic bacteria Pectobacterium spp. and Dickeya spp. on potato (Solanum tuberosum L.)	Czajkowski Robert	2016	NCBiR	Lider	283 353
Anti-Zika vaccine - innovative methods for antigen construction	Król Ewelina	2017	NCBiR	LIDER VII	283 293
Biochemiczna rekonstrukcja kluczowych etapów mitochondrialnej biogenezy centrów żelazo-siarkowych (FeS).	Dutkiewicz Rafał Dominik	2016	NSC	Opus 10	256 682
Targeted exosome-mediated crosstalk between epithelial and antigen presenting cells for effective immunity at barrier sites	Gutowska-Owsiak Danuta	2017	NSC	Polonez 12	224 280
Deciphering malignancy of cancer cells outside the primary tumors through molecular characterization of single circulating tumor cells from breast cancer patients	Markiewicz Aleksandra	2017	NSC	Sonata 12	224 111
Unrevealing the molecular basis of DNA damage recognition and processing in human mitochondria	Szymański Michał	2017	NSC	Polonez 2	223 903
Public health risk assessment, associated with potentially dangerous zoonotic influenza A virus strains, circulating among livestock in Poland.	Łepek Krzysztof	2017	NSC	Sonata 11	177 023
Genetic background and impact of environmental factors on biofilm formation by the beneficial strain of bacteria, Pseudomonas donghuensis P482, in biotic and abiotic conditions.	Rajewska Magdalena	2016	NSC	Sonata 10	160 559
Antimicrobial photoinactivation as an effective tool for sensitization of multidrug resistant ESKAPE pathogenes to antimicrobials	Grinholc Mariusz	2016	NSC	Opus 10	156 966
Determination of biochemical properties and interaction partners of human CLPB protein - its physiological significance and role in MEGCANN syndrome pathogenesis.	Ziętkiewicz Szymon	2016	NSC	Sonata Bis 5	156 388
Characteristics of ubiquitous bacteria of the genus Pectobacterium (plant pathogens) - identification of genes involved in the adaptation to the environment, the rapid spread of and changes in host plant.	Waleron Małgorzata	2016	NSC	Opus 9	152 398
Tick-borne encephalitis virus - search for mechanisms useful in treatment and prophylaxis.	Król Ewelina	2016	NSC	Sonata 10	133 566
Old drugs - new perspectives: modulation of antibiotics activity by caffeine and pentoxifylline	Woziwodzka Anna	2017	NSC	Sonata 11	110 094
Novel biocontrol agent for use in organic / IPM citrus cultivation: biology, phylogeny and biopesticide activity	Szewczyk Bogusław	2016	NCBiR	Współpraca Polska-RPA	94 786
Differential redox potential of tumor and normal cells as a tool for targeting cancer by natural products	Sznarkowska Alicja Anna	2016	NSC	Preludium 9	35 545
Genetic factors causing increased virulence of the baculovirus infecting one of the major forest pests - the gypsy moth (Lymantria dispar)	Krejmer - Rąbalska Martyna Alicja	2016	NSC	Preludium 9	35 541
Biological and clinical significance of RSK2 kinase in breast cancer progression	Czaplińska Dominika	2017	NSC	Etiuda 5	28 900
Gene expression dynamics of main Dickeya solani virulence factors during the infection process in planta	Motyka Agata	2017	NSC	Preludium 11	23 601
Evaluation of the immunogenicity of the highly conserved Hepatitis C virus E2 glycoprotein epitopes exposed on the surface of the Hepatitis B small surface antigen virus-like particles.	Czarnota Anna	2017	NSC	Preludium 12	23 601
Analysis of the mechanism of synergistic action of light-activated porphyrin TMPyP and farnesol against pathogenic bacteria	Kossakowska-Zwierucho Monika	2016	NSC	Preludium 10	23 459
The usage of silver nanoparticles to enhance the antimicrobial potential of naphthoquinones against Staphylococcus aureus.	Krychowiak Marta	2016	NSC	Preluduim 10	22 635
Analysis of ORC proteins' interaction with the single-stranded DNA of origin region – preliminary research	Węgrzyn Katarzyna	2017	NCN	Miniatura	7 819

FNP – The Foundation for Polish Science; NCBiR – The National Center for Research and Development; NSC – National Science Centre

[Facilities and Equipment]

The facilities of IFB comprise laboratories of the Institute of Biotechnology, University of Gdańsk, as well as facilities at the Medical University of Gdańsk campus.

In 2016, IFB relocated the UG based teams to a completely new building of the Institute of Biotechnology situated in the Baltic Campus of the University of Gdańsk. This investment has received a 15 million EUR funding from the Operational Programme Infrastructure and Environment within Structural Funding of the EU. The building is a modern research-teaching complex. The usable area is 7900 m^2 and covers 5 levels. It includes a specialized core facility zone, an area of research laboratories, seminar rooms, computer rooms, an auditory for 180 people, rooms for our Student Scientific Association, a reading room, a room for the Faculty Council, new technical systems (audio-visual systems, access control systems etc.).

Since 2011 IFB has set and expanded its core facility laboratories in which a wide range of methods will be implemented, allowing to analyse interactions among proteins, proteins and nucleic acids, proteomic analyses, lipid analyses, post-translational modifications as well as molecular diagnostics.

Core Facility Laboratories comprise several modules:

▶ Laboratory of Biomolecular Analysis

This laboratory allows insight into molecular structure and interactions within biological systems. It is already equipped with spectro- and fluorometers, FP-8500 (Jasco), Circular Dichroism Spectrophotometer J-1500 (Jasco), advanced microplates reader EnVision (Perkin-Elmer), plasmon resonance analyser Biacore T200, anaerobic chamber (COY Lab Products), ultracentrifuges (Beckman), Atomic Force Microscope BioScope Resolve with scanning head MultiMode8 Lockout Specs (Bruker) and apparatus for microscale thermophoresis Monolith NT.115 (NanoTemper Technologies).

▶ Laboratory of Mass Spectrometry

This unit has been established within the FP7 project MOBI4Health. We have four distinct spectrometers (MassARRAY® Analyzer 4; MALDI-TOF/TOF™ 5800 with MALDI Imaging, QTRAP® 6500 LC/MS/MS, TripleTOF® 5600, CESI 8000 Plus, Eksigent Micro LC 200) providing various applications, for instance in genomics, transcriptomics, proteomics and lipidomics. Mass spectrometry specialists facilitate research work in the MS Laboratory.

▶ Laboratory of Genetic Analysis

Here, the equipment comprises new genetic analysis devices such as: real-time thermocycler Light Cycler 480 (Roche), real time cell analyser xCELLigence DP, homogeniser MagnaLyser, aparatus for the automatic isolation of nucleic acids MagnaPure 2.0 (Roche), apparatus for nucleic acids capillary electrophoresis Tape Station 2200 and automatic pipetting station epMotion 5070 (Eppendorf).




Laboratory of Imaging and Data Analysis

IFB has three confocal microscopes (Nikon PCM-2000, Leica DMI6000 CS SP8 and microscope Leica HCS LSI) as well as several fluorescent ones. The confocal microscope Leica TCS SP8 is equipped with white light laser, which perfectly matches the excitation wavelength ranging between 470 and 670nm of any fluorophore. Up to eight excitation lines can be used - simultaneously. This microscope is equipped with five spectral detectors (350-800nm) working independently. Leica TCS LSI macro confocal is the first super zoom confocal that offers high resolution plus a large 16x16mm field of view for in vivo imaging. Both Leica microscopes are equipped with a special incubation chamber for Live cell imaging.
Nikon PCM 2000 fluorescent confocal microscope equipped with 3 lasers and ultra-sensitive colour camera Hamamatsu.

Laboratory of In Vitro Plant Cultures

The infrastructure consists of ten growth chambers that serve as a controlled environment for the growth of in vitro cultured plants. The growth chambers contain various in vitro cultured endangered plants (e.g. Droseraceae and Orchidaceae species), hairy root cultures, plants containing bioactive compounds and GM plants. These cultures are used for breeding and reintroduction purposes, transformations as well as for obtaining biologically active secondary metabolites.

Isotope Laboratory Type III

The laboratory comprises full equipment indispensable for conducting research with radioisotopes such as 3H, 14C, 32P, 33P and 35S. Two scintillation counters (LC 6000TA Beckmann and MicroBeta LumiJET) are available in the laboratory.

Laboratory for Highly Infectious Pathogens

The IFB core facility established of Institute Biotechnology possesses also two laboratories in Biosafety Level 3 (BSL3) which are designed for working with dangerous animal viruses and bacterial pathogens (for example influenza virus or Mycobacterium tuberculosis). Both laboratories allow safe manipulation with such pathogens and are equipped with laminar chamber class III and several laminar chambers class II. The safety of work is achieved by a strictly controlled access to the lab as well as by a multistep pressure barrier between the working space and rest of the building.

Laboratory of Structural Biology

Recently we started to establish a new laboratory which will focus on solving three-dimension structure of biomolecules. We plan to organize facility for protein and its complex crystallisation and X-ray diffraction.

The Core Facilities are available for Faculty members, research groups from other Faculties at the University of Gdańsk and Medical University of Gdańsk as well as for external users form other scientific institutes as well as commercial institutions.



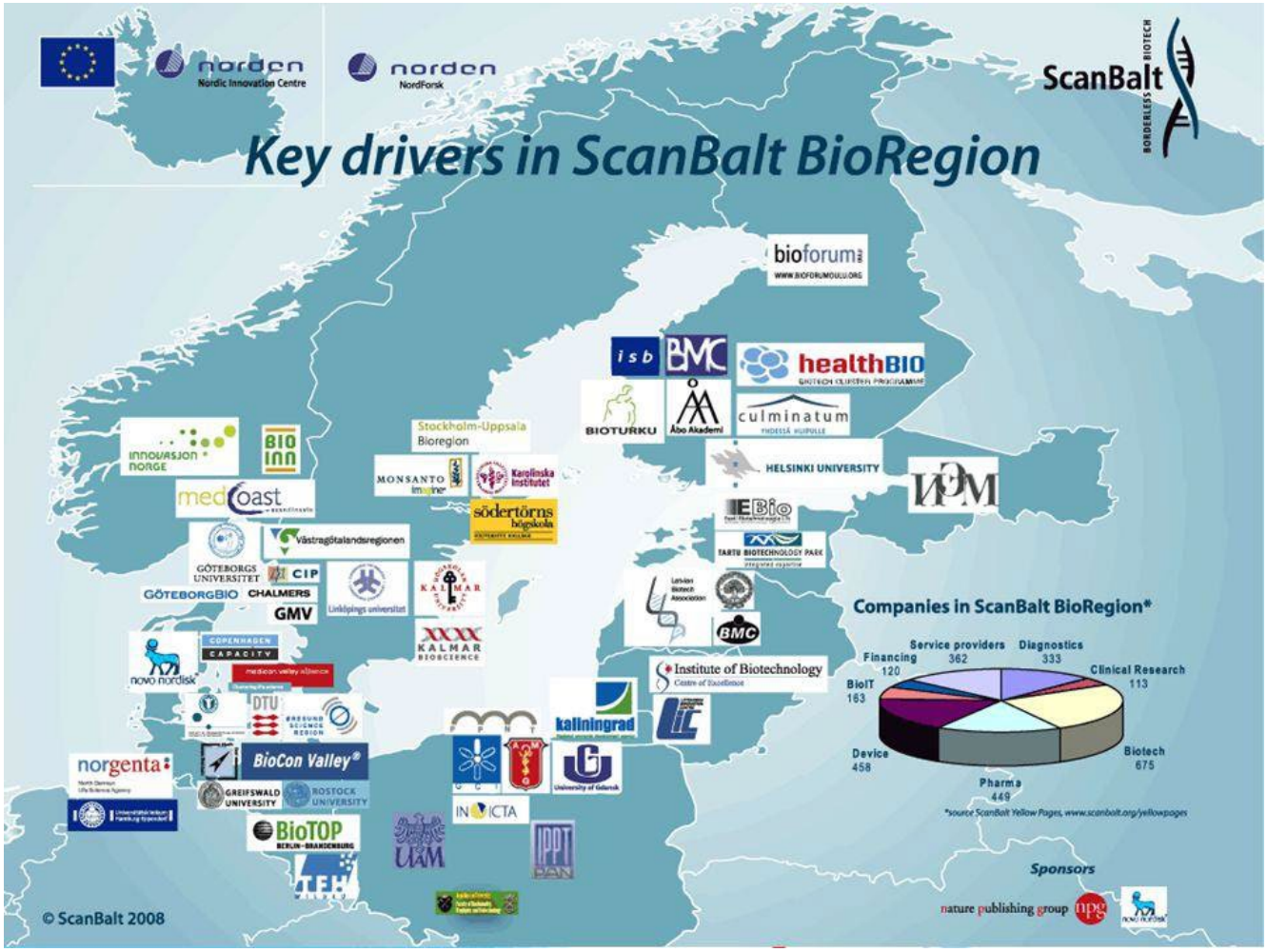



[Partnerships]

IFB cooperates with numerous regional, national and international research, industrial, business, health care and educational institutions, enterprises and networks.

ScanBalt BioRegion

ScanBalt BioRegion is a network composed of the health and bio economy communities in Northern Europe including more than 3000 companies, 50 health care clusters and networks, 75 health care sector science parks and 60 universities (Fig. 4). ScanBalt coordinates the EU Baltic Sea Region Strategy´s flagship "Health Region". Prof. Krzysztof Bielawski, a member of IFB Faculty council, was elected in 2014 as a Vice Chairman of ScanBalt BioRegion.



MOBI4Health Project (2013-2016)

MOBI4Health: Centre of Molecular Biotechnology for Healthy Life: Biotech solutions bringing health to living organisms and environment supported by mass spec-focused research platform (EU 7th Framework Programme)

MOBI4Health project increased the potential of IFB in terms of widening and modernization of its research technologies and expanded the innovative dimension of its scientific achievements through establishing the Centre of Molecular Biotechnology for Healthy Life: MOBI4Health Centre.

Interdisciplinary research in the area of medical biology, molecular biology and molecular biotechnology allows to effectively address issues that are of concern today. Novel ideas for solutions in areas such as vaccines against avian influenza H5N1, antiviral vaccines against HCV virus infections, tools for viral infection monitoring, edible vaccines against bacterium Helicobacter pylori, discovering new tumor markers, neoplasm analysis in in vivo models, nanobiotechnology in treating burns, biobased plant protection, plant nutraceutics as well as basic science research in protein aggregation and disaggregation, molecular chaperones, proteolysis, replication of DNA , infection mechanisms – these are some of the topics, which are currently in the area of interest of the researchers at IFB. New experienced scientists employed within the MOBI4Health project, including scientists with experienced gained abroad, increased the human potential of IFB and work on finding solutions that would contribute to the healthy life of humans, animals and plants.

A previous weakness in form of a lack of an infrastructure and expertise in high throughput mass spectrometry techniques for research projects in proteomics, genomics, lipidomics and other "–omics", has been successfully eliminated. IFB has established a modern, fully operational mass spectrometry laboratory (1.5 million investment in research equipment) that is led by experienced staff trained on the subject. Organization of mass spectrometry workshops has increased skills at IFB, contributed to dissemination of information on the upgraded capabilities of IFB and attracted a large number of participants interested in these technologies.

Twinning with 10 European partners within the project has increased the mobility of IFB researchers and enhanced research partnerships. New joint activities such as ideas for new projects and joint supervision of PhD students have emerged and are expected to result also in an increased number of joint publications of improved scientific quality reaching beyond the project's lifetime. An increase in the quality of journals and an increase of open access publications has already been noticed. This has already contributed to a better recognition and visibility of IFB. The project also allowed to increase the participation in scientific events, such as conferences and workshops, which definitely enhanced the integration in the scientific community.

MOBI4Health partner institutions include:

- University of Nottingham (UK),
- Phillips-University Marburg (Germany),
- Centro de Investigaciones Biologicas (Spain),
- Federico II University of Naples (Italy),
- Georg-August-University Goettingen (Germany),
- INSA Lyon (France),
- University of Konstanz (Germany),
- Agronomy & Environment Laboratory ENSAIA-INPL (France),
- Biomedical Research Institute FORTH (Greece), and
- INSERM U846 Stem-cell and Brain Research Institute (France).

University-business cooperation has been intensified. Specialist staff provided support in the area of IP and innovation-related issues, helped with market analyses and ideas on patent applications as well as advised on new possibilities to cooperate with industry in the future, for example within the Smart Specialization Strategies of the Pomeranian Region.

External evaluation was conducted by three independent experts to assess the project output and recommend possible solutions for further sustainability of the results. The Evaluation Team was composed of the following scientists: Prof. Dr. Marc Vooijs, The Netherlands, Asst. Prof. Dr. Anna Maria Pirttilä, Finland, and Dr. Vanesa Ivetic Tkalcevic, Croatia. Experts' work comprised on-site visits, remote work and summary of evaluation results in form of an evaluation report. During two on-site evaluation visits in Gdańsk (26-28.09.2016 and 14-16.11.2016) and during the phase of remote work, the evaluators undertook a comprehensive analysis of the project output

and IFB's potential. They presented some of their findings during the second visit at an **Evaluation Roundtable Meeting** (15.11.2016) to IFB scientists, MOBI4Health Partners, ISC Members and representatives the University and of local authorities of the Pomorskie Region. The Evaluation Report is confidential, but it can be stated that the evaluation by external experts was positive. The obtained outcomes of the evaluation are implemented to our activities.

The implementation of the MOBI4Health project contributed to sustainable innovative science based on advanced mass spec applications, enhanced future research interactions and provided an excellent basis for a long-lasting cooperation at regional and European level.

MOBI4Health

The project MOBI4Health has received funding within the 7. Framework Programme of the European Commission under grant agreement no. 316094

STARBIOS2 Structural transformation to attain responsible BioSciences (2016 - 2020)

STARBIOS2 is a European project in the frame of the Horizon 2020 Programme involving University of Gdańsk together with 11 partners from Europe, USA and Brazil who work on the concept of responsible research and innovation (RRI) in biosciences. The idea of the project is to develop and implement in selected research institutions individual action plans allowing structural changes related to RRI, especially takin account the five key areas such as societal engagement, gender, education, open access, and ethics.

Our European and international partners are:

- University of Rome Tor Vergata (Italy),
- University of Oxford (UK),
- Agrobioinstitute (Bulgaria),
- University of Primorska (Slovenia),
- University of Bremen (Germany),
- Aarhus University (Denmark),
- Laboratory of Citizenship Sciences (Italy),
- Sparks & Co, Communication Agency for EU Projects (France)
- Oswaldo Cruz Foundation (Brazil),
- University System of Maryland (USA),
- The International Centre for Genetic Engineering and Biotechnology (ICGEB).

STARBIOS2

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 709517.

POTPAT Consortium

Consortium created by IFB, Plant Breeding and Acclimatization Institute - National Research Institute and Norwegian Institute for Agricultural and Environmental Research (Bioforsk, P1) in the frame of Polish-Norwegian Research Programme. The consortium is involved in the project which aims at gaining the knowledge on interactions between host, pathogen and environment in order to reduce the cost of protection against late blight and minimize losses caused by *Pectobacterium* spp., *Dickeya* spp. and *Phytophthora infestans*. POTPAT Project Meeting of the research consortium took place in April 2016 at IFB.

University of Houston – Downtown and Virginia State University

IFB has established long-term collaboration in terms of teaching and practical student trainings with two universities from USA. University of Houston-Downtown (UHD) is our partner in education and teaching affairs. The staff of UHD advise us in teaching program and learning outcomes development. IFB frequently hosts the students form UHD for the summer internship and involved them in the research projects. Both the students and the academic staff of UHD regularly participate in the Biotechnology Summer School. Last year we hosted prof. Janusz Grembowicz, the representative of UHD authorities to discuss the common project for student exchange program. Within collaboration with Virginia State University (VSU) our selected Master program students have opportunity perform their master research project at the VSU laboratories. During last two year we hosted prof. Zygmunt Derewenda from VSU, prof. Anton Kossiakoff from University of Chicago for the presentation of the possibilities for the internship and for the students' recruitment processes.

Pomorskie Smart Specialization

Smart Specialization (ISP) is a principle of the Pomorskie Regional Development Strategy 2020. IFB was one of initiators to create smart specialization in the field of biotechnology and medicine. After long multistage process of evaluation and selection by international advisory board the smart specialization on Medical technologies in the area of civilization and ageing-associated diseases (ISP-4) has been established by Marshal of Pomerania region. The created network consists of more than 100 enterprises, business, companies, venture capitals and higher education institutions in Pomerania region involved in modern solutions in prevention, diagnosis and therapy of civilization diseases and ageing period; support systems for people with disabilities. IFB professors Jacek Bigda and Igor Konieczny are members of ISP-4 council. Prof. Jacek Bigda has been elected as a Chairman.

InnovaBio Pomorze

IFB, together with Pomeranian Science Technology Park, and the I Academic High School in Gdynia, is a co-founder of the educational initiative InnovaBio Pomorze aiming at the practical education for students and pupils through their participation in projects commissioned by entrepreneurs. We support the participation of the students in this initiative and provide the mentorship by our staff.

Academy of Fine Arts in Gdańsk and The ŁAŹNIA Center for Contemporary Art

For years, we have collaborated with the Academy of Fine Arts in Gdańsk and The ŁAŹNIA Center for Contemporary Art. IFB participated in several BioArt projects curated by prof. Grzegorz Klaman. Recently we have hosted the BioArt exhibition at the new building of the Faculty.

Others

For many years, IFB has been cooperating with many organizations and institutions in the fields of education, research and research and development. Examples of such long-term activities are cooperation with the company **Polpharma Biologics** Gdańsk in conducting students' master's projects in the field of medical biotechnology; for many years, under a joint agreement. IFB has been cooperating with **International Institute of Molecular and Cell Biology** in Warsaw as part of the Polish Roadmap of Research Infrastructure programme aimed at developing large scientific infrastructure for research in the field of biotechnology and cell biology.

Pomeranian Voivodship Office in Gdańsk

IFB has been cooperating with the Marshall of the Pomorskie Voivodship on regular basis for several years.

[Invited lectures in 2016-2017]

1. Marielle Afanassieff, PhD (Inserm, Universit Paris, France), *Rabbit Pluripotent Stem Cells: Interest and State of Art*
2. Prof. Robin Fahraeus (Inserm, Universit Paris, France), *Linking viral immune evasion with cell proliferation - Epstein-Barr virus encoded EBNA1*
3. Prof. Zofia Szweykowska-Kulińska (Adam Mickiewicz University in Poznań, Poland) *Splicing pre-mRNA – molecular game of Scrabble*
4. Marcin Okrój, PhD *Role of the complement system in cancer progression and therapy*
5. Danuta Gutowska-Owsiak, PhD *Filaggrin utilize actins to regulate keratinocyte differentiation and cornification during epidermal barrier formation*
6. Mieczysław (Mietek) Mazurek, PhD *Culture of Innovation; Practitioner's Perspective*
7. prof. Marta Miączyńska (International Institute of Molecular and Cell Biology in Warsaw, Poland), *Inflammatory signalling from the endocytic pathway*
8. Michał Szymański, PhD *Structural basis of DNA replication and repair in human mitochondria*
9. Marcin Dembek, PhD (Institute for Cell and Molecular Biosciences, Newcastle University, UK), *Forward genetic studies of gene essentiality and sporulation in Clostridium difficile*
10. Marta Hoffman-Sommer, PhD (Interdisciplinary Center for Mathematical and Computational Modelling, University of Warsaw, Poland, Open Science Platform Platforma Otwartej Nauki), *Open access for scientific publications and*
11. Sebastian Lewandowski, PhD (Karolinska Institute, MBB, Stockholm, Sweden) *Vascular injury accelerates the onset of ALS neurodegeneration: evidence from mouse models and patients*
12. Andrzej T. Wierzbicki PhD (University of Michigan Department of Molecular, Cellular, and Developmental Biology (MCDB), USA), *Mechanisms of RNA-directed DNA methylation*
13. Agnieszka Woźniak PhD (Leuven Cancer Institute, Belgium), *Targeted therapy in mesenchymal diseases - preclinical drug testing in vivo*
14. Magdalena Król, PhD (Warsaw University of Life Sciences, Poland), *Sex-mission in science*
15. Natasza Kosakowska-Berezecka PhD, Magdalena Żadkowska PhD (University of Gdańsk, Poland), *Gender Gap in Biotechnology*
16. Simone Ciofi (CERM, Università degli Studi di Firenze, Italy), *The unique contribution of NMR to elucidate cellular pathways*, XXIII BSS
17. Zohar Kerem (Israel Center for Nutrigenomics and Functional Foods. The Institute of Biochemistry, Food Science and Nutrition, Israel), *Using computational tools to study enzyme – substrate interactions*, XXIII BSS
18. Roland Lill (Institut für Zytobiologie am Fachbereich Medizin der Philipps-Universität Marburg, Germany), *Biogenesis of iron-sulfur proteins in eukaryotes: Mitochondria, mitosomes, mechanisms, DNA maintenance, and maladies*, XXIII BSS
19. Steven E. Lindow (University of California, Berkeley, USA), *Control of Walnut blight disease caused by the bacterium Xanthomonas arboricola pv. juglandis by exploiting insights from the epidemiology of the pathogen*, XXIII BSS
20. Steven E. Lindow (University of California, Berkeley, USA), *Biological control of Pierce's disease of grape caused by Xylella fastidiosa achieved by various strategies leading to pathogen confusion*, XXIII BSS

21. Julius Lukeš (Institute of Parasitology Biology Centre CAS, Czech Republic), *Are human intestinal eukaryotes parasites or commensals?*, XXIII BSS
22. Antonio J. Pierik (University of Kaiserslautern, Germany), *Introduction to iron-sulfur proteins: properties, structure and function*, XXIII BSS
23. Adam Schikora (Institute for Epidemiology and Pathogen Diagnostics, Julius Kühn-Institut (JKI), Federal Research Institute for Cultivated Plants, Germany), *Priming for enhanced defence as a strategy to optimize crop resistance*, XXIII BSS
24. Iris Yedidia (Agricultural Research Organization Volcani Center, Israel), *Interkingdom signaling: elucidating a mechanism by which plant derived small molecules affect bacterial communication and virulence*, XXIII BSS
25. Sophie Vaulont (INSERM, Institut Cochin, France), *Mammalian iron homeostasis: main players and mechanisms*, XXIII BSS
26. Steven E. Lindow (University of California, Berkeley, USA), *Aggregation of phyllosphere inhabitants facilitate cell-cell signaling and community assembly*, XXIII BSS
27. Zohar Kerem (Israel Center for Nutrigenomics and Functional Foods. The Institute of Biochemistry, Food Science and Nutrition, Israel), *Openness and excellence in the Mediterranean diet*, XXIII BSS
28. Steven E. Lindow (University of California, Berkeley, USA), *Biological control of fire blight disease caused by Erwinia amylovora by competitive bacteria*, XXIII BSS
29. Imrich Barak (Institute of Molecular Biology, Slovak Academy of Sciences, Bratislava, Slovakia), *Bacillus subtilis as a tool in basic science and applied research*, XXII BSS
30. Jakub Banaszek (Labsoft – Krzysztof Herman), *The use of atomic force microscopy for imaging and evaluation of the mechanical properties of biological structures*, XXII BSS
31. África González Fernández (Biomedical Research Center (CINBIO), University of Vigo, Spain), *Nanomedicine: immune system as target*, XXII BSS
32. David Lewis (Arrowhead Pharmaceuticals, USA), *Early drug discovery*, XXII BSS
33. David Lewis (Arrowhead Pharmaceuticals, USA), *Intellectual Property in Drug Development*, XXII BSS
34. David Lewis (Arrowhead Pharmaceuticals, USA), *What It's Like to Work in Biotechnology: The Evolution of One Company from a Scientist's Perspective,* XXII BSS
35. Marco Moracci (Institute of Biosciences and Bioresources of the National Research Council, Italy), *Discovery of carbohydrate active enzymes from (hyper)thermophiles: how to exploit natural diversity in biotechnology*, XXII BSS
36. Lars Renner (Leibniz Institute of Polymer Research Dresden, Germany), *Microfabrication meets microbiology – Morphology manipulation of bacterial cells*, XXII BSS
37. Rachna Sadana (University Of Houston–Downtwon, USA), *Balla Cytotoxic coscinamide analogues inhibit tubulin polymerization and cause cell cycle arrest in G2/M phase leading to apoptosis*, XXII BSS
38. Izabela Święcicka (University of Białystok, Poland), *Bacillus thuringiensis – an effective and safe biopesticide*, XXII BSS
39. Kathryn Wheeler (Literacy Network, Madison, USA), *Problem Areas in English for Polish Speakers: Articles, Prepositions, the Present Perfect Tense, and More*, XXII BSS
40. Paweł Żołnierczyk (iTech Innovations Ltd, United Kingdom), *Ballance between blue–sky and applied research within the research group*, XXII BSS

[Teaching Activities and Programmes]

IFB is the leading Faculty in teaching biotechnology, as the Polish Accreditation Committee awarded IFB with a distinction for the quality of teaching, and the Ministry of Science and Higher Education granted the specialty of BIOTECHNOLOGY at IFB the title of The Best Major. For years, IFB has been located on the second top position on the PERSPEKTYWY ranking – 'Fields of Study Ranking – Biotechnology'. The Central Council of Science and Higher Education recognized the set of learning outcomes prepared by the faculty for the specialty of Bio-

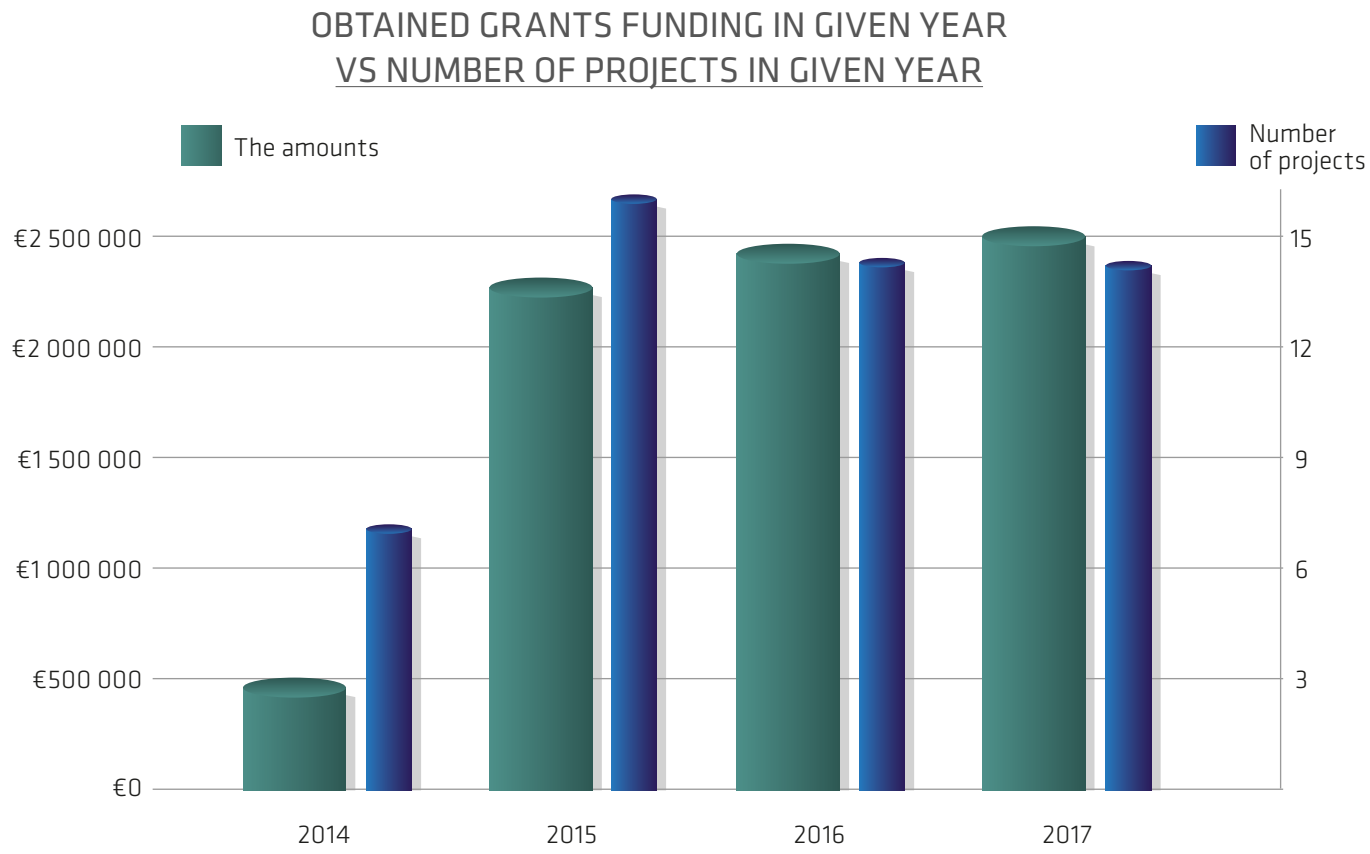


Figure 3. Obtained grants funding

technology as a model set. These are the unique such distinctions in Poland granted in biological sciences. IFB runs BSc, MSc and PhD studies, educating over 360 students, including more than 80 doctoral students. The research activity conducted at IFB is interwoven with a teaching programme that includes an active involvement of students in research. Thanks to the intercollegiate character of the Faculty, all students, independently of the degree they study, use the research and teaching infrastructure offered by both home universities, the University of Gdańsk and the Medical University of Gdańsk. Both the research and the educational programmes at IFB have an interdisciplinary character and are based on international cooperation. Our students may conduct their Master projects and carry out research internships in foreign institutions and in collaboration with the industry. Classes of the second-cycle studies are conducted in English. At present, BSc and MSc studies are run in cooperation with the University of Houston Downtown, Virginia State University in the USA. While designing teaching programmes, we took advantage of our foreign partners' experience and implemented international standards.

Yearly, the Consulting Board at the IFB, composed of representatives of biotech business and industry sector, and the teachers of the high schools, actively supports the process of development of our study programmes.

Each year our teachers are awarded with distinction for the best teacher of the University of Gdańsk, and in 2016 dr Wioletta Żmudzińska obtained 'The Teacher of the Year Mrongowiusz Prize' for the best teacher at UG given by the Students' Committee in recognition of the didactic achievements.

In last year we reached the highest budgetary subvention of 150 000 EUR from the Polish Ministry of Science and Higher Education for our basic activity. We substantially increased subvention for teaching activity (Fig. 3).

We noticed continuously increased of number of foreign students studying at IFB and conducting internships within Erasmus+ Programme. Students from Germany, Italy, Spain, Belgium, Lithuania, Turkey, Belarus, Russia have been successfully studying at IFB.

IFB runs doctoral studies in the frame of the following programmes:

- Doctoral Studies in Chemistry and Biochemistry in cooperation with the Faculty of Chemistry of UG;
- PhD studies 'Life Sciences and Mathematics Interdisciplinary Doctoral Studies (LiSMIDoS).

Annually, we organize a PhD Programme Reporting Session in form of an open conference, where PhD students present the progress of their research projects.

An integral element of teaching and developing young professionals is the organisation of Biotechnology Summer Schools, held annually for 24 years.

[Science and Society at IFB]

At IFB we disseminate knowledge and popularise scientific achievements in biotechnology by organizing events for the Pomeranian community. Every year, we attract a lot of attention among pupils mainly from junior high and high schools. During last two years, we have organized numerous conferences, scientific workshops, doors open days, science events, lectures and classes for children and youth to bring closer important scientific issues. It is important to stress that the researchers, Ph.D. students and students were involved in the organization of these events.

During the workshops the scientific experiments and issues related to science were presented in a very attractive way. The laboratory doors were opened for children, adolescents and the older people, who could visit our well-equipped scientific labs and lecture halls and to gain the knowledge about the achievements of modern biotechnology and research carried out at the faculty. They could see how the scientific work conducted at our Faculty can be used for improving our health and the quality of life.

After moving to the Faculty new building, we organised the Family Day – the Doors Open Day for the Families and Friends of our staff, PhD students and students. During this day, the families and friends visited our new laboratories and got familiar directly with our everyday work environment.

IFB is a co-founder of the educational initiative InnovaBio Pomorze, in which the students and pupils of the high schools carry out the projects commissioned by entrepreneurs. Also, during last two years, we supported the participation of the students in this initiative and provided the mentorship by our staff.



For years, we have collaborated with the Academy of Fine Arts in Gdańsk. In 2016 we hosted the exposition of the BioArt under curator of prof. Grzegorz Klaman, including the Symbiosity of Creation, the artificial, laboratory anthill of leafcutter ants created by Elvin Falmingo (Janusz Czarnecki). This exhibition was enthusiastically welcomed by the public. We also participated in the panel discussion Art and Creativity in The History of Artificial Intelligence and Synthetic Biology organized by The ŁAŹNIA Center for Contemporary Art in Gdańsk.

The events that took place at the Intercollegiate Faculty of Biotechnology include, among others:

- **Biotech Solution for Health and Environment: MOBI4Health Conference & New IFB Building Opening**, April 2016
- **"Learn more about biotechnology"** EU Open days for schools May 2016
- **Horizon 2020: What every scientist should know?** – the workshop, November 2016
- **Smart Specializations, thematic meeting**, November 2016
- **The Night of the Biologists**, January 2017
- **Academia Fairs**, March 2016 and 2017 – the largest educational fair in Pomerania region
- **IFB Doors Open Day**, March 2017
- **Open science: opportunities - challenges – directions (STARBIOS2)**, April 2017
- **Baltic Science Festival**, May 2017
- **Valuation of patents in technology transfer process (STARBIOS2)**, May 2017
- **"Strategic embedding of public engagement into strategy of an institution: the Toolkit on Public Engagement with Science" (STARBIOS2)**, September 2017
- **Women in science (STARBIOS2)**, December 2017
- **Workshops for schools:**
  - DNA - Encyclopedia of Life, April 2016
  - "Be a scientist" workshops addressed to invited students from high school organized by students of theIntercollegiate Faculty of Biotechnology UG and MUG, April 2016
  - Scientific picnics, "University - I like it" April and May 2016 (Kościerzyna, Bytów, Chojnice, Ostróda)
  - Practical workshops on biotechnology. June 2016
  - Kociewski Festival of Science, Starogard Gdański, October 2016
  - Debate on GMO plants "Learning through fun as a tool to learn about myths and facts about GMOs!", June 2016 and May 2017

Since May 2016 IFB has been implementing a pilot project **STARBIOS2: Structural Transformation to Attain Responsible BIOsciences** under funding of HORIZON 2020 EU Programme. The objective of the project's Action Plan is to provide a set of actions for facilitating structural change in the area of RRI at the University of Gdańsk (UG). To achieve this, actions from the 5 key areas of RRI, i.e. societal engagement, gender, education, open access, ethics, have been planned for the time up to April 2020. Sustainability of actions will be based on their impact also beyond the project's lifetime and has been considered in planning as far as possible. The content of the project's Action Plan targets IFB needs, nevertheless, in cases when overall university-wide regulations will be affected, effects of implemented actions are expected to affect also other UG faculties, especially the most related from the topic area of bioscience, i.e. Faculty of Biology (FB) and Faculty of Chemistry and Environmental Protection (FC).

A comprehensive set of actions implemented so far comprise :

- In-depth state-of-the-art analyses in the areas of Societal Engagement and Gender have been conducted. Their results were summarized in the reports "Towards a Better Understanding of Bioscience" and "Gender Gap in Biotechnology" that will serve as a source of information for further actions at IFB;
- Several events have been organized in order to raise awareness and gain more knowledge about RRI related issues including: seminars (Open Access and Copyrights) Invited lectures with panel discussion (eg. Open Science: Opportunities, Challenges, Directions; IP Valuation in the context of responsible research; Women in Science), workshops for IFB researchers (Diversity management)

- Exchange visit to top European TTO (Oxford University Innovations) and resulting hands-on experience in technology transfer which may be implemented at TTO UG
- 24th Biotechnology Summer School dedicated to RRI in September 2018. During this event representatives of bioscience institutions are asked to share their view how the responsibility of science affects their work in their bioscience research. Whereas partners from social science field are asked to give targeted support as best to match the input of bioscience speakers and provide background and further development incentives on selected specific keys of RRI.

STARBIOS2

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 709517.

[Biotechnology Summer Schools]

The main purpose of the Summer School project is to develop so called, soft skills, such as teamworking, techniques of presentation and autopresentation, time management.

Brief history of Biotechnology Summer Schools

Biotechnology Summer Schools are organized annually since 1994. The idea of Biotechnology Summer School (BSS) came from Professor Anna J. Podhajska, who implied that students and young scientists should actively participate in obtaining knowledge and establishing contacts with scientists from all over the world, not only in formal conditions but also outside the University. That is why the participants of BSS are not only biotechnology students but also students in related biological fields from Poland and from abroad, young scientists and even advanced pupils interested in this topic.

Topics of BSS vary from year to year. Prof. Anna Podhajska gained many people's support over her initiative. The number of sponsors increased every year and thanks to all these companies and institutions the organization of Biotechnology Summer School has been possible.

Biotechnology Summer Schools were honored with the presence of many eminent scientists such as professors: Ewa and Ernest Bartnik, Stanisław Bielecki, Klaus Halhlbrock, Waleria Hryniewicz, Robert Huber (Nobel Prize winner in Chemistry in 1988), Berndt Jastorf, Adam Jaworski, Roman

Kaliszan, Władysław Kunicki Goldfinger, Andrzej Legocki, Janusz Limon, Mirosław Matuszyński, Jerzy Paszkowski, Andrzej Płucienniczak, Richard P. Sinden, Piotr Stępien, Wadaw Szybalski, Tomasz Twardowski, Jacques H. Weil, Robert Wells, Brigitte Wittman-Liebold, Maciej Zenktler, Maciej Żylicz.

No less important than learning is having fun. Many entertaining activities for Summer Schools are always planned. A fancy-dress party, a bonfire with singing, field games, sports, playing on words, integrational workshops are the part of every School. We also organize some visits in

local, historical places and regional trips. International experience enables to gain a deeper understanding of another culture, make lifelong friends from a wide variety of backgrounds and benefit from globally-renowned academic excellence.

About XXII Biotechnology Summer School (2016)

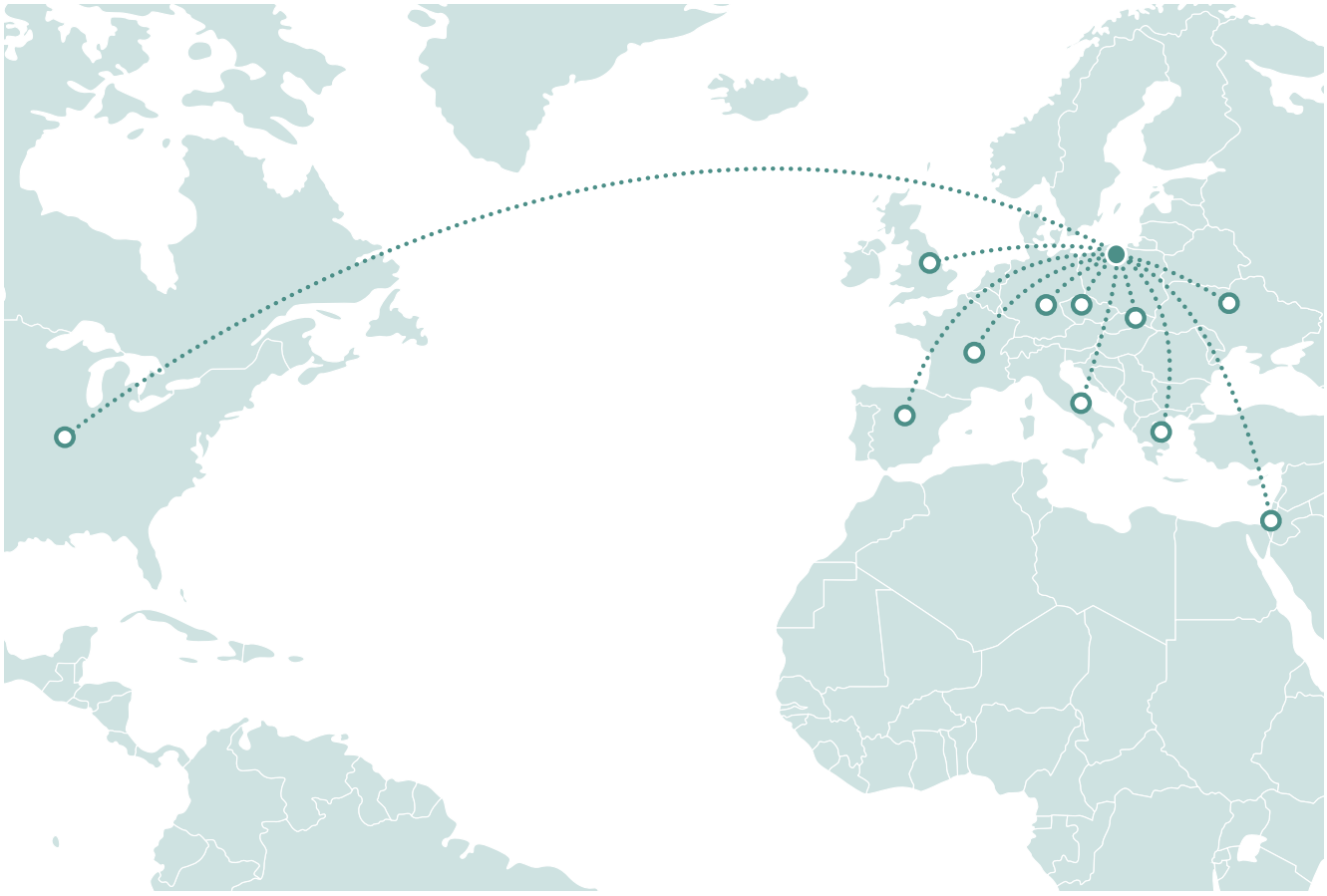
The theme of the XXIII Biotechnology Summer School was: Biotechnologists love every bit of life. The event was organised from 5th to 9th July 2016 in Conference Palace "Osada Danków" among the woods in the charming village near the Elblag Canal. That edition was organized in cooperation with **MOBI4Health project – Centre of**

Molecular Biotechnology for Healthy Life – Biotech solutions bringing health to living organisms and environment supported by mass spec-focused research platform, carried out at IFB UG-MUG. The XXII BSS promoting knowledge about the newest biotechnological achievements as an event integrating young scientists with experience lecturers, was traditionally enriched by additional events such as trip-cruise "Take the boat Through Grass" or field game for all participants. Among invited speakers we hosted: dr Paweł Żołnierkiewicz (UK), dr hab. Izabela Święcicka (Poland), dr Imrich Barak (Slovakia), dr Marco Moracci (Italy), prof. Africa Gonzalez – Fernandez (Spain), prof. Douglas B. Weibel (USA), dr Rachna Sadana (USA), prof. David L. Lewis (USA), dr Kathryn T. Wheeler (USA). Participants represent nearly every Universities in Poland (University of Adam Mickiewicz, Jagiellonian University, Marie Skłodowska-Curie University, Nicolas Copernicus University, Silesian University of Technology, Wrocław University, Wrocław University of Technology, Wrocław Medical University, Warsaw University and University of Gdańsk) research institute's (Nofer Institute of Occupational Medicine) and university from abroad (University of Houston-Downtown, USA).

About XXIII Biotechnology Summer School (2017)

The topic of the XXIII Biotechnology Summer School was *Iron-sulfur clasters* and *bacteriophage as biocontrol agents*. The event took place from 4th to 8th July 2017 in Adler Kaszuby – Medical SPA.

We wanted to improve competences of young scientists in the area of science communication, therefore the participants took part in the English language workshop-course. During that edition we prepared additional activities for our participants like: integration field game, trip to The Centre for Education and Regional Promotion in Szymbark (Kashubia Region) and traditional fancy dress party! The audience of XXIII BSS consisted of students and young scientists interested in experimental sciences, life sciences, especially in biotechnology. The Summer School supplemented existing knowledge with valuable practical and applied training, and allowed to discuss research in depth with the academics who are leading experts in their area.



BSS Participants from Poland and abroad






Among invited speakers we hosted: Charles Cantor (USA), Zbigniew Brzózka (Poland), Rafael Giraldo (Spain), Florian Hollfelder (UK), Takashi Kuwana (Poland), Ezio Ricca (Italy), Paul Williams (UK).

Participants represent nearly every Universities in Poland (Charles University, Jagiellonian University, Medical University of Łódź, Medical University of Silesia in Katowice, Silesian University of Technology, University of Agriculture in Kraków, University of Life Sciences in Lublin, University of Łódź, University of Warsaw, Warsaw University of Life Sciences, Warsaw University of Technology, West Pomeranian University of Technology Szczecin and University of Gdańsk) research Institute's (Institute of Cell Biology NAS of Ukraine), and university from abroad (Aristotle University of Thessaloniki, Greece; Rhine-Waal University of Applied Sciences, Germany).

XXIV Biotechnology Summer School (2018)

The XXIV Biotechnology Summer School in 2018 will be organised under the umbrella of the H2020 Project STARBIOS2: Structural Transformation to Attain Responsible Biosciences and will be dedicated to Responsible Research and Innovation issues.

RESEARCH GROUP PROFILES

[Laboratory of Biologically Active Compounds]

Aleksandra Królicka, PhD

She graduated from Academy of Agriculture and Forestry in Olsztyn in 1994, received PhD in biology (1999) at University of Gdansk and habilitation in biotechnology sciences (2011) at Wrocław University of Environmental and Life Sciences. Group leader since 2012. Author of 59 peer-reviewed publications and 3 course books, supervisor of 3 ongoing PhD's.

Research group

PhD Robert Czajkowski
PhD students:
Rafał Banasiuk
Marta Krychowiak
Angelika Michalak
Jakub Fikowicz-Krośko

Research conducted by the Laboratory of Biologically Active Compounds includes topics relating to the production of biologically active compounds in plant *in vitro* cultures and the use of lytic bacteriophages for biological control applications and focuses on the discovery and study of natural and synthetic antibacterial and antifungal compounds (synthetic peptides, nanoparticles of silver and other metals) as well as on isolation and characterization of lytic bacteriophages to be used in medical and agricultural applications.

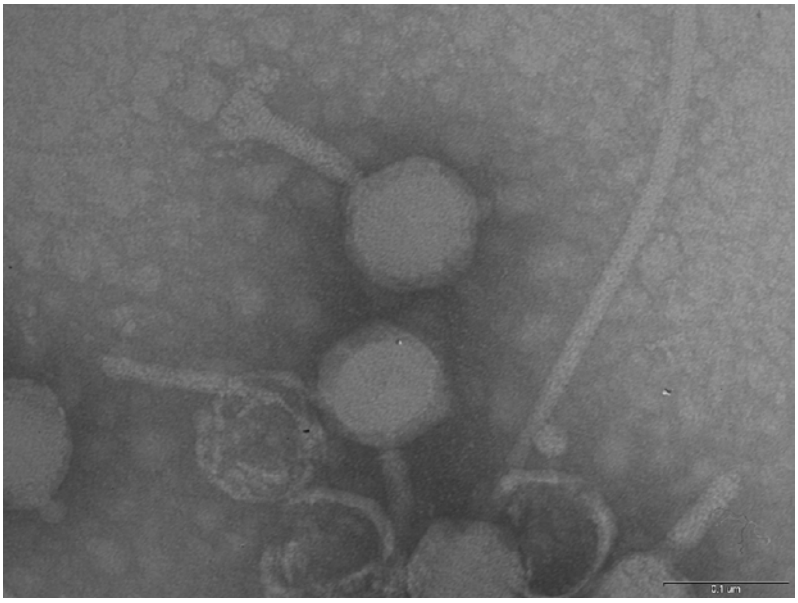
Introduction of antibiotics to medicine has nearly entirely eradicated multiple species of pathogenic microorganisms. However, widespread misuse of these drugs led to the emergence of multiple drug-resistant bacterial species. Considerable problems regarding antibiotic resistance promote the development of novel antibacterial drugs. Search for more effective ways to treat multiple drug-resistant nosocomial infections stimulates the investigation of natural compounds as alternative treatment.

An estimated 50 000 biologically active compounds are derived from plants. They are termed secondary metabolites, as they are not involved in the basic metabolism of plants but are developed as a result of specialised metabolic pathways. Plants have been a source of pharmaceutical compounds since the 7th century B.C. In the second half of the 19th century the interest in phytotherapy decreased and herbs were replaced with synthetic pharmaceuticals. Yet, in the age of chemotherapy a new threat has appeared. The number of drug side effects has increased; moreover not all synthetic drugs are as effective as natural ones. This has led to an increased interest in phytopharmaceuticals.

Similarly, since the early thirties of XX century, bacteriophages were widely used in Eastern Europe in the control and prevention of bacterial infections in humans, animals and (experimentally) plants. The discovery of the first natural antibiotics prevented the development of therapies based on the use of phages in most Western European countries, but did not stop them completely. Only recently, in Western Europe bacteriophages have been widely used in the control of bacterial infections transmitted through water and in the food industry and also to control hospital drug-resistant bacteria.

Our interests include the use of secondary metabolites derived from *in vitro* and *in vivo* cultured plant tissues against bacterial and fungal pathogens of humans and plants, as well as we use lytic bacteriophages to control human, animal and plant pathogens. Moreover, we evaluate activity of lytic bacteriophages and other active compounds to find synergy during application.

In order to increase the content of biologically active secondary metabolites we use abiotic and biotic elicitors, precursors of metabolic pathways and transformation of *Agrobacterium rhizogenes*. The use of biotic and abiotic elicitors increase the synthesis of pharmacologically active compounds (bactericidal and cytotoxic activity). Elicitors play a significant role in the production of secondary metabolites. They induce defense responses in plants, which leads to the accumulation of secondary metabolites. In some cases compounds not synthesized normally by plants in their natural environment are produced upon elicitation.



Scientific collaboration

Université de Lorraine France Laboratoire Agronomie et Environnement Nancy-Colmar, (prof. Frederic Bourgaud); **Medical University of Gdansk**, Department of Pharmacognosy, Poland (prof. Mirosława Krauze-Baranowska and prof. Maria Łuczkiewicz); **Medical University of Lodz**, Department of Biology and Pharmaceutical Botany, Poland (prof. Halina Wysokińska); **AGH-University of Science and Technology**, Poland (Magdalena Ziabka, PhD); **University of California-Berkeley, Berkeley, USA** (Prof. Steven Lindow), Wageningen **University and Research Center**, Wageningen, Holandia (dr. Jan M. van der Wolf).

In order to increase the antimicrobial and antifungal effect of the plant extracts, they are tested in combination with other active agents (synthetic peptides, nanoparticles of silver and other metals). Nowadays the number of chemotherapy treatments based on the multidrug concept continuously increases. The basis of effective multidrug chemotherapy is the multi-target action of several drugs leading to the same therapeutic effect while significantly lowering the production cost. Synergistic combinations of drugs may be extremely effective against antibiotic resistant microorganisms. The mechanism of action of plant extracts, nanoparticles and synthetic peptides on bactera is another important part of our current research.

Ongoing research aims at elucidating the mechanisms determining antimicrobial and antifungal activity as well as developing and improving the process of nanoparticle production. Likewise, ongoing research concern molecular basis of lytic bacteriophages and plant pathogenic bacteria interaction and the use of phages and antagonistic bacteria in biological control of Pectobacterium spp. and Dickeya spp. bacteria in potato and other crops.

Recent publications

- Banasiuk R, Krychowiak M, Swigon D, Tomaszewicz W, Michalak A, Chylewska A, Ziabka M, Lapinski M, Koscielska B, Narajczyk M, Krolicka A. 2017. Carnivorous plants used for green synthesis of silver nanoparticles with broad-spectrum antimicrobial activity. Arabian J. Chem. doi. org/10.1016/j.arabjc.2017.11.013.
- Ziabka M, Dziadek M, Menaszek E, Banasiuk R, Królicka A. 2017. Middle ear prosthesis with bactericidal efficacy – in vitro investigation. Molecules 22: 1681.
- Miklaszewska M, Banaś A, Królicka A. 2017. Metabolic engineering of fatty alcohol production in transgenic hairy roots of Crambe abyssinica. Biotechnol. Bioeng. 114: 1277 – 1282.
- Ogryzek M, Chylewska A, Królicka A, Banasiuk R, Turecka K, Lesiak D, Nidzworski D, Makowski M. 2016. Coordination chemistry of pyrazine derivatives analogues of PZA: design, synthesis, characterization and biological activity. RSC Advances 6: 52009 – 52025.
- Banasiuk R, Frackowiak JE, Krychowiak M, Matuszewska M, Kawiak A, Ziabka M, Lendzion- Bielun Z, Narajczyk M, Krolicka A. 2016. Synthesis of antimicrobial silver nanoparticles through a photomediated reaction in an aqueous environment. Int. J. Nanomedicine, 11: 315 - 324.

Patents

- Patent nr P.405473: Sposób oczyszczania z chlorofili ekstraktów roślinnych zawierających metabolity wtórne. Banasiuk R, Michalak A, Krychowiak M, Królicka A, 30.09.2013.

[Laboratory of Biological Plant Protection]

Sylwia Jafra, PhD

She received her PhD in biological sciences (1999) at the University of Gdansk. She carried out several lab trainings in INSA de Lyon, Lyon, France (1996-1998). She accomplished her postdoctoral training at Plant Research International, Wageningen, The Netherlands (2001-2003). She got habilitation in biochemistry (2011). She has been a Vice Dean for students' and educational affairs f(2012-2016) and continue for the second cadency (2016-2020). She is a member of Marie Curie Fellows Association.

Research group

Dorota Krzyżanowska, PhD
Magdalena Rajewska, PhD
Adam Ossowicki, PhD student
Magdalena Jabłońska, PhD student
Tomasz Maciąg, PhD student
Marta Matuszewska, PhD student

Research interests

Our research focuses on the understanding of the plant-bacteria interaction occurring in the plant rhizosphere with particular emphasis on antagonistic activity of plant beneficial bacteria. Our research goals are to understand the molecular mechanisms determining antimicrobial activity of soil bacteria belonging to, among others, *Pseudomonas*, *Ochrobactrum* and *Bacillus* genera. Conducted research aims to identify the genes responsible for the synthesis and regulation of the production of antimicrobials in the selected environmental bacterial strains, as well as to purify and identify chemical structures of the antimicrobial compounds. Furthermore, we are also interested in bacterial cell-to-cell communication (quorum sensing, QS), a mechanism of regulation of the gene expression involved in the production of virulence factors by many (plant) pathogenic bacteria. The particular emphasis is put on the silencing of the quorum sensing (quorum quenching, QQ) via enzymatic disruption of the bacterial signal molecules by enzymes produced by soil bacteria and the ecological role of QQ in the bacteria possessing the ability to inactivate signal molecules. Recently we have also undertaken the research concerning the molecular mechanisms important for biofilm formation on biotic and abiotic surfaces by the plant beneficial *Pseudomonas*.

Plant rhizosphere (a narrow zone of root adhering soil) is a "hot spot "of microbial activity assuring rich nutrient environment for the growth of microorganisms. It is also characterized by strong intra- and interspecies interactions, where the microorganisms compete for nutrients and ecological niche. Knowledge concerning successful competitive strategies of microbes is essential to understand the dynamics and diversity of microbial communities of rhizosphere. Such knowledge is not only of fundamental scientific interest, but can also be used to improve the efficiency of biocontrol measures of plant pathogens. The competitive mechanisms employed by the plant-beneficial bacteria include better attachment to the roots' surface, effective catabolism of the available nutrients, iron sequestration and successful competition with microbial co-habitants. An important strategy of rhizosphere bacteria to compete with other microbes is the production of growth-suppressing secondary metabolites such as antibiotics, toxins, biosurfactants and volatile organic compounds (VOCs).

Our major research topic concerns the better understanding of the mechanisms involved in plant-microbe and microbe-microbes interactions. *Pseudomonas donghuensis* strain P482 is a tomato rhizosphere isolate, that has been studied in terms of its antagonism towards bacterial (*Pseudomonas syringae*, *Dickeya* spp. *Pectobacterium* spp.), fungal (*Rhizoctonia solani*, *Fusarium culmorum*) and oomycete (*Phytium ultimum*) plant pathogens. We verified that the antagonism of P482 towards bacterial and fungal plant pathogens is based on a new antagonistic activity, different from those previously described for other Pseudomonas. The in silico study of P482 genome sequence and site-directed mutagenesis unveiled the genes curtail for the antimicrobial activity of this strain, and determined that they are a component of the unique accessory genome of this strain. Our study showed that P482 produces a set of VOCs with the strong antifungal activity towards fungal plant pathogens and that the antimicrobial activity remains under the control of GacA/GacS regulatory system (Fig. 1).

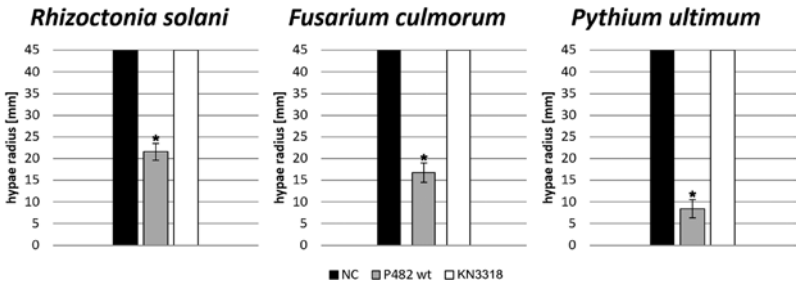


Fig. 1. Average hyphae radius after 4 days (Rhizoctonia solani), 7 days (Fusarium cilmorum) and 5 days (Pythium ultimum) of incubation under influence of volatiles emitted by P. donghuensis (P482 wt), the gacA- mutant (KN3318) and non-treated control (NC). Significant difference between sample and control are indicated by asterisk (one-way ANOVA), error bars represents standard deviation of the mean.

The very recent findings showed that the production of the antimicrobials of P482 is also determined by the carbon source and the iron availability. P482 is able to colonize the roots of tomato (a host plant), maize and potato following artificial plant bacterizaition. Recently, we have discovered that some of the selected genes involved in the antibacterial activity of P482 are also essential for colonization of the root of maize plant by this strain. However, the mechanisms underlying the molecular basis of P482 interaction with roots of various plants have not been elucidated. The questions what genes of P482 are essential for the survival and adaption of this bacterium to the plant rhizosphere remains open. Hence, we have extended our investigation to identification of the genes of P482 specifically induced during root and stem colonization. We also plan to identify the genes of tomato and maize plants, induced in response to bacterization by P482.

In another project, we focus on a potato rhizosphere isolate *Ochrobactrum* sp. strain A44. This bacterium was previously studied by our group in terms of its ability to interfere in quorum sensing mechanism of plant pathogenic bacterium *Pectobacterium cartovorum* and to attenuate plant tissue maceration caused by this pathogen due to the quorum quenching mechanism. *Ochrobactrum* sp. A44 is able to degrade N-acyl homoserine lactones, the signal molecules of many Gram-negative bacteria including P. *carotovorum*, due to the activity of the AiiO hydrolase. Our current goal is to determine the endogenous role of the AiiO-hydrolase from *Ochrobactrum* sp. A44 in its metabolism and the ecological fitness.

Recent publications

- Krzyżanowska D.M., Ossowicki A., Rajewska M., Maciąg T., Jabłońska M., Obuchowski M., Heeb S., and Jafra S. 2016. When genome-based approach meets the 'old but good': revealing genes involved in the antibacterial activity of Pseudomonas sp. P482 against the soft rot pathogens. Front. Microbiol. 7, 782.
- Adam E., Groenenboom A. E., Kurm V., Rajewska M., Schmidt R., Tyc O., Weidner S., Berg G., de Boer W., and Falcão Salles J. 2016. Controlling the Microbiome: Microhabitat Adjustments for Successful Biocontrol Strategies in Soil and Human Gut. Front. Microbiol. 7: 1079
- Czajkowski R., Kaczyńska N., Jafra S., Narajczyk M., Lojkowska E. 2017. Temperature-responsive genetic loci in pectinolytic plant pathogenic Dickeya solani. Plant Pathol. 66, 584-594
- Ossowicki A., Jafra S., Garbeva P. 2017. The antimicrobial volatile power of the rhizospheric isolate Pseudomonas donghuensis P482. PLoS ONE 12(3): e0174362, https://doi.org/10.1371/journal.pone.0174362.

Scientific collaboration

- University of Nottingham, Centre for Biomolecular Science, Nottingham, UK (Prof. Paul Williams)
- Nederlands Instituut voor Ecologie (NIOO-KNAW), Wageningen, The Netherlands (Dr Paolina Garbeva)
- Institute for Sustainable Plant Protection, National research Council of Italy, Portici, Italy (Dr Francesco Vinale)
- Wagenignen UR, Plant Research International, Wageningen, The Netherlands (Dr Jan van der Wolf)
- ARO, The Volcani Center, Institute of Plant Sciences, Ornamental Plants and Agricultural Biotechnology Dep., Bet-Dagan, Israel (Dr Iris Yedidia)

[Protection Laboratory of Biomolecular Systems Simulations]

Rajmund Kaźmierkiewicz, PhD

(was born 1970). He obtained his master degree in chemistry in 1992 at the Chemistry Department of Gdańsk University, where he was employed until 2007. He defended his PhD thesis in 1997. After postdoctoral fellowship (1997-1998) at the Department of Chemistry, University of Arizona, Tucson, USA he visited several times (overall 3 years) the Department of Chemistry and Chemical Biology, Cornell University, USA. Since 2007 is a team leader of Biomolecular Systems Simulations Research Group.

Research group

4 MSc students, 6 PhD students:
Kamil Krystian Belau,
Mateusz Pikora,
Marcin Augustyniak,
Inga Jamrożek,
Paweł Przygocki,
Monika Romanik-Błońska.

Scientific collaboration

- Prof. Harold A. Scheraga from the Department of Chemistry and Chemical Biology, Cornell University, USA.;
- Prof. Baldomero M. Olivera from the Department of Biology, University of Utah and Prof. Grzegorz Bulaj from the Department of Medicinal Chemistry University of Utah, USA;
- Prof. Ulrich H. E. Hansmann from the John von Neumann Institute for Computing, Germany. The past collaboration with prof. Victor Hruby from Department of Chemistry and Biochemistry University of Arizona, Tucson, USA.

PhD Thesis

Paweł Gruszczyński, „The use of molecular modeling methods in conformational analysis and the investigations of protein-ligand interactions using the serine-threonine PrkC kinase complexes with ATP and complexes of sodium ion channels with μ-conopeptides as the examples", 2010.

Roch Jędrzejewski, „Theoretical modeling of the tertiary structures and complexes of proteins from the Ankyrin, MarR and GNAT families, using the molecular dynamics simulations and the functional analysis", 2011.

Dominika Jankowska, „The application of computational methods in research on the bacterial proteins TraR and AiiO", 2016.

Tomasz Makarewicz, "Creation and application of software, with graphical user interface, that allows users to carry out, analyze and visualize molecular dynamics simulations." ,2018

The tools used in our research activities are all contemporary molecular modeling techniques including, but not limited to, quantum *ab-initio* methods, semi-empirical methods, empirical – molecular mechanics (classical force fields methods), molecular dynamics simulations, Monte-Carlo methods, calculations taking into consideration the free energy changes and the influence of solvent. The computers used in research include five supercomputers placed near the beginning of top500 list including the second fastest computer in EU which is IBM Blue Gene located in Forschungszentrum Juelich, Germany.

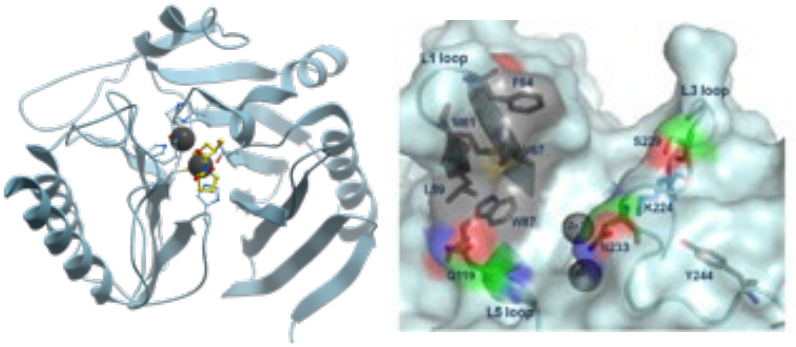
Each of our computer modeling projects takes into consideration the complete environment with the presence of all molecules, as they appear in the living organisms. We are engaged in a couple of state-of-the-art research activities, these are:

Development of the new method of the reconstruction of full-atom protein structure from the coarse-grained protein structure representation or just C^{∂}-trace. The method consists of the Monte Carlo search of global minimum of orientation of the peptide group dipoles. The function minimized is the total energy of interaction of dipoles.

Simulations of folding pathways of quadruplex structures of DNA molecules. We investigate all possible pathways of a series of the DNA quadruplex structures reported so-far in the PDB database. The DNA quadruplex structures are simple models of human telomere DNA fragments. We obtain the quadruplex structure formation pathways and stability of non-B DNA.

Molecular docking studies including virtual screening. The method treats molecular complexes as a pair of objects. The ligand molecule is flexible and its conformation is accommodated to the binding site of the receptor using genetic algorithm minimization in the simplified force field.

Molecular protein-protein docking studies. This project is in accord with current trends as "blind" protein-protein docking studies are the subject of another series of experiments termed the "communitywide experiment on the comparative evaluation of protein-protein docking for structure prediction", in short - CAPRI. This project involves molecular dynamics simulation of the catalytic domain of the serine – threonine PrkC kinase and its complexes with ATP derivatives. The PrkC is able to



The structure of NDM-1/L-captopril complex (panel A). The important residues involved in substrate recognition and specificity of NDM-1. The important residues are shown as gray, green, and blue sticks (panel B)

trans autophosphorylate the second molecule of this enzyme, therefore we investigate also the possible structures of the PrkC dimers.

Theoretical investigation on the forced dissociation of NDM-1 complex with L-captopril after the separation of the ligand using the „Steered Molecular Dynamics" method.

Computer simulations of possible ligand escape pathways. There are quite a few known protein-ligand complexes. The still unsolved problem is how they are formed. Currently it is possible only to simulate realistic physics-based process of dissociating ligand from the complex or simulations of so-called "escape pathways". For that purpose we use the computer modeling technique called Random Acceleration Molecular Dynamics.

The molecular modeling of the TraR protein and autoinducer molecules involved in quorum sensing mechanism. Dominika has modeled TraR/DNA complexes with N-acyl-L homoserine lactones: OOHL, OHL, HHL, OHHL and inhibitors: patulin, droseron, plumbagin and 3-chloroplumbagin for the first time, using Autodock and molecular dynamics in the AMBER empirical force field.

The QM/MM studies on the possible mechanism of action of AiiO enzyme interacting with the N-acyl-L homoserine lactones. There are contradicting literature reports regarding the substrates degradation pathways. They can be verified using the QM/MM simulations.

Future plans

Prof Kaźmierkiewicz's team plans to predict the molecular docking pathways in the homoserine/TraR complex using Random Acceleration Molecular Dynamics method. Another subject of future research is to implement molecular dynamics algorithm in torsional space into the ECEPP empirical force field. One of subjects involves computer simulations of self-assembly process of protein capsids of viruses. It is possible currently with the exception that one needs to design coarse-grained protein models and evaluate protein-protein motions using the simplified empirical force field.

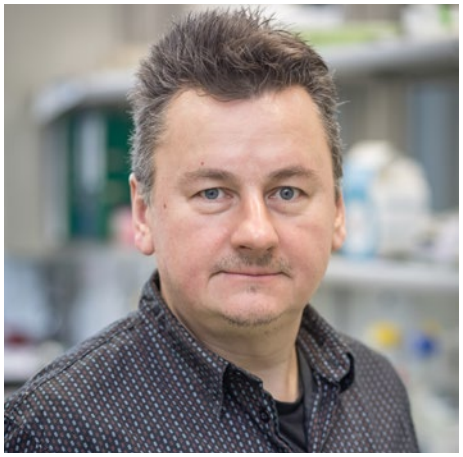
Recent publications

- Kossakowska-Zwierucho M, Kaźmierkiewicz R, Bielawski KP, Nakonieczna J., "Factors Determining Staphylococcus aureus Susceptibility to Photoantimicrobial Chemotherapy: RsbU", Front Microbiol. 2016 Jul 19;7:1141
- Makarewicz T, Kaźmierkiewicz R., "Improvements in GROMACS plugin for PyMOL including implicit solvent simulations and displaying results of PCA analysis", J Mol Model. 2016 May;22(5):109.
- Banecka-Majkutewicz Z., Kadziński L., Grabowski M., Bloch S., Kaźmierkiewicz R., Jakóbkiewicz-Banecka J., Gabig-Cimińska M., Węgrzyn G., Węgrzyn A., Banecki B. "Evidence for interactions between homocysteine and genistein: insights into stroke risk and potential treatment", Metab Brain Dis. 2017 Dec;32(6):1855-1860.
- Borowik A, Prylutskyy Y, Kawelski Ł, Kyzyma O, Bulavin L, Ivankov O, Cherepanov V, Wyrzykowski D, Kaźmierkiewicz R, Gołuński G, Woziwodzka A, Evstigneev M, Ritter U, Piosik J. „Does C60 fullerene act as a transporter of small aromatic molecules? "Colloids Surf B Biointerfaces. 2018 Apr 1;164:134-143.

PhD Thesis

- Paweł Gruszczyński, „The use of molecular modeling methods in conformational analysis and the investigations of protein-ligand interactions using the serine-threonine PrkC kinase complexes with ATP and complexes of sodium ion channels with μ-conopeptides as the examples", 2010.
- Roch Jędrzejewski, „Theoretical modeling of the tertiary structures and complexes of proteins from the Ankyrin, MarR and GNAT families, using the molecular dynamics simulations and the functional analysis", 2011.
- Dominika Jankowska, „The application of computational methods in research on the bacterial proteins TraR and AiiO", 2016.
- Tomasz Makarewicz, "Creation and application of software, with graphical user interface, that allows users to carry out, analyze and visualize molecular dynamics simulations." ,2018

[Laboratory of Biophysics]



Jacek Piosik, PhD

He graduated (1994), received PhD (1999) and habilitation (2011) at University of Gdansk in biological sciences. In 2012 he was appointed associate professor at the University of Gdansk.

Research group

Anna Woziwodzka, PhD,
Agnieszka Borowik, PhD student
Kamila Butowska, PhD student
Grzegorz Gołuński, PhD student

PhD Thesis

- Anna Woziwodzka: „Stacking interactions: the role of caffeine and other methylxanthines in modulation of heterocyclic aromatic amines activity", 16.05.2014

Laboratory of Biophysics conducts research on biologically active low molecular weight compounds, such as anticancer drugs, environmental mutagens and carcinogens, toxins, substances with chemopreventive properties, and nanoparticles. The main objectives of our research are to describe the mechanisms of action of a wide variety of toxic substances, to search for protective compounds and to reveal their mechanisms of action, to develop new effective methods to modulate the activity of drugs with particular emphasis on drugs used in anticancer therapy and antibiotics.

Our recent studies focused on examination of possible direct interactions of small biologically active compounds with commonly used antitumor drugs and antibiotics.

Pentoxifylline as a modulator of anticancer drug doxorubicin: reduction of doxorubicin DNA binding and alleviation of its biological effects

Doxorubicin (DOX) – anthracycline antibiotic – is widely used for treatment of numerous cancer types, such as bladder, prostate or breast cancers, and many others. DOX has numerous systemic adverse effects including cardiomyopathy, hematologic disorders, bone marrow suppression as well as toxic effects at injection sites, such as tissue necrosis or veins inflammation. Numerous reports indicate possibility of DOX activity modulation as well as side-effects reduction by drug administration with other biologically active compound capable to form transient, non-covalent complexes with the drug. Pentoxifylline (PTX) - member of methylxanthines, synthetic derivative of caffeine - is a prospective candidate for such modulation. In our recent work we showed that PTX can directly interact with DOX in the presence of DNA forming stacking complexes. It should be noted that DOX can strongly intercalate to DNA, and additionally it is able to self-aggregate, mainly to form dimers. Using UV-vis spectroscopy we analyzed mixtures containing DOX, PTX and calf thymus DNA. We were able to observe four main forms of DOX molecules in the mixture: DOX alone, DOX in a dimer, DOX in stacking complexes with PTX, and finally DOX intercalated into DNA. Based on newly developed mathematical model, we were able to establish all components' concentrations as well as all association constants. What is more, we observed that DOX-PTX stacking complexes formation disrupts equilibrium between all DOX' forms, and in consequence causes to de-intercalation of DOX molecules from DNA (Fig.1). To check possible influence of PTX on the DOX mutagenic activity we used *Salmonella typhimurium* TA98 strain in the Ames test. We showed that mutagenic activity of DOX – PTX mixtures is lowered when PTX concentration increases in the mixture, and it is strongly associated with presence of DOX in a free uncomplexed form. What is more, using the MTT cytotoxicity assay we showed that PTX has protective effect against the DOX biological activity towards non-cancerous HaCaT eukaryotic cells, but we did not observe such protection on cancerous MCF-7 and MEL-Juso cell lines.

Pentoxifylline affects idarubicin binding to DNA

Anticancer drug idarubicin (IDA) – derivative of doxorubicin – is commonly used in treatment of numerous cancer types. However, in contrast to doxorubicin, its biophysical properties are not well established yet. We performed studies, which showed influence of pentoxifylline (PTX) on IDA binding to DNA. Moreover, we showed that direct interactions between IDA and PTX may influence the anticancer drug biological activity in Ames assay.

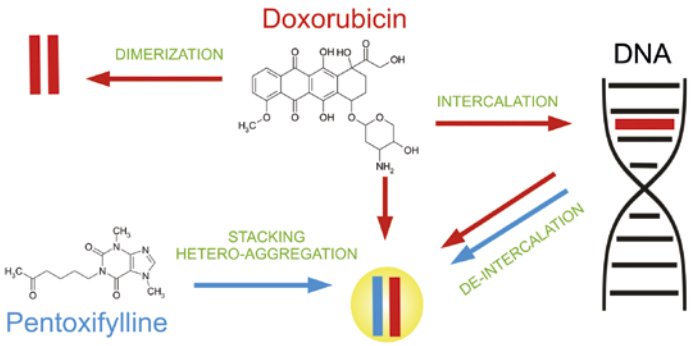


Fig.1. Pentoxifylline promotes de-intercalatation of doxorubicin from DNA

C_{60} fullerene enhances cisplatin anticancer activity and overcomes tumor cells drug resistance

Carbon nanoparticles, especially fullerenes, are another group of biologically active compounds studied by our group in international collaboration. We recently showed that fullerene C60 non-covalently interacts with cisplatin (Cis) forming nano-formulations. We showed that these nano-formulations posses greater cytotoxic activity towards tumor cell lines *in vitro* than Cis alone (Fig. 2). The enhanced proapoptotic activity of the novel complexes was found to be tightly connected with their unique capability to circumvent cancer drug resistance in vitro, as revealed by investigation of human leukemia cells HL-60 together with their sublines resistant towards doxorubicin (HL-60/adr, multidrug resistance protein-1=MRP-1=ABCC1 overexpressing) and vincristine (HL-60/vinc, P-glycoprotein=P-gp=ABCB1 overexpressing). The enhanced anticancer activity of the developed C_{60}+Cis complexes we also confirmed *in vivo* on male C57BL/6J mice bearing Lewis lung carcinoma, effectively inhibiting tumor growth and formation of metastases in comparison to free single Cis.

Methylxanthines as modulators of antibiotics

Despite a broad spectrum of available antimicrobial drugs, effective treatment of infectious diseases in the era of multi-drug resistant superbugs still appears as a major challenge for modern medicine. One of the promising approaches to improve the efficacy of antibiotic treatment is the application of a combination therapy, in which, apart from an antibiotic, an additional substance improving overall antimicrobial effects is used. There are some indications coming from literature that caffeine – purine alkaloid commonly consumed as a component of popular beverages – effectively reduces bacterial growth. On the other hand, caffeine and other xanthines are known to interact non-covalently with other aromatic compounds. As at least some of commonly used antibiotics are aromatic, xanthines may decrease their pharmacological activity. So far the knowledge about possible in vitro antagonistic or synergistic interactions between methylxanthines and antibiotics is scarce. Within the project we are investigating whether caffeine and pentoxifylline are able to potentiate the effects of various antibiotics, or do the opposite.

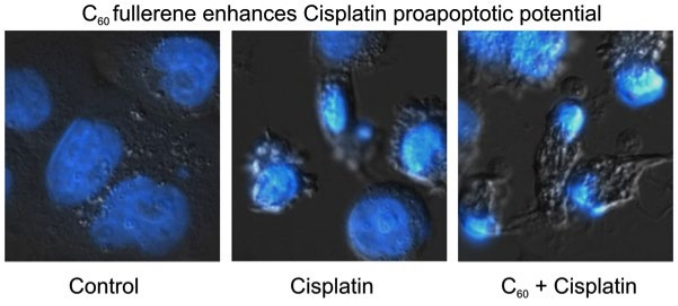


Fig. 2. C_{60}+Cis complex promote apoptosis by hyper-condensation of DNA in human cervix carcinoma cells of KB-3-1 line.

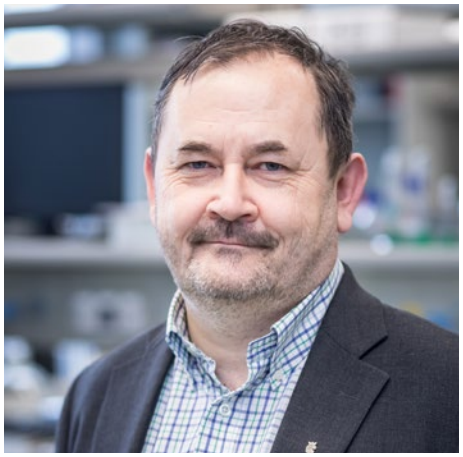
Recent publications

- Prylutska S., Panchuk R., Gołuński G., Skivka L., Prylutskyy Y., Hurmach V., Skorohyd N., Borowik A., Woziwodzka A., Piosik J., Kyzyma O., Garamus V., Bulavin L., Evstigneev M., Buchelnikov A., Stoika R., Berger W., Ritter U., Scharff P. C60 fullerene enhances cisplatin anticancer activity and overcomes tumor cells drug resistance. Nano Research 2017, 10(2): 652–671 (doi: 10.1007/s12274-016-1324-2)
- Gołuński G., Borowik A., Lipińska A., Romanik M., Derewońko N., Woziwodzka A., Piosik J. Pentoxifylline affects idarubicin binding to DNA. Bioorganic Chemistry 2016, 65: 118-125 (doi: 10.1016/j.bioorg.2016.02.005).
- Gołuński G., Borowik A., Derewońko N., Kawiak A., Rychłowski M., Woziwodzka A., Piosik J. Pentoxifylline as a modulator of anticancer drug doxorubicin. Part II: assessment of pentoxifylline influence on biological activity of the drug. Biochimie 2016, 123: 95–102 (doi: 10.1016/j.biochi.2016.02.003).

Scientific collaboration

- Prof. Maxim P. Evstigneev (Faculty of Physics, National Technical University of Sevastopol, Crimea),
- Prof. Yuriy Prylutskyy (Department of Biophysics,
- Taras Shevchenko (National University of Kyiv, Ukraine),
- Prof. Jan Mazerski (Faculty of Chemistry, Gdańsk University of Technology),
- Prof. Janusz Rak, Dr. Dariusz Wyrzykowski (Faculty of Chemistry, University of Gdańsk),
- Prof. Aleksandra Królicka, Prof. Rajmund Kaźmierkiewicz (IFB)

[Laboratory of Biopolimer Structure]



Stanisław Ołdziej, PhD

Received his PhD in Chemistry at the University of Gdańsk (1995). He carried out his postdoctoral training at the University of Montreal, Canada (1996-1998) working with prof. F. Major on modeling structure of small RNA molecules. In the years 2001-2004 he carried out his second postdoctoral training at the Cornell University, USA working with prof H.A. Scheraga on predicting three-dimensional structure of proteins. He became a habilitation doctor at 2005. Author of more than 120 per-reviewed publications.

Research group

Wioletta Żmudzińska, PhD,
Aleksandra Lewandowska – PhD student
Anna Fel – PhD student
Marcel Thiel – PhD student

PhD Thesis

- Wioletta Żmudzińska: "Turn forming sequences and their impact on early stages of protein folding", 19.10.2012
- Anna Hałabis: "The temperature influence on the three-dimensional structure of proteins. Study on model system mini-protein tryptophan cage and its variants", 18.12.2015
- Maciej Baranowski: "Structural analysis of substrate binding region of Hsp40 molecular chaperones". 21.10.2016

Our research is mostly focused on understanding principles governing the protein folding process. Majority of known protein sequences are able to form well organized three-dimensional structures spontaneously. Structural self-organization of proteins is called protein folding, and despite biological importance this process is not well understood yet. Investigation of folding process is very complicated taking into account its speed (most of globular proteins fold in fractions of milliseconds) or sensitivity of the process to environment conditions (temperature, ionic strength, pH, metal ions). One of the approaches to tackle the protein folding problem is to develop a theoretical model capable of reproduction of known experimental data as well as prediction of properties not available so far. Our group in cooperation with groups of professor H.A. Scheraga (USA) and professor A. Liwo (Poland) participates in development of what is called a coarse-grained (simplified) model of polypeptide chain called UNRES (UNited RESidues), see Fig. 1. The UNRES (www.unres.pl) program is used to investigate protein folding mechanism, to simulate protein dynamics over long period of time or to predict three-dimensional structure based on protein amino acid sequence alone. In recent years UNRES model has been extended to be able to treat also nucleic acids (DNA or RNA) as well as complexes formed between proteins and nucleic acids. Currently, our work in UNRES project is focused on two specific aims: temperature influence on structure of proteins and identification of folding initiation sites. Folding/unfolding of a protein induced by temperature is a well-known phenomenon; however detailed mechanism of such process is not well understood. Complete or partial unfolding of proteins and aggregation associated with them bring more and more attention nowadays, especially in the context of cell malfunction or death. Using NMR spectroscopy and molecular dynamics simulations we could provide detailed (at atomic level resolution) mechanism of how native functional structure of the protein responds to temperature change. During our study of temperature influence on protein structure, we found that some parts of protein sequences (motifs) possess the ability to keep an organized three-dimensional structure (similar to those observed for native folded state) regardless of temperature at which measurements are performed. Surprisingly some of such motifs (6-14 amino acids residues) possessed catalytical properties (ATP hydrolysis).

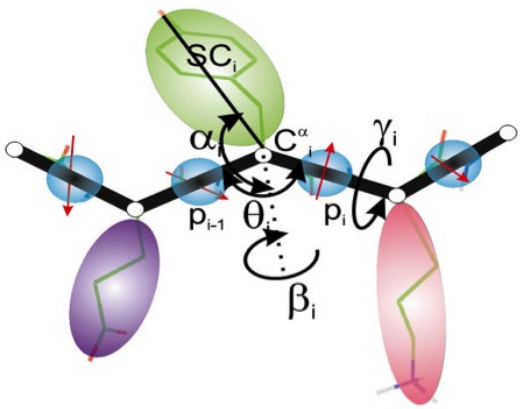


Fig. 1. The UNRES united-residue model of polypeptide chains. The interaction sites are side-chain ellipsoids of different sizes (SC). The polar interaction sites bearing point dipoles (depicted as red arrows) are colored blue and the virtual bonds are shown as thick black lines.

Another area of Laboratory of Biopolymers Structure group's interest is study of proteome composition of human follicular fluid (hFF). Despite the development and increased popularity of assisted reproductive technologies (ART), there is no reliable method of oocyte quality evaluation before fertilization, which leads to embryo overproduction. We focused our research on the proteomic composition of a medium which is the environment of oocyte growth and development in the ovarian follicle – follicular fluid. We developed a method of qualitative and quantitative assessment of peptides and proteins in hFF from separate follicles of a single patient (see Fig. 2.) and devised a preliminary list of differentiating proteins, which we will test in future clinical studies in order to find possible protein markers of good quality of oocytes. In these experiments we closely collaborate with the INVICTA Fertility Clinic and the Laboratory of Mass Spectrometry from IFB Core Facility. Cooperation with the Laboratory of Mass Spectrometry enabled us to use in the project a powerful recently developed method: SWATH-MS (Sequential Window Acquisition of All Theoretical Fragment Ion Mass Spectra). Using established methodology in combination with initial sample fractionation (ultrafiltration, immunodepletion, and high pH RP-HPLC separation), we recently identified 400 distinct proteins and were able to quantify 108 proteins in hFF.

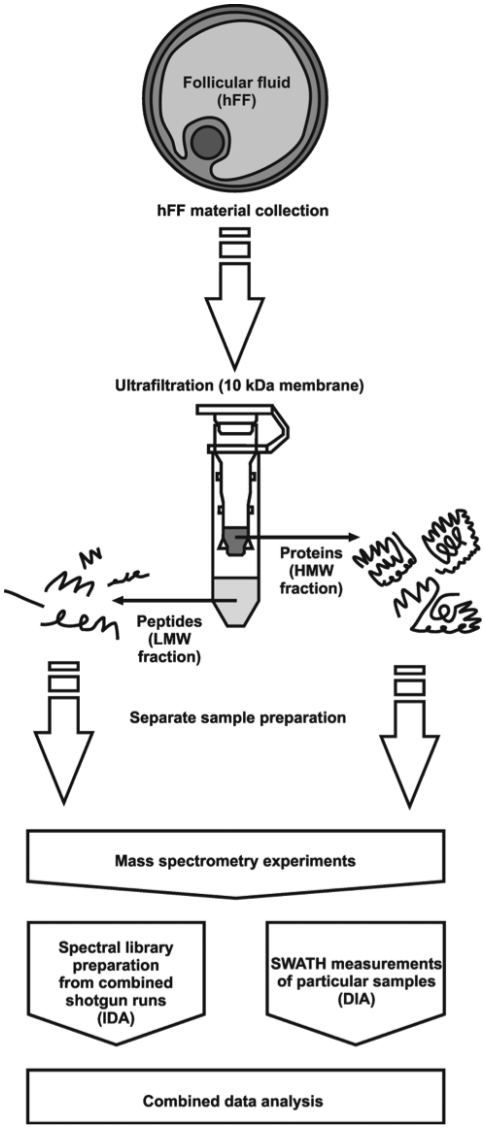


Fig 2. Workflow of the analysis of a single sample of hFF. The material was divided into two fractions: high molecular weight fraction (HMW, >10 kDa) containing whole proteins, and low molecular weight fraction (LMW, <10 kDa) containing endogenous peptides.

Recent publications

- Jaworski Paweł, Donczew Rafał, Mielke Thorsten., Thiel Marcel, Ołdziej Stanisław, Weigel Christoph., Zawilak-Pawlik Anna M. Unique and universal features of Epsilonproteobacterial origins of chromosome replication and DnaA-DnaA box interactions . Frontiers in Microbiology 2016, 7, 1555
- Lewandowska Aleksandra E., Macur Katarzyna, Czaplewska Paulina, Liss Joanna, Łukaszuk Krzysztof, Ołdziej Stanisław. Qualitative and Quantitative Analysis of Proteome and Peptidome of Human Follicular Fluid Using Multiple Samples from Single Donor with LC-MS and SWATH Methodology. Journal of Proteome Research 2017, 16, 3053-3067
- Krupa Paweł, Hałabis Anna, Żmudzińska Wioletta, Ołdziej Stanisław, Scheraga Harold A., Liwo Adam. Maximum Likelihood Calibration of the UNRES Force Field for Simulation of Protein Structure and Dynamics. Journal of Chemical Information and Modeling 2017, 57 2364-2377

Scientific Collaboration

- Prof. H.A. Scheraga, Cornell University,
- Prof A. Liwo, University of Gdańsk,
- Prof J. Brasuń, Medical University of Wrocław,
- Prof. E. Łodyga-Chruścińska, Technical University of Lódź,
- Prof. K. Łukaszuk, Invicta Clinic/Medical University of Gdańsk,
- Prof. W.Kamysz, Medical University of Gdańsk.

[Laboratory of Cell Biology]

Prof. Jacek Bigda

Received his PhD in Medicine at the Medical University of Gdansk (1990). He carried out postdoctoral training at the Weizmann Institute of Science (1991-1993), working with Prof. David Wallach. He underwent also shorter trainings in the Central Laboratory of Dutch Red Cross (1991) and Medical University of Hannover, Germany (1995, 1996). He became a habilitated doctor at 1996. In 2001 he was appointed associate professor at the Medical University of Gdansk and was awarded the full professorship at 2005.

Research group

Prof. Jacek Bigda, MD, PhD
Anna J. Żaczek, PhD
Marcin Okrój, PhD
Patrycja Koszałka, PhD
Anna Supernat, PhD
Grzegorz Stasiłojć, PhD
Aleksandra Markiewicz, PhD
Natalia Bednarz-Kroll, PhD
Dominika Czaplińska, PhD student
Anna Nagel, PhD student
Aleksandra Urban, PhD student
Anna Felberg, PhD student
Anna Jurek, PhD student
Marta Popęda, PhD student
Justyna Topa PhD Student

PhD Thesis

- Aleksandra Markiewicz „Analysis of invasion and metastasis-related markers in breast cancer patients„ (2015)
- Anna Supernat „Clinical significance of selected molecular markers in endometrial cancer" (2015)

Our research is focused on cancer cell biology, with special emphasis on invasion and metastasis. We are interested in mutual interactions of cancer cells with their microenvironment, and their implications for prognosis and therapy of cancer patients. Experiments are carried in vitro, in vivo in animal models and in the clinical setting using broad spectrum of methods. There are three main lines of research related to: I) interaction of cancer cells with endothelium, II) the role of complement system in tumor evasion and III) evaluation of novel biomarkers of cancer progression.

Vascular endothelium, is presently looked upon as an important autocrine/paracrine/endocrine organ that regulates number of cardiovascular functions. Healthy endothelium is essential for undisturbed functioning of the cardiovascular system, while endothelial dysfunction characterized by impaired production of vasoprotective endothelial mechanisms and excessive production of pro-oxidant, pro-thrombotic, pro-inflammatory endothelial mechanisms leads to various pathologies. Endothelial dysfunction contributes to invasion, survival, chemoresistance and metastasis of cancer cells by various mechanisms. Treatment of cancer metastasis still represent „unmet medical need". Migrating cancerous cells cannot survive for a long time in the circulation and unrestrained trafficking of these cells to endothelium seems critical in metastasis. We have demonstrated that CD73/ecto-5'-nucleotidase knockout slows down the vascularization of subcutaneous tumors and decreases the number of experimental lung metastases.

The complement system as a part of innate immune system is aimed to recognition and elimination of invading pathogens. Noteworthy, complement can be also targeted onto tumor cells. However, tumor cells evade complement attack by overexpression of membrane-bound complement inhibitors and natural antitumor antibodies are often present at low titers or possess low affinity. Importantly, therapeutic modulation of complement activity emerges as an attractive target in clinical approaches and there are several anti-cancer drugs approved, which utilize the complement system as their effector mechanism. Laboratory of Cell Biology undertakes projects related to the role of complement in tumor growth and anticancer therapies. Objectives include investigation of the dual role of complement in progression of lung and breast cancer, introduction of novel markers of complement activation for monitoring of monoclonal antibody-based immunotherapy as well as original concept on how to turn factors fueling autoimmune events into supporters of immunotherapy.

Our research relates also to deeper understanding of cancer spread and metastasis formation, with special interest in early dissemination of cancer cells and significance of epithelial-to-mesenchymal transition in breast cancer. Through the comprehensive investigation of primary tumors, lymph node metastases and circulating tumor cells (CTCs) in blood of patients we are looking into the metastasis cascade to gain deeper knowledge about new molecular markers that could improve diagnosis and treatment of breast cancer. Our team is experienced in carrying out projects related to development and validation of biomarkers as well as designing diagnostic methods for their reliable investigation in routine approach. Currently various projects focused on development of novel blood-based qPCR assays to monitor response to the therapy more precisely are underway. They concern molecular profiling of CTCs in breast

cancer, ctDNA in ovarian cancer and miRNA from tumor-derived exosomes in colon cancer. Additionally, biomarkers and molecular pathways associated with response to tamoxifen in breast cancer are investigated.

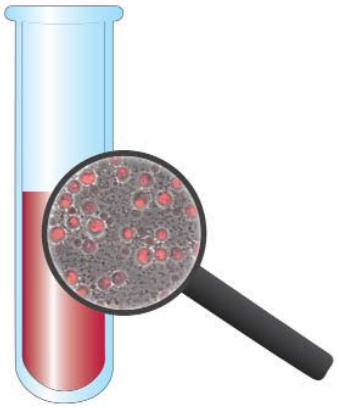
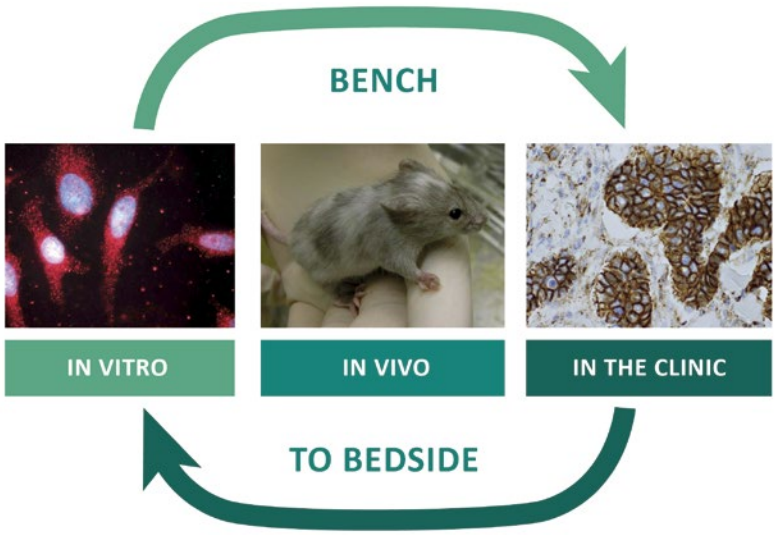


Fig. 1. Liquid biopsy – blood-based assay for detection of tumor cells circulating in the blood of cancer patients

The research of the team is situated at the edge of molecular biology and clinical oncology with mission to translate the results obtained in the laboratory into clinical practice and thus contribute to more effective and individualized management of cancer patients.



Recent publications

- Markiewicz A, Żaczek AJ. The Landscape of Circulating Tumor Cell Research in the Context of Epithelial-Mesenchymal Transition. Pathobiology. 84:264-283, 2017 (invited review).
- Koszałka P., Gołuńska M., Urban A., Stasiłojć G., Stanisławowski M., Majewski M., Składanowski A.C., Bigda J. Specific activation of A3, A2A and A1 adenosine receptors in CD73-knockout mice affects B16F10 melanoma growth, neovascularization, angiogenesis and macrophage infiltration. PLoS One, 11(3): e0151420., 2016.
- Stasiłojć G, Österborg A, Blom AM, Okrój M. New perspectives on complement mediated immunotherapy. Cancer Treat Rev. 45: 68-75, 2016.7

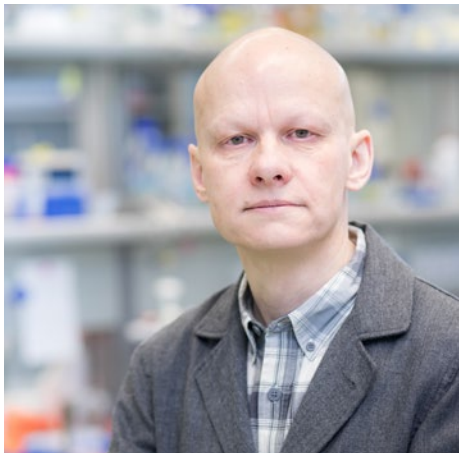
Patents

- PCT/EP2015/070526 Marcin Okroj, Anna M Blom „Antibodies specific for complement component C4d and uses thereof"

Scientific Collaboration

- Dept. of Translational Medicine, Lund University, Sweden
- Radboud University Medical Centre, Nijmegen, The Netherlands
- Latvian Institute of Organic Synthesis, Riga, Latvia
- Cambridge Institute, Cancer Research UK, University of Cambridge, UK
- Department of Pathology, University of Regensburg

[Laboratory of Evolutionary Biochemistry]



Prof. Jaroslaw Marszalek

He graduated from the University of Gdansk (1982), received his PhD in biochemistry at the Medical University of Gdansk (1988) and received his habilitation in biological sciences at the University of Gdansk (1997). He carried out postdoctoral work at the Department of Biochemistry, Michigan State University, USA (1989-1991) and Institut fur Physiologische Chemie der Universitat Muenchen (1995). He has been a Professor in biological sciences since 2004. Beginning in 1999, he has been a Visiting Associate Professor at the Department of Biochemistry, University of Wisconsin-Madison, where he collaborates with professor Elizabeth A. Craig.

Research group

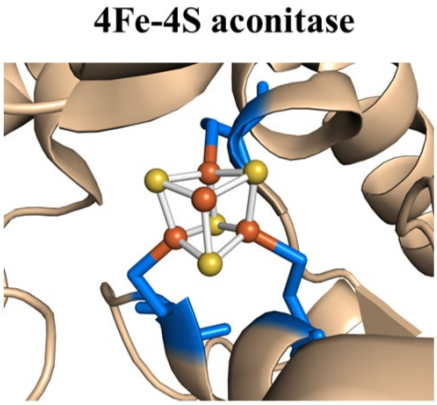
Rafał Dutkiewicz, PhD, Hab.
Bartłomiej Tomiczek, PhD,
Marta Uzarska, PhD,
Wojciech Delewski, PhD student
Małgorzata Kleczewska, PhD student
Marcin Jeleń, PhD student

PhD Thesis

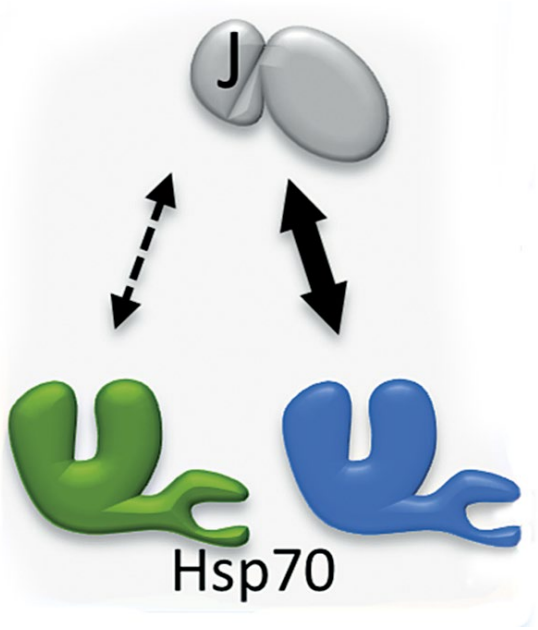
- Szymon Ciesielski (2008-2012) "Characterization of Interaction Between J-type Protein Jac1 and Isu1 Protein Participating in Biogenesis of Iron-Sulfur Clusters"
- Jacek Kominek (2009-2013) "Molecular Evolution of Eukaryotic Hsp70 and Hsp40 Chaperones"
- Mateusz Manicki (2013-2016) "Biochemical reconstruction of protein complexes involved in mitochondrial biogenesis of iron-sulfur clusters"

Proteins are complex and dynamic macromolecules. In all living cells **molecular chaperones** play critical roles in remodeling protein structure i.e. assisting protein folding and preventing protein aggregation, facilitating assembly and disassembling of protein complexes and modulating protein: protein interactions.

Our goals are to understand the basis of: (1) the mechanism of action of molecular chaperones in specific complex biological processes and (2) the evolutionary mechanisms behind functional divergence amongst molecular chaperones allowing them to assist in specific cellular processes. As a model system, we study yeast (*Saccharomyces cerevisiae* and other related species), which allows us to combine biochemical and molecular biology approaches with genetics and evolutionary analyses.



Mitochondria contain a complex system for assembly of iron-sulfur cluster (FeS) prosthetic groups and their insertion into proteins. A specialized Hsp70/J-protein molecular chaperone pair is a critical part of this system, interacting specifically with the scaffold protein on which FeS clusters are first built and facilitating cluster transfer to recipient protein. We aim to unravel the molecular mechanisms of this dedicated chaperone system.



Recent developments in phylo-genomics prompted us to expand our research into the field of protein evolution. We have discovered that the three members of the Hsp70 family present in S. *cerevisiae* mitochondria arose by gene duplication and are unique to S. *cerevisiae* and closely related species. This allows us to ask what molecular mechanisms have governed formation and divergence of duplicated mtHsp70s. Such questions are of general interest as gene duplication is considered a major source of new proteins. Our goal is to determine what structural and functional changes have occurred during Hsp70s evolution that governed their post-duplication divergence. We also ask how multiplication of Hsp70s affected their interactions with J-protein co-chaperone partners and client proteins.

Recent publications

- Kominek J, Marszalek J, Neuvéglise C, Craig EA, and Williams BL (2013) The Complex Evolutionary Dynamics of Hsp70s: A Genomic and Functional Perspective Genome Biology and Evolution 5: 2460-2477
- Manicki M, Majewska J, Ciesielski S, Schilke B, Blenska A, Kominek J, Marszalek J, Craig EA, Dutkiewicz R (2014) Overlapping Binding Sites of the Frataxin Homologue Assembly Factor and the Heat Shock Protein 70 Transfer Factor on the Isu Iron-Sulfur Cluster Scaffold Protein J. Biological Chemistry 289: 30268-30278
- Wojciech Delewski, Bogumila Paterkiewicz, Mateusz Manicki, Brenda Schilke, Bartlomiej Tomiczek, Szymon J. Ciesielski, Lukasz Nierzwicki, Jacek Czub, Rafal Dutkiewicz, Elizabeth A. Craig, Jaroslaw Marszalek (2016) Iron–Sulfur Cluster Biogenesis Chaperones: Evidence for Emergence of Mutational Robustness of a Highly Specific Protein–Protein Interaction. Molecular Biology and Evolution 33: 643-656
- Szymon J. Ciesielski, Brenda Schilke, Jaroslaw Marszalek, Elizabeth A. Craig (2016) Protection of scaffold protein Isu from degradation by the Lon protease Pim1 as a component of Fe-S cluster biogenesis regulation. Molecular Biology of the Cell 27: 1060-1068
- Craig, E.A., Marszalek, J. (2017) How do J-proteins get Hsp70 to do so many different things? Trends in Biochemical Sciences, 42: 355–368.

Scientific Collaboration

- Prof. Elizabeth A. Craig Department of Biochemistry, University of Wisconsin-Madison, 433 Babcock Drive, Madison, WI 53706, USA
- Prof. Roland Lill Institut für Zytobiologie, Philipps-Universität Marburg, Robert-Koch-Str. 6, 35032 Marburg, Germany

[Laboratory of Molecular Bacteriology]

Prof. Michał Obuchowski

He graduated from University of Gdansk in 1993, received PhD in biology (1997) University of Gdansk and habilitation in biological sciences (2006) and was awarded the full professorship at 2014. Since 2004 he work at Medical University of Gdańsk. He carried out postdoctoral work at University of Paris XI, France. Author of more than 50 peer-reviewed publications. He is a Vice-Dean for science of Intercollegiate Faculty of Biotechnology UG & MUG.

Research group

Krzysztof Hinc Phd,
Adam Iwanicki Phd,
Anna Grela PhD student,
Tomasz Łęga PhD student,
Marta Hubisz PhD student.

PhD Thesis

- "Spore based vaccine against pseudomembranous colits" Alessandro Negri (2016)
- „Vaccine against Helicobacter pylori based on Bacillus subtilis spores" Małgorzata Stasiłojć (2015)

Reaserch

Our research includes two main stream of interest: basic research related to process of formation and germination of the *Bacillus subtilis* spore and applied focused on use the spore as universal carrier of peptides or proteins for variety application.

Basic research are focused on different aspects of sporulation process during which time and site specific gene expression lead to functional diversification of ancestor cells after asymmetrical division. In course of such process, the cell which will be converted in metabolically dormant spore undergo several changes including transition DNA conformation from B form to A as well as gaining several protective layer surrounded developing spore. Coordination of such process, and mechanism of deposition of coat proteins is investigated in our laboratory. We focused on the role of PrpE phosphatase in such process. This enzyme is probably involved in the controlling thickness of inner spore coat. Also As part of investigation of sporulation process and spores we pay attention to influence of stress response on such process as well as dinucleotide tetraphosphates present in the living cells.

From the other hand, we also pay attention to the germination process, during which dormant spore is converted into vegetative cells. In this pathway we investigate mechanism of action GerA receptors, which trigger germination in response to presence L-alanine or L-valine in the environment. The germination is irreversible so need to be taken with caution what is manifested at molecular level by interaction between different germination receptors which is also investigated. In a frame of this pathway we are trying to build the model of GerA receptor using bioinformatics approach supported by biochemical experiments and elucidate its mechanism of action.

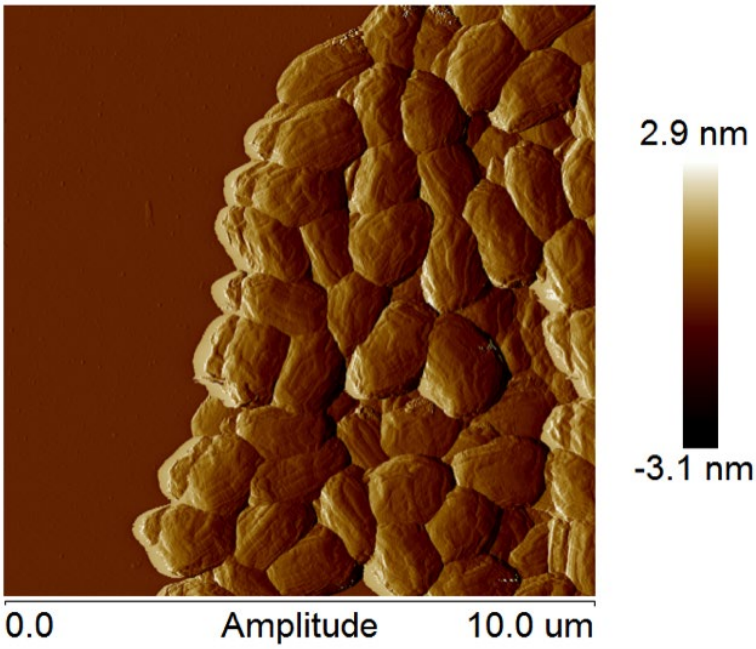
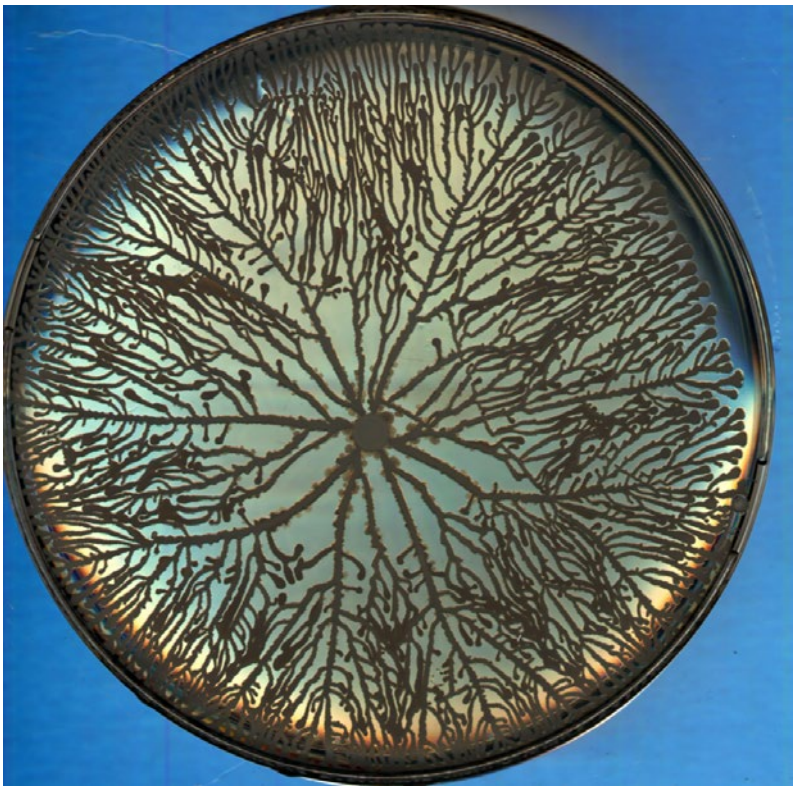


Figure.1. Bacillus subtilis spore image taken by Atomic Force Microscope

Applied research conducted in our laboratory also concern the spore but from different angle. The spore as form of the cells which should survive different harsh condition is extremely resistant for temperature, changes in humidity, low pH, UV irradiation as well as proteolytic enzymes. All this properties make spore a very good choice as carrier particle. This is also supported by fact, that external shield of the spore consist of the proteins. Such create an opportunity to place peptide or protein of choice on the surface of spores by simple creation fusion genes between parts coding coat proteins and coding for passenger part. Using this approach we create set of spores presenting antigens of two pathogenic bacteria: *Helicobacter pylori* and *Clostridium difficile*. Such recombinant spores are used for oral or intranasal immunisation of laboratory animals in order to protect them from infection of pathogens. To make such work more efficient a set of vector for creation of recombinant spores was developed. For maximizing of chance of creation efficient spore based vaccine we also investigate in the mechanism of interaction between administrated spores and immune system components. As site project we also have shown that spores may serve as good support for enzymes which displayed enhanced stability in comparison with soluble form.



Recent publications

- Potocki W, Negri A, Peszyńska-Sularz G, Hinc K, Obuchowski M, Iwanicki A., 2017, The combination of recombinant and non-recombinant Bacillus subtilis spore display technology for presentation of antigen and adjuvant on single spore. Microb Cell Fact. 16:151. doi: 10.1186/s12934-017-0765-y
- Łęga T., Weiher P., Obuchowski M., Nidzworski D., 2016, Presenting influenza A M2e antigen on recombinant spores of Bacillus subtilis. PLoS ONE DOI:10.1371/journal.pone.0167225.
- Stadsiłojć M., Hinc K., Peszyńska-Sularz G., Obuchowski M., Iwanicki A., 2015, Recombinant Bacillus subtilis spores elicit Th1/Th17-polarized immune response in a murine model of Helicobacter pylori vaccination. Molecular Biotechnology 57: 685-691.
- Iwanicki A., Piątek I., Stasiłojć M., Grela A., Łęga T., Obuchowski M., Hinc K., 2014, A system of vectors for Bacillus subtilis spore surface display. Microbial Cell Factories 13:30
- Hinc K., Stasiłojć M., Piątek I., Peszyńska-Sularz G., Isticato R., Ricca E., Obuchowski M., Iwanicki A., 2014, Mucosal adjuvant activity of IL-2 presenting spores of Bacillus subtilis in a murine model of Helicobacter pylori vaccination. PLoS ONE 9:e95187

Patents

- „Oral vaccine containing spores of Bacillus subtilis and its application for immunisation against Helicobacter pylori" granted at 2014-06-17, number: PL398658
- „New probes for detection bacteria of the species Acinetobacter baumannii, oligonucleotides and the protocol for analysis of medical and environmental samples" granted at 2015-12-01, PL223163
- „Oral vaccine against Clostridium difficile, based on Bacillus subtilis spores presenting FliD protein. Granted at 2016-02-11, PL223730

Scientific Collaboration

- Laboratory of microbiology, University of Frideric II (Naples, Italy), prof.Ezio Ricca;
- Military Institute of Medicine (Warszawa, Polska), dr Zbigniew Dąbrowiecki;
- Department of Immunology and Infection biology, University of Łódź, prof. Magdalena Chmiela;

[Laboratory of Molecular Biology]

Prof. Igor Konieczny

Received his PhD in Molecular Biology at the University of Gdansk in 1994 and habilitation in 2000. He is a full-professor in biological sciences since 2004. He carried out postdoctoral training at University of California San Diego, USA. From 1998 a member of International Society for Plasmid Biology and other Mobile Genetic Elements (ISPB) (2010-2012) secretary of ISPB elected. A member of COST Biomedical Domain (2008-2015). He was awarded by EMBO and HHMI YIP Programmes. He got prestigious awards from Foundation for Polish Science and Polish Ministry of Science. Author of 39 peer-reviewed publications, supervisor of 12 defended PhD thesis. Since 2012 he is a Dean of IFB UG & MUG.

Research group

Katarzyna Bury, PhD,
Urszula Uciechowska, PhD,
Katarzyna Węgrzyn, PhD
PhD students: Andrzej Dubiel, Marta Gross, Anna Karłowicz, Małgorzata Ropelewska, Elżbieta Zabrocka.

PhD Thesis

- Anna Karłowicz "Structural-functional analysis of Lon protease from Escherichia coli – identification of DNA interaction site", (2018).
- Anna Wosinski „The influence of metabolites level on the DNA replication in Escherichia coli cells", (2018).
- Aleksandra Wawrzycka „The mechanism of Escherichia coli polymerase III interaction with the RK2 plasmid origin", (2017).

Our research is focused on the analysis of molecular mechanisms responsible for DNA replication in bacterial cells. We mainly investigate the mechanisms responsible for the initiation and regulation of DNA replication of bacterial plasmids an antibiotic resistance factors in bacterial cells. Model used in our investigations is RK2 plasmid that belongs to the group of broad-host-range replicons that can be stably maintained and transferred between cells of various bacterial species, including plant, animal and human pathogens. The research utilizing such a unique system, allowing for the analysis of cellular mechanisms in various organisms, makes the significant contribution towards the general understanding of the fundamental cellular processes important for future development of new antimicrobial therapeutic strategies.

In our investigations we focus on (i) multi-molecule complexes formed on DNA by replication initiation proteins (Rep), their structural bases, functions and dynamics, (ii) analysis of the mechanism of protease activity on substrates bound to DNA and effects of proteases on DNA replication regulation and stably maintenance of plasmids, and (iii) analysis of the function of plasmid encoded post segregational killing systems in the context of its components' interactions with DNA and their stability.

Current understanding of structure and functions of multi-protein complexes formed on DNA is still limited. Especially challenging is the analysis of intrinsically disordered proteins and their complexes with single-stranded DNA (ssDNA). After discovery that Rep proteins bound both double-stranded DNA (dsDNA) and similar, as chromosomal DnaA, they also interact with ssDNA (Wegrzyn K. *et al., Nucleic Acids Res.* 2014), we try to structurally characterize this complex. In our studies we are applying *in vivo* and *in vitro* experiments including reconstituted DNA replication assays, real time kinetics of protein-DNA complexes, Mass Spectrometry (MS), Atomic Force Microscopy (AFM) and crystallographic analysis.

In our research we also challenge the question about the molecular mechanism(s) of proteases activity modulation by interaction with nucleic acids. The controlled proteolysis is a long term task as a potential tool in developing anti-microbial therapies. Recently we extended our investigations on the role of proteases in nucleoprotein complex dynamics in bacterial cells. By constructing mutants of *Escherichia coli* Lon protease, using bioinformatics and phenotypic analysis we demonstrated engagement of positively charged amino acid residues, located on the ATPase domain surface, in interaction with DNA. *In vivo* tests revealed essentiality of Lon interaction with DNA for Lon activity associated with cell division (Karłowicz A., Węgrzyn K. *et. al., JBC* 2017).

In the same lane of investigations we tested the influence of proteases on handcuff complex responsible for controlling DNA replication and stable maintenance of plasmids in bacterial cells. We found that bacterial proteases, particularly Lon and ClpAP, disrupt handcuff by degrading Rep proteins interacting DNA, thus affecting plasmid stability. Moreover, we demonstrate that Rep monomers are able to dissociate handcuffed plasmid molecules and re-initiate DNA synthesis (Bur K. *et. al., NAR* 2017). We assume that those mechanisms are important for plasmid maintenance.

We are also developing the line of research considering the mechanisms of replication complex formation in bacterial cells. Our study on the replisome assembly at plasmid RK2 replication origin (Wawrzycka A, *et al., Proc Natl Acad Sci USA*. 2015) revealed that specific interaction between the plasmid

Rep protein and β subunit of DNA Polymerase III holoenzyme (β-clamp) is required for polymerase complex assembly at plasmid origin. Currently conducted experiments are directed towards understanding of the regulatory mechanisms involving β-clamp interaction with host and plasmid encoded proteins. We are directing our investigations towards the analysis of the stability of an essential replication proteins and mechanisms involving protease activities for the regulation of both chromosomal and plasmid DNA replication in stress conditions.

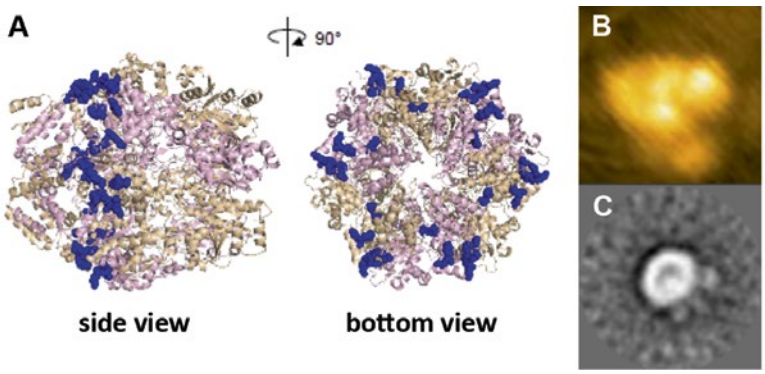


Fig. 1. Investigation on Lon protease structure and its interaction with DNA. (A) A schematic representation of the hexameric ring structure of the protein Lon with selected positively-charged amino acid residues (blue spheres) engaged in interaction with DNA. The hexameric ring is represented by the monomers alternately colored with wheat and pink. The N-terminal domain (1-245 aa of the full-length Lon protease) was removed for clarity. (B) Atomic force microscopy imaging of Lon hexamer. (C) Negative staining electron micrograph of Lon protease. Representative 2D class image of Lon hexamer.

Recent and Important Awards

2016 ELSEVIER-Plasmid prize award for dr. Katarzyna Węgrzyn for the best poster presentation during Plasmid Biology Conference, Cambridge

2015 Award from The Committee of the Cell Molecular Biology of Polish Academy of Science (PAN) for the best publication in microbiology published in Polish laboratories

2002 HHMI (Howard Hughes Medical Institute) Young Investigator

2000 EMBO YIP (Young Investigator Programme), EMBO Heidelberg

Recent Research Grants

2018-2021 National Science Center SONATA "Structural-functional analysis of nucleoprotein complexes of plasmid Rep proteins and ssDNA DUE origin region." (2017/26/D/NZ1/00239)

2017-2018 National Science Center MINIATURA 1 "Analysis of ORC proteins interactions with ssDNA of origin region – preliminary research"

2012-2018 National Science Center MAESTRO "Nucleoprotein complexes in DNA replication, proteolysis and plasmid post segregational killing (2012/04/ANZ1/00048)"

2009-2012 Ministry of Science and Higher Education "Rep protein and AT-rich region of origin- structure and function analysis" (2958/B/P01/2009/37)

Recent publications

- Bury K, Wegrzyn K and Konieczny I, (2017) Handcuffing reversal is facilitated by proteases and replication initiator monomers Nucleic Acids Res. 45(7):3953-3966
- Karlowicz A ,#, Wegrzyn K,#, Gross M, Kaczynska D, Ropelewska M, Siemiatkowska M, Bujnicki J, Konieczny I (2017) Charged patches on the surface of ATPase domain of Lon protease are essential for its interaction with DNA and activity associated with cell division J. Biol. Chem. 292(18):7507-7518
- Wegrzyn K, Gross M, Uciechowska U, Konieczny I. (2016) Replisome Assembly at Bacterial Chromosomes and Iteron Plasmids. Front Mol Biosci.;3:39.doi:10.3389/fmolb.2016.00039. PMID:27563644
- Karlowicz A, Wegrzyn K, Dubiel A, Ropelewska M, Konieczny I. (2016) Proteolysis in plasmid DNA stable maintenance in bacterial cells. Plasmid ;86:7-13. doi: 10.1016/j. PMID:27252071
- Yano H, Wegrzyn K, Loftie-Eaton W, Johnson J, Deckert GE, Rogers LM, Konieczny I, Top EM. (2016) Evolved plasmid-host interactions reduce plasmid interference cost. Mol Microbiol.;101(5) :743-56.
- Wawrzycka A, Gross M, Wasaznik A, Konieczny I. (2015) Plasmid replication initiator interactions with origin 13-mers and polymerase subunits contribute to strand-specific replisome assembly. Proc Natl Acad Sci U S A.;112(31):E4188-96.

*Award from Polish Academy of Science for the best Polish publication in microbiology

- Wegrzyn K, Fuentes-Perez ME, Bury K, Rajewska M, Moreno-Herrero F, Konieczny I (2014) Sequence-specific interactions of Rep proteins with ssDNA in the AT-rich region of the plasmid replication origin Nucleic Acids Res. Jul;42(12):7807

Scientific Collaboration

- CIB-CSIC (Madrid, Spain) Prof. Rafael Giraldo, Prof. Ramon Diaz-Oreja, Prof. Gloria del Solar Dongil
- University of Idaho (USA) Prof. Eva Top
- CNB-CSIC (Madrid, Spain) Prof. Fernando Moreno-Herrero, Prof. Maria Jose Valpuesta
- IIMCB (Warsaw, Poland) Prof. Janusz Bujnicki
- IIMCB (Warsaw, Poland) dr hab. Marcin Nowotny

[Laboratory of Molecular Diagnostics]

Prof. Krzysztof P. Bielawski

He graduated from University of Gdansk in 1985, received PhD in medical biology (1999) at Medical University of Gdansk and habilitation in biological sciences (2006). He carried out postdoctoral work at University of Muenster, Germany, Lund University, Sweden and INSERM U827, France. He is a full-professor in biological sciences since 2011. Author of more than 90 peer-reviewed publications, supervisor of 9 finished and 3 ongoing PhD's. He is a Director of the Technology Transfer Office at UG and CEO of TechTransBalt Ltd., the UG company for commercialization. Since 2016 he is a Vice-Rector for Development and Cooperation with Business and Industry of University of Gdansk.

Research group

Agnieszka Bernat-Wójtowska, PhD,
Mariusz Grinholc, PhD,
Joanna Nakonieczna PhD,
Monika Kossakowska-Zwierucho, PhD
Alicja Sznarkowska, PhD,
Anna Woziwodzka, PhD,
Anna Wróblewska, PhD,
Grzegorz Fila,
Patrycja Ogonowska,
Michał Pierański,
Aleksandra Rapacka-Zdończyk,
Agata Woźniak.

PhD Thesis

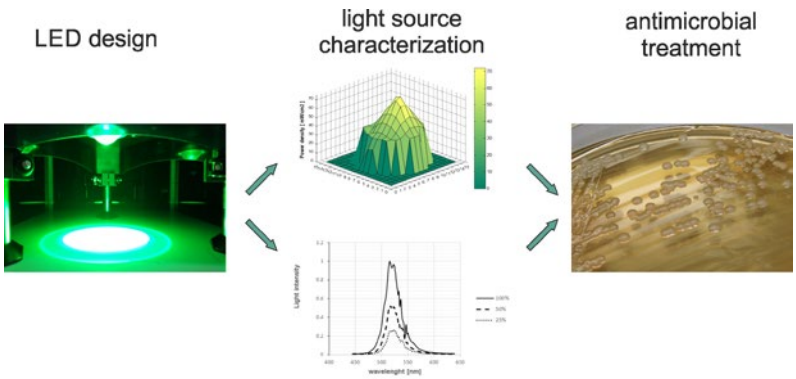
- Monika Kossakowska-Zwierucho: „Analiza cech genotypowych i feno-typowych warunkujących odpo-wiedź Staphylococcus aureus na inaktywację fotodynamiczną", 08.12.2017

Our research includes two fields of interest: research re- lated to the photodynamic inactivation (PDI) of bacterial infections as well as the application of modern tools of mo- lecular biology in the diagnosis of cancer, metabolic and in- fectious diseases.

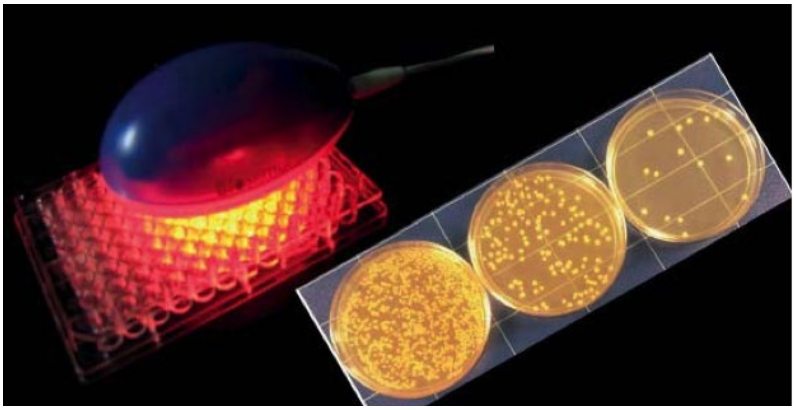
PDI is based on the concept that metabolically active cel- ls, like bacteria, fungi accumulate a photosensitizer (PS), a small molecular compound, which is excited by visible light. In the oxygen-rich environment, the surplus of energy or an electron is passed to molecular oxygen, giving rise to singlet oxygen and other reactive oxygen species. This action cau- ses a cytotoxic effect on living cells. PDI is a method, whe- re generation of resistance has never been shown so far. Moreover, PDI acts equally effectively on microbial strains that are either susceptible or resistant to classical antimicro- bial drugs. Therefore, it seems to be a promising therapeu- tic option for treatment of multidrugresistant-related local infections.

The research carried out in our laboratory focuses on both: basic and applied research. In our group we are stu- dying the mechanisms, which govern different response of microorganisms to photoinactivation, including biofilm for- mation, antioxidative enzymes activity, DNA damage, bacte- rial transporters. As the one of the main limitations of the method is low selectivity of PS used in PDI, the idea is to de- sign a PS molecule efficient against Gram(+) and/or Gram(-) pathogens, specifically multiresistant strains and functiona- lisation of the PS molecule with a cell delivery systems to im- prove the action of PDI. PS must be accumulated inside the bacterial cell or in a proximity of its envelope to efficiently kill bacteria but to be non toxic for human tissue.

According to the latest report by the European Medicines Agency (EMEA) and the European Centre for Disease Prevention and Control (ECDC), the introduction of antibiotics for routine treatment has led to revolutionary changes in the field of bacterial infections. Currently, the emerging and growing multidrug resistance microorganisms poses a huge threat to the health and lives of patients both in Europe and around the world. Just 70 years after the introduction of the first antibiotic, we are faced with the prospect of a future lacking of effective antibiotics in the fight against the most common human pathogens. Although establishment of a monitoring of resistant strains and the level and consumption structure of antibiotics, the problem of bacterial infections continue to grow, especially in the case of multidrug resistant strains. Multidrug resistant strains of microorganisms, belonging to the so-called group of alert



ESKAPE pathogens (*Enterococcus spp., Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter spp.*) are the most common etiological agent of many infections and according to the EMEA/ECDC report works on the development and creation of therapeutic options leading to a reduction in the use of antibiotics and reduction of the ratio of emerging drug resistance mechanisms should be one of the main directions of research. Our research projects lie within the desired research area.



In case of the major multidrug resistant human pathogens such as microorganisms from the ESKAPE group revealing the XDR (*extensively drug resistant*) type of antibiotic resistance we analyze the impact of photodynamic inactivation (PDI), both using blue light treatment (405 nm) or in combination with the photosensitizing compounds facilitating complete eradication of microorganisms *in vitro* (both in planktonic and biofilm culture) and *in vivo*. In our research we investigate a mouse model of a wound infected with methicillin-resistant *Staphylococcus aureus*, and multidrug resistant *Pseudomonas aeruginosa* to mimic the same disease in humans. In the mouse model, a stable and reproducible wound infection is analyzed and demonstrated by bioluminescence imaging. The use of bioluminescent strains allow us the real-time monitoring of the infection in mouse wounds. We believe that this alternative approach would facilitate rapid wound healing and would be the alternative therapeutic option for treating infected wounds.

Recent publications

- Fila G, Kawiak A, Grinholc MS. Blue light treatment of Pseudomonas aeruginosa: Strong bactericidal activity, synergism with antibiotics and inactivation of virulence factors. Virulence. 2017 Aug 18;8(6):938-958.
- Fila G, Kasimova K, Arenas Y, Nakonieczna J, Grinholc M, Bielawski KP, Lilge L. Murine Model Imitating Chronic Wound Infections for Evaluation of Antimicrobial Photodynamic Therapy Efficacy. Front Microbiol. 2016 Aug 9;7:1258
- Nakonieczna J, Kossakowska-Zwierucho M, Filipiak M, Hewelt-Belka W, Grinholc M, Bielawski KP. Photoinactivation of Staphylococcus aureus using proto-porphyrin IX: the role of haem-regulated transporter HrtA. Appl Microbiol Biotechnol. 2016 Feb;100 (3):1393-405.
- Kossakowska-Zwierucho M, Kaźmier-kiewicz R, Bielawski KP, Nakonieczna J. Factors Determining Staphylococcus aureus Susceptibility to Photoanti-microbial Chemotherapy: RsbU Acti-vity, Staphyloxanthin Level, and Membrane Fluidity. Front Microbiol. 2016 Jul 19;7:1141.
- Rybicka M, Woziwodzka A, Romanowski T, Stalke P, Dręczewski M, Bielawski KP. Differences in sequences between HBV-relaxed circular DNA and covalently closed circular DNA. Emerg Microbes Infect. 2017 Jun 21;6(6):e55.
- Wróblewska A, Bernat A, Woziwodzka A, Markiewicz J, Romanowski T, Bielawski KP, Smiatacz T, Sikorska K. Interferon lambda polymorphisms associate with body iron indices and hepatic expression of interferon-responsive long non-coding RNA in chronic hepatitis C. Clin Exp Med. 2017 May;17(2):225-232.

Scientific Collaboration

- Institute of Molecular Oncology, Ibbenbueren (Dr. Ulf Vogt)
- University of Freiburg, Germany, (Prof. Michael Nassal)
- INSERM U846 Stem-cell and Brain Research Institute, France (Prof. Pierre Savatier)
- University of Toronto, Canada (Prof. Lothar Lilge)
- Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University (prof. Tadeusz Sarna)

[Laboratory of Molecular Enzymology]

Prof. Andrzej C. Składanowski

Received his PhD in Biochemistry at the Medical University of Gdansk (1980). He carried out postdoctoral work on AMP deaminase at the Bern University, Switzerland (1981, 1983) and at the Wales University College of Medicine in Cardiff, UK working with Prof. Andrew Newby on adenosine metabolism in the heart (1988-90). Later he studied metabolism of purine nucleotides in ischemic human heart at Erasmus University Rotterdam, and structure of 5'-nucleotidase binding sites at the Bremen University. He became a habilitated doctor at 1997. In 2001 he was appointed associate professor at the Medical University of Gdansk and was awarded the full professorship at 2007. He is member of Editorial Board of the Elsevier's Toxicology in Vitro and is chairing the Gdansk Section of the Polish Biochemical Society.

Research group

Rafał Sądej, PhD DSc
Kamila Kitowska, PhD
Łukasz Turczyk, PhD student
Magdalena Mieszkowska, PhD student
Kamil Mieczkowski, PhD student
Dima Antoun, PhD student
Monika Górska, PhD student

PhD Thesis

- „Analysis of FGFR2 function and mechanism of action in breast cancer" Łukasz Turczyk, 2018,
- „Tetraspanin CD151 in progression of prostate cancer" Alicja Grudowska, 2015,

Progesterone impairs Herceptin effect on breast cancer cells

Kamila Kitowska, Agnieszka Kowalska, Magdalena Mieszkowska, Dominika Piasecka, Andrzej C. Skladanowski, Hanna M. Romanska, Rafal Sadej

Breast cancer (BCa) is the most common cancer affecting women worldwide. Overexpression of human epidermal growth factor receptor 2 (HER2) occurs in ca. 20 25% of invasive ductal breast carcinomas and is associated with the more aggressive phenotype. Herceptin, a humanized antibody against HER2, is a standard therapy in HER2 overexpressing cases. Approximately one third of patients relapse despite treatment. Therefore numerous studies have investigated the molecular mechanisms associated with Herceptin resistance. An interaction between HER2 signaling and steroid hormone receptor signaling pathways has been previously investigated, but the effect of this relationship on Herceptin resistance has never been studied. The present study analyzed an impact of the steroid hormone, progesterone (PG), on Herceptin dependent cell growth inhibition. Results indicated that Herceptin inhibited proliferation of breast cancer cell lines overexpressing HER2 (BT474 and MCF/HER2) in 3D culture is abolished by PG (see Fig. 1). Other results demonstrated that PG led to the activation of HER2/HER3 mediated signaling. PG treatment induced also a shift of Herceptin dependent cell cycle arrest in G1 phase towards S and G2 phases with concomitant upregulation of cyclin dependent kinase 2 (CDK2) and downregulation of CDK inhibitor p27Kip1. These results all together demonstrate a clear PG involvement in the failure of Herceptin treatment *in vitro*. Our observations also suggest that cross talk between PG and HRG/HER2 initiated signaling pathways may lead to the acquisition of resistance to Herceptin in patients with BCa.

Future plans

Further investigations on the role of FGFR1 in promoting growth of cancer cells and metastasis are carried on. Chemical compounds inhibiting FGFR-associated protein kinase are being tested as the mechanism-based anticancer drugs.

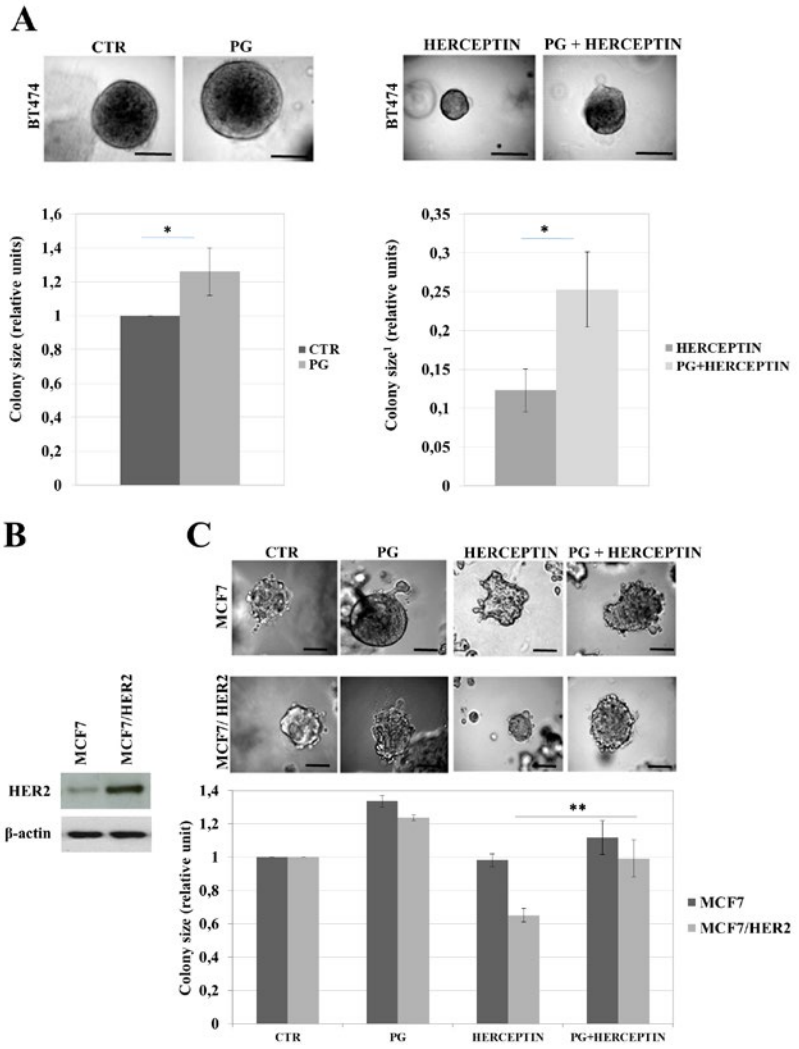


*Fig. 1. PG affects Herceptin-mediated cell growth inhibition. (A) BT474 cells were cultured in 3D Matrigel in the presence of PG (100 nM) and/or Herceptin (10μg/ml). (B) HER2-overexpressing cell line variant MCF7/HER2 was derived from MCF7 cells transfected with pBABEpuro-ERBB2. Expression level of HER2 was analyzed by WB in MCF7 and MCF7/HER2 cells. (C) MCF7 and MCF7/HER2 cells were cultured in 3D Matrigel in the presence of PG (100 nM) and/or Herceptin (10μg/ml). Representative pictures of colonies (for A and C) were taken after 10 days of growth. Magnification x200. Colony size was determined with ImageJ software. The values presented are means ± SD (n=3), *P<0.05; **P<0.01. Scale bar 100 μm. Relative unit = ratio to control (mean colony size of untreated cells). from Kitowska et al., Oncology Lett. 2018, 15:1817-1822.*

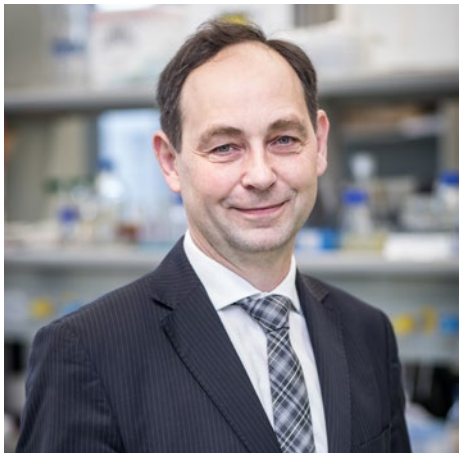
Recent publications

- Kitowska K, Kowalska A, Mieszkowska M, Piasecka D, Składanowski AC. Romanska HM, Sądej R, Progesterone impairs Herceptin effect on breast cancer cells. Oncology Lett. 2018, 15:1817-1822.
- Turczyk L, Kitowska K, Mieszkowska M, Mieczkowski K, Czaplinska D, Piasecka D, Kordek R, Skladanowski AC, Potemski P, Romanska HM, Sadej R. FGFR2-Driven Signaling Counteracts Tamoxifen Effect on ERα-Positive Breast Cancer Cells. Neoplasia 2017, 19(10):791-804.
- Grudowska A, Czaplińska D, Polom W, Matuszewski M, Sądej R, Składanowski AC. Tetraspanin CD151 mediates communication between PC3 prostate cancer cells and osteoblasts. Acta Biochim Pol. 2017, 64(1):135-141.
- Piasecka D, Kitowska K, Czaplinska D, Mieczkowski K, Mieszkowska M, Turczyk L, Skladanowski AC, Zaczek AJ, Biernat W, Kordek R, Romanska HM, Sadej R. Fibroblast growth factor signaling induces loss of progesterone receptor in breast cancer cells. Oncotarget 2016, 7(52):86011-86025.
- Czaplinska D, Mieczkowski K, Supernat A, Skladanowski AC, Kordek R, Biernat W, Zaczek AJ, Romanska HM, Sadej R. Interactions between FGFR2 and RSK2-implications for breast cancer prognosis. Tumour Biol. 2016 Oct;37(10):13721-13731.

Scientific Collaboration

- Division of Cancer Studies, University of Birmingham (UK) Professor Fedor Berditchevski,
- Department of Pathology, Medical University of Łódź (Poland) Professor Radzisław Kordek, Dr. Hanna M. Romańska
- Celon Pharma SA (Poland)

[Laboratory of Physical Biochemistry]



Bogdan Banecki, PhD

PhD, 1985, University of Gdańsk, PL Post-doctoral training: ETH Zurich, University of Utah, USA, University of Ancona, Italy Habilitation, 2003, University of Gdańsk, PL Group leader since 2004.

Research group

Leszek Kadziński, PhD,
Michał Grabowski,
Grzegorz Gawron,
Paulina Werner,
Bartłomiej Żerek.

PhD Thesis

- Wojciech Bartosz Sawuła, 2009 Analysis of risk factors and molecular mechanisms of pathogenesis of ischemic stroke
- Leszek Piotr Kadziński, 2013
The impact of silicone polymers on the structure and activity of proteins

The Laboratory of Biochemical Physics deals with functional analysis of the structure and function of proteins. The team studies structural changes in proteins and the influence of such on the activity and stability of these compounds using advanced spectroscopic, biophysical and biochemical techniques. Employed research techniques include stopped flow measurements, titration and scanning microcalorimetry, biochemical and genetic fluorescent techniques. The team is interested both in basic as well as applied research. Apart from spectroscopic studies, members of the team specialize in chromatographic analyses using liquid (HPLC) and gas (GC-MS) chromatography.

Laboratory participates in four main projects:

▶ Studies on functions of MTHFR and CBS genes during formation of homocysteine in the context of therapeutic and preventive aspects in patients with ischemic brain stroke. The aim of the research, performed in collaboration with Medical University of Gdańsk, is to describe the mechanism of homocysteine action in the organism as one of risk factors in the ischemic stroke. The initial research suggests that heat shock proteins significantly modify the activity of the MTHFR enzyme

▶ Development and studies of biocompatible and bioregenerative materials. We analyzed the side effects of silicone implants by determining the influence on the stability and structure of proteins. The aim of the current research is characterization of interactions of small molecule polymethylsiloxanes with proteins. The conducted research indicates significant affinity of silicones to fibrinogen and collagen, which can be of significance in the development of clinical side effects of using implants.

▶ Isolation and implementation of new nutraceuticals containing natural extracts with the use of efficient, economical and environmentally friendly methods. The project involves the structural identification and determination of possible modifications for increasing the activity and bioavailability of anti-inflammatory and antimicrobial compounds. As a result the project would yield a group of active compounds that will be implemented into the industrial practice. With the collaboration between our team and the laboratory of Biovico sp. z o.o. Gdynia, Poland, we developed new preparation of ointment based on one of the nutraceutical being examined in the project, which has been already released to the market.

▶ Analysis of interactions between silica-based biomaterials and proteins. Silica based biomaterials have gained great interest among scientists due to the possibility of their use in medicine as scaffolds and drug carriers. Their superiority over other biomaterials lie in the way of their synthesis as well as their non-toxicity and biocompatibility in vivo. Gained knowledge could benefit in better understanding the wound healing process and bone regeneration. Moreover, I will study the possibility of application of the biomaterials in the controlled drug release

Future plans

Future plans of our laboratory involve the continuation of the project connected with ischemic stroke risk factors. We are planning to investigate the possible role of inhibitors of nitric oxide synthases – symmetric and asymmetric dimethyloarginine. We hope to be able to correlate its serum level with the ischemic stroke development. Futhermore, we aim to broaden the scope of the project about the neutraceuticals to test different plants in the context of their neutraceutical content. According to the future analysis of silica-based biomaterials, we are planning to investigate the interactions between those with collagen, as well as to check this protein stability and function after being attached to the silica-based material structure. Also we would like to examine the structure of obtained biomaterial with the use of different type of microscopy techniques, like surface electron mictroscopy (SEM), transmission electron microscopy (TEM) and atomic force microscopy (AFM). Basing on the gained knowledge we would broaden our project to the use of different proteins to check its interactions. Performed research of the desired proteins will involve their interactions with the biomaterial both external as well as the internal one in the context of its possible use as a drug delivery system in the future.

Recent publications

- Banecka-Majkutewicz Z, Kadziński L, Grabowski M, Bloch S, Kaźmierkiewicz R, Jakóbkiewicz-Banecka J, Gabig-Cimińska M, Węgrzyn G, Węgrzyn A, Banecki B. Evidence for interactions between homocysteine and genistein: insights into stroke risk and potential treatment. Metab Brain Dis. 2017 Dec;32(6):1855-1860. doi: 10.1007/s11011-017-0078-1. Epub 2017 Jul 26. PMID: 28748495
- Kadziński L, Prokopowicz M, Jakóbkiewicz-Banecka J, Gabig-Cimińska M, Łukasiak J, Banecki B. Effect of silicone on the collagen fibrillogenesis and stability. J Pharm Sci. 2015 Apr;104(4):1275-81. doi: 10.1002/jps.24351. Epub 2015 Jan 14. PMID: 25589402 Free PMC Article
- Mozolewski P, Jakóbkiewicz-Banecka J, Węgrzyn G, Banecki B, Gabig-Cimińska M. Non-steroidal anti-inflammatory drugs are safe with respect to the transcriptome of human dermal fibroblasts. Eur J Pharmacol. 2018 Jan 5;818:206-210. doi: 10.1016/j.ejphar.2017.10.040. Epub 2017 Oct 24.PMID: 29074415

Patents

- The extraction method of sulfonamides, secondary metabolites or semi-synthetic compounds. The patent application (UP RP) No. 402299 dated 2012-12-28.

  (Sposób ekstrakcji sulfonamidów, metabolitów wtórnych lub związków półsyntetycznych. Zgłoszenie patentowe (UP RP) nr 402299 z dnia 2012-12-28.)

Scientific Collaboration

- Medical University of Gdańsk
- Biovico sp. z o.o. Gdynia, Poland

[Laboratory of Plant Biochemistry]

Prof. Antoni Banaś

Graduated from the University of Gdańsk in 1978, where he received PhD in biology (1985). In 1994 received habilitation in biological sciences at Warsaw University. He carried out post-doctoral work at Swedish University of Agricultural Sciences and at Scandinavian Biotechnology Research AB. He is a full-professor in biological sciences since 2009. He is co-author of 88 articles (citied over 1350 times) and around 150 conference communications. He is also co-inventor of 8 patents granted more than 50 times as national patents. He is a supervisor of 4 finished and 4 ongoing PhD's.

Research group

Katarzyna Jasieniecka-Gazarkiewicz, PhD,
Kamil Demski, PhD student,
Bartosz Głąb, PhD student,

PhD Thesis

- Magdalena Miklaszewska "Substrate specificity of selected fatty acid reductases and wax synthases", Gdańsk, 2015
- Katarzyna Jasieniecka- Gazarkiewicz "Substrate specificity and physiological functions of selected acyl-CoA: lysophospholipid acyltransferase", Gdańsk, 2015
- Anna Grzesiuk "Effect of graminicides on selected processes of sensitive plants", Słupsk, 2002

Research: Biochemical basis for improvement of plant oil production

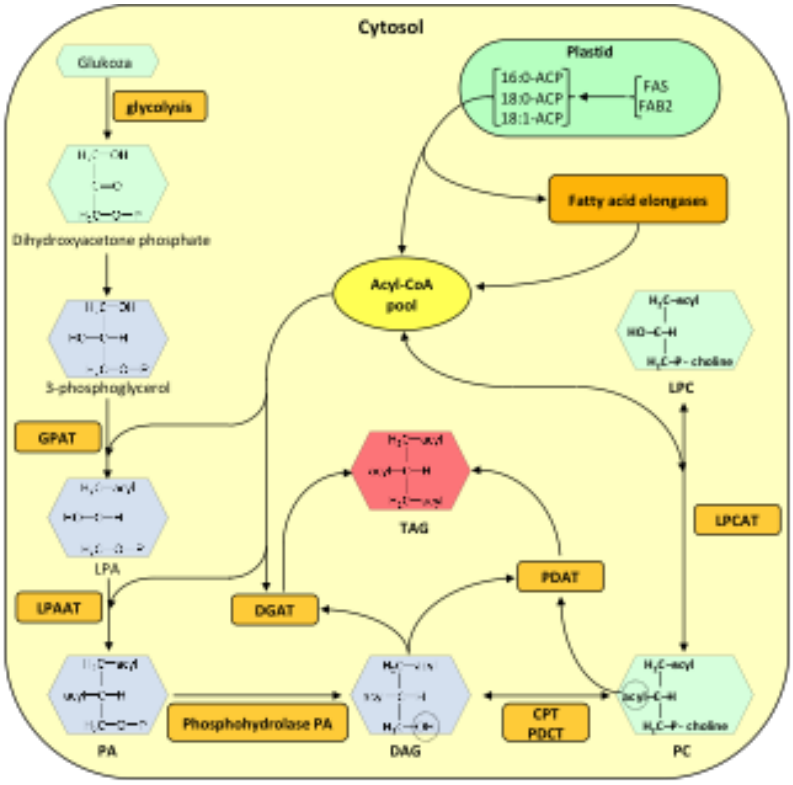
The research interests of the laboratory mainly concern biochemistry and biotechnology of plant lipids.

During the last few years, the laboratory participated in a worldwide integrated project "Industrial Crops producing added value Oils for Novel chemicals – ICON" financed by the Seventh EU Framework Program. The key goal of this endeavour was production of different kinds of wax esters in industrial crops, such as *Crambe abbysinica*, *Camelina sativa* or *Brassica carinata*. Our lab has specialised in characterization of substrate specificities of various fatty acid reductases (FAR) and wax synthases (WS) – the key enzymes of wax esters synthesis. Additionally, the biochemistry of wax ester mobilisation in germinating: (a) jojoba seeds (plant naturally accumulating wax esters) and (b) seeds of transgenic industrial crops producing wax esters have been investigated. Several of these research strands are continued now beyond ICON project.

Beside the above mentioned research we are involved in:

- biochemical characterization and determination of substrate specificity and physiological functions of selected acyl-CoA:lysophospholipid acyltransferases;
- biochemical characterization, determination of substrate specificity and physiological function of enzyme of DGAT type (acyl-CoA: diacylglycerol acyltransferase) and PDAT-type (phospholipid: diacylglycerol acyltransferase) – key enzymes involved in triacylglycerols biosynthesis;
- potential use of biotechnology to create commercially viable plants accumulating storage lipids in leaves and roots

Generally speaking, the group aims at characterisation of different enzymes connected with lipid metabolism (Fig. 1) and evaluation of their potential application in production of different kinds of oil (demanded by chemical industry) in transgenic industrial oil crops as well as providing the biochemical basis for genetic engineering aimed at increase of the oil production capacity both by traditional oilseed crops, as well as new plants producing oil in organs other than seeds (e.g. tubers, leaves, roots).



GPAT – acyltransferase acyl-CoA:3-phosphoglycerol; **LPAAT** – acyltransferase acyl-CoA:lysophosphatidic acid; **DGAT** – acyltransferase acylo-CoA:diacylglycerol; PDAT – acyltransferase phospholipid:diacylglycerol; **CPT** – cholinephosphotransferase **CDP**-choline:diacylglycerol; **PDCT** – cholinephosphotransferase phosphatidylcholine: diacylglycerol; **LPCAT** – acyltransferase acyl-CoA: lysophosphatidylcholine; **FAS** – fatty acid synthase; **FAB2** – stearyl-ACP desaturase

Figure 1.The general scheme of the biosynthesis of triacylglycerols in seeds of oilseeds plants.

Future plans

For the next few years the research connected with the newly granted NCN project "The role of acyl-CoA:lysophosphatidylethanolamine acyltransferases (LPLATs) in plants" as well as the continuation of the current work concerning other aspects of plant lipid metabolism is planned.

Recent publications

- Jasieniecka-Gazarkiewicz, K., Demski, K., Lager, I., Stymne, S., Banas, A. 2016. Possible role of different yeast and plant lysophospholipid:acyl-CoA acyltransferases in acyl remodeling of phospholipids. LIPIDS, 51:15-32
- Miklaszewska, M., Banaś, A. 2016. Biochemical characterization and substrate specificity of jojoba fatty acyl-CoA reductase and jojoba wax synthase. Plant Science, 249: 84-92.
- Miklaszewska, M., Banaś, A., Królicka, A. 2017. Metabolic engineering of fatty alcohol production in transgenic hairy roots of Crambe abyssinica. Biotechnology and Bioengineering, 114 (6):1275-1282
- Jasieniecka-Gazarkiewicz, K., Lager, I., Carlsson, AS., Gutbrod, K., Peisker, H., Dörman, P., Stymne, S., Banaś, A. 2017 Acyl-CoA: lysophosphatidylethanolamine acyltransferase activity regulates growth of Arabidopsis. Plant Physiol 174: 986-998

Scientific Collaboration

Prof Banaś's team collaborates closely with researchers from the Department of Plant Breeding and Biotechnology of the Swedish University of Agricultural Science. Moreover, Prof Banaś' laboratory cooperates with several leading laboratories from Europe, USA, Canada and China.

[Laboratory of Plant Protection and Biotechnology]

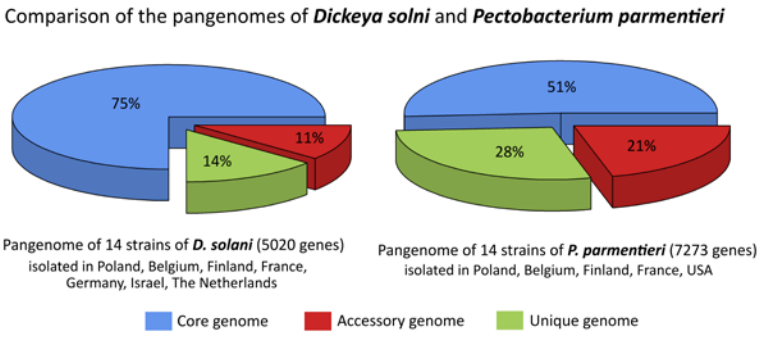
Prof. Ewa Łojkowska

She graduated from University of Toruń in 1977, received PhD in 1984, habilitation in 1991. She carried out postdoctoral work at University of Madison-Wisconsin, USA and INSA, Lyon, France. Professor in biological sciences since 2001. Dean of the IFB UG & MUG in 2015-2012. Author of more than 110 peer-reviewed publications, supervisor of 17 finished and ongoing PhD's. Vice-head of Committee for Biotechnology PAS, member of Central Commission for Scientific Degrees, President of the Jury L'Oreal Poland for Women in Science and member of the L'Oreal International Rising Talents Selection Committee.

Research group

Małgorzata Waleron, PhD, DSci;
Anna Ihnatowicz, PhD;
Anna Kawiak, PhD;
Marta Potrykus, PhD;
Joanna Siwińska, PhD;
Wojciech Śledź, PhD.
PhD students:
Natasza Kaczyńska, Agnieszka Misztak, Agata Motyka, Izabela Perkowska, Sabina Żołędowska,

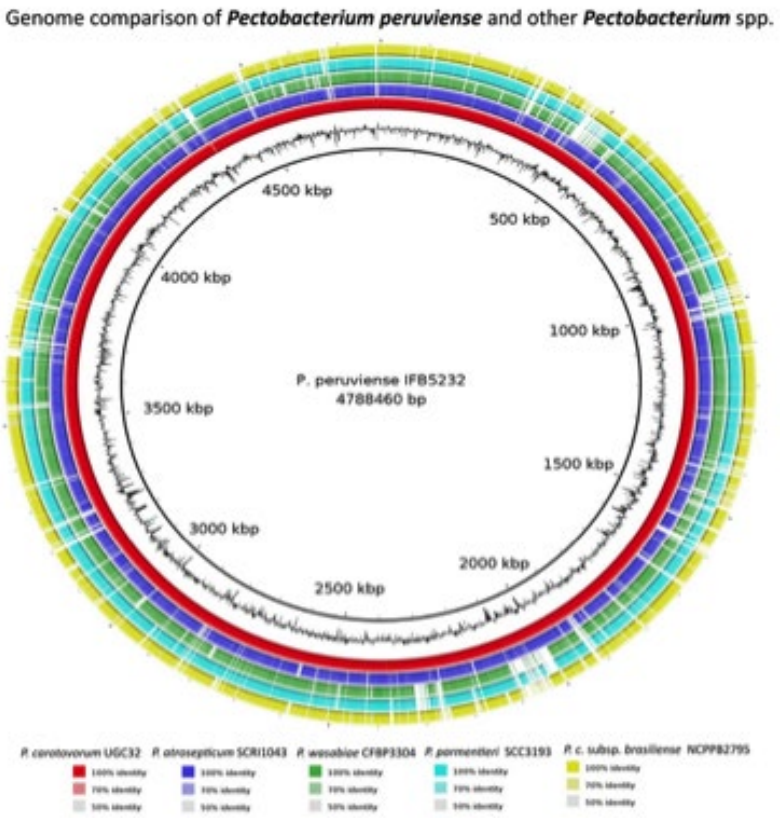
1) Study of the molecular mechanisms involved in the interaction of pectinolytic plant pathogenic bacteria and plant tissue. The goal of our current research is to elucidate the molecular basis of the Dickeya and Pectobacterium virulence on potato. Our studies were concentrated on the regulation of the synthesis of enzymes degrading plant cell wall, especially pectate lyases but also other enzymes and factors important in pathogenesis e.g. cellulases, siderophores, biofilm formation. The performed study expanded the knowledge on molecular mechanisms involved in this interaction. We also study the pangenome and panregulon of Dickeya solani and Pectobacterium parmentieri. The mentioned microbes differ significantly in their biodiversity and pangenome structure. D. solani strains exhibit homogeneity of the genomes (about 75% of genes in core genome) contrarily to their diverse virulence levels, whereas P. parmentieri strains display higher divergence concerning both traits indicated (only about 50% of genes in core genome), (Fig. 1). The presented characteristics determine profound potential of these species as the models for identification of the genes crucial for virulence and adaptation to different environmental niches.



2) Molecular taxonomy, monitoring, adaptation to stress and control of bacteria from genus *Pectobacterium*. We are developing methods for detection and identification of plant pathogenic bacteria. Multiplex-PCR test for simultaneous detection of 3 different species of pectinolytic bacteria was developed, patented and is currently used for diagnostic purposes (Patent PL 223540 B1). Application of modern techniques allowed also to describe a new species of pectinolytic bacteria *Pectobacterium peruviense* (Fig. 2). The study is concentrated on comprehensive genetic and phenotypic characterization of selected cosmopolitan Pectobacterium strains capable of infecting several species of plants. Characteristics of bacteria of the genus *Pectobacterium* allowed for identification of the genes involved in the adaptation to the environment and the rapid spread. Our studies were also devoted to the control of plant pathogenic bacteria by newly isolated and characterized bacteriophages with wide and narrow host specificity to different group of *Pectobacteriaceae* and also by application of direct current atmospheric pressure glow discharge (dc-APGD) generated in contact with flowing bacterial suspensions acting as the liquid cathode.

3) Study of plant secondary metabolites biosynthesis and their role in plant resistance to abiotic and biotic stresses. In this study, we aim to elucidate the function of selected genes and corresponding proteins involved in plant secondary metabolism and responses to various

environmental stresses using a model plant *Arabidopsis thaliana*. We are particularly interested in the metabolic pathway of coumarin biosynthesis and its involvement in iron homeostasis in plants. The study allowed to better understand the genetic and molecular basis of plant responses to different environmental factors and possibly to get insight into the plant adaptation to changing environmental conditions. A set of different functional genomics techniques (ionomics, metabolite profiling, proteomic analysis of thylakoid membranes, transcriptomics) is used, as well as the biochemical and molecular biology methods.



4) Role of Drosera spp. naphthoquinones in the induction of apoptosis. The study aimed at determining the activity of naphtoquinones: plumbagin and ramentaceone toward breast cancer cells and the characterization of the metabolic pathway involved in naphtochinons-mediated cell death induction. The results showed that naphtochinons exhibited high antiproliferative activity toward breast cancer cells, in particular HER2-overexpressing breast cancer cells. The mode of cell death induced was through apoptosis.

5) Genetics, molecular taxonomy and adaptation to stress of Cyanobacteria. We investigate edible cyanobacteria from the genus *Arthrospira* and *Nostoc*. For *Arthrospira* strains, we are performing detailed polyphasic analyses using techniques such as MLSA, fatty acid profiling, comparative genomics and carrying out bioinformatics analysis to improve taxonomy of this genus. We are also studying adaptive abilities of cyanobacteria; their survivability in stress conditions like temperature, salinity, UV or heavy metals. We examined the response of cyanobacteria to stress by means of metabolomic, lipidomic and transcriptomic analyzes. What's more, themetagenomic studies allowed identification of bacteria accompanying edible cyanobacteria from the genera *Nostoc* and *Arthrospira*. Some of the microorganisms from the *Nostoc* and *Arthrospira* microbion indicated an ability to transform biologically active compounds such as, e.g. xanthohumol or naringenin.

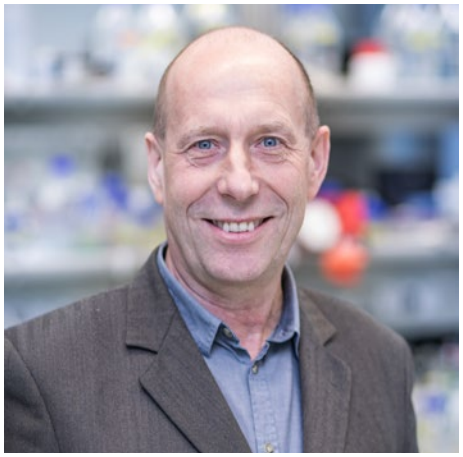
Recent publications

- Furmaniak M., Misztak A., Franczuk M., Wilmotte A., Waleron M., Waleron K. Edible Cyanobacterial Genus Arthrospira: Actual State of the Art in Cultivation Methods, and Application in Medicine. Front. in Microbiol. 2017, 8: 2541
- Kawiak A., Domachowska A., Jaworska A., Łojkowska E. Plumbagin sensitizes breast cancer cells to tamoxifen-induced cell death through GRP78 inhibition and Bik upregulation. Scien. Rep. 2017, 7: 4378
- Motyka A., Dzimitrowicz A., Jamróz P., Łojkowska E., Śledź W., Pohl P. Rapid eradication of bacteria by atmospheric pressure glow discharge generated in contact with a flowing liquid cathode. Biotech. & Bioengin. 2017. (in press).
- Potrykus M., Hugouvieux-Cotte-Pattat N., Łojkowska E. Interplay of classic Exp and specific Vfm quorum sensing systems on the phenotypic features of Dickeya solani strains exhibiting different virulence levels. Mol. Plant Pathol. 2017 (in press)
- Siwinska J., Siatkowska K., Olry A., Grosjean J., Hehn A., Bourgaud F., Carey M., Łojkowska A., Ihnatowicz A. Scopoletin 8-hydroxylase: a novel enzyme involved in coumarin biosynthesis and iron-deficiency responses. J. Exper. Bot. 2017 (in press).
- Żołedowska S., Motyka A., Żukowska D., Śledz W., Łojkowska E. Population struc-ture and biodiversity of Pectobacterium parmentieri isolated from potato in tempe-rate climate. Plant Dis. 2017 (in press).

Scientific Collaboration

- EUPHRESCO – Phytosanitary ERA NET, "Dickeya and Pectobacterium in potato and management strategies".
- Prof. Alessio Mengoni, University of Florence, Italy.
- Dr. Nicole Hugouvieux-Cotet-Pattat, INSA, Lyon, France,
- Prof. Alain Hehn, ENSAIA, Nancy, France,
- Prof. Anick Wilmotte, Belgium.
- Prof. Paweł Pohl, Wroclaw University of Science and Technology, PL,
- Prof. Zbigniew Kaczyński, University of Gdańsk, PL

[Laboratory of Protein Biochemistry]



Prof. Krzysztof Liberek

He graduated from physics at the Technical University of Gdansk (1982), received his PhD in biology at the University of Gdansk (1990) and received his habilitation in biological sciences at the University of Gdansk (1996). He carried out postdoctoral work at Department of Viral, Cellular and Molecular Biology, University of Utah, USA (1990-91) and Department of Medical Biochemistry, University of Geneve, Switzerland (1992-93). He is a full-professor in biological sciences since 2002. In 2006 he was elected to EMBO.

Research group

Anna Janta, PhD,
Agnieszka Kłosowska,PhD
Szymon Ziętkiewicz, PhD
Tomasz Chamera, PhD student
Dagmara Mróz, PhD student
Igor Obuchowski, PhD student
Artur Piróg, PhD student

PhD Thesis

- "The mechanism of chaperone- dependent disaggregation of complexes comprising small heat shock proteins and their substrates" Szymon Żwirowski, 2016,
- "The mechanism of cooperation between Hsp70 and Hsp104 chaperones in the reactivation of aggregated proteins" Agnieszka Kłosowska, 2017

We are interested in the role and mechanisms of chaperone proteins action in different cellular processes. The chaperone protein network controls both initial protein folding and maintenance of proteins in the cell. The linear polypeptide chains newly synthesized on ribosomes have to fold into native three-dimensional structures. Although the native structure of a protein is principally encoded in its amino acid sequence, the process of folding in vivo very often requires the assistance of molecular chaperones. Chaperones also play a role downstream of protein synthesis in a quality control system and thus are required to maintain the proper conformation of proteins in changing environmental conditions. Many factors leading to unfolding and misfolding of proteins result eventually in protein aggregation. High temperature was one of the first aggregation inducing factors studied, and remains one of the main model approaches. With massive protein aggregation occurring in response to heat exposure, the cell needs chaperones to control and counteract the aggregation process. Elimination of aggregates can be achieved by two alternative pathways, solubilization of aggregates and either refolding of liberated polypeptides or their proteolysis. In our research we focus on the mechanisms by which Hsp70, Hsp100 and small heat shock proteins (sHsps) liberate and refold polypeptides trapped in the protein aggregates.

Cooperation between Hsp100 and Hsp70 in protein disaggregation. The Hsp100 family of chaperone proteins plays a wide variety of important cellular functions, including survival to environmental stress, regulation of genetic competence, transposition, proteolysis, and control of protein-based genetic element (prion). These different roles are unified by a common biochemical mechanism, the ability of Hsp100 proteins to promote the disassembly of aggregated proteins and high order protein complexes. During disaggregation a polypeptide is disentangled from the aggregate, translocated through the central channel, and enabled to fold into the native structure. However, Hsp100 chaperones are not able to act on its own. Functional cooperation between Hsp100 and Hsp70 and its cochaperones is required at several stages of this process. In our research we are trying to determine the molecular mechanism of cooperation between chaperones from Hsp70 and Hsp100 families in disaggregation and refolding of aggregated proteins.

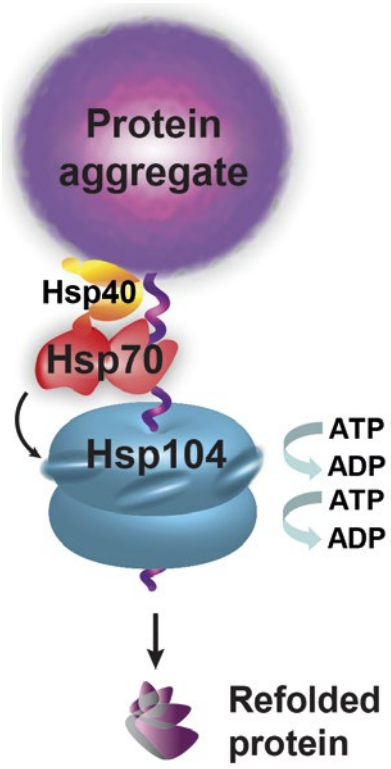


Figure 1. Model for the mechanism of action of Hsp70 and Hsp100 chaperones in disaggregation of protein aggregates

Role of sHsps in control of aggregation and disaggre- gation. Small heat shock proteins are an evolutionary conserved class of ATP-independent molecular chaperones. Members of this family are characterized by a low molecular mass (15-43 kDa) and the presence of the conserved α-crystallin domain. At physiological conditions sHsps form oligomeric structures. Under heat stress conditions deoligomerization process takes place and sHsps form complexes with misfolded proteins, preventing them from further aggregation and keeping them in a refoldable state that facilitates subsequent solubilisation and refolding by AT- P-dependent Hsp70 and Hsp100 chaperones. Using different biochemical approaches we are investigating the molecular events leading to deoligomerization of sHsps and subsequent interaction between these chaperones and their substrates leading to formation of sHsps-substrate complexes. We also analyse the mechanism of misfolded protein refolding from such complexes. While the initial binding of sHsps to substrates is beneficial by preventing the formation of large aggregates and increasing the accessible surface for Hsp70-Hsp100 action, this interaction also hamper Hsp70-Hsp100 association and has to be broken to allow for substrate refolding. How this Janus-faced sHsp feature is circumvented has not been addressed so far. Recently, we have identified a novel Hsp70 activity, displacing sHsp molecules from the surface of the complex at the very initial phase of the reactivation process.

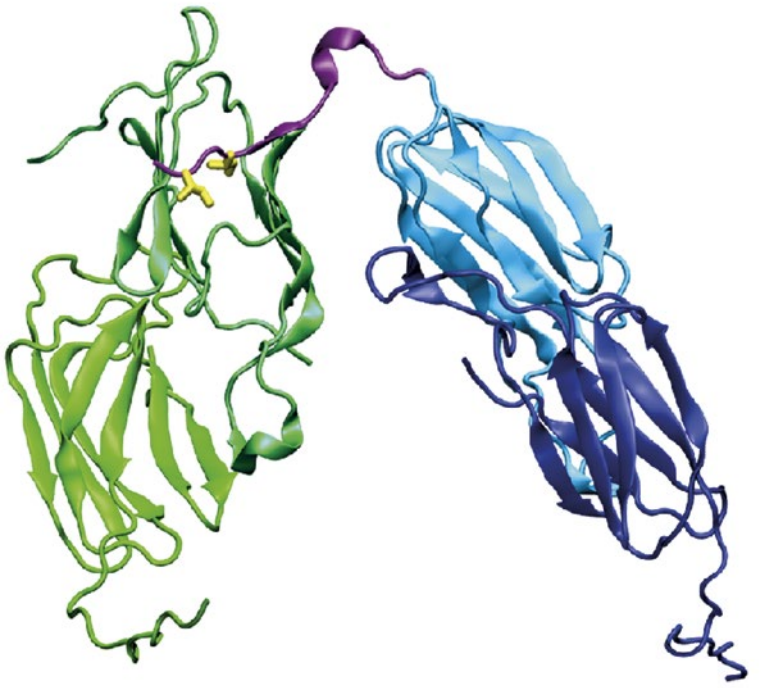


Figure 2. Model of two homodimers of sHsps, IbpA chaperone proteins from Escherichia coli, interacting through the C-terminal motif.

Our studies contribute to the understanding of the fun- damental processes of chaperones functioning. Our long term goal is to understand the functional interactions and crosstalk be- tween components of a chaperone network in different cellular processes.

Recent publications

- Wortmann, S.B. Ziętkiewicz, S. et al., (2015) CLPB mutations cause 3-methylglutaconic aciduria, progressive brain atrophy, intellectual disability, congenital neutropenia, cataracts, movement disorder Am. J. Hum. Genet. 96, 245-57
- Kłosowska, A., Chamera, T., Liberek, K. (2016) Adenosine diphosphate restricts the protein remodeling activity of the Hsp104 chaperone to Hsp70 assisted disaggregation. eLife 2016; 5:e15159. DOI: 10.7554/eLife.15159
- Żwirowski, S., Kłosowska, A., Obuchowski, I., Nillegoda, N. B., Piróg, A., Ziętkiewicz, S., Bukau, B., Mogk, A., Liberek, K. (2017) Hsp70 displaces small heat shock proteins from aggregates to initiate protein refolding. EMBO J. 36, 783-796

Scientific Collaboration

- Center for Molecular Biology of the University of Heidelberg (Germany), Professor Bernd Buka

[Laboratory of Recombinant Vaccines]

Prof. Bogusław Szewczyk

Graduated in 1974 at the Faculty of Chemistry, Technical University of Gdansk. Obtained PhD degree at the Faculty of Chemistry, University of Gdansk in 1984. Habilitation was awarded in 1996 at the Faculty of Biology, Geography and Oceanology, University of Gdansk. Full professorship since 2001.Group leader at IFB since 1996.
Postdoctoral research was done at: University of California San Francisco, USA; University of Utah, Salt Lake City, USA; University of London, United Kingdom.

Research group

Ewelina Król, PhD
Łukasz Rąbalski, PhD
Krzysztof Łepek, PhD
Gabriela Brzuska, PhD student
Martyna Krejmer, PhD student
Karolina Uranowska, PhD student
Maciej Kosiński, PhD student
Sara Boch-Kmnikowska, PhD student

Patents

- DNA vaccine, method of inducing the immune response, method of immunisation, antibodies specifically recognizing the H5 haemagglutinin of an influenza virus and use of DNA vaccine, Patent No. US 9,505,806 granted on 29.11.2016r.
- Selected strain of baculovirus LdMNPV-PL for application in biopesticides. Application P.405607, patent granted on 03.11.2017

The main field of interest of the Laboratory is the application of different expression systems for the production of viral proteins which can be used as potential vaccines or constituents of modern diagnostic tests. Apart from using a wide array of classical methods of molecular biology, the Laboratory specializes in expression of foreign genes in insect cells using baculovirus expression system. Some of the research projects carried out in the Laboratory are listed below:

Construction of recombinant vaccines against bird flu viruses: H5N1, H7N9, H9N2; against human pandemic and seasonal influenza viruses and against Newcastle virus (NDV)

The research on the construction of recombinant vaccines against human and animal influenza was carried out in close collaboration with three scientific institutions which constitute Polish Vaccine Consortium: Institute of Biochemistry and Biophysics Polish Academy of Sciences, Institute of Biotechnology and Antibiotics, and National Veterinary Research Institute. Polish Vaccine Consortium succeeded in construction of a variety of potential anti-influenza vaccines against bird flu H5N1. Two approaches: expression of hemagglutinin in bacteria *Escherichia coli* and in yeast *Pichia pastoris* fulfilled the requirements for large scale protection of chickens, that is excellent protection and very low price for a dose. At present the Consortium is working on the construction of vaccines against two other very dangerous avian strains of influenza: H7N9 and H9N2.

Simultaneously the Consortium constructs the anti-influenza vaccines for humans, both for seasonal as well as for pandemic strains. In case of human vaccines, the criterion of low price though important, is not crucial, therefore other expression systems such as baculovirus or mammalian cells are being used for the production of antigens. The potential vaccines are based on the viral-like particles (VLPs), that is the outer coats of viruses without its genetic material. At present it is the most effective approach to currently produced vaccines.

Though the influenza A/H1N1 responsible for the first pandemic of the twenty- first century turned out to be relatively mild when compared to other influenza pandemics of the past, such a situation may be transient and there are concerns that the virus may reassert during mixed infections of a single host with different variants of influenza A virus. The resulting recombinant virus may have unpredictable properties when it establishes itself in the human population. Therefore, we monitor these processes in animals. Additionally we are trying to develop an universal vaccine against influenza virus which may protect against many strains of the virus. This may be achieved by efficient production of constant regions of viral proteins, e.g. the stalk region of influenza hemagglutinin.

Another devastating disease of poultry is the Newcastle disease. We have changed the classical approach of vaccination, that is using the attenuated strains for vaccination, by replacing it with a recombinant vaccine based on live attenuated turkey herpesvirus (licensed as a vaccine against Marek's disease in many countries) where two genes of Newcastle disease virus are inserted in dispensable part of herpesvirus genome. Animal studies on the efficacy of this vaccine are practically finished. The protection of birds is very good and we are planning to commercialize the vaccine. Another approach to Newcastle disease vaccine is to employ safe, inexpensive and fast platform for the production of the vaccine

candidate using caterpillars as a natural bioreactor. The product will be also based on virus-like particles containing few viral proteins. This approach is also intensively pursued in our laboratory.

Effect of synthetic glycosylation inhibitors on viral entrance and propagation in host cells.

Lack of effective drugs against most of viral diseases calls for an intensive research in this field. We have concentrated our efforts on the development of structural analogs and mimetics of tunicamycin, an effective inhibitor of N-glycosylation of glycoproteins. A large number of synthetic compounds was obtained from Pharmaceutical Institute in Warsaw and Silesian Technical University in Gliwice. We have tested these compounds using a few model viruses which included hepatitis C virus, classical swine fever virus, pseudorabies virus and influenza A virus. A few of these compounds exhibited promising antiviral properties and are further studied with the aim to elucidate their mechanism of action. Some of the inhibitors interfere with the mechanism of glycosylation, while the other inhibit viral propagation by other molecular mechanisms.

Monitoring of baculoviruses controlling the populations of lepidopteran pests in forests and orchards.

Apart from being an excellent system for expression of foreign genes, baculoviruses are used as biological pesticides which are safe for the environment and very selective with respect to a pest. In cooperation with Forest Research Institute in Warsaw we have isolated, and performed extensive sequencing of baculoviruses attacking gypsy moth and other members of the family *Lymantridae*. These studies gave us insight into virulence factors of this family of lepidopteran pests. Recently we have started cooperation with Grahamstown University in South Africa on characterization of baculoviruses which can be used for the protection of orange orchards. The studies are funded by South African and Polish governments.

Future plans

The epidemiology of viral diseases, to a large extent, is a constant chase for new pathogenic viruses. One of the emerging threats for Middle and Western Europe is the tick-borne encephalitis virus (TBEV). Due to the changing climate conditions, the European variant of the virus is quickly translocated to completely new ecological niches in Europe. Additionally, there is an increasing threat of genetic recombination between European variant and even more dangerous Siberian variant of the virus. In our research we are committed to interfere with the spread of this virus and we are constructing a recombinant vaccine against TBEV as well as we are monitoring the genetic changes of the emerging viruses.

Finally, we are preparing tools for prevention by vaccination and for quick molecular diagnosis of viral diseases which may appear in the nearest future. We have concentrated our efforts on Zika virus and hepatitis E virus which are of increasing importance for the whole world. For all these viruses we shall also test the inhibitory effect of our glycosylation inhibitors and their potential application as pharmaceutical compounds.

Scientific collaboration

- Grahamstown University, South Africa.
- Biological Control Unit EMBRAPA, Brasilia, Brazil.
- Forest Research Institute, Warsaw
- Pharmaceutical Institute, Warsaw,
- Silesian Technical University, Gliwice
- Institute of Biotechnology and Antibiotics, Warsaw

Recent publications

- Lepek, K., Pajak,B., Rabalski, L., Urbaniak, K., Kucharczyk, K., Markowska-Daniel, I., Szewczyk, B., (2015) Analysis of co-infections with A/H1N1 strain variants among pigs in Poland by MultitemperatureSingle-Strand Conformational Polymorphism (MSSCP) BioMed Res. Int , Article ID 632347, doi. org/10.1155/2015/535908
- Rąbalski Ł., Krejmer-Rąbalska M., Skrzecz I., Wasąg B., Szewczyk B. (2016) An alphabaculovirus isolated from dead Lymantria dispar larvae shows high genetic similarity to baculovirus previously isolated from Lymantria monacha – An example of adaptation to a new host. Journal of Invertebrate Pathology 139, 56-66 (doi: 10.1016/j.jip.2016.07.011)
- Saczynska V., Romanik A., Florys K., Cecuda-Adamczewska V., Kesik-Brodacka M., Smietanka K., Olszewska M., Domanska-Blicharz K., Minta Z., Szewczyk B., Plucienniczak G., Plucienniczak A. (2017) A novel hemagglutinin protein produced in bacteria protects chickens against H5N1 highly pathogenic avian influenza viruses by inducing H5 subtype-specific neutralizing antibodies PLoS ONE, 12, e0172008, doi:10.1371/journal. pone. 0172008
- Pastuk-Gawolek, G., Chaubey, B., Szewczyk, B. Krol, E., (2017) Novel thioglycosyl analogs of glycosyltransferase substrates as antiviral compounds against classical swine fever virus and hepatitis C virus. European Journal of Medicinal Chemistry 137, 247-262; doi.org/10.1016/j. ejmech.2017.05.051

PhD Thesis

- Ewelina Król „Classical swine virus (CSFV) as the model for testing the activity of novel inhibitors against hepatitis C virus (HCV), (2012)
- Łukasz Rąbalski „Application of ssDNA separation and real-time PCR for the detection and differentiation of Newcastle virus strains", (2014)
- Dawid Nidzworski „Novel methods for the detection of influenza virus and Newcastle disease virus", (2014)
- Krzysztof Łepek „Differentiation of influenza strains by new diagnostic methods", (2016)
- Marcin Zieliński (SGGW-Warszawa) „Production of PAM enzyme in eukaryotic cell cultures and its use for human recombinant insulin analogue modification", (2017)

[Laboratory of Virus Molecular Biology]

Prof. Krystyna Bieńkowska - Szewczyk

Graduated in 1976 at University of Gdansk, obtained PhD in biochemistry (1982) at the Faculty of Biology, Geography and Oceanology of University of Gdansk, habilitation awarded at the same Faculty in 2002. Full professorship since 2008. Postdoctoral research: Max Planck Institute, Tubingen (Germany), University of California San Francisco (USA), University of Utah, (USA), The Institute for Animal Science and Health, (The Netherlands). Since 1998 a partner in five EU international projects founded by European Framework Programs. Vice-dean of IFB for 6 years. Co-founder of International Center for Cancer Vaccine Science (ICCVS)

Research group

Andrea Lipińska, PhD
Małgorzata Rychłowska, PhD
Michał Rychłowski, PhD
Katarzyna Grzyb , PhD
Alicja Chmielewska, PhD
Krzysztof Lacek, PhD
PhD students:
Natalia Derewońko, Mirosława Panasiuk, Karolina Zimmer, Małgorzata Graul, Joanna Belkiewicz, Magda Wąchalska, Anna Czarnota, Kinga Grabowska

Research

Viruses that are currently studied in our lab include herpesviruses and hepatitis C virus. We investigate various aspects of virus-host interaction, with the focus on virus entry, spread and the modulation of immune response. To study the structure and functions of viral proteins and their interactions with host cells, we construct live viral mutants with deleted or modified genes as well as the stable cell lines expressing the genes of interest. The intramolecular localization and transport of viral proteins in infected cells is analyzed by laser confocal microscopy. The construction of recombinant viral particles labeled with fluorescent markers allows us to make direct observations of virus multiplication and spread in live cells.

The examples of research projects include the study of direct cell-to-cell mode of viral spread. Many enveloped viruses, apart from "free entry" (binding of viral particles to the surface of permissive cells), can be also disseminated by direct fast "cell-to-cell" spread mode, without being secreted to the extracellular environment and being exposed to the immunological response. We study direct transmission of alpha-herpesviruses using as a model bovine herpesvirus 1 (BHV-1) , a pathogen of cattle, closely related to human pathogens (HSV-1, VZV). We investigated the role of viral proteins (gE, gI, and protein kinase Us3) in viral spread, using a wide panel of viral mutants and seeking for cellular partners of viral proteins by biochemical methods and mass spectrometry. Using laser confocal microscopy and a panel of fluorescent viral mutants we analyzed cell-to-cell spread of BHV-1 between various types of cells and confirmed the essential role of viral envelope glycoproteins gE/gI in this process. We also demonstrated that herpesviruses can be transmitted between distant cells via tunneling nanotubes (TNT), recently discovered long range intercellular connections.

In other projects we study the mechanism of immune evasion – the strategies used by viruses to avoid recognition by the immune system of the host. We explore the molecular mechanism of activity of UL49.5 protein, main immunomodulatory protein in some herpesviruses, which downregulates major histocompatibility class I (MHC I) expression. To identify active amino acid sites and domains mediating the activity of UL49.5, we used structural studies and protein modeling followed by side-directed mutagenesis. We also studied interactions of UL49.5 with another viral protein – glycoprotein M and cellular trafficking of this protein complex. Using fluorescently labeled cellular target protein -TAP transporter and CRISPR/Cas9 libraries, next generation sequencing and proteomics we attempt to identify cellular proteins involved in the mechanism of inhibition.

In another project we studied the role of exosomes, nanosized vesicles of intercellular origin, in alphaherpesvirus infection. Exosomes can carry specific cargo (nucleic acids, microRNA, proteins) which may affect the immune response, mediate signaling, promote oncogenesis. We look for crossroads between exosomes and herpesviruses, by studying specific incorporation of viral proteins and microRNA to exosomes.

Hepatitis C virus (HCV) is a one the most dangerous human pathogens and the methods of its control, despite the recent progress in drug development are not efficient. There is no available vaccine to prevent HCV infection. Our group has been involved in several international projects, funded by EU Framework Programs, aimed at the development of new

strategies of HCV control. We participated in the large project (Hepacivac) aimed at the development of HCV vaccine and have constructed and characterized numerous adenovirus vectors expressing HCV envelope glycoproteins. As tools for our studies , we produced HCV recombinant proteins in mammalian cells , baculovirus system and recently in a novel expression system based on protozoan Leishmania tarentolae. We also explore the possibility of the construction of a bivalent prophylactic vaccine against HBV and HCV, introducing conserved epitopes of HCV E2 glycoprotein into hepatitis B small surface antigen (sHBsAg), which forms subviral particles used widely in prophylactic control of HBV infection.

Future plans

We plan to continue to study the role and mechanism of formation of intercellular connections involved in virus transmission between. cells. Our new research area is the interaction between virus infection and tumor cells. We have discovered that BHV-1 , a cattle pathogen , contrary to its restricted species-specificity, is capable to infect and kill many types of human cancer cells. We plan to study the infection of tumor cells with viral pathogens and try to identify the cellular factors important for tumor cell susceptibility for virus infection. In another project we started to investigate the antiviral properties of interferon induced transmembrane proteins (IFITM). IFITM proteins inhibit the entry of many viruses, like influenza, Denga or ZIKA virus into host cells . We will try to elucidate the mechanism of IFITM function during hepatitis C (HCV) virus infection in humanized mice model. In collaboration with the new International Center of Cancer Vaccine Science (ICCVS) , we plan to develop new oncolytic vectors and viral vectors for expression of tumor antigens.

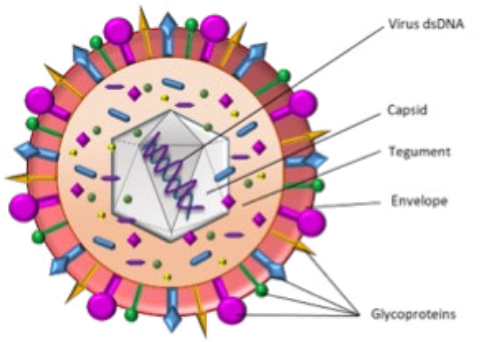


Fig .1.
The herpesviral particle

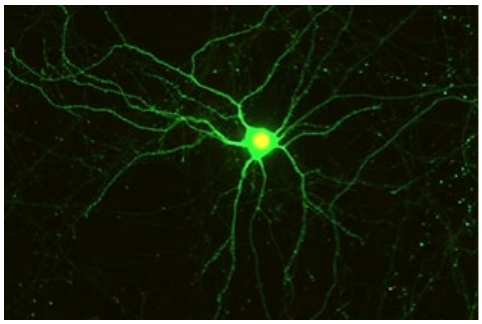


Fig2.
Neurons transfected with BHV-1 US3 gene fused to GFP

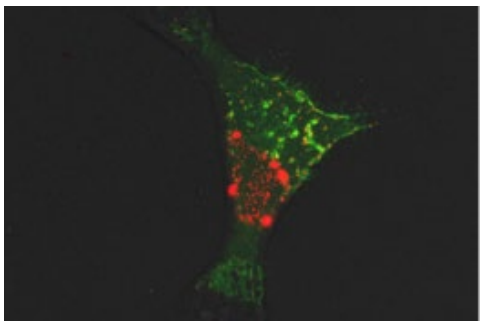


Fig 3
Fibroblast infected with dual-label BHV-1 virus (green: envelope glycoprotein gE-GFP, red- capsid VP26 -m-Cherry)

Recent publications

- Brzozowska A, Lipińska AD, Derewońko N, Lesiak D, Rychłowski M, Rąbalski Ł, Bieńkowska-Szewczyk K.(2017) Inhibition of apoptosis in BHV-1-infected cells depends on Us3 serine/threonine kinase and it. s enzymatic activity. Virology. 513:136-145. doi: 10.1016/j.virol.2017.09.029
- Kurzynska-Kokorniak A, Pokornowska M, Koralewska N, Hoffmann W, Bienkowska-Szewczyk K, Figlerowicz M. (2016) Revealing a new activity of the human Dicer DUF283 domain in vitro. Sci Rep.,6:23989. doi: 10.1038/srep23989
- Czarnota A, Tyborowska J, Peszyńska-Sularz G, Gromadzka B, Bieńkowska-Szewczyk K, Grzyb K. (2016) Immunogenicity of Leishmania-derived hepatitis B small surface antigen particles exposing highly conserved E2 epitope of hepatitis C virus. Microb Cell Fact. 15:62. doi: 10.1186/s12934-016-0460-4.
- Grzyb K., Czarnota, A, Brzozowska, A Cieślik, A., Rabalski, L., Tyborowska, J. Bieńkowska-Szewczyk, K. (2016)Immunogenicity and functional characterization of Leishmania-derived hepatitis C virus envelope glycoprotein complex . Sci. Rep. 6, 2;6:30627. doi: 10.1038/srep30627

Scientific Collaboration

- Institute of Virology, MRC Glasgow (Prof. Arvind Patel)
- Reithera company, Italy (Prof. Alfredo Nicosia)
- Gent University, Belgium (Prof.Philip Meuleman)
- University of Edinburgh, UK (Prof. Kathryn Ball)
- University of Utrecht, Netherlands (Prof. Emmanuel Wiertz)

[New Researchers at IFB]

The IFB employment policy supports young researchers whose previous achievements are good predictors for becoming strong and active research group leaders. In October 2017 Faculty authority acting in such way successfully recruited two perspective researchers currently establishing their research groups.

Dr. Danuta Gutowska-Owsiak is an immunologist with a strong interest in allergy and inflammation. After she graduated from the Medical University in Gdańsk, she moved to the UK, where she undertook research training at the University of Liverpool (PhD in 2010).

In 2009 she joined MRC Human Immunology Unit at the University of Oxford, where she became interested in the epidermal barrier and immunity of the skin. In 2017 she received the "Young Investigator Award" from British Society for Investigative Dermatology for her contribution to dermatology research.

She joined the Intercollegiate Faculty of Biotechnology in October 2017 to develop a programme of immunological research. Her team investigates communication between cells in the skin during allergy and infection and the role of exosomes in this process.

Dr. Michał Szymański studies proteins involved in basic DNA replication and repair processes. He graduated from the University of Houston, USA, in 2007 and obtained his PhD in Biochemistry and Molecular Biology from the University of Texas, USA, in 2011. He became J.B. Kempner Postdoctoral Fellow at the Pharmacology Department, UTMB, USA, where contributed to mechanistic understanding of human mitochondrial DNA replication.

After receiving POLONEZ (NCN) and FIRST TEAM (FNP) grants, in October 2017, he joined Intercollegiate Faculty of Biotechnology. Research in Szymanski's group combines structural biology (x-ray crystallography and electron microscopy), protein biochemistry and biophysics to understand the assembly of macromolecular complexes and use this knowledge in possible therapeutic strategies.

[Important Dates and Facts]

2017

- Committee for Evaluation for Scientific Units completed comprehensive evaluation of the Polish scientific units granting IFB the highest possible mark A+ as a leading unit with the highest standard of scientific activities and research potential
- XXIII edition of the Summer Biotechnology School organized by IFB

2016

- The first Academic Year inauguration in the new building of IFB
- XXII edition of the Summer Biotechnology School organized by IFB
- Project STARBIOS 2 (Structural Transformation to Attain Responsible BIOSciences) funded for the EU Horizon 2020 research and innovation has started in May 2016
- Official opening of the new IFB building at the campus of University od Gdańsk – one of the most modern research and educational academic units in Poland

2015

- The last Academic Year inauguration in the old IFB premises at ul. Kladki 24 in Gdańsk
- The completion of the construction of the new building of the Institute of Biotechnology
- Prof. Krzysztof Bielawski re-elected Vice – President of ScanBalt
- XXI edition of the Summer Biotechnology School organized by IFB

2014

- 25 April - laying of the cornerstone for the new biotechnology building at University of Gdansk Campus. of the construction of the new building of the Institute of Biotechnology at University of Gdańsk Campus
- XX edition of the Summer Biotechnology School organized by IFB
- Establishing the units of Core Facility Laboratories and Teaching Laboratories at IFB

2013

- Establishing of a new unit at IFB dedicated to facilitating research management & administration: Dean's Office for Research and Project Management
- Start of the FP7 project MOBI4Health - CENTRE OF MOLECULAR BIOTECHNOLOGY FOR HEALTHY LIFE Biotech solutions bringing health to living organisms and environment supported by mass spec-focused research platform" (2013-2016, 7. Framework Programme of the European Union), coordination by Prof. Krzysztof Bielawski
- XX Anniversary of IFB

2012

- Funding from the National Centre for R&D for the construction of a new building of the Institute of Biotechnology obtained (EU Structural Funds).
- Consortium agreement between IIMCB (Warsaw) and IFB signed
- FB again receives funding for the so-called commissioned study programmes and for improving the alumnis' opportunities on the labour market

2012

- Biotechnology at IFB as one of the best study courses receives additional funding from the Mini- stry for Science and Higher Education for further improving the study programme
- Distinction for the Best Major for the study course Biotechnology at IFB granted by the Ministry for Science and Higher Education

2011

- Distinction for the study course Biotechnology (B.Sc. and M.Sc.) at IFB granted by the Polish Accreditation Committee
- Establishing of IFB Advisory Council to intensify cooperation with institutions and companies from the biotech sector
- International Institute of Molecular and Cell Biology in Warsaw (IIMCB) joins the Life Sciences and Mathematics Interdisciplinary Doctoral Studies (LiSMIDoS)

2010

- IFB obtains the first category in the National Evaluation of Scientific Institution (tor the 3rd time) and is ranked in the 1st place within the group of biology at Polish universities
- Prof. Ewa Łojkowska is elected vice-chairwoman of the ScanBalt Association
- The Central Commission for Scientific Titles and Degrees licenses the Faculty to confer habilitation in biological sciences in the discipline of biochemistry
- Establishing of Life Sciences and Mathematics Interdisciplinary Doctoral Studies (LiSMIDoS)
- Opening of the International Doctoral Project, financed by the Polish Science Foundation from the Innovative Economy Programme, EU Structural Funds, coordination by Prof. Jarosław Marszałek
- IFB obtains the premium category in the National Evaluation of Scientific Organizations

2009

- IFB is funded by Ministry of Science and Higher Education within the frame of Commissioned fields of studies in Polish universities under the Human Capital Program, EU Structural Funds, co- ordination by Prof. Igor Konieczny.

2008

- Start of collaboration and exchange activities for Master degree students with the University of Chicago, USA and University of Virginia, USA

2007

- IFB is granted with accreditation for teaching biotechnology by the Polish University Accreditation Commission (for the 2nd time)

2006

- IFB becomes partner in the INTERREG III project ScanBalt Campus (2006-2008). The Centre of Knowledge on Molecular Diagnostics for Medicine, Plant and Animal Diseases in Gdańsk, coordination by Prof. Ewa Łojkowska and Prof. Jacek Bigda
- Prof. Krzysztof Liberek elected as member of the European Molecular Biology Organization

2005

- IFB is granted the accreditation for teaching biotechnology granted by the State Accreditation Commission
- IFB obtains the first category in the National Evaluation of Scientific Institution (for the 2nd time)

2005

- Opening of new laboratories belonging to the Faculty at the Medical University of Gdańsk (Tricity Academic Experimental Animal House – Research Service Centre of the Medical University of Gdańsk)

2003

- IFB establishes the Centre of Excellence BioMoBiL – Centre of Bio-safety Research and Molecu- lar Biomedicine – Integration in Education and Research Towards the Knowledge and Technology Transfer Level (2003-2006, 5. Framework Programme of the European Union); coordination by Prof. Jacek Bigda and Prof. Ewa Łojkowska.

2002

- IFB is granted with accreditation for teaching biotechnology by the Polish University Accreditation Commission

2001

- IFB becomes member of the ScanBalt association. Prof. Anna Podhajska elected as vice-chairwo- man of ScanBalt (2001-2005)
- IFB obtains first category in the National Evaluation of Scientific Institutions
- The Faculty becomes a partner in the consortium of 10 European Universities and participates in the establishment of a new teaching program: Job Creation Biotechnology Diploma – International First Level Degree (3 years), coordinated by prof. Mariapia Viola Magni from Universita degli Studi di Perugia, Italy

2000

- Prof. Wacław Szybalski is granted the title of Doctor Honoris Causa of the Medical University of Gdańsk. The initiative comes from and is supervised by the IFB. Prof. Wacław Szybalski is also ho- noured at the Marie Curie-Skłodowska University of Lublin (1980) University of Gdańsk (1989) and Technical University of Gdańsk (2002)

1999

- Opening of new laboratories in the Institute of Biotechnology, UG. Main lecture hall named in the memory of late prof. Karol Taylor, the founder of molecular biology in Gdańsk
- Central Commission for Scientific Titles and Degrees licenses IFB to confer PhD degrees in biologi- cal sciences in the discipline of biochemistry

1994

- Successful application for a first EU project: Creation and development of a novel Faculty of Bio- technology (TEMPUS, 1994-1997), coordination by Prof. Wiesław Makarewicz, Dean of IFB
- 1st Biotechnology Summer School organized at Wilga, near Warsaw, by Prof. Anna Podhajska. Prof. Wacław Szybalski is the honorary guest at the event

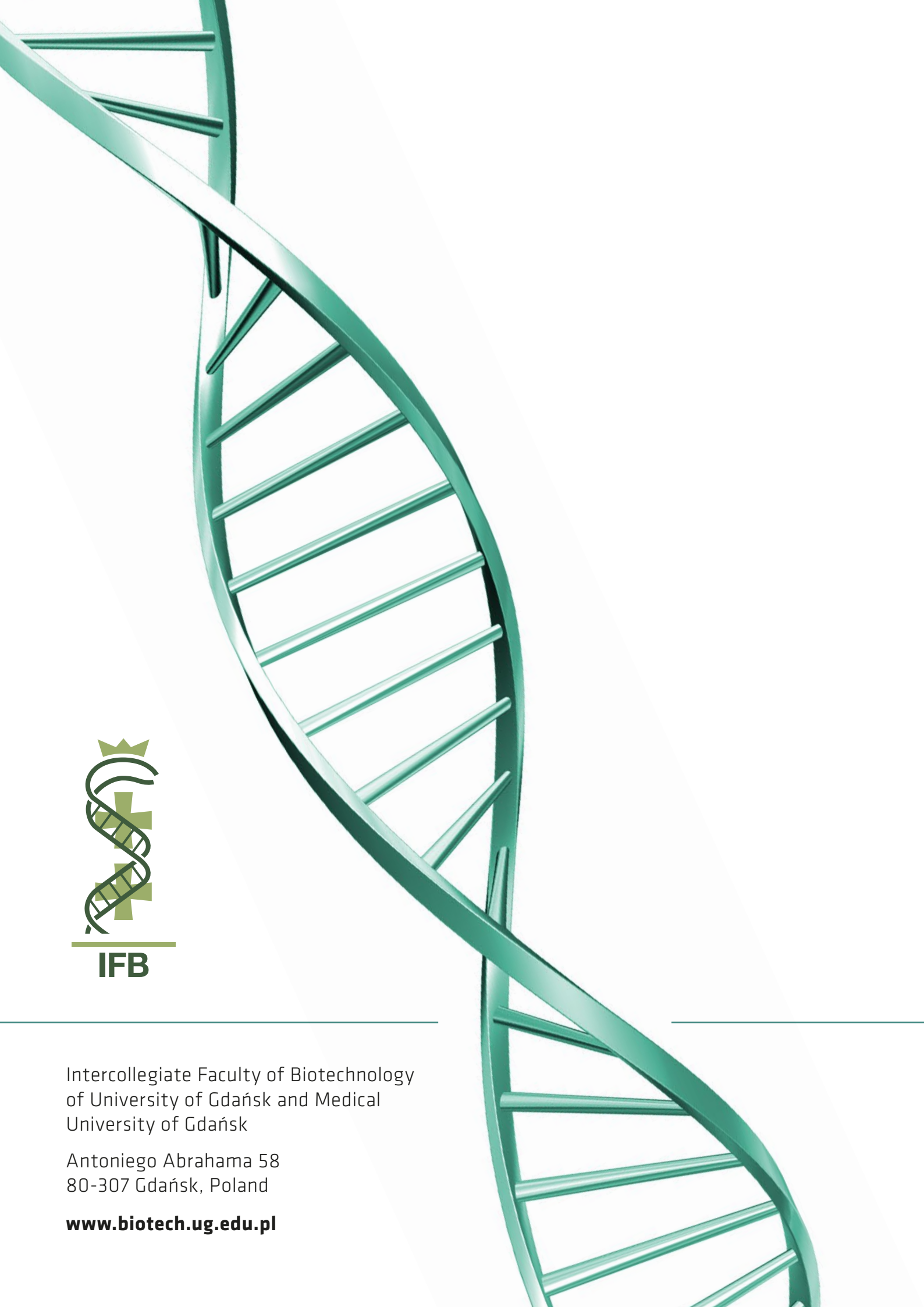
1993

- Senate of the Medical University of Gdansk and Senate of the University of Gdansk decide to establish the Intercollegiate Faculty of Biotechnology UG & MUG

1992

- Crystallization of the idea to create a joint unit for teaching biochemistry among the universities in Gdansk. Rectors of the University of Gdansk, Medical University of Gdansk and Technical University of Gdansk appoint Prof. Anna J. Podhajska as the person responsible for organizing and establishing the structure of this faculty

[Notes]



IFB

Intercollegiate Faculty of Biotechnology
of University of Gdańsk and Medical
University of Gdańsk

Antoniego Abrahama 58
80-307 Gdańsk, Poland

www.biotech.ug.edu.pl