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Honorary Patronage

1970 U G 2020 University of Gdańsk 50th Anniversary

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STARBIOS2

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

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About organizers of the *ScanBalt Forum 2019*

- **ScanBalt MTÜ**

ScanBalt is the first EU macro-regional concept targeting modernization and digitalization of the health care, distribution of health and advancing an innovation-based health economy and related cross-over disciplines in bioeconomy.

ScanBalt mobilizes European, regional and national public-private investments for transnational collaboration based on a common mission, vision and strategy.

ScanBalt will achieve this by:

- ✓ promoting innovation and business
- ✓ fostering interregional collaboration
- ✓ reducing barriers
- ✓ enhancing visibility
- ✓ attracting resources

By doing so ScanBalt aims for impact leading to new health care products/services, development of eHealth and promotion of digital care, promotion of healthy lifestyles, cross-border healthcare, innovation and competence development, policy development and better use of funding instruments.

https://scanbalt.org/

- **International Centre for Cancer Vaccine Science (ICCVS)**

The International Centre for Cancer Vaccine Science project is carried out within the International Research Agendas Programme (IRAP) of the Foundation for Polish Science and the European Union under the European Regional Development Fund. IRAP involves establishment of joint research units by Polish institutions and international partner institutions. The University of Gdańsk partners with The University of Edinburgh; established in 1583 and ranked as one of the top universities in the world with a special commitment to global interactions in science, engineering, informatics, and health care. The formation of a joint research unit between the University of Gdansk and the University of Edinburgh will combine expertise from both organization to ensure that PhD and MD training programmes and mentoring are innovative and interdisciplinary, global in vision to develop transferable skills needed for the 21st century, and industrial collaborations will be drive translational clinical developments and commercialization.

https://iccvs.ug.edu.pl/

- **Intercollegiate Faculty of Biotechnology UG&MUG (IFB)**

The Intercollegiate Faculty of Biotechnology of the University of Gdansk and Medical University of Gdansk (IFB UG & MUG) has been established in 1993 as an very unique establishment in Poland created by two institutions. This leads to the interdisciplinary character of the conducted research and teaching by combining biomedical and biomolecular research and their applications in biotechnology for health and improved life quality**.**

The Faculty runs BSc, MSc and PhD programmes, educating over 360 students, including 90 doctoral students**.**

IFB is a leading research and teaching institution in Poland, having held the the status of the European Centre of Excellence in Molecular Biomedicine since 2002. In 2017the Faculty was obtained category A+ status during the Ministry of Science and Higher Education evaluation and ranked1st place amongst Polish biotechnology faculties. The teaching quality has been frequently appreciated(distinction of the Polish Accreditation Committee in 2011, the title of The Best Major from the Ministry of Science and Higher Education in 2012)**.**

https://en.biotech.ug.edu.pl/

- **University of Gdańsk (UG)**

The University of Gdańsk (UG) is a dynamically developing institution of higher education and one that combines respect for tradition with a commitment to the new. It offers education in nearly all fields of academic knowledge and in sought-after professions on the job market. It benefits from the state-of-the-art facilities located at campuses in Gdańsk, Sopot and Gdynia; it is currently one of the most modern academic centres in Poland. As the largest university in the Pomeranian region, it has had an indisputable influence on the development of modern Poland, science and higher education. UG consists eleven faculties and nearly twenty six thousand students, doctoral students and post-graduates, taught by close to two thousand academic staff. The University of Gdańsk is one of the best institutions in Poland for Biology, Biotechnology, Chemistry, Oceanography, Quantum Physics, Pedagogy, Psychology, Law and Economic Sciences.

The University of Gdańsk was founded on 20th of March 1970 as was formed as a merger of two institutions of higher education: the Higher Economics School in Sopot and the Higher Pedagogical School in Gdańsk. Later, it also included the Higher Teacher Training School. The precursor of the Higher Economics School in Sopot was the Higher School of Maritime Trade in Sopot, which opened in 1945 and awarded its first degree in 1947.

2020 will mark the celebrations of the 50th anniversary of the founding of the University of Gdańsk.

https://en.ug.edu.pl/

- **Medical University of Gdańsk (MUG)**

The Medical University of Gdańsk (MUG) is the largest medical university in the Northern Poland. The MUG ranked 1st for Medicine and in the top ten of the best Polish state universities in the 2018 higher education

ranking of the Perspektywy Education Foundation. The MUG gathers more than 6,000 undergraduate and postgraduate students at 4 Faculties: Faculty of Health Sciences, Faculty of Medicine, Faculty of Pharmacy and the Intercollegiate Faculty of Biotechnology. The MUG also offers Premedical Course, Medicine Doctor Programme, Pharmacy Programme, Nursing Programme which are taught fully in English.International students constitute more than 15% of the MUG's students and represent more than half of all international students in Gdańsk. Students benefit form the access to modern Sports Centre.

The MUG constantly improves its clinical and teaching facilities. In the end of 2011 the University Clinical Centre has been successfully modernised. The main hospital, the Invasive Medicine Centre (IMC), is one of the most modern hospitals in Europe. Together with the new investment of the MUG, the Non-Invasive Medicine Centre (NIMC), IMC is the one of the largest and newest hospital complexes in Poland.

https://mug.edu.pl/

- **Fundation for the Development of the University of Gdansk (FRUG)**

Currently the aim of the Foundation for the Development of the University of Gdańsk is to support the activities and development of the University of Gdańsk. This goal is realized through financial and material assistance as well as cooperation with the University units. Financial assets for the realization of the statutory goal are received by the Foundation's activity as well as, partially, by subsidies and donations from various institutions, companies and enterprises.

FRUG provides service, commercial and training activities. Among other things, it is involved in organization of conferences, symposia, scholarly workshops and implementation of academic projects. The Foundation has broad experience in management of educational, environmental and investment projects.

http://www.frug.ug.edu.pl/en/home/

Program of the *ScanBalt Forum 2019*

Day I: Tuesday, 24 September 2019		
9:00	Morning coffee	
9:30	-Piotr Stepnowski (University of Gdańsk Vice-Rector for Research and Foreign Cooperation) -Jaanus Pikani (ScanBalt Chairman)	Welcome & Opening word
Opening lecture		
9:45	Jan Dumański (3P-Medicine/Medical University of Gdańsk/Uppsala Universitet)	Loss of Y in leukocytes, dysregulation of autosomal immune genes and disease risks
10:45	Coffee break	
Session I: Cancer Biology *Chairs: Natalia Marek-Trzonkowska, Aleksandra Markiewicz*		
11:00	Ted Hupp (International Centre for Cancer Vaccine Science/University of Gdańsk/University of Edinburgh)	Interferon signalling pathways in human cancer
11:30	Anna Żaczek (Intercollegiate Faculty of Biotechnology UG&MUG)	Circulating tumor cells – stroma crosstalk in breast cancer progression
12:00	Wojciech Niedźwiedź (Institute of Cancer Research, London)	Small mistakes with grave consequences. Unravelling the mechanisms of genome instability to treat cancer
12:30	Karin Jirström (Lund University)	Next-generation pathology: reporting of tumor heterogeneity and evolution
13:00	Lunch break/Poster session	
Session II: Cancer Immunology *Chairs: Danuta Gutowska-Owsiak, Marcin Okrój*		
14:00	Vittorio Colizzi (UNESCO Biotechnology & Bioethics/University of Rome Tor Vergata/ Faculty of Science & Technology of the Evangelic University of Cameroon)	Effects of plant microvesicles containing miRNAs on proliferation and apoptosis in tumour cell lines
14:30	Michael Kirschfink (Universität Heidelberg)	The complement system in cancer: ambivalence between tumour destruction and promotion
15:00	Margarida Rei (University of Oxford)	Playing hide and seek: Epigenetic modulation to unravel cancer testis antigens and neoantigens in glioblastoma
15:30	Andrzej Mackiewicz (Adam Mickiewicz University/Medical University of Poznan)	Next generation of cancer genetic vaccines
16:00	Coffee break	
Keynote speaker		
16:15	Susanne Gabrielsson (Karolinska University)	Exosomes in cancer progression and as immunotherapeutic tools for cancer
17:15	General Assembly (for ScanBalt Members only)	
19:00	Conference networking reception	
21:00	End of day 1	

Day II: Wednesday, 25 September 2019		
9:00	Morning coffee	
Academia-Industry Cooperation		
Session I: EIT Health – European Commission support instrument for innovation in healthcare *Chair: TBC*		
9:30*	Inês Matias (EIT Health InnoStars)	EIT Health and its support for business creation and business growth
10:00	Q&A	
10:15	Merike Leego (Innovation Manager and "Biobanks and Registers in Transition" program manager, EIT Health Scandinavia)	Biobanks and Registers in Transition – program to facilitate industry access to biobanks and health registers
10:30	Q&A	
10:45	Christos Vaitsis (Business Creation Manager at EIT Health Scandinavia)	Scandinavian Business Creation Ecosystem and Digital Sandbox program
11:00	Q&A	
11:15	Katarzyna Waligóra-Borek (Gdańsk RIS Hub EIT Health)	Medical University of Gdansk as Regional Innovation Scheme (RIS) Hub for Pomeranian region
11:30	Q&A	
11:45	Coffee break	
Session II: Presentations Organised by Projects *Chair: TBC*		
12:00	Tero Piispanen (BiC project)	Biomarkers and Cancer
12:45	Krzysztof Bielawski, Claudia Colonnello, Evanthia K. Schmidt (STARBIOS2 H2020)	Responsible Innovation: a promising collaborative approach for research
13:30	Kazimierz Murzyn (Klaster LifeScience Kraków)	Sano Foundation, The Centre for Individualized Computational Medicine
14:00	Networking (Sandwich Lunch)	
Session III: Research Funding and Publishing *Chair: TBC*		
14:30	Anna Dziubczyńska-Pytko (National Contact Point - Poland)	Funding Opportunities for Academia Industry Collaboration in Research
15:15	Lynn Sherrer (Elsevier)	How to write a great paper
15:45	End of day 2	

*9:30-11:30 – a couple of rooms will be available to organize individual meetings, please make reservation of the room during registration

Venue

The *ScanBalt Forum 2019* will take place in the building of the Faculty of Social Sciences of the University of Gdansk in Gdańsk (Poland).
Address: Faculty of Social Sciences, room S207, Jana Bażyńskiego 4, 80-309 Gdańsk (UG campus)

Information on Speakers and Talks

Loss of Y in leukocytes, dysregulation of autosomal immune genes and disease risks

Jan P. Dumanski

Uppsala University, Sweden and Medical University of Gdansk, Poland

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Biography

Jan Dumanski is a Professor of experimental pathology at Uppsala University, Sweden, and visiting professor at the Gdansk Medical University. Jan Dumanski was born in 1960 in Cracow, Poland and studied medicine at Jagiellonian University there (1979-1984). In 1985 he entered a PhD programme at Karolinska Institutet in Stockholm and graduated in 1990 from the Department of Clinical Genetics and Ludwig Institute for Cancer Research, Stockholm branch. In 1994 he received associate professorship at Karolinska Institutet in medical molecular genetics and moved to Uppsala University in February 2000. Between May 2006 and May 2008, he was active as Professor of Genetics at University of Alabama at Birmingham, Department of Genetics and Director of Howell and Elizabeth Heflin Center for Human Genetics. Since 2018, Jan Dumanski is also a Head of 3P-Medicine Laboratory (IRAP) at the Gdansk Medical University.

Abstract

Epidemiological investigations show that mosaic loss of chromosome Y (LOY) in leukocytes is linked to increased risk for morbidity and mortality in men. LOY is the most common acquired mutation and associated with disease e.g. cancer and Alzheimer's disease. We studied DNA, RNA and proteins in bulk, sorted- and single-cells in vivo and in vitro. The results showed that Alzheimer's disease and prostate cancer patients displayed LOY in different types of leukocytes with higher frequencies in NK- and CD4+ T cells, respectively. Furthermore, the expression of autosomal genes was profoundly altered in cells with LOY in a pleiotropic fashion including numerous immune genes such as LAG3 and LY6E. Proteomic analysis also indicated that LOY leaves a footprint in the plasma proteome. Thus, our results support the hypothesis that LOY influence immune system homeostasis and provide an explanation how LOY in leukocytes could increase risk for disease in other organs.

Developing interferon signalling models in human cancer

Ted Hupp

University of Gdansk, International Centre for Cancer Vaccine Science, Gdansk, Poland; University of Edinburgh, Institute of Genetics and Molecular Medicine, Edinburgh, Scotland, United Kingdom; Regional Centre for Applied Molecular Oncology, Masaryk Memorial Cancer Institute, Brno, Czech Republic

Biography

Ted Hupp was educated in microbiology & chemistry in Ohio, USA with a PhD in Biochemistry at Michigan State University (USA). Enzymology principles were applied to the cancer research field in the UK to develop the paradigm that the tumour suppressor p53 could be activated by Biologics, such as peptides and antibodies. His current position of Professor is as the Chair of Experimental Cancer Research at the University of Edinburgh and Director of the International Centre for Cancer Vaccine Science (ICCVS); a project carried out within the International Research Agendas Programme of the Foundation for Polish Science. The ICCVS is forming a centre of excellence in inter-disciplinary research that aims to improve human health by establishing programme teams focused on (i) neoantigen science; (ii) receptors at the cancer-immune synapse; (iii) proteogenomics and computational science; and (iv) translational models in human cancers of high unmet clinical need.

Abstract

Oesophageal adenocarcinoma (OAC) is a cancer of high unmet clinical need. Proteomics and genomics have defined the major signalling landscapes that form therapeutic targets in this cancer type [1, 2]. Proteomics platforms have been used to identify two key therapeutic target pathways in OAC; one plays a role in secretory trafficking [3] and the second comprises the interferon-stimulated DNA damage resistant signature, including the transmembrane receptor, IFITM1 [4]. These data have implications for the developing therapeutic approaches that target the secretory pathway and associated function of receptors mediating interferon-stimulated protein induction as well associated MHC Class I-antigen presentation during oncogenic and anti-viral signalling.

[1] Secrier M, Li X, de Silva N, Eldridge MD, Contino G, Bornschein J, et al. Mutational signatures in esophageal adenocarcinoma define etiologically distinct subgroups with therapeutic relevance. Nat Genet. 2016;48:1131-41.
[2] O'Neill JR, Pak HS, Pairo-Castineira E, Save V, Paterson-Brown S, Nenutil R, et al. Quantitative Shotgun Proteomics Unveils Candidate Novel Esophageal Adenocarcinoma (EAC)-specific Proteins. Mol Cell Proteomics. 2017;16:1138-50.
[3] Mohtar MA, Hernychova L, O'Neill JR, Lawrence ML, Murray E, Vojtesek B, et al. The Sequence-specific Peptide-binding Activity of the Protein Sulfide Isomerase AGR2 Directs Its Stable Binding to the Oncogenic Receptor EpCAM. Mol Cell Proteomics. 2018;17:737-63.
[4] Gomez-Herranz M, Nekulova M, Faktor J, Hernychova L, Kote S, Sinclair EH, et al. The effects of IFITM1 and IFITM3 gene deletion on IFNgamma stimulated protein synthesis. Cell Signal. 2019;60:39-56.

Circulating tumor cells - stroma crosstalk in breast cancer progression

Anna Żaczek

[1] Laboratory of Cell Biology, Department of Medical Biotechnology, Intercollegiate Faculty of Biotechnology University of Gdańsk and Medical University of Gdańsk

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Biography

Assistant Professor at the Department of Medical Biotechnology at the Intercollegiate Faculty of Biotechnology, with specialization in tumor biology. Principal investigator of 13 externally-funded projects. Author of >40 peer-reviewed publications on cancer biology and diagnostics and an inventor in patent on CTC detection. Scholar at the Stanford University within TOP500 Innovators Program and Starship Innovation Fellow (EIT Health) with 1-year training in Bioinnovation at University of Coimbra and IESE Business School. Her research focuses on biology of cancer, particularly on dissecting the role of circulating tumor cells, epithelial-mesenchymal transition and tumor-stroma crosstalk in breast cancer progression. Her team is carrying out multidisciplinary projects dedicated to identification and development of new molecular markers, including liquid biopsy approach, for better cancer diagnosis, prognosis and prediction of treatment response.

Abstract

Stroma cells, considered to play key role in tumor development, contribute to phenotypic plasticity of cancer cells, defined as ability to undergo epithelial-mesenchymal transition (EMT) and the reverse mesenchymal-epithelial transition. Tumor cell plasticity has been recently postulated to be essential for successful completion of metastatic cascade and linked with most aggressive subpopulation of cancer cells, providing them the highest possibility of adaptation to different conditions. The influence of tumor stroma on phenotype plasticity of circulating tumor cells (CTCs) is scarcely known. We have hypothesized that stroma might contribute to the selection of cells with particularly aggressive phenotype that enables effective dissemination of the disease.

Data of the ongoing study on wide range of tumor microenvironment features both at primary site and in peripheral blood in the context of EMT-related phenotypes of CTCs and patients outcome in operable breast cancer will be presented. Intratumoral stroma features include: IHC status of CD68 and CD163 (macrophage infiltration and activation status), vimentin and α-SMA (fibroblasts), CD34 and D2-40 (vascular and lymphovascular endothelium, respectively) markers; expression of 730 immune-related genes assessed with NanoString technology; whereas blood microenvironment is described by standard blood count and Luminex x-MAP-based cytokine profiling (incl. 66 cytokines). Evaluation of CTCs interplay with stroma might potentially define patients at the highest risk of disease progression and contribute to better understanding of the complex network of environmental elements supporting metastatic process.

Research was supported by National Science Centre, Poland (Sonata Bis 2016/22/E/NZ4/00664)

Small mistakes with grave consequences. Unravelling the mechanisms of genome instability to treat cancer

Wojciech Niedźwiedź

Institute of Cancer Research, London

Biography

Wojciech Niedzwiedz obtained a PhD in Radiation Biology from the Institute of Nuclear Physics/Silesian University, Poland in 2000. After postdoctoral research at the MRC-LMB, University of Cambridge (2002-2007), he was awarded personal fellowships by AICR and the MRC to set up his own group at the Weatherall Institute of Molecular Medicine, University of Oxford (2008-2017). In June 2017, he relocated his group to the Institute of Cancer Research (ICR) in London. The same year he was appointed Professor of Molecular Cancer Biology at the ICR. His research is focused on understanding the molecular mechanisms of genomic instability and its implication for cancer treatment.

Abstract

Accurate replication of DNA is essential to preserve genomic integrity and failure to do so results in a variety of chromosomal instability-associated diseases including cancer. Work over the last decade suggests that the key to this is the ability of cells to stabilise and restart stalled replication forks. Here, I will discuss the mechanisms by which cells stabilise and restart stressed replication forks to maintain chromosomal integrity. In particular, I will focus on the role of the recently identified replication fork protection factor termed EXD2.

I will provide evidence regarding EXD2 role in counteracting fork reversal and how this activity is critical for suppression of uncontrolled degradation of newly synthesised DNA, efficient fork restart and suppression of genome instability. Consistent with this, I will present biochemical reconstitution of replication fork processing highlighting the mechanism by which purified EXD2 can resect substrates mimicking regressed forks *in vitro.* Finally, I will describe a novel synthetic lethal interaction between EXD2 and BRCA deficiency and present our recent work towards developing EXD2 nuclease inhibitors to target BRCA1/2 mutated cancers.

Next-generation pathology: reporting of tumor heterogeneity and evolution

Karin Jirström

Division of Oncology and Pathology, Department of Clinical Sciences Lund, Lund University

Biography

Karin Jirström is a Professor and senior consultant in pathology with longstanding experience from tumour-agnostic cancer biomarker research. Her laboratory harbours Sweden´s largest collection of tissue microarrays with retrospectively collected, clinically well-annotated tumours representing several types of major solid cancers, with particular focus on gastrointestinal cancer. She is now in the process of launching several prospective clinical on-treatment biomarker studies. Within these studies, the spatial heterogeneity of mutations and protein biomarkers in resected primary tumours and metastases will be comprehensively mapped, and blood samples will be collected during systemic treatment to study the temporal heterogeneity and clonal evolution of tumours.

Abstract

Tumours evolve, like living organisms, and continuously adapt to the pressure from treatment by selecting resistant clones that may subsequently adapt to therapy through transcriptional reprogramming, each clone affecting the inflammatory tumour microenvironment differently. Although this dynamic and evolutionary nature of tumours is well-recognized, systemic therapies are typically administered in a static, linear fashion, through protocols that *a priori* fix the drug(s), dose and timing. Adding to this, biomarker analyses, if applicable, are only performed on one selected sample from a pretreatment surgical specimen or, in irresectable cases, a biopsy. In a similar fashion, the majority of biomarker studies only consider clinical outcome in relation to analysis of one sample. This is likely the reason why, despite the plethora of scientific literature on promising biomarker candidates, very few ever make it into clinical protocols. Cancer evolution is reflected by tumour heterogeneity, both temporal and spatial. Therefore, understanding tumour heterogeneity, and its clinical consequences, is essential for designing effective therapeutic strategies and more precise companion diagnostics. This talk will discuss some of these aspects and how pathology protocols can be adapted to better monitor and predict the molecular events occurring during systemic therapy.

Effects of plant microvesicles containing miRNAs on proliferation and apoptosis in tumour cell lines

Vittorio Colizzi

Department of Biology, Laboratory of General Pathology and Immunology, University of Rome "Tor Vergata", Rome, Italy and Evangelic University of Cameroon

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Biography

Born in Rome the 7/12/1949, held the medical degree at the University of Rome “La Sapienza” with full honour. VC is specialist in Clinical of Infectious Diseases (University of Rome) and in Hygiene and Public Health (University of Pisa), and PhD in Immunology (Brunel University, UK). VC has been Assistant in Microbiology and Associate professor in Immunology at the University of Pisa. Since 2000 to now, VC is Full Professor of Immunology and Director of the UNESCO Chair in Biotechnology & Bioethics at the University of Rome Tor Vergata, and is the Dean of the Faculty of Sciences and Technologies of the Evangelic University of Cameroon. He is consultants for several agencies of the United Nations. VC has been Scientific Director and member of the Board of the International Reference Centre for AIDS “C. Biya” in Yaoundé, Cameroon and President of the University Spinoff Eurobiopark. VC has been the coordinator of the European Project STARBIOS2. VC published over 300 scientific publications on peer-review journals on Immunology of Infectious Diseases and Cancer.

Abstract

Different studies demonstrated that plant-derived small RNA molecules, like microRNAs, can regulate gene expression in an inter-species manner called “cross-kingdom interaction”. After the discovery of plant microRNAs in human tissues, the cross-kingdom regulation seemed to provide new meaning to phytomedicine: plants used for centuries in the treatment of pathologies may be now redefined for their genetic materials. Minutolo et al. and Potestà et al demonstrated how the synthetic and natural small RNAs from Olea europaea drupes and from Moringa oleifera seeds introduced into hsa-miR34a-deficient tumor cells restored the function associated with the human miRNA, whereas cells with normal expression of endogenous hsa-microRNA34a remained unaffected. More recently the presence of the most conserved plant miRNAs family in microvesicles from M. oleifera was demonstrated and their effects on some tumorigenesis mechanism were evaluated in tumors cell lines: such microvesicles reduced the viability of tumour cell lines and it was associated with the increase of apoptosis, decrease of BCL2 protein expression and depolarization of mitochondrial membrane. All these results highlighted the role of microRNAs as bioactive compounds from natural plants which are able to regulate proliferation and apoptosis in a different way in healthy cells respect to cancer ones. Our results suggest a role for plant microvesicles as natural microRNA carrier in humans and it could be used as a cancer adjuvant therapy.

The complement in cancer: Ambivalence between tumour destruction and promotion

Michael Kirschfink

University of Heidelberg

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Biography

Michael Kirschfink is Professor emeritus of Immunology at the Institute of Immunology, University of Heidelberg, Germany. Studies in chemistry and veterinary medicine were followed by his PhD in Experimental Pathology at the German National Cancer Center (DKFZ). After his postdoc at the National Cancer Institute, NIH, Laboratory of Immunobiology, Frederick, MD, USA, he took over the Laboratory of Immunochemistry at the Institute of Immunology. His research projects focus on complement in health and disease, including immunodeficiencies, cancer immunology and nephropathies. He is a consultant immunologist and with a comprehensive complement analysis in his accredited diagnostic lab he served national and international clinics and pharmaceutical institutions (preclinical, clinical studies). He chairs the IUIS/ICS committee on standardization in complement diagnostics. Prof. Kirschfink has been member of the University senate and faculty board. He holds a honorary Professorship at the Tongji Medical College, Wuhan, China and is member of several national and international societies.

Abstract

Complement acts as first line of defence against infections by orchestrating the immune response through opsonisation, attraction of immune cells to the site of infection and direct cell lysis. The interactions of cancer cells with components of the complement system are highly complex. Complement activation on cancer cells but also in their microenvironment elicits multiple concomitant physiological and immunological responses that may act cooperatively to either mediate cancer cell death or promote cell survival, growth, and metastasis. Malignant cells are heterogeneous in their susceptibility to complement-induced killing, depending on the expression grade of the antigen or the ability of antibodies to activate complement, but also on protective mechanisms, either intrinsically expressed by the malignant cell or induced by various inflammatory or non-inflammatory agents. There is compelling evidence that antibody-based tumour cell killing is impaired by resistance of malignant cells to complement attack, mainly due to over-expression of one or more membrane complement regulatory proteins (mCRPs: CD46-MCP; CD55-DAF and CD59) on the surface of tumour cells. Local inflammatory processes with the generation of certain cytokines and even low grade sublytic complement activation. Furhermore, concomitant drug resistance appears to augment complement resistance of the targeted tumour cells. This has been considered as a major barrier to successful antibody-based immunotherapy.

Recent studies, indicate that activation of the complement system is also an important component of tumour-promoting inflammation primarily by suppressing the cellular anti-cancer immune response with C1q and C5a as key players. We just start to understand that the impact of complement may be either favourable or detrimental to malignant cells, with a significant impact on future developments in cancer immunotherapy.

Playing hide and seek: Epigenetic modulation to unravel cancer testis antigens and neoantigens in glioblastoma

Margarida Rei

MRC Human Immunology Unit, Weatherall Institute for Molecular Medicine, Radcliffe Department of Medicine, University of Oxford, Oxford, UK

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Biography

Margarida Rei is a postdoctoral tumour immunologist in Vincenzo Cerundolo's group. She is currently studying the role of T cells in the tumour microenvironment of cancer patients and how to enhance T cells responses against tumours. During her PhD she discovered a pro-tumour role for gamma delta T cells, mediated by the production of IL-17A, in a mouse model of ovarian cancer [1].

Abstract

Glioblastoma (GBM) is the most common and malignant primary brain tumour in adults. The relentless and inevitable progression of GBM is thought to be facilitated in part by an immunosuppressive microenvironment, which weakens the patient's ability to mount an effective tumour-eradicating response. Despite numerous trials, clinical response in GBM patients to immunomodulatory drugs, including checkpoint inhibitors, is modest which is in part due to the low number of mutations seen in GBM. Epigenetic regulation of tumour cells is becoming increasingly recognised as an important factor in tumour immune escape with downregulation of chromatin modifying genes being shown to lead to increased sensitivity to checkpoint blockade and increased immune-mediated cell killing through increased expression of interferon stimulated genes. Here, we examine the effect of decitabine (DAC), a DNA methyl-transferase inhibitor, on the expression of both cancer testis antigens (CTA) and neoantigens (Nag). Primary GBM and U87MG cell lines were subjected to whole exome sequencing for mutation and neoantigen calling. RNAseq was performed on the cell lines with and without treatment with 1uM DAC to investigate differentially expressed CTA and NAg. We observed that a whole spectrum of CTA are consistently upregulated as well as several NAg following decitabine treatment. Peptide specific T cells were isolated from autologous peripheral blood mononuclear cells (PBMC). Furthermore, we have optimized a protocol for isolation of peptide specific T cells from healthy donors. We observed that these T cells are capable of recognition of the tumours in a neoantigen specific fashion and increased expression of NAg leads to increased T cell mediated killing. We aim to translate this in vitro data to an in vivo model with an aim of bringing combinatorial DAC +/- checkpoint inhibitor therapy into a clinical trial setting.

[1] Margarida Rei, Natacha Gonçalves-Sousa, Telma Lança, Richard G. Thompson, Sofia Mensurado, Frances R. Balkwill, Hagen Kulbe, Daniel J. Pennington, and Bruno Silva-Santos. Proc Natl Acad Sci USA. 2014 Aug 26;111(34)

Next generation of cancer genetic vaccines

Andrzej Mackiewicz

Adam Mickiewicz University, Medical University of Poznan

Biography

Andrzej Mackiewicz, MD, PhD Professor of medicine, board certified in medical oncology, internal medicine and pathology, consultant in clinical immunology and laboratory diagnostics. Chairman of Medical Biotechnology, Head of Department of Cancer Immunology at Poznan Medical University, Head Dept. of Cancer Diagnostics and Immunology in Greater Poland Cancer Centre. He is the funder and CEO of BioContract Sp. z o.o., IntherVax Sp o.o., funder and v-President of AGIRx Ltd. (East Sussex, UK; 2005-11).

Prof. Mackiewicz trained in USA, Sweden, Denmark, France. He was visiting professor in USA and Germany. He was a mentor of 23 PhDs, 7 habilitations. He served as a President of Polish Society for Basic and Clinical Immunology. He was a member of Life Sciences Panel of NATO, The Cancer Genome Atlas Network, Cancer Immunotherapy Consortium (CIMT).

He discovered mechanisms regulating glycosylation of acute phase proteins. Is a pioneer of gene therapy. His expertise is related to cancer research. He invented therapeutic melanoma vaccine. He authored more than 300 papers (cited more than 15000 times, H-index – 42). He is the Editor-in-Chief of *Contemporary Oncology*.

Exosomes in cancer progression and as immunotherapeutic tools for cancer

Susanne Gabrielsson

Dept. of Medicine Solna, Karolinska Institutet, Sweden

Biography

Prof. Gabrielsson has after her PhD at Stockholm University and a postdoc at the Curie Institute in Paris, established a group dedicated to exosome research at the Karolinska Institutet, Sweden. She has been a pioneer in the field of immune effects of exosomes. Dr. Gabrielsson was the first to describe the presence of exosomes in bronchoalveolar lavage fluid, as well as in breast milk. Her work has revealed that exosomes are major players in lung diseases such as asthma and sarcoidosis, where they contribute to inflammation. Her studies in animal models give new insights into how exosome-based therapies can be optimized for immunotherapeutic applications in cancer.

Abstract

Exosomes from antigen presenting cells are potential cancer immunotherapy vehicles due to their capacity to stimulate tumor-specific activity in mice. However, clinical trials using peptide-loaded autologous exosomes showed only moderate T cell responses, suggesting a need for optimization of exosome-based therapy. We are using dendritic cell derived exosomes to induce antigen-specific immune responses with the aim to cure cancer. We have seen that exosomes need to carry whole protein, and not only peptide/MHC complexes, to induce a strong T cell response in vivo. We showed that the reason for this was that B-cells needed to be activated to induce a strong T cell response to exosomes. This has led us to test allogeneic exosomes in a B16 melanoma model, and our results demonstrate that allogeneic exosomes are as efficient in inducing immune responses as syngeneic exosomes. This greatly increases the feasibility of exosome-based immunotherapy. Currently we are working on different ways to further boost immunogenicity of exosomes and data from these studies will be presented.

EIT Health and its support for business creation and business growth

Inês Matias (EIT Health InnoStars)

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Biography

With a degree in Cellular and Molecular Biology and a master's degree in Economics and Management in Science, Technology and Innovation, before joining the EIT Health team as Business Creation Project Manager for the InnoStars region, Inês was Program Director at the Healthcare City, a health and wellness start-up incubator based in Lisbon. For the last 3 years she has been working with healthcare startups, from life science projects to medical devices, and supporting them to become successful businesses.

Abstract

EIT Health Accelerator is a business creation programme, set up to support the best and brightest health industry entrepreneurs. To tackle the future challenges of European healthcare, EIT Health Accelerator creates a favourable environment for innovation, providing skills and services to get promising business ideas into the market. The Accelerator pillar of EIT Health provides support to healthcare entrepreneurs at every stage of the process.

Biobanks and Registers in Transition – program to facilitate industry to access biobanks and registers

Merike Leego (EIT Health Scandinavia)

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Biography

Merike Leego, MBA, MSc, is Innovation Manager in EIT Health Scandinavia (https://www.eithealth.eu/), the European Commission funded network that promotes innovation in health sector and brings together stakeholders to implement close-to-market-ideas into everyday healthcare via supporting its financial instruments. She is also coordinator of program RABBIT (https://www.eithealth.eu/rabbit) that stands for improving access of biobanks and quality registries to industry and academia within EIT Health network. Merike Leego has extensive experience in coordinating research projects funded by the European Commission, NIH and the Estonian Research Council at her previous position in University of Tartu/Estonian national biobank. She has been actively involved in activities of BBMRI-ERIC Estonia and coordinated FP7 funded project BBMRI-LPC activities in Estonia. She has held position of Marketing Manager and Intellectual Property Manager in several biotech companies in Estonia. She also reads lecture on bio-Entrepreneurship at University of Tartu.

Abstract

The strategic activity in EIT Health Scandinavia RABBIT (Biobanks and registers in transition), seeks to address several issues, with the overall goal of simplifying industry access to biobanks and registers in order to gain improvements for R&D, through leveraging assets in biobanks and health registries.

The main activities will include identification of challenges for industry, collecting the fragmented information into one portal and bringing the stakeholders together to matchmaking event on the 21st of October (https://eu.eventscloud.com/ehome/biobanksandregisters) for planning new healthcare solutions. By providing overview on access procedures, national regulations and content of the registers and biobanks in Scandinavia, but also use cases and collaboration models between industry and registers/biobanks, we aim to save the time of the innovators.

Beside EIT Health financial support for large innovation projects, independent EIT Health program “Digital Sandbox” provides support for start-ups and SMEs for their developments that use biobanks and registers.

Scandinavian Business Creation Ecosystem and Digital Sandbox Program

Christos Vaitsis (EIT Health Scandinavia)

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Biography

Christos Vaitsis, MMSc, MSc, is Business Creation (Accelerator) Manager in EIT Health Scandinavia. The Accelerator provides support throughout the entire value chain (incubation, validation and scale up and out) to life science entrepreneurs in Europe and leverages business creation entities and actors such as start-ups, investors, mentors, incubators, accelerators and innovation clusters. He is also Program Manager for the EIT Health Digital Sandbox program. Christos has been working previously in Karolinska Institutet in developing a Master's programme course in ''Designing eLearning interventions in healthcare education'', in different EU funded projects and also in basic research and publications on the contribution of Big Data and Analytics for impacting reasoning and decision making in health education context. He holds a Master of Medical Science with a major in Health Informatics from Karolinska Institutet and a Bachelor in Computer Science with emphasis on Artificial Intelligence and Neural Networks.

Abstract

The EIT Health Scandinavian node is currently operating with Partners in Denmark, Sweden and Estonia. It brings together a strong network of Academic, Indusrty and public sector stakeholders and has a strong profile of public partners representing up to 60% of population in these countries. EIT Health Scandinavia is also cultivating collaborations with national strategic programmes and initiatives having a strong role as the internationalization arm for Europe.

EIT Health Scandinavia is also leading the EIT Health Digital Sandbox program for SMEs requiring access and collaboration with Biobanks, Sample Holders and Quality Registers in Europe, for the further development and/or commercialization of new technologies, products or services, that will lead to improved (quality for) prevention, predicition, diagnosis, treatment and follow up. The main purpose of the EIT Health DS Programme is to enable the leveraging of the ''Health Data Business'' in Europe.

Medical University of Gdańsk as Regional Innovation Scheme (RIS) Hub for Pomeranian Region

Katarzyna Waligóra-Borek (Gdańsk RIS Hub EIT Health)

Medical University of Gdańsk

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Biography

A graduate of the University of Gdańsk carried out a doctoral dissertation at the Faculty of Biology, Geography and Oceanography, she is the author of several scientific publications in a field of life-science. Experience in the internal audit of integrated management systems - Process Management Office Grupa LOTOS S.A. Started career in the medical industry by working at the Tissue and Cell Bank, Hematology and Transplantology Clinic of the University Clinical Center. From May 2015 specialist in Technology Transfer Office, from July 2018 Acting Director in Technology Transfer Office in Medical University of Gdańsk. The main issues: supports the activities of the University in obtaining national and international funds in the field of commercialization of innovative scientific research, creation of spin-off companies, administration of intellectual property rights, activating scientists to cooperate with business entities.

Abstract

From 2018 the Medical University of Gdańsk is a part of the community of the European Institute of Innovation and Technology (EIT) in the field of health, which main goal is to improve the quality of life of Europeans and increase entrepreneurship. The Medical University of Gdańsk as the regional contact center of the Regional Innovation Scheme (RIS) implements tasks resulting from the cooperation agreement with the EIT Health institution. The project assumes strengthening the local ecosystem and expanding the cooperation network of the academic and economic community as well. European Institute of Innovation and Technology is a strong, diverse and sustainable partnership, made up of leading organizations in the fields of education, research, technology and innovation, currently has more than 140 partners from 14 European countries.

The position of the Medical University of Gdańsk as a recognizable full-fledged Gdańsk RIS Hub in Poland and in Europe will be a beneficial instrument for the development of interdisciplinary projects with both commercial and implementation potential. This initiative brings wide support opportunities in a few areas of programs: acceleration, training and scholarship dedicated to researchers, students, PhD students, young innovators and start-ups from the university and the region.

BIC Tools for Biomarker Commercialization

Tero Piispanen (BiC project)

Senior Executive, HealthTurku, Turku Science Park Oy Ltd, BIC – Biomarker Commercialization project

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Biography

Tero Piispanen, MSc (Eng.), MBA. is senior executive in Turku Science Park (TScP) where he currently runs HealthTurku, the largest life science cluster in Finland. He is also a board member of Council of European Bioregions CEBR and a vice president of ScanBalt. Tero has long industrial career in business development, internationalisation, tecnology transfer and risk funding. He has also acted as a board member of life science companies and as CEO of a life science management consultancy company.

TScP is a not-for-profit organisation providing business development services which cover the entire lifecycle of entrepreneurial activities, ranging from testing a business idea and establishing a company to internationalisation and expanding of international business operations. TScP also runs a national Life Science Accelerator programme in Finland.

Abstract

The process of turning biomarker discoveries into commercial products to market and clinical use is long and challenging. BIC - Biomarker Commercialization project (Oct 2017 -Sept 2020) aims to support the commercialization of new biomarkers by providing:

- a 'Master Tool', which includes the key tasks of a biomarker commercialization process, including not only the 'technical' task of the researcher, but also the commercial and regulatory considerations in each development phase
- a screening and selection guide for TTOS for early identification of the best biomarker projects
- a compilation of the best practices and pitfalls in commercializing IVD–applicable biomarkers
- an overview over regulatory challenges and transnational exchanges of clinical data and samples in biomarker commercialization

More information about the project at https://biomarker.nu

The project's budget is EUR 2.55 million, and it is co-financed by the European Regional Development Fund through the Interreg Baltic Sea Region Programme with EUR 1.96 million.

Responsible Innovation: a promising collaborative approach for research

Krzysztof Piotr Bielawski (STARBIOS2 H2020)

University of Gdansk

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Biography

Full Professor for Molecular Biology, Head of the Laboratory for Molecular Diagnostics; Vice-Rector for Development and Cooperation with Business and Industry at University of Gdańsk (since 2016).

Author and co-author of more the 100 publications;

Experienced academic supervisor (7 postdoctoral coworkers and 12 Ph.D. students).

Experienced in management positions in the medical diagnostics sector (Hospital for Infectious Diseases, Regional Blood Bank in Gdansk).

Intensively involved in science-industry relations (CEO of BioBaltica Ltd. (2008-2010), director of the Technology Transfer Office at UG (2014-2016), CEO of TechTransBalt Ltd. (2014-2016).

Vice President of ScanBalt Association since 2014.

Involved in numerous EU projects (Coordinator of FP7 project *MOBI4Health (*2013-2016), Polish Team Leader in FP7/ERA-Net Infect-ERA (2014-2017), WP Leader in STARBIOS2 and RESBIOS projects, Supervisor as a senior scientist in 5th (HepBvar) and 6th (ViRgil) EU Framework Programmes grants on monitoring of drug resistance of viral infections.

EC expert in EU FP7 and HORIZON 2020.

Abstract

The presentation by C.Colonnello, V.Collizzi, E. K. Schmidt and K. P. Bielawski focuses on how social aspects taken into account within bioscience research can enrich the scope the work undertaken.

This part focuses on the introduction to the RESBIOS project (RESponsible research and innovation grounding practices in BIOSciences). The aim of the new H2020 project is to deeply embed societal focused actions in 4 research organizations in the field of Biosciences from 4 European countries. The implementation of a dedicated package of actions in areas such as social engagement, education, gender equality, open access and ethics, is expected to result in sustainable institutional changes in the participating institutions. The project is focused on the biosciences sector which is one of the crossroads in the relations between science and society. In the frame of the project University of Gdańsk will share its previous experience with new partners.

Responsible Innovation: a promising collaborative approach for research

Claudia Colonnello (STARBIOS2 H2020)

Laboratorio di Scienze della Cittadinanza – LSC (Laboratory of Citizenship Sciences)

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Biography

Claudia Colonnello is a social researcher with a long experience in the interdisciplinary study of contemporary social phenomena, from responsible research and innovation and gender perspectives, and in the sociological analysis of the relations between security and privacy within the context of surveillance. She has been involved in projects in Europe, Africa, Latin America and Australia: STARBIOS2 (Structural Transformation to Attain Responsible BIOSciences), GRACE (Grounding RRI Actions to Achieve Institutional Change in European Research Funding and Performing Organisations); CHERRIES (Constructing Healthcare Environments through Responsible Research Innovation and Entrepreneurship Strategies); RICONFIGURE (Reconfiguring Research and Innovation Constellations); SIIP (Speaker Identification Integrated Project); MAPPING (Managing Alternatives for Privacy, Property and Internet Governance); RESPECT (Rules, Expectations and Security through Privacy Enhanced Convenient Technologies); SMART (Scalable Measures for Automated Recognition Technologies); TWIST (Towards Women in Science and Technology); WHIST (Women's careers hitting the target: gender management in scientific and technological research); and PRAGES (Practising Gender Equality in Science).

Abstract

The presentation by C.Colonnello, V.Collizzi, E. K. Schmidt and K. P. Bielawski focuses on how social aspects taken into account within bioscience research can enrich the scope the work undertaken.

This part is entitled: “Structural change to attain Responsible Biosciences: the experience of the STARBIOS2 project“. Science is facing a complex transition which is reshaping its structure, norms, values and practices. Many risks are challenging the advancement of science today, some of which depending on its inadequate alignment with society. The ongoing changes are activating modifications in the structure of research institutions and are requiring a revision of the usual mechanisms of research governance toward, e.g., a multi-actor and public engagement in research and innovation (including citizens), an easier and open access to scientific results, the take up of gender and ethics in the research and innovation content and process, and the enhancement of formal and informal science education. In this framework, some lessons will be presented on effective strategies for fostering structural change drawn from the EU-funded STARBIOS2 (starbios2.eu) Project, involving 9 bioscience research institutions from Europe, South Africa, Brazil and US.

Responsible Innovation: a promising collaborative approach for research

Evanthia K. Schmidt (STARBIOS2 H2020)

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Biography

Dr. Evanthia K. Schmidt is Associate Professor and Research Director at the Department of Political Science Aarhus University. She specializes in science and innovation policy, Responsible Research and Innovation (RRI), gender in knowledge production and research organizations, European gender policies, European research policy and governance, and evaluation of policy interventions. She has been involved in a number of projects funded by the EU and Nordic research councils and has been frequently engaged by the European Commission as an expert in the evaluations of FP6, FP7, and H2020 project proposals. She was appointed by the EC as member of the FP7 Expert Group to carry out the Ex-post Evaluation of International Cooperation Activities of the FP7 Capacities Programme and the Ex-ante Impact Assessment of H2020, Environment and Climate Change Programme. Dr. Schmidt is the appointed Danish expert member of the European RTD Evaluation Network and has been an expert member of the H2020 Advisory Group for Gender.

Abstract

The presentation by C. Colonnello, V. Collizzi, E.K. Schmidt and K.P. Bielawski focuses on how social aspects taken into account within bioscience research can enrich the scope the work undertaken.

This part entitled: “Monitoring and Assessing RRI Structural Change in Biosciences” will focus on key aspects of the monitoring and evaluation of the actual experience of promoting RRI structural change within research organisations in the STARBIOS2 project. The main objectives of the monitoring and assessment activities are: (i) to examine and assess the process and progress towards the objectives of the actions, (ii) to provide input as to the quality of the activities during the implementation process, and (iii) to assess the achievement of planned objectives and expected impacts. The monitoring and assessment activities also contribute to RRI knowledge exchange and mutual learning.

Sano Foundation, The Centre for Individualized Computational Medicine

Kazimierz Murzyn (Klaster LifeScience Kraków)

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Biography

Managing Director of the LifeScience Krakow Klaster; Member of Biotechnology Committee of Polish Academy of Science; Member of the Board of Agriculture University in Krakow; Member of strategic group of SCANBALT; Chairman of the Malopolska Smart Specialization Working Group "Life Science".

He has working expertise in the fields of business development, creativity and innovation management, cluster management and organizational learning, modeling of behavior of complex systems, systems thinking and systems dynamics, strategic and scenario planning, creative problem solving.

Abstract

This presentation describes the creation in Kraków, Poland, of a new research and innovation centre – Sano Foundation, The Centre for Individualized Computational Medicine. The Centre aims to be a major driver for European advancement in this rapidly growing sector, developing sophisticated engineering methods for the diagnosis and treatment of disease, optimising the use of patient data, and meeting the overarching worldwide need for personalised, precision healthcare.

Computational medicine (In Silico medicine) was born as a field of science based on the advancements of computer technologies and their computing power and the increase in the quantity and quality of data, which constitute a basic, in principle exclusive research material. Contemporary computational medicine deals with modelling, simulation and visualization of biological and medical processes in computers in order to mimic real biological processes in a virtual environment.

This is the domain of the Sano Foundation. Sano project creates the opportunity for researchers to engage in projects and programs aimed at developing and implementing new methods, tools and skills in the clinical practice using computer techniques and technologies as ultimately clinically validated, clinically ready-to-use decision support systems.

Funding Opportunities for Academia Industry Collaboration in Research

Anna Dziubczyńska-Pytko (National Contact Point – Poland)

Biography

2014 till now - the National Contact Point (NCP) to the Social Challenge 1. Health, demographic change and wellbeing in Horizon 2020 and to the Innovative Medicines Initiative 2 (IMI2) Joint Undertaking. Polish member to the State Representatives Group IMI2 and the expert to the Health H2020 Program Committee.
2002 - 2013 - Deputy Director of the NCP – Poland (KPK PB UE).
Partner in 12 projects of the Framework Programmes and coordinator of QUALITYMEAT project (2004-2006, 11 European partners).

Abstract

The National Contact Point – Poland supports Polish research community (public, private, science, business, (non)governmental etc.) in participation in the EC FPs since 1999.

The NCP offers:

- information
- info days, trainings, workshops, conferences, brokerage/partnering events
- proposal consultation, mentoring
- financial and legal advice for proposals and projects
- partner search
- support for scientists coming from abroad (EURAXESS).

Information service: www.kpk.gov.pl and http://en.kpk.gov.pl/ncp-poland/

The EC invests €11 billion in new solutions for societal challenges and drive innovation-led sustainable growth for the last year of Horizon 2020. It is the largest annual tranche under EU research and innovation funding programme for the period 2014-2020.

Societal Challenge 1: Health, demographical changes and wellbeing budget for calls 2020 is €698 million. 30 topics which have deadline in April 2020 will be introduced on ScanBalt Forum 2019 in Gdansk. Those topics are in 3 calls:

1. “Better Health and Care, economic growth and sustainable health system” in areas (1) Personalised medicine, (2) Innovative health and care industry, (3) Infectious diseases and improving global health, (4) Innovative health and care systems - Integration of care, (5) Decoding the role of the environment, including climate change, for health and well-being, (6) Supporting the digital transformation in health and care.
2.“Digital Transformation in Health and Care”.
3.“Trusted digital solutions and Cybersecurity in Health and Care”, Focus Area on Digitising and transforming European industry and services.
Horizon Europa is the next EU Research & Innovation Investment Programme (2021 – 2027).

How to write great papers

Lynn Sherrer (Elsevier)

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Biography

Lynn Sherrer is a Publisher in Life Sciences at Elsevier, where she manages a portfolio of 19 biotechnology journals, overseeing strategy of journal quality, content, and growth, the journals' Editors, finance, and marketing. Lynn has been with Elsevier for 10 years, for the first 5 as Editor-in-Chief of the Cell Press journal, *Trends in Parasitology*. She has a B.S. in Microbiology from University of Georgia, and a Ph.D. in Biochemistry & Molecular Genetics from University of Alabama at Birmingham, where her work focused on RNA transport in African trypanosomes. Her postdoctoral studies in the Department of Molecular Biophysics & Biochemistry at Yale University focused on tRNA-mediated selenocysteine biosynthesis in Archaea and *Plasmodium falciparum*. Her time in academia, as an editor, and now publisher, she has been on all sides of the publishing journey.

Abstract

Navigating the process of publishing in scientific journals can be a daunting task full of frustration. Understanding how to structure your paper during the writing process and deciding on an appropriate journal will greatly increase your chance of ending with acceptance. Knowing in what manner editors think and having a clear picture of the peer review process are also invaluable insights into publishing your paper. To avoid the disappointment of having your paper rejected, each of the steps of the publishing cycle, from title to references, and submission to acceptance will be covered.

Poster Abstracts

Converting pathogenic gain of function variants of complement factor B into enhancers of anti-CD20 immunotherapy

Authors

A. Felberg-Mietka[1], A. Urban[1], A. Borowska[1], G. Stasiłojć[1], M. Taszner[2], A. Hellmann[2], A. M. Blom[3], M. Okrój[1]

Affiliations

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Abstract

Anti-CD20 monoclonal antibodies rituximab and ofatumumab, approved for treatment of B cell malignancies, are potent activators of the classical complement pathway. However, complement exhaustion and overexpression of complement inhibitors by cancer cells diminishes their therapeutic potential. The strategies of targeting membrane complement inhibitors by function-blocking antibodies and the supplementation with fresh frozen plasma have been proposed to overcome tumour cell resistance. We present a novel approach which utilizes gain of function variants of complement convertase forming proteins. The proof of our concept is exemplified by factor B (FB), a component of alternative C3/C5 convertases which augment mAbs activated reaction by the amplification loop. If complement concentration is limited, an addition of quadruple gain-of-function FB mutant p.D279G p.F286L p.K323E p.Y363A (or selected single mutants) results in significantly increased complement mediated lysis of ofatumumab resistant tumour cells, as well as the complete lysis of moderately sensitive cells. Importantly, this effect cannot be achieved by further increasing ofatumumab concentration. Addition of hyperactive FB but not wild-type protein could compensate the loss of cytotoxic potential of serum collected from the NHL and CLL patients after infusion of rituximab. Residual levels of rituximab in such sera, in combination with added FB, were able to efficiently lyse tumor cells. The novelty of the proposed solution consists in the use of such potentially pathogenic proteins as an immunotherapy supplement significantly increasing the cytotoxic activity of the immunotherapeutics.

Project was supported by two grants from National Science Centre Poland (2015/18/M/NZ6/00334 and 2014/14/E/NZ6/00182) and Cancerfonden (Sweden).

Blocking the TNF-TNFR2 interactions - a promising cancer treatment

Authors

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Affiliations

[1] Department of Biomedical Chemistry, Faculty of Chemistry, University of Gdansk, Gdansk, Poland, [2] International Centre for Cancer Vaccine Science, University of Gdansk, Gdansk, Poland, [3] Department of Theoretical Chemistry, Faculty of Chemistry, University of Gdansk, Poland, [4] The Royal (Dick) School of Veterinary Studies and the Roslin Institute, Roslin, Midlothian, United Kingdom

Abstract

According to the World Health Organization, cancer is the second leading cause of death globally and was responsible for 9.6 million deaths in 2018. Conventional cancer treatments are losing their therapeutic use due to drug resistance and lack of tumour selectivity, and thus there is a need to develop new therapeutic agents. Biological treatments are currently seen as very promising methods. One such treatment is immunotherapy using checkpoint blockades and engineered T cells, which has achieved great success in recent years. Immune checkpoint inhibitors (ICIs) have revolutionized cancer therapy but exhibit variable efficacy, relapse and can induce autoimmunity. Tumour necrosis factor receptor II (TNFR2) is expressed both by some cancer cells and by tumour infiltrating immunosuppressive regulatory T cells (Tregs). TNFR2 stimulates the activation and proliferation of Tregs, a major checkpoint of anti-tumour immune responses, promotes cancer cell survival and tumour growth. The main goal of this project is to design and synthesize peptides and peptidomimetics which will be able to block the TNF – TNFR2 complex formation, and therefore suppress tumour growth and activate the immune system by suppressing Treg lymphocytes. In this project, the fragments of TNF, their analogues and designed peptidomimetics will be synthesized and examined whether they can inhibit TNF – TNFR2 complex formation and, in this way, block the proliferation of Tregs and ovarian cancer cells.

Nanotechnology as a tool for detecting drugs on the example of valrubicin

Authors

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Affiliations

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Abstract

Currently, many methods are used to detect pharmaceutical compounds, including fluorescent techniques. However, we often struggle with problems related to the small sample volume, fluorescent nature background, or the low quantum yield of the test compound. These limitations and difficulties can be overcome by using the phenomenon of enhancing the efficiency of lighting and photostability of the fluorophore in the presence of thin layers or nanostructures of precious metals (silver, gold). Recently, it has been observed that even greater fluorescence intensities can be obtained due to traveling plasmons. Speech is then about the so-called plasmonic platforms. Designing and preparing appropriate surfaces for recording and analyzing enhanced fluorescence is currently extremely important. The benefits that this brings with it are many times higher fluorescent signal intensities and greater photostability of samples.

As part of the study, the drug used was valrubicin, a semi-synthetic derivative of doxorubicin. This medicine is used to treat bladder cancer. The limitation in the detection of this molecule is the low quantum fluorescence yield, which is about 6%. This means that the drug in the samples tested is undetectable by ordinary spectroscopic methods. Core-shell structures were used to obtain new plasmonic platforms. As a result of the use of new plasmonic platforms, a new quality in biosensing was obtained, thanks to an improvement in detection sensitivity by about 50 times.

Interactions of recombinant TRF1 and TRF2 and their binding domains Myb1 and Myb2 from shelterin complex protein with telomeric DNA

Authors

M. Prusinowski, J. Żebrowska, D. Krefft, M. Fiutak, P. Laszczuk, P. Maciszka, I. Sobolewski, A. Żylicz-Stachula, P. M. Skowron

Affiliations

Department of Molecular Biotechnology, Faculty of Chemistry, University of Gdansk, Poland

Abstract

The human hTRF1 (Telomeric repeat-binding factor 1) and hTRF2 (Telomeric repeat-binding factor 2) belong to the shelterin complex protecting telomeres. This structure ensures the stability of the chromosome by rolling the telomeric DNA into two specific loops and protects against undesirable activities of the DNA repair cycle. The hTRF1 and hTRF2 exhibit high affinity for double-stranded telomeric DNA and bind to DNA as homodimers by TRFH domain. The hTRF1 is a negative regulator of the telomeres length. TRF1 along with TRF2 normally prevents telomerase from adding more telomere units to telomeres. Additionally the hTRF2 covers and protects the ends of the chromosomes. The removal of hTRF2 from telomeres results in the loss of the cell's ability to discriminate the natural ends of DNA from cracking and cutting off the single-stranded chain at the end of 3‘ hanging, leading to telomere dysfunction. Both hTRF1 and hTRF2 contain the TRFH homodimerization domain and the Myb type domain which specifically recognizes and binds telomeric DNA.

The aim of the study is to demonstrate the importance of the use of recombinant TRF1 and TRF2 proteins to study in vitro protein-DNA interaction model. It will allow testing of chemical compounds which may be a potential solution in the fight against cancer cells.

Genes encoding recombinant TRF1/2 as well as binding domains of human hTRF1 and hTRF2 proteins (Myb1/Myb2) were designed, synthetized, cloned and overexpressed in E. coli system. The ability of specific binding to telomeric DNA by both TRF1/2 proteins and their binding domains Myb1/2 was confirmed.

FUNDING: Project was supported by National Center for Research and Development, Warsaw, Poland, grant no STRATEGMED3/306853/9/NCBR/2017, entitled „New anticancer compounds interfering function of telomeres (project's acronym: TARGETTELO).

Long-term memory of transcription – a case of trained immunity

Authors

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Affiliations

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Abstract

Stable mitotic transmission of gene expression is essential for development and maintenance of tissues. Chromatin, the histone/DNA nucleoprotein complex, is implicated in preserving the transcriptional status of genes. However, while local chromatin-based feedback loops have been described to play a role in maintenance of gene silencing, no such mechanisms have been reported for active states. In order to discover epigenetic mechanisms that drive the maintenance of active gene expression it is crucial to uncouple the role of chromatin structure from the process of transcription itself. Here we capitalize on a phenomenon called trained immunity where cell-autonomous gene activation by cytokines, such as interferon gamma (IFNγ), result in priming of a subset of genes that are maintained in a poised but inactive state which is revealed by stronger re-activation at a later stage. This mitotically stable, poised character forms a paradigm for long-term epigenetic memory of gene activation.

We aim to discover mechanisms driving transcriptional memory. We have identified key human genes strongly primed by IFNγ, most notably those encoding Guanylate Binding Proteins. By using GBP5 as readout, we established a robust assay to dissect the kinetics of memory at the single cell level. We discovered that priming leads to an increase in the number of cells that reactivate the gene. In addition we are currently characterizing which specific chromatin features contribute to long term maintenance of the primed state, providing new mechanistic insights into the phenomenon of trained immunity.

Emerging roles of BRCA1 alternative splicing in patogenesis of ovarian cancer

Authors

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Affiliations

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Abstract

The BRCA1 (17q21.31) is the prime gene for susceptibility to ovarian cancer (OC). It is estimated that approximately 44% of women being carriers of BRCA1 pathogenic variant will develop OC. Today, more than 2189 different BRCA1 mutations have been recorded. The main challenge toward a better understanding of BRCA1 and its role in ovarian cancer are alterations located within splicing regulatory elements that might result in the formation of an alternative or non-functional form of protein. The alternative splicing of BRCA1 is poorly understood, and besides several relatively well-studied isoforms, the role of the majority of alternative transcripts remains unknown.

The main aim of the study is to evaluate the incidence of alternative BRCA1 transcripts in the group of BRCA1/2 negative, ovarian cancer patients.

The screening for the presence of alternative transcripts was done using PCR followed by direct sequencing, while analysis of common BRCA1 isoforms (Δ10-11, Δ11, Δ11q) was conducted with ASA-PCR. In the present study, we did not identify novel aberrant transcripts; however, all, naturally occurring, isoforms were detected. Moreover, statistical analysis revealed significant differences in their frequency between patients and healthy controls.

Characterization of tumour-infiltrating lymphocytes from non-small cell lung cancer

Authors

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Abstract

Lung cancer is the most prevalent cancer worldwide (over 2 million new cases estimated in 2018) and the one with the highest mortality, according to the World Health Organization. Non-small-cell lung cancer (NSCLC) accounts for 85% of all lung cancer cases and its main cause is cigarette smoking [1]. Despite all the recent advancements in treatment only 18% of patients with lung cancer survive 5 years after diagnosis [2]. It was shown that high level of tumour-infiltrating lymphocytes (TILs) in NSCLC correlates with improved disease-free survival and decreased risk of recurrence [3]. Therefore, we are setting up a protocol of lymphocyte-based cellular therapy of NSCLC. In this project we are isolating TILs from fresh samples of NSCLC, characterizing their phenotype and assessing therapeutic potential. We are also comparing the phenotype, activation status and antigen specificity of TILs with lymphocytes isolated from regional lymph node and peripheral blood of each patient. As lung cancer has the second highest mutation burden of all tumour types, it expresses mutated neoantigenic peptides, which can be targeted by T cells [4]. Therefore, our studies are also focused on neoantigen discovery in aim to induce antigen-specific immune response against NSCLC.

Our preliminary data show that immune response against NSCLC is strongly suppressed by tumour infiltrating regulatory T cells (Tregs). However, peripheral blood is a good source of effective T cells for anticancer treatment.

Cancer dormancy: promising therapeutic target

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Abstract

Cancer dormancy is a pivotal stage in cancer progression in which residual disease is present but remains asymptomatic. In favorable conditions, dormant cancer cells can awaken and promote metastasis, leading to relapse in patients that are in seemingly complete remission. Experimental and clinical evidence shows the existence of various mechanisms of cancer dormancy, including cellular dormancy and tumor mass dormancy. But what is the actual cause of awakening of dormant cancer cells? How can we target and eradicate those cells? Herein I summarize the major molecular pathways underlying the dormancy and analyze the current pharmacological strategies aimed at dormant cancer cells.

Biosynthesis in Escherichia coli bacterium and purification of Myb1 protein

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Abstract

Background: Myb1 is protein domain of TRF1 protein. TRF1 is one of six protein subunits which build shelterin complex. TRF1 protein is able to bond with DNA, because of affinity Myb1 domain to recognize tandem arrays of DNA 5' – TTAGGG – 3' sequence repeats. Shelterin complex is able to create a T- loop which is occurred in human telomeres. T – loop formation provides stability of chromosomes by protect them from degradation or fusion.

Aim: The aim of this work is biosynthesis in bacteria expressive system and purification of Myb1 protein.

Results: After bacterial transformation, Myb1 protein was expressed in Escherichia coli BL Star (DE3) bacterial strains in temperature: 37oC. The protein was eluted in gradient by buffer contains imidazole on NGC Medium – Pressure Liquid Chromatography System by Ni – NTA agarose columns. Results of protein expression and purification were checked by separating proteins in Tris Tricine SDS – PAGE gel. Myb1 protein was identified in western blotting technique by immunodetection with polyclonal antibodies: anti – His tag and anti – TRF1.

Conclusions: The product obtained in protein biosynthesis in Escherichia coli BL21 Star (DE3) bacterial strain, has got degradation fragments. Myb1 protein was eluted by 500 mM imidazole concentration in elution buffer on Ni – NTA agarose columns.

Immune escape of breast cancer cells and its link with epithelial to mesenchymal transition

Authors

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Abstract

Epithelial to mesenchymal transition (EMT) is a physiological process hijacked by cancer cells, which allows them to acquire invasive phenotype, leading to more efficient metastasis formation. Recent studies indicate that EMT may also be involved in immune escape of cancer cells. Direct mediators of metastasis process, circulating tumour cells (CTCs), may escape from immune system control by disruption of antigen presentation.

In this study we aimed at evaluating the expression of immunoproteasome (PSMB8, PSMB9, PSMB10) and genes involved in antigen preparation (B2M, TAP1, TAP2) in breast cancer cell lines, and further establish a method of profiling the above mentioned genes in CTCs from breast cancer patients.

Forty two breast cancer cell lines spanning all molecular subtypes of breast cancers were investigated. Expression of immune escape genes PSMB8, PSMB9, PSMB10, TAP1, TAP2, B2M was elevated in cell lines with more mesenchymal features, whereas epithelial marker expression correlated with decreased immunoproteasome (PSMB8, PSMB9, PSMB10) subunits expression. In the established breast cancer CTCs model single MCF7 and MDA-MB-231 cell lines were isolated from blood samples. On the single cell level decreased expression of PSMB8, PSMB9, PSMB10 and B2M was observed in epithelial MCF-7, in comparison to mesenchymal MDA-MB-231 cell line.

Breast cancer cell lines with more epithelial characteristics show features which could contribute to more efficient immune escape. Analysis of CTCs from breast cancer patients are currently performed to validate this finding.

miR-410-3p is induced by vemurafenib via ER stress and contributes to BRAF inhibitor resistance in melanoma

Authors

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Abstract

Despite significant development of melanoma therapies, death rates remain high. MicroRNAs, controlling posttranscriptionally gene expression, play role in development of resistance to BRAF inhibitors. In our study, FFPE tissue samples of 12 primary nodular melanomas were analyzed. With the use of Laser Capture Microdissection, parts of tumor, transient tissue, and adjacent healthy tissue were dissected. In vitro studies were performed on human melanoma cell lines A375, G361, and SK-MEL1. IC50s of vemurafenib were determined using MTT method. Cells were transfected with synthetic miR-410-3p mimic, anti-miR-410-3p and their non-targeting controls. ER stress was induced by thapsigargin. Expression of isolated RNA was determined using qRT-PCR.

We have found miR-410-3p is downregulated in melanoma tissues compared to healthy tissues and other type of cancer. Its expression is induced by vemurafenib in melanoma cells. Upregulation of miR-410-3p level increased melanoma cells resistance to vemurafenib, while its inhibition leads to the decrease of resistance. Induction of ER stress upregulated the level of miR-410-3p. miR-410-3p upregulated the expression of AXL in vitro and correlated with markers of invasive phenotype in starBase.

Our study shows a novel mechanism of melanoma resistance. miR-410-3p is induced by vemurafenib in melanoma cells via ER stress. It drives switching to the invasive phenotype that leads to the resistance to BRAF inhibition.

Cytoplasmic beclin 1 indicates prostate cancer progression

Authors

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Abstract

Beclin 1 is a protein involved in autophagy regulation. In tumor, it might facilitate both its development, progression as well as therapy resistance. The overexpression and loss of beclin 1 are considered to correlate with advanced tumor stage. Its prognostic significance was shown e.g. in liver and breast cancer, whereas little is known about its role in prostate cancer (PCa).

Thus, the aim of this study was to examine the status and clinical significance of beclin 1 gene (*BECN1*) and protein in PCa.

Beclin 1 was detected in (i) cytoplasm, (ii) cytoplasm and nuclei, and (iii) nuclei of tumor cells in 86 (52%), 49 (30%) and 3 (2%) of 165 informative PCa patients, respectively, whereas its lack was observed in 27 (16%) patients. *BECN1* gene loss and gain were observed in 14% and 2% of the analysed tumors, respectively. Patients with beclin 1 expressed exclusively in cytoplasm of tumor cells showed the shortest time to biochemical recurrence in comparison to other subcohorts of patients (p=0.012). Tumors with cytoplasmic beclin 1 showed also more frequently the increased levels of CK14 (basal cell marker; p=0.009), CK18 (luminal cell marker; p=0.004), XIAP (apoptosis inhibitor; p=0.041), Snail (EMT-related transcription factor; p=0.004) and decreased level of ApopTaq (apoptosis signature; p=0.001).

In the current study, beclin 1 expression localized in cytoplasm seems to indicate PCa progression potentially *via* EMT induction, regulation of differentiation and apoptosis inhibition.

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Nrf2 role in immune surveillance

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Abstract

Background: The nuclear factor erythroid 2 related factor 2 (Nrf2) is a relevant basic leucine zipper (bZIP) transcription factor that is essential in the regulation of cell cycle homeostasis, cytoprotection, and innate immunity when cells are under stressful conditions. Nrf2 was shown to protect cells against multiple redox-induced and xenobiotic-induced diseases including cancer and its activation is beneficial in terms of prevention of chronic diseases. Nrf2 activity is desirable in early stages of tumorigenesis, when the host is seeking to control premalignant carcinogenesis, but is undesirable in later stages of tumorigenesis, when it could make fully malignant cancer cells become resistant to treatment. Though Nrf2 function in mounting an immune response is still unsolved, it is widely accepted that Nrf2 speeds up growth and proliferation of cancer cells and confers chemoresistance.

Aim: Investigation of the role of transcription factor Nrf2 in MHC class I expression in normal vs cancer cells.

Results: The results show that depletion of Nrf2 decreased MHC class I expression on protein and cell surface level, in normal lung fibroblasts and in non-small cell lung cancer cell line (A549) with functional knockout of Nrf2. Interestingly, this effect was not observed on transcriptional level where the depletion of Nrf2 increased the expression of MHC class I, in both normal lung fibroblasts and A549 cells.

Conclusion: Nrf2 indeed has a role in immune surveillance and can regulate translation of MHC class I molecules or affect the degradation of HLAs.

Implementation and application of an external high performance data acquisition system on Orbitrap mass spectrometers

Authors

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Abstract

FTMS Booster (Spectroswiss, Lausanne, Switzerland) is an innovative time-domain signal acquisition and processing device designed to work in parallel with manufacturer-supplied acquisition system on Orbitrap mass spectrometers (Bremen, EU). The FTMS Booster directly collects time-domain data (transients) that is not readily available from the manufacturer's software. These transients can then be processed using methods available to all Fourier transform (FT) mass spectrometers including the basics of FT independently after the data acquisition. This circumvents the truncation of data that the manufacturer carries out automatically to decrease file size which in turn results in loss of data.

The benefits of using the FTMS Booster on an LTQ Orbitrap FTMS as available at ICCVS include the following: 1) resolving power increase (up to 2 times) in comparison to standard processing and 2) signal-to-noise ratio improvements. The most important difference in data processing is the ability to carry out full absorption mode Fourier transform data processing and to perform data averaging directly on transients which represent the true raw data produced by Orbitrap mass analyzers.

We report on performance improvements obtained on LTQ Orbitrap by comparing the mass spectra of various samples obtained by FTMS Booster along with the mass spectra acquired using manufacturer's hardware. The expected benefits will be of a great importance for applications involving analysis of trace amounts of the samples or requiring high mass accuracy. It is the case in field of cancer vaccine research, where usually the sample amount is limited, and *de novo* peptide sequencing required for identification of potential cancer neoantigens benefits from the highest possible mass accuracy.

Synthetic flavonol derivatives affect crucial cellular processes in cancer cells

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Abstract

Background: The emerging increase in morbidity and fatalities caused by malignant neoplasms is the cause of the constant search and development of drugs exhibiting anti-cancer activity. The substances that are easily available and widespread in the daily diet turn out to be widely used in research on cancer therapy. In addition, attempts are made to obtain synthetic compounds based on the chemical structure of natural substances that would have better therapeutic effect than the initial compounds, including greater activity, better bioavailability and selectivity.

Aim: In this research the antiproliferative potential of synthetic compounds based on the chemical structure of flavonol against prostate cancer cells (PC-3 cell line) and breast cancer cells (T47D cell line) was investigated. The activities of synthetic derivatives were compared with natural compounds from flavonol group - quercetin and kemferol.

Results: The obtained results demonstrate that some synthetic flavonol derivatives exhibit better than parental compounds antiproliferative activity against both cell line studied. Synthetic derivatives modulate crucial cellular processes in cancer cells. They, induce cell cycle arrest, senescence and apoptosis. They also induce autophagy and inhibit migration of cancer cells. Moreover, the properties of the tested derivatives depend on the structure of the heterocyclic ring substituent.

Conclusions: Modification of flavonol structure is promising strategy to obtain compounds with high anti-cancer potential.

Potential of ctDNA in pre-operative diagnosis of endometrial cancer

Authors

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Abstract

Background: The classification of endometrial cancer (EC) into type I and II is very important when planning surgical procedures. For benign type I, hysterectomy is recommended, while type II tumors are aggressive and require more radical approach. Unfortunately, the actual scope of surgical intervention is assumed, rather imprecisely, during surgery and only the post-operative histological evaluation ultimately indicates what the optimal treatment should have been. As each type of EC carries a set of characteristic mutations, we hypothesized that ctDNA mutational profile in plasma samples could discriminate between type I and II EC patients prior to treatment.

Aim: The study included sequencing results of 520 primary EC tumor samples downloaded from TCGA (The Cancer Genome Atlas). TCGA samples served as a training cohort, used for machine learning to classify mutations characteristic for each EC type. The evaluation cohort consisted of 48 plasma samples collected preoperatively from patients suffering from both type I and II EC. Plasma samples were subjected to DNA extraction, size selection with Pippin and gene panel sequencing.

Results: Random Forest Classifier was trained and evaluated on the TCGA data, using a subset of 71 genes and the mutations' Variant Effect Predictors (VEPs). The classifer was cross-validated (10-fold) on a set of 416 cases (0.8 of the total TCGA data; the rest used for the final testing) reaching F1-score of 0.881. The classifier applied to 15 ctDNA samples showed classification accuracy of 0.867 (13/15 samples classified correctly).

Conclusions: It was shown that the presented approach, based on machine learning and ctDNA mutational profile, can be used to discriminate between type I and II EC in pre-operative samples. Further works include improvement of the classifier quality by exploring the use of Gene Ontology and pathway models for the tumor classification.

Proteomic Analysis of Barrett's Esophagus Cells

Authors

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Abstract

Background: Barrett's esophagus is a disorder in which the normal squamous mucosa in the esophagus is replaced by metaplastic columnar epithelium and is the highest risk for esophageal adenocarcinoma. Patients with Barrett's esophagus have at least ten times greater risk of developing esophageal adenocarcinoma.

This study aims to determine differentially expressed proteins between wild type (WT) Barrett's esophagus cell lines (CPA) and p53 knockout (KO) and p53 Smad4 KO CPA treated with lithocholic acid (LCA) or X-ray. For proteome profiling of the cells we used microdroplet processing in one pot for trace samples (µPOTS) platform, benchtop workflow for analysis of low-number of cells.1 µPOTS platform enabled detection of the differentially expressed proteins from cells previously treated by LCA or X-ray.

Material and methods: CPA p53 KO and p53 Smad4 KO were generated with the CRISPR/Cas9 genome-editing technology and stimulated with LCA or X-ray. Samples consisting of ~200 cells were digested with trypsin using the µPOTS strategy and analyzed by LC-MS/MS on an Orbitrap Fusion Lumos. Protein identification was performed with MaxQuant.

Results: High sensitivity of the µPOTS platform was demonstrated by identification of more than 2500 protein groups from samples containing ~ 200 cells. More than 100 differentially expressed proteins were found with transferrin receptor overexpressed in CPA WT LCA compared to CPA WT. Details of proteins and biochemical pathways found to be significantly different between the groups will be presented.

CD73 (ecto-5'-nucleotidase) regulates various aspects of tumor cell's differentiation

Authors

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Abstract

Background: Changes in cell differentiation are common in cancers and play crucial role in transition to invasive phenotype. Phenomena such as Epithelial-to-Mesenchymal Transition, anaplasia and presence of Cancer Stem Cells can be modulated by tumor microenvironment. Extracellular adenosine generated by ecto-5'-nucleotidase (CD73), is thought to be an important player in cancer progression through influence on both tumor and immunomodulatory cells. Therefore, CD73 can have a potentially significant role in regulation of differentiation process in cancer.

Aim: Analysis of the CD73 role in regulation of differentiation in melanoma and breast cancer.

Results: Inhibition of CD73 with AOPCP (α,β-Methylene-ADP) stimulates the ability of murine B16F10 melanoma cells to migrate and invade ECM, but decreases it in some of the breast cancer cell lines analyzed. These changes are regulated through adenosine receptors and dependent on type of receptors expressed, with activation of A3 and A2A adenosine receptors having an opposite effect on invasiveness of 4T1 breast cancer cell line. Interestingly, in B16F10 melanoma these changes are present only when cells are melanized, while melanization itself modifies cellular distribution of CD73 and CD73 inhibition decreases melanization. Furthermore, CD73 inhibition and stimulation of A2A and A3 receptors impairs process of vasculogenic mimicry. AOPCP also induces significant changes in expression of cytokines regulating EMT and cancer stem cell differentiation.

Conclusion: CD73 regulates various aspects of tumor cell differentiation through extracellular adenosine in tumor microenvironment and thus affecting cancer progression. However, it looks like differentiation may also affect CD73, possibly forming a control loop interactions.

Gain-of-function complement C2 mutant as a supporter of anti-CD20 therapy

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Abstract

Introduction of anti-CD20 mAbs (e.g. rituximab) has revolutionized the management of B-cell lymphoma and leukemia patients. Although it remains first-line treatment, many patients do not respond to treatment or develop resistance, mainly due to overexpression of complement inhibitors by tumor cells. These proteins inactivate particular components of complement cascade and disable pivotal effector mechanism. Due to their activity, the majority of early complement proteins deposited onto the target cells after introduction of anticancer antibodies will not support the terminal stages of the cascade but instead will be unproductively depleted. The problem mostly concerns early complement components (e.g. C2) as their serum concentration can be at least ten times lower than other complement proteins. Thus, C2 emerges as a bottleneck of complement activation pathway and a limiting factor of successful anti-CD20 therapy. We present a novel idea, that supplementation of anti-CD20 mAbs with complement C2 mutant resistant to cancer-derived complement inhibitors may significantly improve the efficacy of complement-mediated cell killing. A panel of single and multiple C2 mutants was created based on naturally occurring mutations in homologue protein factor B. Some of them were able to significantly increase anti-CD20 cell lysis, even of primarily non-sensitive cell line. Importantly, best-performing C2 mutant was able to restore the cytotoxic potential of post-infusion serum samples obtained from rituximab treated patients, without the addition of therapeutic antibodies. Obtained results clearly indicate that administration of our GOF C2 mutant can significantly potentiate the activity of anti-CD20 monoclonal antibodies.

Technology platform designed for the development and study of therapeutics used in cancer immunotherapy. Development of small molecules for the immune checkpoint blockade in combination cancer immunotherapies

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Abstract

Targeting the interaction between PD-1 and its ligand-1 PD-L1 comprises a game changer in oncology - in many cases rendering formerly lethal cancers into a well treatable disease. The currently approved monoclonal antibodies, which block the signaling between PD-1 and PD-L1, show impressive clinical results in several cancers. However, these antibodies are effective only in a subset of patients and display disadvantages such as no oral bioavailability, poor solid tumor penetration and poor control of pharmacokinetics and thus mAb related toxicities. Development of chemical and biologic inhibitors for this pathway lags the antibody development mostly because of insufficient structural information available until very recently. We believe that the identification of the small-molecule and biologic inhibitors of the immune checkpoint proteins is of the highest importance as this could lead to inexpensive cancer therapeutics. The main goal of our research is to discover small-molecule chemical antagonists and bispecific antibody inhibitors that would effectively antagonize the immune checkpoint proteins; like for example, the interaction between the programmed cell death protein-1 (PD-1) and programmed cell death protein ligand-1 (PD-L1). We propose to use and to synthesize a large library of small-molecule chemical fragments and screen for binding against a number of immune checkpoint proteins, PD-1, PD-L1, PD-L2, CD80, and VISTA, using the in-silico computational screening, the methods of high-throughput screening (HTS), and the nuclear magnetic resonance (NMR)-based fragment screening. Medium-to-high affinity binding compounds are identified and then resynthesized; their affinity to the targets are assayed using NMR and other biding assays followed by co-crystal structure analysis.

Immune-related transcriptome profiles associated with negative prognostic factors for operable breast cancer

Authors

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Abstract

Background: Formation of metastasis is mediated by circulating tumour cells (CTCs). Their mesenchymal phenotype is associated with the most aggressive disease course. Platelets are reported to promote survival of CTCs in the circulation, contributing to tumour aggressiveness.

Aim: The aim of this study was to (1) evaluate the interaction between mesenchymal CTCs (mesCTC) and platelet count (PLT) as prognostic factors for breast cancer and (2) to determine the concomitant immune-related primary tumour transcriptome profiles.

Results: In the analysed group (n=86), shorter overall survival was associated with mesCTC (HR=6.6, 1.8-24.6, p=0.005) and higher normal PLT (hPLT; HR=5.8, 1.5-23.4, p=0.013). Coexistence of the factors (mesCTC-hPLT) had an additive negative effect (HR=14.5, 2.4-87.0, p=0.003) on patient prognosis, independent of their interaction ($p<0.05$). For a subset of patients (n=35), expression of 730 immune-related genes was assessed in the primary tumour using NanoString technology. Presence of mesCTC and hPLT alone corresponded with 65 and 16 overexpressed genes, respectively. All 3 groups (mesCTC, hPLT, mesCTC-hPLT) demonstrated elevated expression of 10 genes, involved e.g. in immune response stimulation and T cell chemotaxis. Interestingly, 90 genes were upregulated uniquely in mesCTC-hPLT patients; gene set enrichment analysis revealed upregulation of genes implicated in chemokine receptor binding, response to IL-1, or neutrophil and eosinophil chemotaxis.

Conclusions: Our data suggest that the aggressiveness of early breast cancer is correlated with mesenchymal CTCs and higher normal platelet count that have an additive negative prognostic significance. The effect may be mediated by increased expression of genes involved in chemokine signalling in primary tumours.

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Prognostic significance and molecular profile of tumor associated macrophages in breast cancer

Authors

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Abstract

Breast cancer (BC) is the most frequently diagnosed cancer and the second leading cause of cancer-related death in women worldwide. Despite advances in early detection and comprehensive treatments approximately 30% of patients with early-stage breast cancer still experience recurrence of the disease. Tumor stroma is considered to play key role in the carcinogenesis, tumor dissemination and metastasis formation. One of the most abundant stromal cells in tumor microenvironment are tumor-associated macrophages (TAMs) which play a critical role at each stage of cancer progression. Mostly, TAMs resemble the alternatively activated macrophages - M2.

The aim of the study was to determine correlation of tumor-associated macrophages with breast patient's clinico-pathological characteristics and survival. Moreover, association of TAMs infiltration with genes expression involved in tumorigenesis and progression of breast cancer was assessed using NanoString nCounter assay.

Clinical samples from 107 breast cancer patients treated in University Clinical Centre in Gdańsk (2011 – 2013) were analyzed. Presence of macrophages was confirmed by immunohistochemical staining with anti-CD163 (M2 marker) antibodies. Infiltration of CD163+ macrophages into primary tumor stroma correlated with patients' poor survival, larger tumor size and Triple Negative Breast Cancer phenotype. Overexpression of genes associated with tumor progression (S100A7, CEACAM6, CD1A, PRAME, CCL17, BST2) was detected in CD163-positive patients, what suggests potential mechanism of TAMs influence on patient's poor survival.

This study was supported by National Science Centre, Poland (Sonata Bis 2016/22/E/NZ4/00664).

Altered desaturation of polyunsaturated fatty acids in colorectal cancer cells

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Abstract

Background: Fatty acid (FA) metabolism, including fatty acid desaturation, is an essential process in cancer cells growth and proliferation. One of the cancers in which alteration in lipids metabolism occurs is colorectal carcinoma (CRC). However, still little is known about changes in FA profile in colorectal cancer cells and consequences of these changes on lipid metabolism.

Aim: The aim of the study was to examine if CRC is associated with changes in fatty acid desaturation and to evaluate if these changes are result of altered gene expression. Materials and Methods: FA profile in normal colon mucosa and CRC tissue samples from patients were measured using GC-MS. Total cellular RNA was extracted from cancer and healthy tissue. Gene expression was measured by real-time PCR.

Results: In CRC tissue samples changes in FA profile, especially in polyunsaturated fatty acid (PUFA) content were found. In cancer tissue higher n-3 PUFA and n-6 PUFA levels were observed in comparison with control tissue. The mRNA level of FADS1 and FADS2 (the enzymes involved in fatty acid desaturation) were highly elevated in cancer tissue comparing to normal tissue.

Conclusions: Colorectal cancer cells have induced polyunsaturated fatty acid desaturation. This finding gain more insights into CRC carcinogenesis and can help in development of novel therapeutic strategies.

Synergistic antitumor effect of histone deacetylase inhibitor scriptaid and proteasome inhibitor bortezomib in vitro against ovarian cancer cells

Authors

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Abstract

Background: Histone deacetylase (HDAC) inhibitor - scriptaid can sensitize ovarian cancer cells and reverse resistance of cancer cells to drugs used in currently established therapeutic protocols. That was the justification for combining the former together with conventional chemotherapeutics or bortezomib. Cytotoxic effect of the agents was tested in a MTT assay. Apoptosis assay was performed using annexin V-FITC/PI assay. Apoptotic proteins: caspase-3, caspase-9 and protein p21 were determined by Western blotting.

Aim: To investigate antitumor activity of scriptaid, used either alone or in combination with standard chemotherapeutics: paclitaxel, doxorubicin, carboplatin, etoposide, as well as, bortezomib, on ovarian cancer cells (SKOV-3, OVP-10, MDAH 274) in vitro.

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

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

Immunohistochemical study of tumour-infiltrating lymphocytes in non-small cell lung cancer

Authors

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Abstract

According to the International Agency for Research on Cancer (IARC) of the World Health Organization (WHO) lung cancer remains the most frequent cancer worldwide with fatal consequences, as it is the leading cause of cancer-related mortality in many countries [1]. Adenocarcinoma and squamous cell carcinoma are most common histotypes and they belong to the group of non-small cell lung cancers (NSCLC) [2]. Increased density of tumour-infiltrating lymphocytes (TILs) in NSCLC is associated with better prognosis [3, 4].

Using the formalin-fixed paraffin-embedded postoperative samples, the tumour tissue microarrays (TMA) were made and used for further analysis. TMAs were stained with antibodies focused on immune markers. The percentage of positively stained cells, their staining pattern, and distribution of immune cells in both adenocarcinoma and squamous cell carcinoma were evaluated.

Our preliminary data demonstrates the variability of amounts and intensity of staining of immune cells in lung tumours and suggests a potential impact on the outcome.

Cancer associated fibroblasts subpopulations defined by ERα36 expression and their action on different breast cancer subtypes

Authors

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Abstract

Cancer associated fibroblasts (CAFs) are the most abundant cell type in the tumour microenvironment (TME), they may be involved in disease progression pushing cancer cells towards aggressive phenotype and treatment resistance. However, the role of CAFs in different breast cancer (BC) subtypes is not well described.

The study aimed to discover the role of two different CAFs populations defined by low and high expression of oestrogen receptor isoform – ERα36.

Six CAFs cultures were isolated from chemotherapy naïve breast cancer patients and characterized for ERα36 expression. Conditioned media from CAFs cultures were used to assess the influence of CAFs on clonogenicity and migration abilities of breast cancer cells representing different BC molecular types: hormone receptor-positive cell line - MCF7, triple negative - MDA MB 231 and non-cancerous cell line - HB2. The levels of α-SMA as a CAFs marker in tumour stroma were assessed in the group of 134 BC patients by immunocytochemistry and results were correlated with patients clinical data.

CAFs characterized by low expression of ERα36 significantly increased clonogenicity ($p<0.001$) and migration ($p<0.001$) of MCF7 cell line and decreased clonogenicity in MDA MB 231 cell line ($p=0.001$) with no impact on migration. The α-SMA level was significantly correlated with poor patients survival in hormone receptor-positive group ($p=0.02$).

CAFs are a significant player in breast cancer progression, understanding the dialogue between cancer cells and tumour environment can result in new ways of treatment and diagnosis.
The study was supported by the National Science Centre, Poland (Sonata Bis 2016/22/E/NZ4/00664).

Anticancer potential of selected flavonol derivatives

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Abstract

Background: The growing problem of cancer forces to search for new anti-cancer compounds. The subject of research are often natural compounds present in the diet because of their safety and good tolerance by the organism. Flavonoids are a group of secondary metabolites present in plants. They exhibit numerous health-promoting activities including anti-inflammatory, anti-aggregation, antipyretic, analgesic and anti-cancer properties.

Aim: In this study, the effect of synthetic flavonol derivatives on breast cancer cells (T47D line) and prostate cancer (PC3 line) was examined. The derivatives were tested for their effect on cancer cell viability and their ability to migrate as well as their effect on cell cycle progression, autophagy stimulation and induction of apoptosis.

Results: The obtained results demonstrated the anticancer activity of the tested derivatives against both prostate and breast cancer cells, although the effect on individual cellular processes depended on the cell line used. Importantly, the tested derivatives proved to be selective against cancer cells. The reduction of cells' viability was caused by inhibition of the cell cycle and cell death by apoptosis. Moreover, derivatives affected autophagy and cells migration. In addition, the performed research allowed to select the derivatives with the strongest antiproliferative activity against prostate and breast cancer cells.

Conclusions: The flavonol derivatives seem to be promising compounds in the fight against cancer, although their potential still requires verification in cancer cell lines of different origin and in *in vivo* models

Herpesvirus entry mediator - signaling receptor present on the surface of melanoma cells

Authors

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Abstract

Herpesvirus entry mediator (HVEM), a member of TNF-receptor superfamily, plays an important role in the regulation of the immune system. This protein was found on the surface of T and B lymphocytes and cancer cells, including melanoma cells. This receptor serves as a bimolecular switch to regulate the host immune response. Depending on which ligand it binds to, HVEM can stimulate (LIGHT and LTα) or inhibit (BTLA and CD160) T lymphocyte function.

The main objective of this research is to recognize the interactions between cancer cell and immune cells in the context of anticancer drugs design. The development of the efficient method of expression and purification of HVEM and it characteristic is necessary to plan further experiments which may help to understand the function of this receptor.

Expression of His-tagged HVEM was performed in Escherichia coli. Unfortunately, protein was accumulated in insoluble fraction. Protein renaturation was performed using three methods: dialysis, dilution and column chromatography. Purification was performed using affinity chromatography followed by gel filtration. In addition, was carried out size exclusion chromatography to determine protein monomericity and ELISA tests to check the ability to form a complex with its natural ligand - BTLA receptor.

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Enzymatic production of lipid A using synthetic biology approaches

Authors

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Abstract

Lipopolysaccharides (LPS) are the major component of outer membrane of Gram-negative bacteria. LPS consist of three parts: lipid A, core oligosaccharide and O-antigen. Lipid A part of the LPS triggers proinflammatory response through the TLR4-MD2 complex. Owing to its role in immunomodulation, it has been used as a vaccine adjuvant in cancer treatment. However, lipid A cannot be exploited with its full potential, because it is chemically synthesised – which is expensive and labour intensive. This project therefore aims to synthesize lipid A enzymatically and build an optimal lipid A genetic cassette for its production. As a first step towards the optimal genetic cassette, metabolic flux through the lipid A biosynthesis pathway (Raetz pathway) should be analyzed and rate-limiting step of the pathway should be identified. For this purpose, modular plasmids have been designed, constructed and verified. Additionally, in order to have a strain with the ideal genetic background for the metabolic analysis, an *Escherichia coli* strain is designed which includes deleting the *rfaD* and *cdh* genes from CGSC #12119. Several lipid extraction methods have been tested including weak anion exchange solid phase extraction (WAX SPE), modified Folch and sodium acetate extraction. WAX SPE is decided to be the most suitable method for this research. Furthermore, mass spectrometry measurements were taken using MALDI and ESI-MS for the extracts and standards. The results of this study will hopefully increase the use of bacteria in cancer treatment which was first recognized two centuries ago.

Investigating tumour intrinsic PD-1/PD-L1 signalling in canine osteosarcoma cell lines as a spontaneous model of human disease

Authors

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Abstract

Osteosarcoma (OS) is a fatal disease both in dogs and humans. One of the problems in development of novel treatment approaches is relatively low frequency of osteosarcoma in humans. In fact, no major changes in osteosarcoma therapy have been applied in clinics over last 30 years. Although rarely diagnosed in humans, osteosarcoma in 27 times more prevalent in dogs. Interestingly, the disease in both species shares many pathological and genetic similarities. Recently, much attention has been brought to immunotherapies as a potential breakthrough in cancer treatment. Indeed, PD-1/PD-L1 monoclonal antibodies showed great success rates in number of patients and types of cancers. Even though the implementation of immunotherapy is getting wider, there are still some diseases with no significant progress in therapeutic approach over decades, including osteosarcoma. It has been proposed that besides well characterized PD-1/PD-L1 effects on T-cells, PD-1/PD-L1 intrinsic signalling may play currently undefined role in cancer cells, stimulating their growth, proliferation and survival. The aim of our work is to investigate PD-1/PD-L1 intrinsic signalling in canine osteosarcoma cell lines as a potential model for human disease. Taking into consideration higher prevalence of the disease in dogs and many pathological and genetic similarities between the disease in both species, makes dogs a perfect model to study osteosarcoma and to potentially apply the results into human studies.

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