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Pompe (recent activity)

**Research ongoing:**
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Determination of PEGylated substances in plasma and FDP/FC
Tissue analysis

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Dear Colleagues, Partners, Scientists, Clinicians, Bioengineers and Friends,

Advances in fundamental, translational and clinical research as well as in environmental sciences and the availability of biomarkers are beginning to transform the healthcare landscape. Biomarker platforms construe the work that goes into bringing the most promising experimental therapies, diagnostic and monitoring technologies to the clinic after extensive testing in experimental models and being validated.

In this context, we at I.M. Sechenov First Moscow State Medical University and Moscow Engineering Physical Institute (MEPhI) jointly with the United Scientific Group (URG) hosting the Conference, look forward to welcoming you to the fantastic International Conference on Biomarker Research in Clinical Medicine, to be held in the City of Paris. The meeting planned would bring in a new spin on conferences by presenting the latest scientific improvements in Biomarkers and its Translational and Clinical impacts. The conference will provide a forum for researchers, clinicians and drug designers to present cutting edge research and learn about the latest breakthroughs and technologies in biomarker-related areas.

The Conference will provide the ideal forum to stimulate ideas and establish collaborations as well as to initiate intense discussions. The Program will discuss how biomarkers can be used to improve drug discovery and development and to treat disease, and how it is helping to centralize and organize medical knowledge. The Conference will also include a Satellite Symposium on Educational Aspects and on how to apply biomarkers in the daily clinical practice, with insights from entrepreneurs who have made the transition from academic-based translational research to the clinical and industrial sector.
At the gathering, we hope to build on the conventional approach to biomarker-aided strategy by fostering a method in which practitioners undertake a comprehensive evaluation of Biomarker Impact while accounting for information such as genomic, proteomic, metabolomics and related biomarker platforms through the use of the newest analytical technologies. Our goal is to open a forum to facilitate the exchange of knowledge and experience and to invigorate the field with young clinicians and scientists. The Conference would secure the attracted participation from many of established leaders as well to open a green light for concentrating focus on generating solutions to the field’s challenges. The latter would propose ways to encourage investment in innovation and stimulate the adoption of personalized and translational medicine in the daily practice.

In keeping with the theme, we have collaborated with the United Scientific Group (URG) and National Alliance on Translational Medicine (NATM) partners in Russia and our colleagues from different parts of the Globe to hold an additional program off-site and plans and programs to be added to the Program. We are delighted to assist the Organizers in order to foster and promote excellence in biomarker-related discussions as well as to secure leadership in promoting Research, Clinical, Industrial and Educational development of this field. And the Conference will bring together scientists and entrepreneurs who are interested in biomarker-related future and research to be implemented into healthcare tools and biopharma services.

We look forward to seeing you at the Meeting, and to providing you with an unforgettable scientific and social experience in Paris which whilst being the global capital for elegant sophistication and thus the emotional and cultural capital of the world is also a place where many different cultures, brilliant academic science and clinical experience, artistic excellence and sophisticated tastes meet in interesting and fascinating ways.

Personally we are convinced that the international partnership and collaboration would play a crucial promoting role for the jointly set projects from any points of view. We do hope that your interaction with your colleagues from many different countries will stimulate a creative ex-change of ideas and will be personally rewarding.
Key Concepts

- Clinical & Translational Biomarkers
- Cancer Biomarkers
- Biomarker Discovery & Validation
- Biomarkers in Clinical Research
- Neuro & Immuno Biomarkers
- Genomic Biomarkers
- Biomarkers Imaging & Dynamics
- Computational Biomarkers
- Biomarkers in Personalized Medicine
- Cardiac Biomarkers
- Biomarkers in Nutrition
- Biomarkers in Drug Discovery & Development
- Emerging Trends in Biomarker R&D
February 19

Monday
The Search for Infectious Agents in Human Cancers: Where and Why?

Harald zur Hausen, Ethel-Michele de Villiers
German Cancer Research Center, Deutsches Krebsforschungszentrum, Heidelberg, Germany

Abstract

Although globally ~20% of human cancers have been linked to predominantly viral infections, epidemiological patterns point to a possible role for infections in the etiology of additional cancers. This accounts in particular for colon, breast, and prostate cancers. We specifically suspected infectious nutritional factors, originating from the consumption of Eurasian cattle meat and dairy products. We isolated about 50 novel single-stranded circular DNA genomes (1200-3000 nucleotides), many of them closely related to bacterial plasmids.

Upon transfection into specific human cells, those tested were transcriptionally active and produced specific proteins. We are presently investigating their possible role by analyzing presence of their DNA and proteins in the cancers mentioned before, in addition to immune reactivity to a major protein (rep) of these isolates.

Biography

Harald zur Hausen studied medicine from 1955-60. After two years of medical internship he received the license to practice medicine. Subsequently, he went into research and worked in Düsseldorf, Philadelphia, and Würzburg for about 3½ years, respectively. In 1972 he was appointed as founding Director of the Institute of Virology at the University of Erlangen and moved 5 years later to a similar position at the University of Freiburg from 1983-2003. He was Director of the German Cancer Research Center in Heidelberg. In 2008, he has been awarded with the Nobel Price for Physiology or Medicine for the discovery of specific human papillomavirus types and their role in cervical cancer. At present he heads a Division at the Heidelberg Cancer Research Center.
The Proton Preparation NSC-631570 (Ukrain) and its Selective Effect

Dr. Techn. Wassil Nowicky, Dr. Med. Askold Nowicky
“Nowicky Pharma”/Ukrainian Anti-Cancer Institute, Vienna, Austria

Abstract

First indications on the selective effect of NSC-631570 on the cancer cells were provided in an early study when different oxygen consumption by normal liver cells and Ehrlich's tumor ascitic cells after the incubation with NSC-631570 was revealed.

In the tests on the Jurkat lymphoma model, NSC-631570 has been proven to be a strong apoptosis inductor. Profound research showed NSC-631570 brought about the depolarization of mitochondrial membranes and consequently the activation of caspases.

NSC-631570 induced apoptosis in a panel of cancer cell lines (cervical cancer HeLa, HeKB, HeKS32, HeBcl3, HeNFR and HeIKK, human colon cancer SW480, human renal carcinoma HEK293, human osteosarcoma MG-63) by activating the caspases of the intrinsic cell death pathway. Interestingly, non-transformed fibroblasts (hTERT) cell line was insensitive to the drug.

In the tests on human cervix carcinoma cells HeLa, squamous carcinoma cells WHCO5, normal kidney cell line Graham 293, and transformed kidney cell line Vero from African green monkey, NSC-631570 inhibited the tubulin polymerization and caused a metaphase block in cancer cells which is characterized by abnormal chromosomal distribution, and results in the formation of micronuclei and in apoptosis.

The effects of NSC-631570 on cell survival, alteration of the cell cycle and induction of apoptosis without and in combination with ionizing radiation (IR) were investigated on the exponentially growing human tumor cells MDA-MB-231 (breast), PA-TU-8902 (pancreas), CCL-221 (colon), U-138MG (glioblastoma), and human skin and lung fibroblasts HSF1, HSF2 and CCD32-LU.

Without IR, NSC-631570 exerted a time- and dose-dependent cytotoxic effect, more pronounced against the cancer cells. The combination of NSC-631570 plus IR enhanced toxicity in CCL-221 and U-138MG cells with their accumulation in the G2/M phase, but not in MDA-MB-231 and PA-TU-8902 cells. A radio protective effect was found in normal human fibroblasts.

NSC-631570 caused the accumulation of prostate cancer cells as well as epidermoid carcinoma cells in the G2/M phase, however, not of normal cells. The cytotoxic effects of NSC-631570 were evaluated in primary pancreatic cancer cell lines (PPTCC), fibroblasts derived from pancreatic ductal adenocarcinoma specimens (F-PDAC), and an immortalized epithelial ductal pancreatic cell line HPNE. Cytotoxic effects of NSC-631570 in PPTCCs were significantly higher than those observed in F-PDAC and HPNE cells. Furthermore, it was revealed that PPTCCs cells consumed more drug than F-PDAC and HPNE cells. This selective effect of NSC-631570 in PPTCCs may be related to a different transport system or higher metabolism of the drug in PDAC.

Altogether, in comparative studies NSC-631570 has been tested on 18 cancer and 12 benign cell lines at identical conditions so far. In all these experiments the selective effect of NSC-631570 against cancer cells was confirmed. This selective effect of NSC-631570 against cancer cells explains its good tolerability in clinical use.

Biography

Wassil Nowicky (Dipl. Ing., Dr. techn., DDDr.h.c.) is the Director of Nowicky Pharma and President of the Ukrainian Anti-Cancer Institute (Vienna, Austria). He finished his study at the Radiotechnical Faculty of the Technical University of Lviv (Ukraine) at the end of 1955 with graduation to “Diplomingenieur” in 1960 which title was nostrificated in Austria in 1975. Inventor of the anticancer preparation on basis of celandine alkaloids “NSC-631570”. He is the author of over 300 scientific articles dedicated to cancer research. He is a real member of the New York Academy of Sciences, member of the European Union for applied immunology and of the American Association for scientific progress, honorary doctor of the Janka Kupala University in Hrodno, doctor “honoris causa” of the Open international university on complex medicine in Colombo, honorary member of the Austrian Society of a name of Albert Schweizer. He has received the award for merits of National guild of pharamsists of America, the award of Austrian Society of sanitary, hygiene and public health services and others.
Personalized & Translational Medicine as a Tandem of the New Philosophy, Updated Mentality and Technological Platforms

Sergey Suchkov1-6, Abner Notkins7, Trevor Marshall8

1 Sechenov University, Russia
2 Moscow Engineering Physical Institute (MEPhI), Russia
3 A.I. Evdokimov Moscow State University of Medicine & Dentistry, Moscow, Russia
4 EPMA, Brussels, EU
5 PMC, Washington, DC, USA
6 ISPM, Tokyo, Japan
7 NIDCR, National Institutes of Health, Bethesda, MD, USA
8 Autoimmunity Research Foundation, Los Angeles, CA, USA

Abstract

Personalized and Precision Medicine (PPM) has been the grand challenge to forecast, to personalize, to predict and to prevent is rooted in a big and a new science generated by the achievements of Systems Biology and Translational Armamentarium whilst integrating OMICS platforms and Bioinformatics as well.

The development and application of systems strategies to biology and disease are transforming medical research and clinical practice in an unprecedented rate. Translational research is the science that aims at making scientific discoveries available for application in relation to life sciences, medicine, bio-design and bioengineering. Translational Medicine (TM) is thus an area of research and applications that aims to improve human health and longevity by determining the relevance to human disease of novel discoveries as applicable to PPM.

TM seeks to coordinate the use of new knowledge in clinical practice, biotech and biopharma and to incorporate clinical observations and questions into scientific hypotheses in the laboratory. Thus, it is a bidirectional concept, encompassing so-called bench-to-bedside factors, which aim to increase the efficiency by which new diagnostic, predictive, prognostic & therapeutic strategies developed through basic research are tested clinically, and bedside-to-bench factors, which provide feedback about the applications of new treatments and how they can be improved. TM facilitates the characterization of disease processes based on monitoring of biomarkers-related dynamics and the generation of novel hypotheses based on direct human observation.

PM as being as a model of healthcare services to be updated via the new philosophy and translational bridges, would unite patients and persons-at-risk, community health service centers, hospitals, remote clinics, and education centers to improve the quality and efficiency of healthcare.

So, the goals of PM and TM as a tandem in academia and bio-industry are complementary. Thus, a balanced approach that encourages partnership between those entities could establish a positive feedback loop in which benefits raised in academia would lead to the development of new products in bio-industry and then to be implemented in clinical practice.

To optimize translational research, policy could consider refining translational research models to better reflect scientists’ experiences, fostering greater collaboration to suit strategic alliances and buy in from all types of scientists.

Biography

Sergey Suchkov (PhD, MD) was born in the City of Astrakhan, Russia, in a family of dynasty medical doctors. In 1980 he graduated from Astrakhan State Medical University and was awarded with MD. In 1985 maintained his PhD at the I.M. Sechenov Moscow Medical Academy and Institute of Medical Enzymology, Moscow, Russia. In 2001, maintained his Doctor’s Degree at the National Institute of Immunology, Russia. From 1985 through 1987 worked as a Post Doc Research Associate, Institute of Medical Enzymology. From 1987 through 1989 was a Senior Researcher, Koltsov Institute of Developmental Biology, USSR Academy of Sciences. From 1989 through 1995 was being a Head of the Lab of Clinical Immunology, Helmholtz Eye Research Institute in Moscow. From 1995 through 2004 was being a Chairman of the Department for Clinical Immunology, Moscow Clinical Research Institute (MONIKI). In 1993-1996 he was an Executive
Irina Zavestovskaya
National Research Nuclear University MEPhI (Moscow Engineering Physical Institute), Russia
P.N. Lebedev Phisical Institute of Russian Academy of Science, Moscow, Russia

Abstract

The first Russia’s Alliance of Translational Medicine (ATM) was created in December 2016 a Consortium agreement signed by the universities participating in the Russian academic excellence Program “5-100”: N. I. Lobachevsky Nizhny Novgorod state University, National Research Nuclear University “MEPhI”, National Research Tomsk State University, and the “Center for Strategic Research North-West” Foundation.

The goal of Alliance creation is to bring the Russian science into the global scientific and technological leadership in the breakthrough fronts of Biomedicine. Our strategy is to integrate biomedical technologies in the educational process, which corresponds to the practical solution to global problems, such as diagnostics and therapy of socially significant diseases. Joint technology programs with industrial partners will be running from the fields of medicine, industries and the research results will be commercialized.

The ATM activity object is the translational, personalized and predictive medicine, which the participants defined as high-tech efficient performance and services to support development of therapeutics, support clinical decision based on specialized digital platforms, developing advanced and unique technologies of early and extra-early diagnosis and treatment.

Area of scientific specialization of the Alliance covers the key challenges of medicine – oncology, cardiology, neurodegenerative diseases. The group of participants and their partners will dramatically accelerate and reduce the cost of translation of scientific ideas into clinical and industrial practices that produce based on scientific evidence new personal medicines, to develop new methods of preventive diagnostics. To do this, the Alliance members to integrate a database of research data and open each other access to a unique infrastructure.

The strategic objective of the Alliance is the training of medical professionals: doctors, researchers, trained to work with high-tech equipment. We have developed the new network educational programs in the space of three universities.

The scientific potential of universities in the declared specialization – more than 20 internationally recognized research groups working in such emerging fields as nanotechnology, neuroscience, biosensing, imaging, computer modelling. The main feature of the Alliance is to focus on the industry to achieve outstanding results in translational medicine, we must concentrate the resources, money and time.

Trust and co-operation in the scientific world will dominate.

The Alliance of translational medicine is open to cooperation, to associate of the different types of participants: universities, hospitals, research centers and industrial companies.

Biography

Irina Zavestovskaya, PhD was born in the city of Krasnoyarsk (Russia). In 1977, Irina graduated from Basov High Physicists School of MEPhI with honors. In 1980 she received her PhD in the field of theoretical research of degradation processes of semiconductor lasers. In 2013 she was awarded her Doctor’s Degree. The theme of Doctor’s dissertation: “Theoretical modeling of processes of surface treatment of materials by laser pulse radiation".
At present Irina Zavestovskaya is Executive Director of Institute Of Engineering Physics For Biomedicine of MEPhI, professor in the Department of Semiconductor Quantum Electronics and Biophotonics, Leading Researcher of the Lebedev Physical Institute of RAS. She delivers lectures to the students of the MEPhI on “Laser-matter interaction”, “Basics of synchrotron radiation”. She was repeatedly invited to lecture at universities in Germany, USA, France, Japan, Britain and Italy.

In 2005 Irina Zavestovskaya was awarded the Presidential Prize in the field of education. Member of the Board of Moscow Physical Society. She is the member of the editorial board of the journal “Physics in Higher Education”. Member of the program and organizing committees of many international conferences, Chairman of the Organizing Committees of the International Symposium on “Physics, Engineering and Technologies for Bio-Medicine”.

Dr. Zavestovskaya is an author of more than 150 articles, 2 textbooks, 1 monograph. Her scientific interests include laser-matter interaction, laser nanostrucrurization and fragmentation, bionanophotonics, nanomedicine.

Clinical Trials on the Way to Secure the Translational and Clinical Efficacy

Vladimir Lazar
WIN Consortium, France

Abstract

Position of the problem: To date only 10% of NSCLC patients are detected in stage I, at a stage when the disease is curable by surgery alone (90% of patients are alive at 5 years). Most of the patients, over 60%, are unfortunately detected in late metastatic stage IV and remain incurable, with a median survival of 12 months, and less than 5% of patients alive at 5 years. The lecture will present WIN Consortium efforts to significantly improve the clinical outcome of lung cancer patients: A major component is international collaboration to improve molecular profiling and data management and design of innovative trials, driven by new biomarker tools and strategies.

Combination of targeted therapies: The key feature of future therapies in metastatic NSCLC, is switching from current monotherapies to combination of targeted therapies, as only way to fight against secondary resistance that occurs in all patients. This switch will need the identification and validation of new tools to match individually the patient’s tumor biology profile to the most appropriate combination of therapies.

The main limitations of current biomarkers mainly companion diagnostics (Cdx) are:

a) multiplicity of drugs that require a large number of tests (and different technologies) to be performed on limited amount of biological samples.

b) inability to prioritize the best therapeutic options for each individual patient.

The lecture will present the Simplified Interventional Mapping System (SIMS), a Systems Biology based novel generation of multiplex combinatorial Cdx which provides biological support to prioritize and to select the classes of drugs that are predicted to be most effective at the individual patient level. The example used is metastatic Non Small Cell Lung Carcinoma (NSCLC), but the method applies to any solid tumor. SIMS is based on the use of dual biopsies in order to compare tumor with its histologically matched normal tissue from the same patients. SIMS algorithm integrates data of DNA sequencing, CNV, and the differential expression of mRNA and miRNA between tumor and matched normal tissue from 121 NSCLC patients. SIMS converts thousands of genomic and transcriptomic measurements into a simple and actionable result (a 1 to 10 score) that may be usable by physicians to select the optimal drug or drugs’ combinations therapy. One of the most interesting hypothesis being the tri-therapy approaches, following the historical success in AIDS. Comparing tumor and normal tissue biopsies has proven feasible in the ongoing WINTHER trial (NCT01856296) SIMS outlines novel therapeutic possibilities by focusing on pertinent classes of targeted therapeutics to be used in combinations, and is a novel generation of combinatorial multiplex companion test enabling to match patients to drugs.

Biography

Vladimir Lazar obtained his MD (1989) at The University of Timisoara (Romania), First in Class and Certificate of Merit “Magna cum Laudae”. He became a specialist in Clinical Biology (DIS, 1977, University René Descartes in Paris) and obtained his PhD in molecular biology (1997) at the University René Descartes in Paris, with the highest degree and the Prize of University. Dr. Vladimir Lazar is specialized in clinical biology, molecular biology, molecular pathology and
has a broad training, education and postgraduate degrees in biotechnology (first in class) and project management. He is recognized specialist in translating research to clinical applications. He was the founder and Head of Gustave Roussy’s Genomic Center and Integrated Biology Platform (2002–2015) running the Agilent European reference and training center. He is the founder and current Chief Operating officer of the WIN Consortium (www.winconsortium.org). In these positions he has built a strong expertise in project design, technology evaluation and implementation, use of genomics and biomarkers in oncology, companion test development, and biology driven clinical trials. He has also developed leadership and entrepreneurial skills through the creation of his initiatives. He is author of 6 patents and author-co-author of more than 100 publications.

How Biomarker Validation Platforms Can Accelerate “Bench to Bedside” Efficiency

Catherine Larue
Integrated BioBank of Luxembourg, Luxembourg

Abstract

After a huge hype for innovative biomarkers when clinically useful biomarkers such as troponin, procalcitonin, PSA etc appeared, after considerable amounts of investments in H2020 “omics” calls or IMI consortia such as “safety” biomarkers, it is time for disappointment on both sides of academic research and health industry. Every year, thousands of biomarkers are published through an abundant literature, but less than 5% of those are used clinically mainly because they are not properly validated.

This issue has led to particularly in Europe, a delay in using new biomarkers e.g. in translational medicine, to a misunderstanding by academic researchers of the needs for investigating the biomarker robustness further and deeper, to a certain degree of risk adversity by Pharma or IVD industry and globally to a decrease of the impact of our research & innovation.

By conducting pre-analytical and analytical validations, clinical verification to verify the performance of a biomarker in well-qualified clinical sample sets, IBBL biomarker validation platform can provide the academic researcher with a full report and scientific arguments, and therefore better promote his discovery to industry.

Building bridges between academic research and health industry, such as biomarker validation platforms, can dramatically help European research to be more efficient, more productive, particularly in light of translational medicine where bench to bedside efficiency must be quickly achieved.

Biography

Catherine Larue, PhD began her career at Sanofi, Montpellier (France) in the cardiovascular R&D department soon after pursuing PhD in Immunology and at Sanofi she participated in the discovery of innovative biomarkers such as troponin I and natriuretic peptides.

She then joined Sanofi Diagnostics Pasteur, at Minneapolis MN (USA) for 3 years where she was responsible for Assay Development in the immunodiagnostic area. She completed an Executive MBA in 2003 and had worked for 7 years as a Director of Business Unit at Bio-Rad. After installing the Biomarkers department in Genfit (Lille, France), she took over the CEO position of the Institute IBBL (Integrated Biobank of Luxembourg). She is an author of 87 publications and filed 13 patents.

She served in standardisation committees on Cardiovascular Biomarkers at AACC and IFCC for 15 years. She also created and chaired the “Biomarkers Group” in the Competitiveness Bio-cluster (Medicen, Paris). She is currently serving as an expert for the European Commission (H2020 and IMI programmes) and for the first Luxembourg Plan Cancer.
Biomarkers in Basics, Clinical and Translational Research to Get the Translational Pipeline Succeeded

Anastasiia Voronkova
Sechenov University, Moscow, Russia

Abstract

The use of biomarkers in basic and clinical research as well as in translational research has become so commonplace that their presence as primary endpoints in clinical trials is now accepted almost without question. In basic research they play an important role of milestones during the verification of theory of disease pathway. In clinical practice biomarkers are used to evaluate drug efficiency and for patients' condition monitoring. And eventually translational research is hardly thinkable without a deep system of multilevel biomarkers. In this speech current progress and issues of biomarker armamentarium will be discussed.

Biography

Anastasiia S. Voronkova graduated faculty of Biology of Lomonosov Moscow State University in 2013. Thereafter she worked in the field of basic and clinical genomics and transcriptomics. Scientific interests: molecular genetics, molecular physiology, physiology of energy deficiency, hereditary disorders, mitochondrial disorders, gene networks, gene expression dynamics.

Nanobiotechnologies and Nanobiomicroscopy as a New Research, Clinical and Educational Tool to Biomedicine

Vladimir Oleinikov
National Research Nuclear University MEPhI, Russia

Abstract

The rapid development of nanotechnology, further miniaturization and possibility to place an increasing number of functional elements in all the smaller volumes dictate the drifting of classical medicine to nanomedicine, namely, to the creation of increasingly sophisticated nanodevices that can effectively label, identify, and denote the boundaries of damaged tissues from healthy ones. Now, we have an opportunity to create micro- and nanosensors, to determine the parameters in local areas of biological cells and tissues. Multicolor systems, so-called fluorescently encoded colloidal microchips, are developed and created, allowing to carry out diagnostics, simultaneously fixing a large complex of characteristic features and markers. Multifunctional micro- and nanoparticles are increasingly being used as carriers for targeting drugs to their targets, providing programmable or controlled release of drug agents.

A limitation that prevents the comprehensive use of modern micro- and nano-tools is the backlog in the development of macro instruments that do not always and not completely implement the possibilities of nano-tools from the point of view of extracting, analyzing and presentation of extensive data.

This report considers various types of nano- and micro-instruments for diagnostics and therapy (mainly based on conjugates of biological molecules with semiconductor fluorescent nanocrystals and plasmonic nanoparticles from noble metals) as well as ways to develop macroinstruments, mainly associated with the transition from correlation microscopic methods to micro spectroscopic and to use all the power of scanning probe microscopy techniques.

A new dimensional vertical from nano to macro has already yielded new nano-, micro- and macro-tools. There is also a strong need in a new level of expertise in research, technical approaches and instruments. We are also going to consider issues related to education and training of high level specialists to work with the newest nano and macro-tools in medicine.

Biography

Vladimir A. Oleinikov was born in Yelets, Russia. In 1973 he graduated from the Moscow Physical Engineering Institute (MEPhI) and was qualified as an engineer-physicist. In 1985 maintained his thesis at the MEPhI with a specialty in Molecular Physics. In 2003 maintained his Professor degree, Dr. of Sciences in Physics and Mathematics, in the St. Petersburg Polytechnic University, in biophysics. From 1973 through 1985 he worked as a researcher at MEPhI in the field of mass spectrometry. From 1987 through 1995 he is senior researcher of the Shubnikov Institute of Crystallography of
the Russian Academy of Sciences. The field of his interests was the nanotechnology, based on the use of track membranes (nuclear filters) and structures prepared by the replication of the track membranes surfaces. Since 1995 - an employee of the Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences (IBCh RAS). Since 2003 headed the group of mass spectrometry of the Institute, since 2008 - the scientific secretary of the Institute, since 2011 head of the Laboratory of Molecular Biophysics.

At present he is the head of the Department of Biomaterials and Bionanotechnology, IBCh RAS, Scientific Secretary of IBCh RAS, Professor of the Department of Translational Medicine of the Institute of Engineering Physics for Biomedicine MEPhI. Dr. Oleinikov is the author of more than 200 publications, including 12 patents and 3 monographs.

Neurotoxic Peptides and Proteins: Biomarkers for Screening and Identifying Ion Channel Subtypes in Healthy/Diseased Conditions and for Drug Design

Victor Tsetlin
Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, RAS and MEPhI, Moscow, Russia

Abstract

Cys-loop receptors comprising nicotinic acetylcholine receptors (nAChRs), glycine-, ionotropic GABA and serotonin receptors exist as several subtypes differing in localization and role in normal functioning/ pathologies. Contrary to antibodies, their identification is more efficient with neurotoxic peptides and proteins from animal venoms, highly selectivity for a particular receptor subtype. Naturally-occurring neurotoxins are used in electrophysiology, while their radioactive/ fluorescent derivatives help to measure the receptor subtypes at normal state and diseases. Such measurements are important, for example, for αβ2 nAChRs involved in nicotine addiction, for α7 neuronal nAChRs implicated in β-amyloid peptide binding and for “non-neuronal” α7 nAChR regulating anti-inflammatory response and lung cancer growth. X-ray analysis of the neurotoxin complexes with the receptor models shed light on the binding sites and on possible functional effects of certain disease-associated mutations. Neurotoxins give hints for new drugs or become drugs themselves: like a strong analgesic ω-conotoxin (Prialt) blocking one Ca2+ channel subtype. Several α-conotoxins blocking α9/α10 nAChRs are considered as possible analgesics emphasizing that fundamental research of ligand-receptor interactions is important for solving practical medical tasks. Our recent work on (1)nAChRs and other Cys-loop receptors will be illustrated with novel high-affinity α-conotoxins, (2)snake venom α-neurotoxins (3)human endogenous proteins that have the same three-finger folding as α-neurotoxins and regulate the nAChR activities.

Biography

Victor Tsetlin got both his PhD degree in chemistry (1973) and D. Sci. degree (1987) at the Shemyakin-Ovchinnikov Institute. He was Head of the Laboratory of Neuropeptide Receptors (1987-2009) and now a Head of the Department for Molecular Basis of Neurosignaling. He was elected a Professor (1996) and corresponding member of the Russian Academy of Sciences (2006) with the awards: Russian State Prize in Science and Technology (1985), the Humboldt Prize (1992). He worked as an invited scientist at the Uppsala University, Sweden (1979), Imperial College, London (1983-1984), Institute of Protein Research, Osaka (1992-1993), Free University of Berlin (1993-1994). He published about 200 papers, including those in PNAS, Neuron, Nature Str. Mol. Biol, J.Biol. Chem., J. Neurochemistry, Sci. Rep. and other. He was a member of the Advisory Board of the FEBS J., from 2000-2011, and then from 2013 till present he is a member of the Advisory Board of the Biochem. J. Citation Index 3950, Hirsh index 32.
**In vivo** Degradation Kinetics of 3D Scaffolds Traced with a Fluorescence Marker

Peter Timashev  
*Sechenov University, Moscow, Russia*

**Abstract**

*In vivo* scaffold degradation is one of the main points in tissue engineering. There are many studies on the *in vitro* estimation of scaffold degradation kinetics (Zhu et al. 2013; Costa-Pinto et al. 2014; Oliveira et al. 2014). However, *in vivo* assessment of this parameter remains a problem; and a new *in vivo* non-invasive visualization method is needed to reduce the number of surgical procedures. There are several approaches to solving this problem: biopolymer crosslinking with fluorescent dyes or nanoparticles, fluorophore encapsulation into material, development of auto fluorescent polymers. Auto fluorescent biodegradable materials are the most attractive because this approach requires no use of additional fluorescent agents, which cannot be homogeneously distributed within scaffolds. This leads to incorrect degradation kinetics values. Moreover, fluorescent agents are toxic and increase the burden on normally functioning organs and tissues (liver, kidney, spleen, etc.). We showed that two-photon polymerization (2PP) enables the fabrication of auto fluorescent biodegradable scaffolds, which can be observed in real-time via *in vivo* non-invasive methods. We used successfully this approach in our study and revealed that polylactide 2PP scaffolds possessed auto fluorescence and were implanted after cell seeding into C57/B16 mice. The *in vivo* degradation rates were assessed due to changes in fluorescence intensity in real time.

**Biography**

Peter Timashev is the Deputy Director of Institute for Regenerative Medicine, Sechenov University. His work covers the development of biodegradable and biocompatible materials for laser additive technologies. His studies, which discuss the 2PP formation of 3D scaffolds inducing the osteogenic differentiation of stem cells, their mechanical and surface features, and *in vivo* fluorescent imaging of their degradation rates, underlie the development of laser-induced structure formation for tissue engineering. Moreover, his research team optimized approaches to 2PP structuring polysaccharide and protein hydrogel systems for soft tissue restoration. For these 3D matrices, Peter Timashev et al. developed non-destructive procedures of their surface and mechanical modification that increased cell compatibility.

Markers of the Cell Differentiation as a Tool to Assess the Feasibility of Implantable Tissue-Engineered Constructs

Anastasia Shpichka*, Anastasia Gorkun, Elena Istranova, Denis Butnaru, Peter Timashev  
*Sechenov University, Moscow, Russia*

**Abstract**

Nowadays, remarkable achievements in tissue engineering bring closer the day when we will be able to create biomimetic tissues and organs for each patient. To fabricate a tissue-engineered construct, which can be implanted, most scientists use stem or progenitor cells that are seemed to differentiate towards a particular lineage and mature. Therefore, it is crucial to understand the importance of cell differentiation markers. They can be applied to assess the feasibility of such constructs to prevent undesirable side effects caused by uncontrolled cell differentiation. This approach will permit us to develop criteria system for future application of tissue engineering in clinical practice.

**Biography**

Anastasia Shpichka, PhD is a senior researcher at the Institute for Regenerative Medicine, Sechenov Moscow State Medical University. She received her PhD in Biotechnology at the Lomonosov Moscow State University in 2013 and graduated with honors from the Penza State University majoring in Pharmacy. Her study mainly focuses on the 3D complex tissue fabrication and microfluidic lab-on-a-chip systems.
Tissue-Engineered Construct for Urethral Reconstructive Surgery

Anastasia Shpichka*, Anastasia Gorkun, Elena Istranova, Denis Butnaru, Peter Timashev

Sechenov University, Moscow, Russia

Abstract

Nowadays, the common treatment of urethral stricture is substitute urethral reconstruction using a buccal mucosa graft or an acellular matrix. However, most studies showed that their use can cause the development of fibrosis, recurrent stricture, necrosis, and graft rejection (Atala et al., 2017). Therefore, this study aimed to fabricate a tissue-engineered urethral wall construct and test it in preclinical and clinical trials. We developed a system from mechanically strong hybrid matrix from collagen and glycolide and L-lactide fibers and spheroids from buccal epithelial cells. Epithelial cell in spheroids could save their phenotype and form epithelial lining on a matrix surface. The developed construct successfully passed preclinical trials (rabbits); and we have initiated its clinical trials (NCT03205670). Thus, this tissue-engineered construct is promising; and after ending trials, its use can be easily translated into clinical practice.

Biography

Anastasia Shpichka is a senior researcher at the Institute for Regenerative Medicine, Sechenov Moscow State Medical University. She received her Ph.D. in Biotechnology at the Lomonosov Moscow State University in 2013 and graduated with honors from the Penza State University majoring in Pharmacy. Her study mainly focuses on the 3D complex tissue fabrication and microfluidic lab-on-a-chip systems.

Novel Advanced Laser-Synthesized Nanomaterials for Cancer Theranostics

Andrei V. Kabashin

Aix Marseille University, CNRS, LP3 UMR 7341, Campus de Luminy, France
National Research Nuclear University MEPhI, Institute of Engineering Physics for Biomedicine (PhysBio), Bio-Nanophotonic Lab., Moscow, Russia

Abstract

Some inorganic nanomaterials demonstrate extremely promising characteristics for biological imaging and therapy, but biomedical prospects of such nanomaterials are complicated by toxicity issues arising as a result of relatively dirty pathways for their fabrication. As an example, Si nanoparticles are biocompatible and even biodegradable in pure state, but conventional chemical and electrochemical routes for their synthesis inevitably lead to a surface contamination by toxic products. As a solution of the toxicity problem, we recently introduced a series of physical nanofabrication methods based on ultrashort laser ablation in aqueous biocompatible solutions. This talk will present the laser synthesis method and overview results of first tests on interaction of some promising laser-synthesized nanomaterials (Si, Au) with biological systems. In particular, our tests in vitro demonstrate excellent safety of nanoparticles, while protein covering after the incubation of nanoparticles in real biological environment suggests potential successful transport of nanoparticles in vivo. In vivo tests in small animal model using systemic administration of Si nanoparticles also do not reveal any sign of toxicity effects, which is confirmed by behaviour of mice, stability of blood content and other biochemical parameters, as well as by histology analyses of all organs and biodistribution of nanoparticles in tissues. Furthermore, the nanoparticles rapidly biodegrade in the organism and are completely cleared 2-3 days after their injection. The talk will also describe optical, photochemical and photo-thermal characteristics of laser-synthesised nanomaterials in the view of their potential cancer theranostic (therapy + diagnostics) applications. As an example, we recently introduced a novel method for mild cancer therapy, in which Si nanoparticles are used as sensitizers of radio-frequency induced hyperthermia. The efficiency of this method is confirmed by successful tests in vitro and in vivo.

Biography

Andrei V. Kabashin is one of world leading experts in plasmonics/metamaterial-based biosensing and laser-ablative nanofabrication. He obtained his MS Degree in 1990 from Moscow Institute of Physics and technology (MIPT) and his PhD degree in 1994 from A.M. Prokhorov General Physics Institute, Moscow, Russia. From 1999 to 2008 he worked as Research Professor of the University of Montreal, Canada. Since 2009 he holds a Research Director position of the French
National Center of Scientific Research (CNRS) in Aix-Marseille University, Marseille, France. He is also a Scientific Director of the Institute of Engineering Physics for Biomedicine (PhysBio) and the Head of International Laboratory “Bionanophotonics” of the National Nuclear Research University (MEPhI), Moscow, Russia. Finally, he holds an Adjunct Professorship in the Institute of Lasers, Photonics and Biophotonics in State University of New York at Buffalo (USA) and an Associate Professorship the University of Sherbrooke (Canada).

Nuclear Medicine Through the View of Personalized Healthcare

Andrei Postnov  
National Research Nuclear University MEPhI and N.N.Burdenko Institute of Neurosurgery, Moscow, Russia

Abstract

Modern clinical practice relies to a big extent upon general technologies with limited information about the patient. Formal diagnosis initiate a treatment pipeline which considers patient as an average person who receives standard treatment. However, in case of socially significant diseases (cardiovascular disease, Alzheimer disease, cancer, schizophrenia etc.) these pipelines frequently fail and do not guarantee cure or even survival.

Taking clinical practice in oncology as an example we see that sometimes modern treatment techniques can be successful. But the core problem persists: the patient condition and the disease current state is not known well enough. Aggressive treatment with chemotherapy, radiotherapy, ions or gamma rays exposure are given with no good enough predication on the outcome. The situation is complicated by the fact that all these treatments have severe side effects and can't be repeated. Doctors take vital decisions on the cure path in the condition of information shortage.

Nuclear medicine and especially its diagnostic branch (PET and SPECT) offers huge and currently underestimated surplus to the disease characterization. PET as the only instrument for functional imaging provides volumetric and quantitative information on metabolic activity of the ligand injected. Nuclear medicine owns capacity to label any endogenous compound with positron emitting isotope as well as creating artificial compounds capable to bind to almost any target with high affinity and selectivity.

At the same time the follow-up of the tumor metabolic activity during treatment allows collecting data to better understanding of the fundamentals of the tumor progression. Big data of metabolic history during tumor evolution combined with genetic information, biopsy analysis, molecular imaging etc. opens prospective for truly individual approach based on retrospective analysis of similar cases supported by machine learning.

As an illustration the clinical importance of the modern PET tracers (18-F-FLT, 18-F-FMISO, 11-C-Choline, 11-C-MET, 18-F-FET, newly designed tracers in trials) and combined multimodal imaging will be discussed on how to create new standard in brain tumors description to optimize the most aggressive treatment for each particular patient. The examples of surgery planning, irradiation planning, biopsy site definition, tumor staging, chemotherapy response based on metabolic imaging will be demonstrated. Prospective of introduction of dynamic PET imaging and following pharmacokinetic analysis to the benefit of the patient will be considered.

How to Develop a Novel Type of Strategic Alliances to Move Ahead: Business Ecosystems Grown, Developed and Powered by FiZ

Christian Garbe  
Frankfurt Innovation Center Biotechnology GmbH, Germany

Abstract

In the age of digitalization, innovation is increasingly taking place across different sectors. The key components of this precision medicine are the collection of a large number of samples in hospitals, transfer of the biological material into data with the help of sequencing, availability of high-performance information and communication technologies (ICT), access to databases for analysis and result representation, and follow-up of the treatment in hospitals using blood-based biopsy companion diagnostics tests.
Over the past few years, innovation research has brought to light that the added value of innovation emerges less from purely technological development than by a market-oriented connection of companies and technologies. The use of the mp3 technology at Apple is one example of this. This example also impressively shows how new business models developed in digitization and caused a massive change in the market for consumer electronics. Similar profound changes are expected for the health sector as well.

For one, FiZ has a network of companies and researchers in the field of precision medicine and, for the other, the necessary IT infrastructure for adding future value via digitalization business models is available at the Frankfurt site. FiZ developed the project German Genethics (GG) on the following basis:

German Genethics (GG) supports doctors who (want to) work with precision medicine to define individual therapies. The special aspect here is: GG has a worldwide unique database based on complex algorithms.

The database connects information from renowned specialist magazines and highly specialized molecular biology databases that contain research results from clinical studies with knowledge from recognized treatments. This big-data solution can categorize the characteristics of each individual DNA sample and match it to existing knowledge. In this way, “big data” becomes “intelligent data.”

GG is a joint FiZ project on a global scale. The network initiated and coordinated by FiZ consists of highly specialized companies, some of which are headquartered at the FiZ campus in Frankfurt am Main.

My passion is the interaction and the network of the companies at FiZ and the collaborative approach of the international research institutes. This will make the term “New.German Engineering” a new quality concept in the strong growth markets, which, while making use of the past, will experience expansion in the age of digitalization. With GG, the foundation is laid for establishing a system, which can then be extended into other disease areas, e.g., diabetes, autoimmune diseases, etc. This is how translational medicine gets its daily routine in the clinics and for the benefits of the patients.

Biography

Christian Garbe has been the Managing Director of FiZ Frankfurter Innovationszentrum Biotechnologie GmbH since its founding in 2002. He completed his studies in agricultural sciences at Georg-August University in Göttingen and earned his doctorate in 1996 with emphasis in economics and social sciences. Subsequently, he began his professional career at Novartis in Basel, where he assessed potentials of biotechnology for product developments. After transitioning to DZ BANK AG in Frankfurt, he analyzed pharmaceutical and biotechnology companies there and successfully managed a biotech fund.

The focus of his work is in the development of international business models and innovative, data-driven technologies. In doing so, he consistently implements the megatrend of digitalization and the topic of industry 4.0, in which processes are digitized in a platform-based manner and used in practical applications.

How to Develop a Medical School of the Newest Generation: From Canonical Integrity Through a Bridge of the Challenge to the Multi-Integrative Approach

Sergey Suchkov1-6, Noel Rose7, Mariya Studneva1,4

1Sechenov University, Moscow, Russia
2Moscow Engineering Physical Institute (MEPhI), Russia
3A.I.Evodikimov Moscow State University of Medicine & Dentistry, Moscow, Russia
4EPMA, Brussels, EU
5PMC, Washington, DC, USA
6ISPM, Tokyo, Japan
7Johns Hopkins University, Baltimore, MD, USA
8Harvard Medical School, Boston, MA, USA

Abstract

Rapid market penetration of new medicines and technologies demands the implementation of reforms not only in biopharma, but also in medical education. Therefore, the problem of the updated education of specialists in bioengineering, drug design and affiliated fields is becoming particularly urgent, and it requires significant revision of training programs and curricula. Modernization and integration of widely accepted standards require consolidation of both the natural and medical
sciences that may become the conceptual basis for the biopharma education.

The main goal of this training is not simply to achieve advanced training and expansion of skills, but to provide development of novel multifaceted approaches to build academic schools for future generations. So, it becomes obviously that a higher, secondary and primary education as a TRIO should be integrated into the circuit! Based on current trends and own experience, we have made the first steps towards reshuffling the canonical educational tandem “School-University” and restructuring of Specialized Groups (with targeted disciplines) to get the mentees to be involved into having the existing healthcare system advanced and stepped forward. Moreover, non-canonical approach has been used to create a team of young researchers and biopharma students which has been recognized as The International Research Team of Youngsters under the aegis of EPMA, Brussels, EU, and ISPM, Tokyo, Japan. This model of multistage training has included (1) the 1st level of education - familiarize of schoolchildren with biopharma and drug discovery; (2) the 2nd level of education - deep study of fundamental and applied aspects of drug design; and (3) the 3rd level of education - study of interdisciplinary aspects of bioengineering and drug design among post-graduate students. Thus, integration of the primary and secondary education provides: (1) development in the chosen direction; and (2) optimization of the jointly set activity of a student and the teacher within a PAIR or a TANDEM (mentor-mentee).

The need for teachers to be competent in all areas of professional practice has never been greater. So, a phrase “What Does It Mean to Be a Professional?” would attribute to a schoolchild, the child’s family, the mentoring teacher and the microenvironment, for sure! The above-mentioned has pre-determining value, because under the disintegration of the world community expressed the competition in quality of the scientific intellect dramatically increases. The same occurs in the areas of quality of all of three segments of the educational process, i.e., Pre-College (secondary school), University and Graduate.

**Biography**

Sergey Suchkov was born in the City of Astrakhan, Russia in a family of dynasty medical doctors. In 1980 he graduated from Astrakhan State Medical University and was awarded with MD. In 1985 he got his PhD from I.M. Sechenov Moscow Medical Academy and Institute of Medical Enzymology, Moscow, Russia. In 2001 he pursued his Doctor’s Degree from National Institute of Immunology, Russia. From 1985 to 1987 he worked as a Post-Doc Research Associate at the Institute of Medical Enzymology. From 1987 to 1989 he was a Senior Researcher at Koltzov Institute of Developmental Biology, USSR Academy of Sciences. From 1989 to 1995 he was the Head of the Lab of Clinical Immunology, Helmholtz Eye Research Institute in Moscow. From 1995 to 2004 he was the Chairman of the Department for Clinical Immunology, Moscow Clinical Research Institute (MONIKI). In 1993-1996 he was an Executive Secretary-in-Chief of the Editorial Board, Biomedical Science, an international journal published jointly by the USSR Academy of Sciences and the Royal Society of Chemistry, UK.

At present Prof. Sergey is the Director for Center for Personalized Medicine, and Professor, Department of Pathology, Sechenov University, Moscow, Russia; Chair of Department of Translational Medicine, National Research Nuclear University MEPhI; Secretary General of United Cultural Convention (UCC), Cambridge, UK. He is an author of more than 500 publications including 10 patents and more than 10 monographs, handbooks and textbooks published in Russia and USA. A fellow of 10 International Societies and Associations and a member of International Editorial Boards of 15 journals.
Different Whole Genome Sequencing Strategies for the Clinical Management of Patients with Oropharyngeal Squamous Cell Carcinoma

David I Smith
Mayo Clinic, USA

Abstract

Oropharyngeal squamous cell carcinoma (OPSCC) is a cancer of the base of the tongue and tonsils. This cancer was previously found in individuals with a smoking and drinking history but is increasingly being promoted by the presence of high risk types of human papillomavirus (HPV). In an attempt to determine the exact role that HPV plays in the development of this cancer we have been using mate-pair next generation sequencing (MP-Seq). Using MP-Seq we have found that HPV is only integrated into the human genome in 30% of HPV-positive OPSCCs, which is dramatically different than what is found in cervical cancer. MP-Seq not only can determine the physical status of HPV in a given sample, but can also ascertain genome-wide changes in any cancer. We describe how MP-Seq could be used in the clinical management of HPV-positive OPSCC patients. We have also explored another whole genome sequencing strategy that has been developed by the Beijing Genomics Institute. They can currently do whole genome sequencing for a total cost (and this includes analysis) of $600 and are developing methodologies to reduce this to $100. I will describe how these types of whole genome sequencing strategies could be used to direct therapies for these patients including facilitating the use of the liquid biopsy to monitor patients during their clinical treatment.

Biography

David I Smith received his PhD in Biochemistry from the University of Wisconsin in Madison. He is currently a Professor in the Department of Laboratory Medicine and Pathology at the Mayo Clinic. He is also the Chairman of the Technology Assessment Group for the Mayo Clinic Center for Individualized Medicine. His laboratory studies the role that the common fragile sites play in the development of a variety of different cancers. They are also studying the different ways that human papillomavirus is involved in the development of different cancers and how genome sequencing strategies could be used in the clinical management of cancers with an HPV etiology.

Aurora-A Kinase and Cancers: A Biomarker to Detect and a Target to Inhibit

Claude Prigent
Institute of Genetics and Development of Rennes, CNRS, France

Abstract

In 1995, the Aurora-A kinase was discovered in Drosophila. In 1997, it was found to be overexpressed in breast cancer cell lines. In 1998, the function of the kinase in the assembly of the mitotic spindle was identified as well as its oncogenic activity. These results immediately triggered an intensive search by pharmaceutical companies for kinase inhibitors to be used in the treatment of cancer.

Overexpression of the kinase is sufficient to transform NIH3T3 cells that induce tumor formation when implanted in nude mice. A more direct relationship between Aurora-A and cancer was discovered in 2006 by demonstrating that its overexpression in the mammary epithelium was sufficient to induce cancer. Aurora-A is then a key cell cycle kinase, whose overexpression induces cancer, making it indeed a good target for the treatment of cancers. A large number of inhibitors have therefore been manufactured and used in clinical trials for the treatment of cancers. However, after 20 years, none has yet managed to pass any phase III. So how can we improve the effectiveness of Aurora-A inhibitors in cancer treatments?

Biography

Claude Prigent is the Director of Research in the National Center for Scientific Research in France. He finished his PhD in Biology University of Rennes 1 and Post-doc in UK under the direction of Dr. Thomas Lindahl (Nobel Prize in Chemistry 2015). He was the Director of the Institute of Genetics and development of Rennes (2004-2016) and Director of the MRic imaging core facility (2000-2016). He is the Associate Professor at University Laval, oncology department, Quebec, Canada (2015-2017). He is the head of the “The Cell Cycle Team” since 1996. He studies cell division mechanisms with a focus on mitosis and its regulation by protein kinases in particular Aurora-A.
Biomarker-Assisted Drug Development in Oncology – 20 Years and Counting

Baolin Zhang  
*Center for Drug Evaluation and Research, Food and Drug Administration, USA*

**Abstract**  
Oncology drugs target discrete molecular aberrations or pathways in tumor cells; due to the intrinsic heterogeneity of tumors, many drugs are only active in a subset of patients. Predictive biomarkers, measured using *in vitro* companion diagnostics (IVD), help identify patients likely to respond to treatment and are increasingly integrated into drug development programs. This presentation will provide an update of biomarker-assisted oncology drugs approved by the US Food and Drug Administration. Case studies will be presented on therapeutic monoclonal antibodies selectively targeting HER2, EGFR, or PD-1/PD-L1 signaling pathways. This information will be further discussed with respect to biomarker discovery in the development of novel cancer therapeutics.

**Biography**  
Baolin Zhang is Senior Investigator and Review Team Leader in the Office of Biotechnology Products of the Center for Drug Evaluation and Research (CDER) at the US Food and Drug Administration (FDA). Dr. Zhang has 16 years of FDA experience regulating biotechnology drug product applications, including therapeutic monoclonal antibodies. He also directs a research program on cancer drug resistance and cancer biomarkers. He has published over 80 original studies in high profile journals, and presented at numerous scientific and regulatory conferences. He has received numerous awards including the FDA Awards for Excellence in Laboratory Science, Excellence in Regulatory Science, and Excellence in Mentoring and Leadership.

Resistance to Tyrosine Kinase-Targeted Therapy in Lung Cancer: Autophagy and Metabolic Changes

Hongde Li¹, William B Stokes², Emily Chater², Ewa Rupniewska², Rajat Roy², Francesco A Mauri², Xin Xue Liu², Maciej Kaliszczak², Julian Downward³, Eric Aboagye², Huiru Tang¹, Yulan Wang¹, Michael J Seckl², Olivier E Pardo²  
¹Centre for Nuclear Resonance, Wuhan Institute of Physics and Mathematics, Wuhan, China  
²Department of Surgery and Cancer, Imperial College London, UK  
³Signal Transduction laboratory, CRUK-LIF, London, UK

**Abstract**  
Lung cancer is the commonest cancer killer worldwide. Tyrosine-kinase inhibitors (TKI) are novel agents in the treatment of this cancer. However, their efficacy is impaired by the rapid development of drug-resistance through a variety of mechanisms. Here, we will discuss resistance to the first-generation EGFR inhibitors (eg. Erlotinib) and SRC inhibitors (eg. Dasatinib).

The principal mechanism of resistance to first-generation EGFR inhibitors is the appearance of the T790M receptor mutation. While the reason for resistance was proposed to be changes in affinity of the receptor for ATP, our metabolomics analysis additionally revealed that resistance is associated with decreased cellular levels of glutathione (GSH), a direct consequence of the T790M mutation. This occurred because of decreased SQSTM1/NRF2-mediated transcription of GSH synthesising enzymes in cell lines and clinical samples with T790M-EGFR. We demonstrate that increasing GSH levels in resistant cells re-sensitises these to first-generation EGFR inhibitors *in vitro* and *in vivo*. As compounds exist in the clinic to achieve this, our finding may have profound therapeutic and economic consequences.

Src family kinases (SFK) are commonly overexpressed or hyperactivated in lung cancer cell lines and clinical samples. However, despite their on-target efficacy, SRC inhibitors have failed to prevent tumour growth and improve patients’ survival in multiple clinical trial. Here we show that this failure is associated with the induction of autophagy in treated cells that prevents these compounds from triggering apoptosis cell death. Targeting autophagy, either genetically or using our novel small-molecule inhibitor, C1A, sensitises lung cancer cell lines to Dasatinib both *in vitro* and *in vivo* by unlocking the apoptotic response. These findings propose new combinational therapeutic strategies that could resurrect the use of SRC inhibitors in the treatment of lung cancer.

**Biography**  
Olivier E. Pardo graduated from the Faculty of Pharmacy Paris-V, France where he was awarded a Doctorate in Industrial Pharmacy (1997). He then completed his PhD in Biochemistry and Molecular Biology at Imperial College-London (2002). He obtained post-doctoral experience in the laboratory of Prof. Julian Downward at the CRUK-London Research Institute where he worked on the regulation of apoptotic cell death and cell migration. In 2006, he created the Cellular Regulatory Networks lab at Imperial College, Department of Surgery and Cancer. His team focuses on understanding the molecular mechanisms underlying chemo-resistance and metastasis in lung and other cancers.
Wnt Signaling in Tumorigenesis of Astrocytic Brain Tumors

Nives Pecina-Slaus¹, Anja Kafka¹, Anja Bukovac¹, Niko Njiric¹, Mateja Bacic², Davor Tomas³

¹Laboratory of Neurooncology, Croatian Institute for Brain Research, and Department of Biology School of Medicine University of Zagreb, Croatia
²Research Gate GmbH, Germany
³Department of Pathology, School of Medicine, University of Zagreb, and Hospital Center "Sisters of Charity", Croatia

Abstract

Wnt pathway has been established as one of the basic signaling pathways whose malfunctioning often governs tumorigenesis. Investigations on key players of the Wnt signaling: beta-catenin (CTNNB1), TCF1, LEF1, SFRP3, SFRP1 and DVL3 are here presented. We have found that beta-catenin was upregulated in 50% of investigated glioblastomas while its nuclear localization was observed in 52.1%. Transcription factors of the pathway TCF1 and LEF1 were also upregulated in 51.6% and 71% of glioblastomas, respectively. Discriminant function analysis showed that strong expression levels of LEF1 discriminated between astrocytomas of lower grades and glioblastomas offering LEF1 as a potential progression marker. Promoter methylation of SFRP1 gene was found in 29, 2% of astrocytomas, and was progressively rising in higher grades with the highest distribution found in glioblastoma (P = 0,066). Cases with methylated SFRP1 expressed less SFRP1 protein than unmethylated ones (P = 0,013). Furthermore, samples with unmethylated SFRP1 promoter had significantly less beta-catenin (P = 0,046). SFRP3 protein behaved differently demonstrating decreased nuclear but increased cytoplasmic expression in higher grade astrocytomas. This may suggest that SFRP1 acts as tumor suppressor while SFRP3 acts as an agonist of Wnt signaling promoting invasive behavior. DVL3 expression levels showed significant positive correlation to higher tumor grades (P<0.001). Also significant positive correlation between DVL3 and both TCF1 (P = 0.020) and LEF1 (P = 0.006) was noted. Our findings contribute to better understanding of human glial tumor genetic profile and suggest that Wnt signaling plays important role in its etiology.

Biography

Nives Pecina-Slaus is a professor at the Department of biology and Head of Laboratory of neuro-oncology Croatian institute for brain research. B.S and MS Faculty of Sciences, PhD School of Medicine, University of Zagreb. She was trained at Cold Spring Harbor Laboratory, New York, and Georgetown University, Washington DC. She was granted 5 scientific projects. She is author of more than 100 publications – 60 scientific papers, a book, abstracts, book chapters. Her main fields of interest include cancer genetics, Wnt signaling, genetics of brain tumors. She is the Editorial board member of Frontiers in Bioscience, Acta Clinica Croatica, Cancer Cell International and Croatian Medical Journal. She received scientific awards from Croatian Medical Association, Academy of Medical Sciences, School of Medicine University of Zagreb, and in 2011 she received National Science Award.

Peripheral Blood Mitochondrial DNA Copy Number is a Potential Biomarker for Progress of Diabetic Nephropathy in Type 2 Diabetes Patients

Ghada Al-Kafaji*, Abdulla N. Aljadaan, Moiz Bakhiet

Department of Molecular Medicine and Princess Al-Jawhara Center for Molecular Medicine, Genetics and Inherited Disorders, College of Medicine and Medical Sciences, Arabian Gulf University, Kingdom of Bahrain

Abstract

Mitochondrial DNA (mtDNA) copy number is a surrogate measure of mitochondrial function, and altered mtDNA copy number has been associated with diabetic nephropathy (DN), a leading cause end stage renal disease in diabetic patients. We investigated whether mtDNA copy number in peripheral blood could be utilized as a biomarker for DN progress in type 2 diabetes (T2D) patients. A total of 50 non-diabetic and 100 diabetic subjects were recruited. The diabetic subjects were sub-divided based on urinary albumin-creatinine ratio (ACR) into T2D patients with normoalbuminuria (ACR <30mg/g, n = 50), DN patients with microalbuminuria (ACR 30-300mg/g, n = 29), and DN patients with macroalbuminuria (ACR >300mg/g, n = 21). The mtDNA copy number was measured as relative quantity of mtDNA compared to nuclear DNA using real-time PCR. Overall, the mtDNA copy number was lower in T2D and DN patients than in controls (P<0.001). Sub-group analyses by ACR showed that lower mtDNA copy number was significantly associated with high levels of albuminuria even after adjusting for conventional risk factors (odds ratio [OR] 0.47, confidence interval [CI] 0.299-0.74 for microalbuminuria and OR 0.21, 95% CI 0.1-0.436 for macroalbuminuria). Moreover, mtDNA copy number was correlated negatively with albuminuria (r = -0.546) and positively with glomerular filtration rate (r = 0.572). The
areas under the receiver operating characteristic curves (AUCs) of mtDNA copy number in discriminating DN patients from T2D patients and healthy controls were 0.80 (P<0.001) and 0.885 (P<0.001), respectively. Our results showed that peripheral blood mtDNA copy number was associated with the development of DN and could serve as a biomarker during DN progression.

Biography

Ghada Al-Kafaji has completed her PhD in molecular genetics from King’s College London, University of London, UK. Currently, she is an Associate Professor and the director of Personalized Medicine Master program at the College of Medicine, Arabian Gulf University, Bahrain. She has abundant publications in the area of molecular genetics that have been cited over 130 times. She has been serving as a reviewer and an editorial board member of reputed journals and received several certificates of excellence in reviewing scientific articles. She also received a number of awards for best presentations and outstanding work in regional and international conferences.

miRNA Expression Profiling of Mouse Colon Cancer Stem Cells: A Tumour-Specific Signature Traceable Along Colorectal Cancer Progression with Prognostic Value in Human Colon Cancer

Mariangela De Robertis
Laboratory of Molecular Medicine and Biotechnology, University Campus Bio-Medico of Rome, Italy
Department of Bioscience, Biotechnology and Biopharmaceutics, University of Bari, Italy

Abstract

Background: The definition of cancer stem cells (CSC) still lacks conclusive experimental evidence. Colorectal cancer (CRC) EphB2 and EphA2 cells have been correlated to stem-like properties and tumor malignancy. Here, we investigated a panel of miRNA involved in the self-renewal and cell fate during cancer development using murine CRC EphA2 and EphB2 sorted cells and tumor tissues as well as public datasets of hCRC data.

Methods: FACS-isolated murine EphA2high and EphB2high cells were analyzed by gene expression and IHC analyses in order to characterize the stem-like/differentiation phenotype. miRNAs expression profiling was performed using TaqMan LDA both on murine sorted cells and tissue and validated on public hCRC datasets (TCGA and GEO).

Results: miRNAs differentially expressed in murine tumor EphA2/EphB2 cells and tissues were found to orchestrate functions related to stem-like properties or to proliferation, metastasis and drug-resistance. Particularly, the EphA2 cells showed a molecular pattern reflecting the activation of EphA2 and EGFR pathways and a coherent dysregulation of mir-26b and mir-200a. This pattern displayed prognostic significance for stage I–III CRC. In patients with stage IV and WT KRAS, EphA2/Efna1/Egfr gene expression status was significantly associated with poor response to cetuximab treatment. EphA2 and EGFR overexpression showed a combined effect relative to cetuximab resistance, independently from KRAS mutations. The EphA2/EphB2-specific signatures resulted to be clinically relevant.

Conclusions: These data provide a comprehensive miRNAs signature implicated in the regulation of tumorigenesis, stemness and pharmacoresistance that could be exploited for diagnosis, therapeutic design and could be proposed as novel CRC prognostic biomarkers.

Biography

Mariangela De Robertis is currently Post-Doc fellow at the Department of Bioscience, Biotechnology and Biopharmaceutics, University of Bari, Italy. After graduation in Medical Biotechnology at the University of Bari, she moved to the University Campus Bio-Medico of Rome, Italy. She received her PhD in Experimental Oncology from the University of Foggia and she was Post-Doc visiting scientist at the University of Navarra, Pamplona (Spain). Her research interests cover topics in the field of tumor heterogeneity, epigenetics, and identification of novel biomarkers for colorectal cancer. Her published scientific work includes book chapters, papers in peer-reviewed international journals and proceedings of international conference.
How Detecting Change-Points in Biomarkers Time Series Can Aid the Diagnostic of Ovarian Cancer

Inés P. Mariño¹,², Oleg Blyuss², Andy Ryan², Aleksandra Gentry-Maharaj², John F. Timms², Anne Dawnay³, Jantiderpal Kalsi², Ian Jacobs³,⁴, Usha Menon², Alexey Zaikin²

¹Rey Juan Carlos University, Spain
²University College London, UK
³University College London Hospitals, UK
⁴University of New South Wales, Australia

Abstract

Ovarian cancer is the fifth most common cause of cancer-related deaths among women, with more than 150,000 deceases worldwide each year. One of the main problems of ovarian cancer is that, usually, is detected at later stages, for which the survival rates are relatively low. Thus, the development of new approaches for longitudinal multi-marker analysis that result in earlier detection may significantly impact on mortality. An issue of specific interest is to determine whether the baseline level of a biomarker changes significantly at some time instant (change-point) prior to the clinical diagnosis of cancer. Here we apply a hierarchical Bayesian change-point model to jointly study the features of time series from multiple biomarkers, such as the serum biomarker Cancer Antigen 125, the Human Epididymis Protein 4, matrix metalloproteinase-7, Cytokeratin 19 fragment, glycodelin and mesothelin, using data from a nested case-control study of women diagnosed with ovarian cancer in the UK Collaborative Trial of Ovarian Cancer Screening. In this way we assess whether some of these biomarkers can play a role in change-point detection and, therefore, aid in the diagnosis of the disease. The main conclusion of our study is that the combined analysis of a group of specific biomarkers may possibly improve the detection of change-points in time series data (compared to the analysis of Cancer Antigen 125 alone, the most commonly used oncomarker in the screening of ovarian cancer) which, in turn, are relevant for the early diagnosis of ovarian cancer.

Biography

Inés P. Mariño (MSc 1995, PhD 1999) is an Associate Professor at the Department of Biology and Geology, Physics and Inorganic Chemistry, Universidad Rey Juan Carlos (Spain) and a Honorary Senior Research Associate in the Institute for Women's Health, University College London (UK). Her interests are in the fields of dynamical systems, computational statistics and their applications in biology and medicine. She is a co-author of over 50 publications in international journals and proceedings of international conferences.

Anti-FIRs (PUF60) Auto-Antibodies are Detected in the Sera of Early-Stage Colon Cancer Patients

Sohei Kobayashi and Kazuyuki Matsushita∗
Department of Laboratory Medicine & Division of Clinical Genetics and Proteomic, Chiba University Hospital, Japan

Abstract

Anti-PUF60, poly(U)-binding-splicing factor, autoantibodies are reported to be detected in the sera of dermatomyositis and Sjogren's syndrome but little is known whether it is detected in the sera of cancer patients. PUF60 is identical with far-upstream element-binding protein-interacting repressor (FIR) that is a transcriptional repressor of c-myc gene. In colorectal cancers, a splicing variant of FIR that lacks exon2 (FIRΔexon2) is overexpressed as a dominant negative form of FIR. In this study, to reveal the presence and the significance of anti-FIRs (FIR/FIRΔexon2) antibodies in cancers were explored in the sera of colorectal cancer patients. The autoantibodies for FIRs were examined in the sera of 87 colorectal cancer patients. The sera of 42 healthy subjects were used as controls. Anti-FIRs antibodies were surely detected in the preoperative sera of 28 colorectal cancer patients (32.2% of positive rates), and the detection rate was significantly higher than that in healthy control sera (Mann–Whitney U test, p < 0.01). Anti-FIRs antibodies were detected even in early stage cancers in which anti-p53 antibodies, CEA, and CA19-9 were negatives. Furthermore, the area under the curve of receiver operating characteristic for anti-FIRs antibodies was significantly larger (0.85) than that for anti-p53 antibodies or CA19-9. In conclusions, Anti-FIRs antibodies were detected in relatively early-stage colorectal cancers. Therefore, the combination of anti-FIRs antibodies with other clinically available tumor markers such as anti-p53 antibodies, CEA, and CA19-9 further improved the specificity and accuracy of diagnosis.
Biography

Kazuyuki Matsushita was born in the City of Chiba, neighbor of Tokyo area, Japan. In 1988, graduated from Chiba University and was awarded with MD. In 1995 maintained his PhD at the Graduate Scholl of Medicine, Chiba University in Japan. From 1990 to 1997 worked as a resident of surgery at Chiba Cancer Center Hospital, Chiba University Hospital and National Sakura Hospital. From 1997 to 2000 was a visiting fellow, of the NCI, NIH, USA. From 2006 to 2008 was as an assistant professor of Department of Emergency and Critical Care Medicine; Division of Artificial Organs and Hemodialysis, Chiba University, Japan. From 2008 to 2016 he was Clinical Professor of Department of Molecular Diagnosis and Laboratory Medicine, Chiba University Hospital, Japan. In 2015, he was listed as a Board of Laboratory Medicine, Japanese Society of Laboratory Medicine, Japanese Board of Medical Genetics, form the Japan Society of Human Genetics. In 2010, he got the Board of Specialty in Cancer Treatment from Society of Japanese Cancer Treatment Society.

At present he is a Professor of Department of Laboratory medicine, Director of Laboratory Medicine, Division of Clinical Genetics and Proteomics, Chiba University Hospital, Chiba, Japan. He has been studying c-myc transcriptional regulation, especially demonstrated on c-myc transcriptional repressor FIR (FBP interacting repressor) in carcinogenesis. Proteomic and genomic analysis in carcinogenesis and DNA damage repair pathway for clinical validities such as cancer treatment and diagnosis. Establishment of biobanks network of human clinical samples in Japan for novel biomarkers research are studied in his group. His current research is studying FIR-SAP155 (SF3b1) interaction in c-myc regulation and p27Kip1 pre-mRNA splicing because SAP155 is required for proper p27Kip1 pre-mRNA splicing regulation. FIR-SAP155 interaction thus affects c-myc and cell cyclen. Proteome analysis in terms of FIR-SAP155 interaction is also applied to the studies in carcinogenesis and their clinical validities to cancer treatment and diagnosis.

Translational Potential of Non-Coding RNAs in Oncology

Ondrej Slaby
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Masaryk Memorial Cancer Institute, Czech Republic

Abstract

For many years, central dogma of molecular biology has been that RNA functions mainly as an informational intermediate between DNA sequence and its encoded protein. One of the great surprises of modern biology was discovery that protein-coding genes represent less than 2% of total genome sequence, and subsequently that almost 90% of human genome is actively transcribed. Thus, human transcriptome was found to be more complex than collection of protein-coding gene transcripts and their splice variants. Recent evidences have clearly shown that non-coding RNAs (ncRNAs) play major biological roles in cellular development, physiology and pathologies. NcRNAs are grouped into two major classes based on transcript size; small ncRNAs and long ncRNAs. Each of these classes can be further divided, whereas novel subclasses are still being discovered and characterized. In last ten years, class of small ncRNAs called microRNAs was studied most intensively with more than fifty thousand hits at PubMed database. Huge amount of evidence has been accumulated to describe molecular mechanisms of novel RNA species functioning, providing insight into their functional roles in cellular biology and in human disease, especially in cancer. Knowledge regarding ncRNAs functioning in cancer biology and their translational potential to serve as disease biomarkers and novel therapeutic targets in cancer will be summarized and demonstrated on several examples based on our recent observations.

Biography

Ondrej Slaby is an Associate Professor of Biochemistry at the Faculty of Science at Masaryk University in Brno and the 1st Faculty of Medicine at Charles University in Prague, Czech Republic. He also works as research group leader (group Molecular Oncology II) at the Central European Institute of Technology at Masaryk University in Brno and as a scientific secretary at the Masaryk Memorial Cancer Institute in Brno. Dr. Slaby has published extensively in the field of non-coding RNAs and cancer with special focus on their translational potential in diagnostics and as the therapeutic targets.
Faster Detection of Ischemia in Free Tissue Transfers by Use of Microdialysis

Hanne Birke-Sorensen*, Andreas Rauff-Mortensen
Aarhus University, Denmark

Abstract

Microdialysis is a sensitive and specific method for collection of metabolic biomarkers detecting secondary ischemia after microvascular surgery performing reconstructions by use of free tissue transfers.

Microdialysis is a minimal invasive method for collection of dialysate representing the molecular composition in the tissue of interest. By using the traditional microdialysis setting with a perfusion flowrate of 0.3µl/min, we have demonstrated a very high sensitivity and specificity clinically as well as experimentally regarding ischemia. Despite these demonstrations, there has been a hesitation to the use of microdialysis especially due to the diagnostic delay of 1-2 hours.

In a laboratory study and later in a porcine experiment we have demonstrated that the system can work faster by increasing the microdialysis perfusion flowrate from 0.3µl/min to 1.0µl/min. The median detection time for arterial ischemia in a pure muscle transfer can be reduced from 60 to 28 minutes. The monitoring system can be accelerated without reducing sensitivity or specificity. Furthermore, it is possible to alternate between the traditional and the new faster method without changing the ischemic alarm values.

The microdialysis system is not a screening method but a final answer of whether the transfer is ischemic and the patient has to be taken back for a reoperation. The microdialysis system can be used in all sorts of free tissue transfers and by use of this faster method, the microdialysis monitoring system is approaching the demands of an ideal monitoring system for detection of ischemia in free tissue transfers.

Biography

Hanne Birke-Sorensen received her medical degree from Odense University, Denmark in 1983 and completed her residency in Reconstructive Plastic Surgery at Aarhus University Hospital, Denmark 1998. She was head of the Section of Microvascular Reconstructions at Aarhus University Hospital from 2000 to 2010, specializing in free tissue transfers to head and neck, esophagus, breast and the extremities.

Throughout her professional career, Birke-Sørensen has been interested in optimizing wound healing and surgical procedures and finding ways to monitor tissue at risk to avoid complications. She has authored several peer-reviewed papers within these topics including 20 papers including the use of microdialysis, experimentally as well as clinically. She completed her PhD-thesis on monitoring of free intestinal transfers for esophageal reconstruction using microdialysis in 2009. She is currently working freelance at private hospitals and as associate assistant professor at the Faculty of Health, Aarhus University, Denmark.

Clinical and Translational Biomarkers for Lysosomal Storage Disorders

Christiane Auray-Blais*, Pamela Lavoie, Mona Abaoui, Michel Boutin
Faculty of Medicine and Health Sciences, University of Sherbrooke, Canada

Abstract

Lysosomal storage disorders (LSDs) are characterized by the accumulation of metabolites, mainly due to enzyme deficiencies. There is a wide range of clinical manifestations in affected patients due to a marked variability in the genotype and phenotype. It is thus important to find reliable biomarkers for early detection (high-risk/mass screening), confirmation of diagnosis and monitoring treated patients. Results from biomarker studies using mass spectrometry approaches for two groups of LSDs will be presented: 1) Fabry disease (FD), an X-linked, multisystemic LSD characterized by the accumulation of glycosphingolipids in different organs, and biological fluids; and 2) Mucopolysaccharidoses (MPSs), a group of LSDs resulting from primary defects in enzymes involved in the glycosaminoglycan (GAG) catabolism. First, using metabolomic approaches with time-of-flight mass spectrometry, our results show the detection of novel biomarkers for Fabry disease patients in urine and plasma, called analogs of globotriaosylsphingosine (lyso-Gb₃). After devising and validating high sensitivity tandem mass spectrometry (MS/MS) methods for these analogs, we have established a positive association with some of these biomarkers and the left ventricular mass index, and/or the Mainz Severity Score Index for FD patients having a cardiac variant mutation. Secondly, we have devised and validated a multiplex MS/MS method for the
quantitation of urinary dermatan sulfate, heparan sulfate, chondroitin sulfate, and keratan sulfate. Patients under enzyme replacement therapy treatment have shown reduced levels of these GAGs. Other spectrophotometric methods were shown to be unreliable leading to false-negative results. These translational research studies allowed a technological transfer of these biomarkers to the clinic.

**Biography**

Christiane Auray-Blais is the Director of the Provincial Neonatal Urine Screening Program for hereditary metabolic disorders in Sherbrooke, QC. She holds a PhD in Radiobiology (Université de Sherbrooke) and postdoctoral studies from Duke University Medical Center, NC, USA. She has a master’s degree in Health Law from the Faculty of Law (Université de Sherbrooke). She is the author of more than 250 publications/abstracts/articles. She is a professor at the Medical Genetics Division, in the Pediatrics Department at the Faculty of Medicine and Health Sciences in Sherbrooke. She is the Scientific Director for the Waters-CHUS Expertise Centre in Clinical Mass Spectrometry.

**Clinical Applications of cfDNA Methylation in Breast Cancer**

Bodour Salhia*, Gerald Gooden, Tim Triche Jr.
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**Abstract**

A number of clinico-pathological criteria and molecular profiles have been used to stratify breast cancer (BC) patients into high and low risk groups. Currently, there are still no effective methods to determine which patients harbor micrometastatic disease after standard BC therapy and who will eventually develop local or distant recurrence. Cell-free (cf) DNA has attracted attention for clinical use in the context of risk prediction, prognostication and prediction of response to chemotherapy in human cancer. Several groups including ours have reported the detection of tumor-associated methylation changes in cfDNA extracted from plasma or serum. We are specifically interested in the use of cfDNA methylation biomarkers for the prediction of cancer metastasis in the early stage setting. Accordingly, we are validating a DNA methylation signature, referred to as CpG4C, which discriminates metastatic BC from healthy individuals or disease free survivors using a targeted bisulfite amplicon sequencing approach. In addition, we have been investigating whether a surge of cfDNA levels after cytotoxic chemotherapy affects the sensitivity and specificity of the CpG4C assay. Lastly, we are also working on determining the technical and biological limits of detection of CpG4C in plasma. CpG4C is a potential blood-based biomarker that could be advantageous at the time of surgery and/or after the completion of chemotherapy to indicate patients with micrometastatic disease who are at high-risk of recurrence, and who could benefit from additional therapy.

**Biography**

Bodour Salhia is an Assistant Professor at the University of Southern California and is a translational genomics scientist with extensive knowledge and expertise in mechanisms that underlie tumorigenesis and tumor biology. She merges cutting edge genomics/epigenomics analyses with cell biological and functional studies towards the investigation of clinically relevant problems in human cancer. Dr. Salhia received her Honors Bachelor of Science Degree (1998), Master of Health Science (2001) and PhD. (2006) degrees in human molecular and cellular biology from the University of Toronto. She completed a postdoctoral fellowship from 2006–2011 at the Translational Genomics Research Institute (Phoenix, Arizona) in cancer genetics and epigenetics.
Biosensors and Nanobiosensors for Rapid Point of Care Measurement of Biomarker Proteins

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2ELISHA Systems Ltd, UK

Abstract

The current gold standard for protein biomarker measurement is the ELISA, which shows good sensitivity and specificity but is typically quite slow and requires expensive and complex equipment. For applications such as early cancer diagnosis, this may limit access, whilst for critical conditions such as acute kidney injury (AKI), sepsis, stroke then rapid measurement has the potential to drive the clinical response. Other applications such as immediate confirmation of bacterial vs viral infection to inform antibiotic prescribing, also require a fast analysis. Biosensors offer the prospect of reagent-less, processing-free measurements at the patient’s bedside. We have fabricated electrochemical immunosensors against a wide range of medical analytes; such sensor operate by virtue of an immobilized bioreceptor, typically an antibody or antibody fragment, or more recently a synthetic binding protein (Affimer) onto an electrode surface. Sensor readout after exposure to the biomarker, in blood, urine or other bio-fluid is then by electrochemical impedance measurement. We have also developed lanthanide ion doped nanoparticles, typically 20-40 nm diameter which are surface-functionalized with antibodies or Affimers. Here, readout after biomarker presentation is via alteration of luminescence intensity, either quenching or enhancement. Also since the nanobiosensors are in suspension and the emission profile can be tuned, then real time measurement, e.g. of the AKI biomarker NGAL in urine should be possible. With all of these devices, the surface nanostructure is absolutely key to performance and this will be discussed.

Biography

Paul Millner received his PhD from the University of Leeds in 1979 followed by Postdoctoral Fellowships at Purdue University, USA and Imperial College, London. He returned to Leeds in 1986 as Lecturer in Biochemistry. Since mid-2009 he has been the Professor of Biomaterials and until recently Head of the School of Biomedical Sciences at Leeds. His research group works to interface biomolecules with non-biological surface to build a range of devices at both the macro-scale (electrochemical biosensor chips, functional nanofiber mats) to nanoscale (nanobiosensors) and targeted nanoparticles for imaging and drug delivery.

Monocyte Chemoattractant Protein-1 (MCP-1) is a Prognostic Biomarker and a Therapeutic Target in Diabetic Nephropathy

Frederick W. K. Tam
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Abstract

Diabetic nephropathy is the common cause of kidney failure worldwide. Despite optimal use of inhibitors of renin-angiotensin system (RAS), a significant proportion of diabetic patients developed progressive kidney disease. Novel mechanistic biomarker will be beneficial in identifying patients with high risk of progression.

MCP-1 (also known as CCL2) is a potent chemokine for monocytes and macrophages. Increased amount of urinary MCP-1 were detected in urine from patients with diabetic nephropathy. Earlier work from our laboratory showed that urinary MCP-1/creatinine ratio is prognostic of the rate progression (loss in estimated glomerular filtration rate (eGFR)) over 6 years prospective follow up. Recently, the prognostic values of urinary MCP-1 in diabetic nephropathy have been validated by other research groups.

Multiple mechanisms, including high concentration of glucose, may contribute increased synthesis of MCP-1 by glomerular mesangial cells. Our recent work also showed that stimulation of P2X7 receptor with extracellular ATP synergized with high concentration of glucose in mesangial cell production of MCP-1.

The receptor for MCP-1 has been targeted in a recent clinical trial in diabetic nephropathy. Furthermore, P2X7 receptor may also be a novel therapeutic target in diabetic nephropathy. In conclusion, MCP-1 is both a prognostic biomarker and a
therapeutic target in diabetic nephropathy.

Biography

Frederick W. K. Tam is the Ken and Mary Minton Chair of Renal Medicine at Imperial College London. He has been investigating the importance of cytokines in pathogenesis of glomerulonephritis, diabetic nephropathy and renal allograft rejection. He has also applied the experience from cytokine analysis and proteomics to development of non-invasive biomarkers for renal diseases. The expertise of his research group has been applied in the preclinical and early clinical development of anti-inflammatory therapies, in collaboration with the industry.

Phase Imaging of Axonal Integrity of Cranial Corticospinal Tract in Experimental Spinal Cord Injury at 9.4T

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3High Magnetic Field Lab of Chinese Academy of Sciences, Hefei, China
4Department of Neurology, Anhui NO.2 Province People’s Hospital, Hefei, China

Abstract

Spinal cord injury (SCI) leads to neuronal cell death, axonal damage and demyelination. Both spinal cord and brain undergo anatomical changes following SCI. Recently MR phase imaging (PI) has shown promising application in visualizing demyelination or axonal damage. Therefore, in this study we explored the possibility to investigate integrity of cranial corticospinal tract (CST) in SCI using PI. Diffusion tensor imaging (DTI), and its metrics, e.g. axial diffusivity \( \lambda_\parallel \) were also used to verify the axonal integrity and preclude the potential contribution of axonal injury to the observed decrease in frequency contrast. We also correlated the MRI findings to immunohistochemistry.

Results show that the phase contrast decreased mainly in contralateral pyramid two weeks post-injury compared to pre-injury levels. Significant reduction in contralateral pyramid two weeks post-injury compared to pre-injury levels when quantified radial diffusivity \( \lambda_\perp \) values. The \( \lambda_\parallel \) in all those regions did not significantly change 2 weeks post-injury compared to pre-injury levels.

The reduction of frequency contrast along with no significant changed \( \lambda_\parallel \) were observed in the contralateral pyramids, suggestive of demyelination without obvious axonal damage in the CST white matter. These MRI findings were confirmed by immunohistological results, i.e. myelin basic protein staining lost but without obvious reduction in neurofilament staining after two weeks after injury. The reduced \( \lambda_\perp \) in the contralateral pyramids, which may be associated with activated astrocytes according to the increased expression of GFAP in those regions. In conclusion, PI is a potential endogenous biomarker for brain axonal integrity after spinal cord injury.

Biography

Junchao Qian received his BS in Clinical Medicine from Anhui Medical University in 2003. He received his PhD in Biophysics from High Magnetic Field Laboratory of Chinese Academy of Sciences (CAS) in 2015. Before that he worked as a research fellow at University of Texas Medical School at Houston from 2008 to 2010. Now he is an Associate Professor with tenure in Center of Medical Physics and Technology of CAS, and Deputy Scientific Director of Medical Imaging Department at Cancer Hospital of CAS. His interest is to apply novel MRI techniques to study tumor and brain plasticity after injury.
**Profiling Signaling Proteins in Human Spermatozoa: Biomarker Identification for Sperm Quality Evaluation**

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**Abstract**

In this study we unraveled human spermatozoa signaling pathways and correlated the activity of sperm signaling proteins with clinical data. Thirty seven semen samples were used and basic semen parameters, sperm DNA fragmentation and the expression levels of 75 protein kinases and the phosphorylation/cleavage patterns of 18 signaling proteins were evaluated to determine the correlation between semen basic parameters and the expression and activity of signaling proteins. We have contributed towards establishing a biomarker “fingerprint” to assess sperm quality based on molecular parameters.

**Biography**

Margarida Fardilha is working as an assistant professor at the Medical Sciences Department of the University of Aveiro where she directs the Biomedical Sciences Bachelor. At the same time, she coordinates the Signal Transduction Lab at iBiMED, at University of Aveiro. She has a Bachelors in Biochemistry (University of Porto) and PhD in Biology from University of Aveiro. Her research is focused on the modulation of Protein Phosphatase 1 complexes in sperm motility and prostate cancer.

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**PTPRQ as a Potential Biomarker for Idiopathic Normal Pressure Hydrocephalus**

Yuki Nagata¹, Masahiko Bundo¹, Saiko Sugiura¹, Masahiro Kamita², Masaya Ono², Kotaro Hattori¹, Sumiko Yoshida¹, Yu-ichi Goto¹, Katsuya Urakami¹, Shumpei Niida¹

¹National Center for Geriatrics and Gerontology, Japan
²National Cancer Center Research Institute, Japan
³National Center of Neurology and Psychiatry, Japan
⁴Tottori University, Japan

**Abstract**

Idiopathic normal pressure hydrocephalus (iNPH) is caused by the accumulation of cerebrospinal fluid (CSF) and is characterized by gait disturbance, urinary incontinence, and dementia. iNPH dementia is treatable by shunt operation; however, since the cognitive symptoms of iNPH are often similar to those of other dementias such as Alzheimer’s disease (AD), accurate diagnosis of iNPH is difficult. To overcome this problem, finding new diagnostic markers to distinguish iNPH and AD is warranted. Using comparative proteomic analysis of CSF from iNPH and AD patients, protein tyrosine phosphatase receptor type Q (PTPRQ) was identified as a candidate biomarker protein for discriminating iNPH from AD. ELISA analysis indicated that the PTPRQ concentration in the CSF was significantly higher in iNPH patients than in AD patients. In addition, the PTPRQ concentration in the CSF of non-responders to shunt operation (SNRs) tended to be relatively lower than that in the responders. PTPRQ would be a useful biomarker for discriminating iNPH from AD patients and may be a potential companion biomarker to identify SNRs among iNPH patients. Additional large-scale analysis will allow understanding new aspects of iNPH.

**Biography**

Yuki Nagata was born in the City of Kagoshima, Japan. In 2005, she graduated from Graduate School of Life Sciences, Tohoku University. She got a PhD in the field of DNA damage and repair system, by studying the relation between DNA polymerase activity and spontaneous mutations in *Escherichia coli*.

From 2005 to 2009, she worked as a Post Doc Researcher at Iwate medical university. In this period, she studied the mechanism of differentiation of mouse hematopoietic stem cells and mesenchymal stem cells. From 2010 to present, she works at National Center of Geriatric Gerontology. She studied about elderly specific diseases, such as sarcopenia and dementia.
At present, she is trying to find new diagnostic biomarkers for dementias by several kinds of comprehensive analyses, including proteomics, metabolomics and transcriptomics. Recently, she performed exome and RNA-seq analysis with next generation sequencer to obtain additive information for elderly specific diseases.

Label Free Detection of Sensitive Mid-Infrared Biomarkers of Glomerulonephritis in Urine Using Fourier Transform Infrared Spectroscopy

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1Pediatric Nephrology, Department of Pediatric Nephrology, Chang Gung Memorial Hospital at Lin-Kou and Chang Gung University, Taiwan
2Imperial College Kidney and Transplant Centre, Renal and Vascular Inflammation Section, Department of Medicine, Imperial College London, UK
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5UCL Center for Nephrology, University College London Medical School, Royal Free Campus and Hospital, UK

Abstract

More reliable biomarkers using near-patient technologies are needed to improve early diagnosis and intervention for patients with renal disease. Infrared (IR) vibrational spectroscopy/microspectroscopy is an established analytical method that was first used in biomedical research over 20 years ago. With the advances in instrumentation, computational and mathematical techniques, this technology has now been applied to a variety of diseases such as cancer, bone and neurodegenerative disease; however, applications in nephrology are just beginning to emerge. In the present study, we used Attenuated Total Reflectance Fourier Transform infrared (ATR-FTIR) spectroscopy to analyze urine samples collected from rodent models of inflammatory glomerulonephritis (GN) as well as from patients with crescentic GN, with the aim of identifying potential renal biomarkers; several characteristic mid-IR spectral markers were identified in urine samples. Specifically, a 1545 cm⁻¹ band increased in intensity with the progression and severity of GN in rats, mice and humans. Furthermore, its intensity declined significantly in response to corticosteroid treatment in nephritic rats. In conclusion, our results suggest that specific urinary FTIR biomarkers may provide a rapid, sensitive and novel non-invasive means of diagnosing inflammatory forms of GN, and for real-time monitoring of progress, and response to treatment.

Biography

Mei-Ching Yu graduated from China Medical University in Taiwan and completed her residency and fellowship training in Chang Gung Memorial Hospital, Lin-Kou medical Centre, Taiwan. And then, she moved forward to get her PhD in Renal Medicine from Imperial College London, UK by researching with the pathogenic mechanism of renal inflammation and fibrosis, developing the new platform of early detection of kidney disease and cytokine/growth factor-based therapy. At present, she is working as a consultant pediatric nephrologist and physician scientist in Lin-Kou CGMH, carrying on clinical and basic research for translation to clinical applications.

Autoantibodies Against Aquaporin-5, A Novel Biomarker of Primary Sjögren’s Syndrome

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2Seoul St. Mary’s Hospital, Korea

Abstract

The pathophysiology of exocrine dysfunction observed in Sjögren’s syndrome (SS) is not fully understood. We identified autoantibodies against human AQP5 in the sera of primary SS patients. The screening of 53 control and 112 SS samples by an indirect immunofluorescence (IIF) assay using the AQP5-expressing MDCK cells revealed the presence of significantly higher levels of anti-AQP5 IgG in the SS samples than in the control samples with sensitivity of 0.73 and a specificity of 0.68. Furthermore, the presence of anti-AQP5 autoantibodies was associated with low resting salivary flow in SS patients. Subsequently, epitope analysis of the anti-AQP5 autoantibodies was performed by IIF assay in the presence or absence of peptides corresponding to the second transmembrane helix and extracellular loops A, C and E of AQP5. Overall, SS samples (n = 27) were inhibited by peptides corresponding to A, C, and E by approximately 40 to 50%, whereas control samples (n = 14) were inhibited only by peptides corresponding to E by less than 20%. A cyclized peptide mimicking E
(E1) was most frequently recognized and best differentiated between SS and control samples. To determine functional epitopes, the effects of purified IgG and neutralizing peptides on the transepithelial osmotic permeability (PfT) of MDCK cells expressing AQP5 were measured. Incubation of MDCK-AQP5 cells with SS-, but not with control-IgG, significantly decreased PfT, which was reversed by the neutralization of IgG binding to any of the extracellular loops. In conclusion, anti-AQP5 autoantibodies may be a potential biomarker and therapeutic target in SS.

Biography

Youngnim Choi has completed her PhD at the State University of New York at Buffalo and postdoctoral studies at the National Human Genome Research Institute/National Institute of Health, USA. She is a full professor at the Seoul National University School of Dentistry. She has published more than 60 papers in reputed journals and has been serving as an editorial board member of Journal of Dental Research. Her current research is focused on the role of host-microbe interaction in the pathogenesis of periodontitis, oral mucosal diseases, and autoimmune diseases.
The Effects of Dietary Polyunsaturated Fatty Acids on Prostate Cancer: Unbiased Proteomic and Phosphoproteomic Studies

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2Department of Urology, Roswell Park Cancer Institute, Buffalo, USA

Abstract

A line of evidence has suggested that early inference and dietary prevention are beneficial in prostate cancer (PCa) patient care. Fish oil (FO), which contains mostly omega-3 polyunsaturated fatty acid, is one of the most widely studied candidate supplements for PCa prevention; however, the molecular mechanism remains elusive. The goal of this study is to evaluate the regulatory role of FO on PCa through a global unbiased proteomic analysis and a global phosphoproteomic profiling. In the global protein expression study, we found only a few proteins with statistically significant changes, including sequestosome-1 (p62), MSMP, a newly identified proinflammation factor, and a few in the glycolysis pathway. In the global phosphoproteomic study, we confidently identified 828 phosphopeptides from 361 phosphoproteins with FDR<1%. Quantitative comparison between treatment and control groups suggests that FO induces changes in protein phosphorylation of proteins involved in pathways associated with cell viability and metabolic processes, specifically significant decreases in the levels of phospho-PDHA1Ser232 and phospho-PDHA1Ser300, suggesting a role for n-3 polyunsaturated fatty acids in controlling the balance between lipid and glucose oxidation. This study confirmed that FO changed PCa cell function through diverse pathways including glycolysis, cell cycle, cytotoxicity induced stress, anti-inflammation and also provided useful details about the mechanism of these effects. A global proteome and phosphoproteome clinical study in PCa clinical samples would validate and extend these findings to the patient population and potentially provide novel opportunities for therapeutic development.

Biography

Mu Wang is a tenured Associate Professor at Indiana University School of Medicine. He earned his PhD in Bio-Organic Chemistry from Washington University in St. Louis, Missouri, USA, and was an NIH postdoctoral fellow studying mechanisms of DNA repair in mammalian system. He joined the faculty of Indiana University School of Medicine in 2001 and has served as a Proteomics Core director since. His research interest include biomarkers and drug target discovery, and deciphering the protein interaction networks in complex human diseases with the use of high throughput proteomics technologies and bioinformatics.

NFL in CSF and Serum, A Potential Translational Dynamic Biomarker of Neurodegeneration in Preclinical Models

Nathalie Schussler1*, Anthony Brureau1, Veronique Blanchard-Bregeon2, Catherine Pech1, Stephanie Hamon3, Pascal Chaillou2, Jean-Claude Guillemot2, Pascal Barneoud1, Philippe Bertrand1, Laurent Pradier1, Thomas Rooney1
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3Evotec, France

Abstract

Accumulation of Neurofilaments (NFs), the major constituents of the neuronal cytoskeleton, is a distinctive feature of neurological diseases and several studies have shown that soluble NFs can be detected in the cerebrospinal fluid (CSF) of patients with neurological diseases, such as multiple sclerosis and frontotemporal dementia. We have used an inducible transgenic mouse model of neurodegeneration, CamKII-TetOp25 mice (Tsai et al., 2003), to evaluate whether NF-L levels in CSF or blood can be used as a biochemical biomarker of neurodegeneration. Induction of p25 transgene brain expression led to increases in CSF and serum NF-L levels that correlated with increased neuronal stress and neurodegeneration. When p25 transgene expression was switched off this prevented further increases in both CSF and serum NF-L levels which correlated with the block of further increases in neuronal stress and neuronal loss. The levels of CSF NF-L detected in p25 mice are about 4-fold higher than the CSF levels detected in patients with chronic neurodegenerative diseases, such as symptomatic FTD (bvFTD). We also report increase with aging in CSF and plasma NFL in two other transgenic mouse models, ThyTau22 (Schindowski et al., 2006) and APPxPS1 mice (Balnchard et al., 2003). Finally, Western blot and

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NanoLC-MS/MS data indicate that the NF-L detected in CSF is most likely a cleaved form of NF-L. These results suggest that CSF and serum NF-L could be used as potential translational dynamic biomarkers of neurodegeneration in preclinical animal models and in clinical studies.

**Biography**

Nathalie Schussler is a senior scientist in Neuroscience Therapeutic area. Working at Sanofi for 20 years, she has acquired knowledge and expertise in *ex-vivo* evaluations from mechanism of action elucidation, evaluation of target engagement and biomarker identification/validation. She has first validated several biochemical readouts in the brain for the characterization of transgenic mice models and the activity of chemical compounds. She then moved on to biochemical markers evaluation in bio-fluids (cerebrospinal fluid and blood) both on human samples and animal models of neurodegenerative diseases to contribute to the identification of translatable biomarkers for proof of activity in early PhII clinical trials.

**Microdialysis Monitoring – A Method for Monitoring Organ and Tissue Chemistry**

Katarina Asberg  
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**Abstract**

Microdialysis is a technique for sampling the chemistry of individual organs and tissues. The basic principle is to mimic a capillary blood vessel by perfusing a thin semi-permeable dialysis membrane tube implanted in the tissue with a physiological solution. In the tissue substances from the interstitial fluid diffuse through the dialysis membrane into the perfusion fluid. The perfusate is analyzed chemically and reflects the tissue or the organ chemistry.

Today there are CE-approved Microdialysis catheters available for implantation in brain, liver, abdomen, muscle, subcutaneous tissue as well as intravenously. There are Microdialysis perfusion pumps, micro-vials and analyzers suitable for intra-operative as well as bedside use in the Intensive Care Unit. The presentation will give a brief overview of the different applications of clinical Microdialysis.

**Biography**

Katarina Asberg (maiden name Fransson) was born 1968 in Motala city, Sweden. In 1989, she graduated from the Stockholm University College of Health Sciences at the Institution for Laboratory Medicine. During the education she had working practice at the Pharmacology Institution of Professor Urban Ungerstedt at the Karolinska Institute in Stockholm. From 1989 until 2011 she worked as a Product Manager and Sales Manager for CMA Microdialysis AB in Stockholm, a spinoff company from the Karolinska Institute founded by Professor Urban Ungerstedt. At present she is the Sales and Marketing Director at the company M Dialysis AB in Stockholm a leading supplier of Clinical Microdialysis products, and she is a member of the company Management team. She is also the responsible Educator at the company.

**Application of Bioinformatics for Biomarkers Research, Drug R&D and Clinical Practice**

Andrey Khudoshin*, Anton Yuryev\(^2\)  
\(^1\)Elsevier, Russia  
\(^2\)Elsevier, USA

**Abstract**

Liver toxicity is a key reason why new drugs fail in clinical trials, or once they are in broader use. Drug-induced cholestasis is a common form of liver toxicity. Yet currently there is no model or test to predict which drugs may induce cholestasis in patients.

This report demonstrate how bioinformatics approach on the example of using Elsevier’s Pathway Studio® pathway analysis software can be used to create complex, predictive mechanistic models of biological processes, providing novel insights to researchers and helping them direct the course of their studies. The report will highlight application of bioinformatics and mechanistic models approach to biomarkers research. Presented examples include following: prediction of biomarkers based on reconstructed liver toxicity model, identification of new potential candidates for drug targets, identification of drug efficacy biomarkers or safety biomarkers and assessment of clinical biomarker specificity.
Biography

Andrey Khudoshin have 7 years of research experience in field of conversion of natural compounds before 2012 when he switched to drug R&D processes and start to work in Bio-Rad Laboratories in field of biologic drugs purification technologies. From 2015, Andrey, implement his chemistry and biology experience in Elsevier where collaborate with leading centers in field of medicinal chemistry, personalized and evidence based medicine, system biology, drug R&D to enhance research performance by implementation of data-driven approach. His fields of scientific interests include innovative drug R&D, data-driven research at the intersection of chemistry, biology and medicine and behavioral and neurobiological science.

Cancer Biomarkers in Biosensors Fabrication for Diagnostic Purposes

Samar Damiati

Institute for Synthetic Bioarchitectures, Department of Nanobiotechnology, University of Natural Resources and Life Sciences (BOKU), Vienna, Austria
Department of Biochemistry - Science, King Abdulaziz University (KAU), Jeddah, SA

Abstract

Cancer is one of the leading causes of death worldwide and the number of deaths is increasing due to the limitations of the available diagnostic tests. Early diagnosis plays an important role in controlling disease progression and response to therapy. Hence, cancer biomarkers are widely exploited in oncology to detect the presence of tumors and to evaluate the subsequent treatment of patients. Biomarker-based biosensors have attracted attention due to their simplicity, rapidity, selectivity and sensitivity. The main obstacle that prevents the development of biosensors is the fact that cancer is a complex set of diseases and only a few biomarkers are exploited by oncologists to detect cancer. This talk will be focusing on the fabrication of biosensors for cancer biomarker detection and highlights various biomarker detection techniques. It will also discuss the limitations associated with some developed systems for immunoassay technology.

Biography

Samar Damiati is an Assistant Professor of Nanobiotechnology, received her PhD in 2013 from the Department of Nanobiotechnology at the University of Natural Resources and Life Sciences - Vienna, Austria. Currently, her research focuses on synthetic biology, biosensors, nanomedicine, lab-on-a-chip and microfluidics.

Particles-Induced Osteoblast Apoptosis and Inflammation Mediated by Endoplasmic Reticulum in a Murine Model of Periprosthetic Osteolysis

Guoyin Liu¹²³, Yong Zhang¹, Jin Wang¹, Jiangning Chen¹, Jianmin Chen¹, Junfeng Zhang¹, Jianning Zhao²

¹Bayi Hospital Affiliated to Nanjing University of Chinese Medicine, Nanjing, China
²Jinling Hospital affiliated to the School of Medicine, Nanjing University, China
³School of Life Sciences, Nanjing University, China

Abstract

Macrophage apoptosis and inflammation in interface membrane have been shown to play a significant role in the pathogenesis of osteolysis. However, osteoblasts have not been fully explored as a participant in the process of osteolysis, despite their critical role in bone growth, remodeling and maintenance. The purpose of our study was to identify whether endoplasmic reticulum (ER) stress participates in particle-induced osteolysis (PIO), osteoblasts apoptosis and inflammation within osteolytic bone tissues in PIO animal models. We examined the histopathologic changes of osteolysis and the expression of ER stress-related apoptotic markers (Ca²⁺, IRE1-α, PERK, GRP78/Bip, CHOP, JNK and Caspase-12) and inflammatory markers (TNF-α, IL-1β, and IL-6; ROS and Ca²⁺; NF-κB and c-Fos), and analyzed apoptosis and apoptotic regulators (Bcl-2 and Bax) within the osteolytic bone tissues. Our results demonstrated that wear particles were able to induce ER stress, and were associated with the inflammation and apoptosis of osteoblasts in vivo and vitro. Blocking ER stress with 4-PBA dramatically decreased particle-induced osteolysis symptoms, lessened the infiltration of inflammatory cells, reduced the inflammatory response, diminished the capability of osteoclastogenesis, and promoted the differentiation of osteoblasts. However, the ER stress blocker unexpectedly aggravated cell death of osteoblasts, which was of vital importance to the osteosynthesis of the ostotytic and absorptive bone. Given that the ER chaperone conforms to the definition of true moonlighting proteins with two quite distinct roles in nucleus and cell surface, making modulators of ER potentially attractive targets for therapeutics discovery. Thus, a better understanding of the mechanisms that orchestrate the ER may help to devise future strategies of safely modulating this process for therapeutic benefit.
Biography

Guoyin Liu has completed his Master’s degree from Medical School of Nanjing University. He is the Orthopedic Surgeon of Bayi Hospital Affiliated to Nanjing University of Chinese Medicine. He is also the Secretary and Research Director of Orthopaedics Department. He worked mainly on the immunization therapy and the signaling pathways of apoptosis and inflammation, and has published 2 papers in reputed journals.
**Genomics Testing and its Applications in Personalized Pediatric Services (mtDNA)**

Anastasiia Voronkova  
*Sechenov University, Moscow, Russia*

**Abstract**

The confirmation or exclusion of mitochondrial diseases remains a challenge in clinical practice, especially for pediatric cases, which show enormous variation in clinical presentations. Demonstrative example are infant myopathies. Different manifestations of congenital myopathy may mask mtDNA alterations. Of times mitochondrial disorders are not suspected and manifest unexpectedly. In this regard, molecular mtDNA testing is getting increasingly important as a stage of diagnostics. In the speech, the results of mitochondrial DNA sequencing in the group of unrelated patients with mitochondrial encephalomyopathy diagnosed are presented. Significance of individual genetic particularities is evaluated through example of several patients with different ethnical background. In spite of not revealing confirmed pathogenic variants, we found several individual particularities of mitochondrial DNA, which may have clinical significance, in each patient. Through these examples modern approaches of personalized diagnostics are considered. In addition, robust relationship between laboratory and post-laboratory methodics in molecular genetic analysis are demonstrated.

**Biography**

Anastasia S. Voronkova graduated faculty of Biology of Lomonosov Moscow State University in 2013. Thereafter she worked in the field of basic and clinical genomics and transcriptomics. Scientific interests: molecular genetics, molecular physiology, physiology of energy deficiency, hereditary disorders, mitochondrial disorders, gene networks, gene expression dynamics.

**AFM of Tissue Sections is a Useful Complementary Tool as a Biomedical Marker**

Peter Timashev, Svetlana L. Kotova  
*Sechenov University, Moscow, Russia*

**Abstract**

The aim of the study was to demonstrate a good diagnostic potential of atomic force microscopy (AFM) in tracking morphological changes in the extracellular matrix (ECM) of connective tissue due to pathological processes. Here we summarize our experience in AFM application in a number of biomedical studies on the connective tissue disease, both for research and clinical purposes. AFM has been shown to reveal visible deviations from the normal morphology of the extracellular matrix in diseased tissues. We found that AFM and related techniques are capable of tracking disease-related changes at different levels of collagen organization in the ECM. AFM may also monitor a ratio between collagen and non-fibrous material of the ECM, for example, in inflammatory and neoplastic processes. The FNS parameters provide quantification of the morphological changes visualized by AFM. The PeakForce QNM and nanoindentation studies give a further insight into the state of ECM via tracking changes in the local mechanical and adhesive properties. All our AFM studies appeared in a good agreement with the histological findings and generally had a superior sensitivity to the ECM pathological changes. AFM may serve as a valuable complementary diagnostic tool for tracking pathological changes in the connective tissue.

**Biography**

Peter Timashev is the Deputy Director of Institute for Regenerative Medicine, Sechenov University. His work covers the development of biodegradable and biocompatible materials for laser additive technologies. His studies, which discuss the 2PP formation of 3D scaffolds inducing the osteogenic differentiation of stem cells, their mechanical and surface features, and in vivo fluorescent imaging of their degradation rates, underlie the development of laser-induced structure formation for tissue engineering. Moreover, his research team optimized approaches to 2PP structuring polysaccharide and protein hydrogel systems for soft tissue restoration. For these 3D matrices, Peter Timashev et al. developed non-destructive procedures of their surface and mechanical modification that increased cell compatibility.
Novel Microengineered Environments for Mouse Embryonic Stem Cell (mESC) Differentiation towards Cardiomyocytes

Natalia Bakhtina
Karlsruhe Institute for Technology (KIT), Institute of Microstructure Technology (IMT), Germany

Abstract

Cardiomyocytes (CMs) are the contractile cells of the heart. Their regenerative capacity is lost after birth. Embryonic stem cells (ESCs) are able to differentiate into functional CMs, however this process is not yet efficient. The elucidation of ESCs’ differentiation into CMs could provide an additional avenue for therapeutic interventions and disease modeling. This interdisciplinary project will result in a unique platform that targets precise quantification of the fundamental molecular mechanisms underlying mouse ESC cardiac differentiation at the single cell level. The platform takes the advantages of 3D tailored conductive microscaffolds (3DTCMSs) to deliver precise mechanical and electrical stimulation patterns to individual cells in vitro. Co-integrated 3DTCMSs have the necessary infrastructure for long-term cell culturing. The platform is accessible for in situ high-resolution, real-time microscopic observation of essential molecular information due to transparent materials. Advanced two photon polymerization photolithography will be utilized for the exact reconstruction of 3DTCMSs based on a novel optically transparent, conductive ionic liquid-polymer composite. ESC pluripotent factors and CM markers will be monitored comparatively by live microscopy and molecular analysis. This project aims to integrate expertise in materials science, engineering, cellular and molecular biology. As a result, a novel in vitro CM differentiation model will be developed, which has a potential to open a completely new window of research in systems biology.

Biography

Natalia Bakhtina received her diploma in electrical engineering at the department of advanced technologies of radio-electronics, Russian State Technological University named after K.E. Tsiolkovsky (MATI), Moscow, Russia in 2009. In 2011 she received her MSc degree in microsystems engineering from the Hochschule Furtwangen University of Applied Sciences, Germany. Since 2012, she is a PhD candidate at the Department of Microsystems Engineering (IMTEK), University of Freiburg, focusing on the detection and immobilization of C. elegans.

Nanofiltration of Extracellular Vesicles from Human Plasma & Their On-Chip Qualification and Quantification with a NanoBioAnalytical Platform

Obeid Sameh1, Benoit Le Roy de Boiseaumarie1, Celine Elie-Caille1, Wilfrid Boireau1, Ming Li Chou2, Thierry Burnouf2,3, Pei-Shan Sung4, Shie-Liang Hsieh4,5,6
1Institut FEMTO-ST, Univ. Bourgogne Franche Comté, CNRS, France
2Graduate Institute of Biomedical Material and Tissue Engineering College of Biomedical Engineering, Taipei Medical University, Taiwan
3International PhD Program in Biomedical Engineering, College of Biomedical Engineering, Taipei Medical University, Taiwan
4Institute of Clinical Medicine, National Yang Ming University, Taipei, Taiwan
5Genomic Research Center, Academia Sinica, Taiwan
6Department of Medical Research, Taipei Veterans General Hospital, Taiwan

Abstract

One complication of plasma transfusion is non-immune transfusion related acute lung injury (TRALI), which is associated with the formation of neutrophil extracellular traps (NETs) resulting from polymorphonuclear neutrophil (PMN) activation.

Activated platelets have recently been shown to trigger NETs formation. We hypothesized that (a) NETs could be promoted by platelet derived microparticles (PMPs) and (b) that 75 nm-nanofiltration of plasma, by removing parts of PMPs, could avoid NETs formation. To better characterize the large spectrum of size and concentration of PMPs in complex media, we combined conventional approaches (Flow Cytometry, TRPS) with an original nanobioanalytical (NBA) platform based on Surface Plasmon Resonance imaging (SPRi) and Atomic Force Microscopy (AFM) techniques. We will demonstrate that this new analytic solution allows:

• a label-free follow-up of PMPs capture in real time from various complex media,
• a multiplex detection of different PMPs subpopulations,
• the determination of the size and morphology of captured PMPs in a range of 20nm to 1µm their proteomic studies.
We expect that such platform will contribute to (i) a better understanding of the physiological function of Evs subpopulations, (ii) the discovery of specific biomarkers and (iii) to therapeutic follow-up.

**Biography**

Wilfrid Boireau obtained his PhD degree in enzymatic engineering from the University of Technology of Compiègne (UTC, France) in 1999. After a post-doctoral position in the Center of Molecular Genetics (CGM, Gif/Yvette, France) in 2000-2001, he joined the CNRS as a permanent researcher in 2001 in a laboratory of Physics (LPMO) at Besançon, France. In 2004, at the creation of the FEMTO-ST institute (UMR6174 CNRS), he was responsible for a transversal project called “microtechniques for proteomic” at the University of Franche-Comté involving physicists and biochemists. In 2008, he co-founded the “Clinical - Innovation Proteomic Platform” (CLIPP), a platform devoted to clinical proteomics between UFC and University of Burgundy.

In 2012, he became responsible of the Multiphysics Microsystems team (MIMU team), one of the three teams of the Micro Nano Sciences & Systems department (MN2S) of FEMTO-ST Institute. In 2015, he became Director of MN2S department and initiated a thematic restructuration that led to the creation of BioMicroDevices Group, a multidisciplinary team of researches involving biochemists, nanobioscientists, physicists and micro/nano technologists. His current researches are based at the interface of bio-engineering, microtechnologies and nanostructured materials for the development of biochips integrated in sensors and analytical platforms for clinical proteomics and diagnosis. Since 2012, he focuses his researches onto nano-biological-particles (virus like particles and extracellular vesicles) and their qualification and quantification in complex biological media.

He co-authored about 54 publications (1062 citations; H Index = 15 in WoS) and of 4 patents since 1998, Dr. Wilfrid Boireau has also presented, during the last decade, around 125 communications in national and international conferences and has been awarded three times for outstanding poster presentation.

**Autologous Cardiac Progenitor Transplantation for Myocardial Repair: A Step Towards Personalized Medicine**

Hendriks M, Jamaer L, Dubois J, Declercq J, Daniels A, Bijnen E, Heuts N, Hendriks F, Bito V, Rummens J-L

*University of Hasselt, Belgium*

**Abstract**

Traditionally the heart is considered a terminally differentiated organ. However, at the beginning of this century increased mitotic activity was reported in ischemic and idiopathic dilated cardiomyopathy hearts, compared to healthy controls, underscoring the potential of regeneration after injury. Due to the presence of adult stem cells in bone marrow and their purported ability to differentiate into other cell lineages, this cell population was soon estimated to be the most suited candidate for cardiac regeneration. Clinical trials with autologous bone marrow-derived mononuclear cells, using either an intracoronary or direct intramyocardial injection approach consistently showed only minor improvement in global left ventricular ejection fraction. This was explained by their limited cardiomyogenic differentiation potential. To obtain more convincing improvement in cardiac function, based on true myocardial regeneration, the focus of research has shifted towards resident cardiac progenitor cells. Several isolation procedures have been described: the c-kit surface marker was the first to be used, however experimental research has clearly shown that c-kit+ cells only marginally contribute to regeneration post myocardial infarction. Sphere formation was used to isolate the so-called cardiosphere derived cells (CDC), and also in this cell population cardiomyogenic differentiation is a rare event. Recently a new type of stem cells derived from atrial tissue (cardiac atrial stem cells – CASCs) was identified, based on the presence of the enzyme aldehyde dehydrogenase (ALDH). Those cells significantly improve both regional and global LV ejection fraction, based on substantial engraftment and consistent differentiation into mature cardiomyocytes (98%).
Myocardial Repair with Customized Exosomes: Stimulation of Proliferation and Cardiomyogenic Differentiation of Cardiac-Committed Transient Amplifying Cells

Galina Belostotskaya*, Michael Galagudsa1, Sergey Suchkov3
1Institute of Evolutionary Physiology & Biochemistry, RAS, Russia
2Almazov’s National Medical Research Centre, Russia
3Sechenov University & National Research Nuclear University MEPhI, Alliance of Translational Medicine, Russia

Abstract

A completely sensible idea of stimulating regenerative cardiomyogenesis with exosomes is complicated by the lack of a clear understanding of which adult myocardial cells are in principle capable of forming new cardiomyocytes. The existing disagreements not only divide scientists into 2 camps, some of whom prefer cardiac stem cells (CSCs), while others insist on the division of pre-existing cardiomyocytes (CMs), but, more importantly, do not allow the development of adequate tactics effects on the regeneration of damaged myocardium. In this regard, our data on the intracellular development of CSCs in CMs with the formation of “cell-in-cell structures” (CICSs), followed by the division of CSCs and their partial cardiomyogenic differentiation, leading to the formation of the transitory amplifying cells (TACs) pool. It is shown that the imitation of ischemia in vitro (hypoxia, acidosis) resulted in a 5-10-fold increase in the number of CICSs, and permanent myocardial ischemia in adult SPF rats showed a 1.5-fold increase in the number of CICSs in the infarction zone compared to the control 2 weeks after coronary occlusion. This data allowed suggest that inflammation in the infarction zone causes resident CSCs to intrude into the surviving CMs by temporarily shutting them out of the regeneration process, but the subsequent CICSs rupture and the release of a significant number (~ 200) of TACs that are capable of proliferation and cardiac differentiation put them on the first plan as candidates for therapeutic effects on cardiomyogenesis in the ischemic heart.

Biography

Galina Belostotskaya graduated from Leningrad State University in 1970 and defended her thesis in 1984 on a specialty “Radiobiology”. Now she is working in Sechenov Institute of Evolutionary Physiology and Biochemistry of the Russian academy of sciences as the Head of Cytoanalysis centre. In recent years, she has been studying the resident muscle stem cells and published more than 15 papers in Russian Journals and several articles in “Cell Cycle” (2014, 2015), Bioelectromagnetics (2014), Carbohydrate Polymers (2015). Being the head of investigations she released 7 specialists and 2 graduate students. The works have been supported by the 11 Russian grants.

Infectious Biomarkers in Autoimmune Diseases - Importance in Personalised Medicine

John M. Aitken
Otakaro Pathways Ltd, New Zealand

Abstract

There is increasing evidence that bacteria may play important roles in the triggering of emerging diseases, including in autoimmune disease, attention deficit disorder (ADD), control of gut diseases, and depression.

Bacterial presence in a susceptible host can be an important biomarker. In TB the presence of Mycobacterium tuberculosis is diagnostic of TB infection. With other members of the Mycobacterium species however, passive carriage or commensal colonisation may be ongoing and have no role in infection of the host.

Atypical mycobacteria may be present in the normal individual and pose no risk, but the same organism may cause significant infections in the immune compromised host, in the elderly, and in children. Recent research into emerging infectious diseases suggests that over the last 40 years mycobacteria have evolved to exhibit novel biological mechanisms to avoid detection by the host and become “stealth pathogens”. The immune status of the host and the virulence of the infecting organism are therefore important considerations in diagnosing infectious diseases, and are challenges for the clinical laboratory. Close communication between the clinician and the medical laboratory staff are important requirements to ensure an optimal clinical response to complex interactions between bacteria and the host.

Biography

John Aitken is a medical laboratory scientist who has worked in medical laboratories in the community and in tertiary institutions for over 40 years. He is Chief Scientist for Otakaro Pathways Ltd, a private company that carries out research on novel probiotics, and organisms producing new antimicrobial compounds. Otakaro Pathways also researches the role of mycobacteria in Crohn’s disease and has developed tests able to monitor mycobacterial presence in the peripheral blood. The company holds intellectual property in these areas.
First Impressions of Two New Brilliant Biomarkers for Pompe Disease (LSD) in Plasma and Urine in Comparison to Hex4 and Glc4 in Urine

Hermann Mascher*, Benedikt Schoser, Stephan Wenneninger
pharm-analyt Labor GmbH, Austria

Abstract

Pompe disease is a glycogen storage disease type II with acid-α-glucosidase (acid maltase) deficiency. People affected with this disease are unable to degrade glycogen stored in the lysosome and this leading to the accumulation of glycogen in lysosomal storage vacuoles. The incidence is approximately 1 to 40,000 live births. The diagnosis is really a challenge because there is almost no biomarker for determination of the intensity and the future development of symptoms (phenotype). Only Hex4 or more in detail Glc4, a four sugar unit in urine, can give some hints: Sometimes Hex4 or Glc4 are useful markers, sometimes they have very unclear levels. Our search for biomarkers in Pompe disease started about four years ago and different attempts had no outcome.

A very intensive check in plasma with HPLC-MS (Orbitrap) and also with HPLC-ELSD (especially fitting for sugars) showed encouraging results. With that knowledge we checked in a preliminary search plasma and urine samples of 19 Pompe patients in comparison to 10 healthy people. The outcome were two brilliant biomarkers fitting for plasma/serum but also for urine. Now these biomarkers will be applied systematically to further samples.

A comparison with the until now “best biomarkers for Pompe” (Hex4 and Glc4 in urine) will be presented.

Biography

Hermann Mascher is the founder and bioanalytical consultant of pharm-analyt Labor GmbH, has more than 100 publications in peer reviewed journals (more than 230 impact factor) including two books by Wiley – VCH e.g. HPLC Methods for Clinical Pharmaceutical Analysis. He is the inventor of 3 patents for biomarkers in the area of rare lysosomal storage diseases (Gaucher, NPC, MLD). pharm-analyt is over 30 years old and known as a highly scientific CRO for bioanalytical services and as a research provider. He got different innovation awards and is cited in the “Who’sWho in the World” since 2002.

Association of ACE Gene I/D Polymorphism with Susceptibility to Osteoarthritis

Banu Bayram
Department of Medical Biology, Medicine Faculty, Muğla Sıtkı Koçman University, Turkey

Abstract

Osteoarthritis (OA) is the major chronic disease leading to musculoskeletal morbidity and functional loss, but is of unknown cause. It is generally agreed that the cause is multifactorial, involving genetic predetermination, age, gender, acute and chronic joint trauma, metabolic and inflammatory mechanisms and dietary factors. Current therapeutic approaches for OA are limited and are insufficient to prevent the initiation and progression of the disease. Genetic studies of patients with OA can help to unravel the molecular mechanisms responsible for specific disease manifestations, including joint damage, nociception and chronic pain. Angiotensin converting enzyme (ACE) is a metalloenzyme converts angiotensin I to a potent vasoconstrictor angiotensin II. It also inactivates bradykinin which is a vasodilator of the kallikrein kinin system and has major implication in inflammatory process including OA. Recent evidence indicates that genetic polymorphisms of distinct genes within the general population are responsible for the susceptibility to many of the major chronic diseases. ACE gene (Gene Bank accession number: NM 000789.2) is localized on chromosome 17 and contains a polymorphism based on the presence (insertion, I) or absence (deletion, D) within intron 16, of a 287 base pair ALU repeat sequence; resulting in 3 genotypes: DD and II homozygotes and ID heterozygote. DD genotype is associated with higher concentrations of circulating ACE. However, as gene pools, life style, and gene-environment interactions vary between the populations, the risk shall not be supposed as identical in every population with respect to genotypes. Therefore, the differences will be manifested in the genetic relationship of ACE gene I/D polymorphism genotypes with OA. As a result of a review study, the association of ACE gene I/D polymorphism with susceptibility to OA from the various populations will be presented and discussed.
Biography

Banu Bayram is particularly specialized on genetic polymorphisms and disease susceptibility, received her PhD degree from Eskişehir Osmangazi, University Medical Faculty, Department of Medical Biology, 2007 and MSc degree from Eskişehir Osmangazi, University Medical Faculty, Department of Medical Biology, 2004 and BSc degree from Gazi University, Science Faculty Department of Biology, 2001. She is an Associate Professor since 2012 at Muğla Şitki Koçman University. She has published nearly 25 scientific papers, as well as 20 presentations and posters, and has nearly 100 citations. She serves as editor in chief for Meta Gene and associate editor for Gene Elsevier.

Innovations in Molecular Biology and Proteomics Adapted to in vivo Peptide Phage Display

Define Active Protein Domains as Biomarkers in Multiple Sclerosis Neuroinflammation

Klaus G. Petry¹, Antonios Vekris¹, Eleftherios Pilalis², Aristotelis Chatziioannou²

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²National Hellenic Research Foundation, Institute of Biology, Medicinal Chemistry and Biotechnology, Greece

Abstract

With the double goal to streamline biomarker discovery of Multiple Sclerosis neuroinflammatory pathology entangled by non-affected Central Nervous System tissue and to better characterize the complex molecular interactions at the altered blood brain barrier (BBB) that becomes permissive to extravasation of blood derived immune cells and compounds, we choose to identify peptide ligands reacting with inflammatory CNS lesions. With no “a-priori” for targets by applying in vivo the phage displayed 12aa peptide screening in CNS neuroinflammation of the experimental autoimmune encephalomyelitis (EAE) rat model of MS and healthy controls, we generated two complex phage displayed peptide repertoires. By developing molecular DNA subtraction of both phage repertoires we generated a subtraction phage repertoire of EAE specific peptides. In a bioinformatics approach aligning the 270612 EAE peptides to the human proteome the formed peptide clusters allowed the ranking of proteins being potential “mimicked” indicators of functional protein interactions. Experimentally, among the most high score mimicked proteins, derived synthesized short peptides (22aa) of mimicked domains were tested for labeling of BBB alterations in CNS sections of MS and other chronic neurodegenerative diseases. In vitro studies using the BBB model hCMEC/D3 confirmed their binding to human endothelial cells under proinflammatory stimulation. Finally, with a derived peptide covalently linked to a nanocarrier contrast agent, we could target in vivo and monitor by MRI, experimentally induced inflammatory CNS lesions. Our strategy of combining the developed molecular biology and bioinformatics approaches adapted to phage display is applicable to many disease models to identify biomarkers and functional proteins/domains.

Biography

Klaus Gunter Petry finished her PhD in Immunoparasitology at Bernhard Nocht Institute for Tropical Medicine, University Hamburg/Germany (1986). Post-doc work at Fred Hutchinson Cancer Research Center Seattle/USA on Characterization of molecular mimicry as active autoimmune mechanism in Chagas’ disease infection. Since 1990 she is Full Research Member and Director/ Head of Department at INSERM (French National Institute for Bio-Medical Research) in Bordeaux. Her research topics include Multiple sclerosis neuroinflammation biomarker discovery; Methodological innovations to monitor in vivo molecular and cellular processes in MS including MRI of macrophage activity with nanoparticles and defining strategies for drug delivery into the CNS.

Conjunction of the Molecular, Cytogenetic and Genetic Biomarkers as Predictor of Vulnerability to Medical Radiation Treatment

Antonina Cebulska-Wasilewska

Radiation and Environmental Biology Department, The H. Niewodniczański Institute of Nuclear Physics PAN, Krakow, Poland
Central Laboratory for Radiological Protection, Warsaw, Poland
5th Military Hospital & Public Polyclinic, Krakow, Poland

Abstract

In previously reported studies of healthy controls, prostate cancer patients, and thyroid disease patients, exposed diagnostically to I-131, voluntarily obtained blood samples, or isolated lymphocytes were exposed in vitro to high challenging dose of X-rays. Before and right after in vitro irradiation; the DNA Repair Competence Assay and cytogenetic methods were applied. Strong variability between individual vulnerability to radiation was reported. For this investigation, using PCR
method the XRCC1(194) and XRCC1(399), that are engaged in base excision and DNA single strand breaks repair, and XRCC3(241) involved in DNA double strand breaks repair via homologous recombination, were investigated in randomly chosen samples from 60 subjects. Results of investigated biomarkers stratified according conjunction of polymorphic alleles have shown insignificant variability between all subjects in the DNA sensitivity to irradiation, detected immediately after challenging exposure in 4°C. In contrast, high differences are observed between subgroups stratified according conjunction of polymorphic alleles of investigated genes, in levels of biomarkers related to DNA repair (DNA RCA and percentage of cells with significantly elevated number of sister chromatid exchanges) as well as biomarkers of cancer risk. One of the highest percentage of not repaired DNA damage evaluated by the DNARCA, and frequency of chromosome aberration, were detected in lymphocytes of prostate cancer patient with homozygous genotype at XRCC3-241/C and XRCC1-194/C, and heterozygous at XRCC1-399A/G locus. Obtained results confirm strong influence of genotypes on the repair efficiency of DNA damage induced by irradiation and levels of biomarkers that are predictor of cancer risk.

Biography

Antonina Cebulska-Wasilewska, was born in Nowy Sacz, in Poland. She graduated from Jagiellonian University (JU), Krakow in 1974-Ph.D in Chemistry. From 1981/1982 she was a Research Fellow of International Agricultural Centre and International Atomic Energy Agency (IAEA) for radiobiology research at Institute ITAL, Wageningen, The Netherlands. In 1986-1990 she was WHO expert in IPCS program. She pursued a course in Radiobiological Basis of Modern Radiotherapy Innovations, Gray Laboratory CRC, UK.

Leader in more 15 national research programs and Author and co-author in more than 250 articles, for 38 years she head the Radiation and Environmental Department at IFJ, Krakow. In 2002&2009 she was as the Director of NATO ARW & A.Hollaender Courses “Human Monitoring of Genetic Effects”. Since 1992 until now she was elected as Council Member of The Maria Skłodowska-Curie Polish Radiation Research Society and IARR. From 2011 until now she is serving as the President of ICRR Congress. Member of International Advisory Board in Korean Journal of Radiation Biology. At present she is Professor Emeritus of Polish Academy of Sciences from IFJ, Krakow.

Serum Level of HMGB1 Indicates Outcome of the Treatment of Tumor Bearing Animals with Antineoplastic Drug NSC631570

Larysa Skivka1*, Mariia Rudyk1, Ievgeniia Hurmach1, Kateryna Stepura1, Niccola Funel2, Ascold Nowicky3, Wassil Nowicky3

1Taras Shevchenko National University of Kyiv, Ukraine
2University of Pisa, Italy
3Ukrainian Anticancer Institute, Austria

Abstract

Background: HMGB1 plays an important role in DNA architecture and transcriptional regulation in all nucleated cells. This protein is released by tumor cells during cellular necrosis and late apoptosis after the treatment with chemotherapeutic agents and acts as a danger associated molecular pattern (DAMP, endogenous alarmin) stimulating immune responses to pathogenic cell death products. Antineoplastic drug NSC631570 induces immunogenic tumor cell death in vitro that is accompanied by the release of HMGB1. This study was aimed at assessing the association of serum level of HMGB1 in tumor-bearing mice with the outcome of the treatment with NSC631570.

Methods: Ehrlich's carcinoma calls as well as two B16 melanoma sublines with different metastatic potentials were used. For in vivo experiments tumor cells were inoculated into Balb/c and C57BL/6 mice correspondingly. The anticancer effect of NSC631570 was characterized by the growth inhibition index. Cell cycle, apoptosis and necrosis were assessed by flow cytometry. The levels of HMGB1 in cell culture medium and in animal serum were determined by ELISA.

Results: Treatment of all mentioned tumor cells with NSC631570 at apoptogenic concentrations induced cell death coupled with dose-dependent HMGB1 release in vitro. The treatment of tumor-bearing mice with NSC631570 was also accompanied by the strong release of HMGB1 in the serum. Therapeutic efficacy of the drug was more pronounced in the case of B16, and was associated with the highest level of this alarmin in animal serum.

Conclusion: Serum level of HMGB1 can be considered as a biomarker of the outcome of the treatment with NSC631570.

Biography

Larysa Skivka has completed her PhD at the age of 28 years from R.E. Kavetsky Institute of Experimental Pathology,
PITX2 DNA-methylation as the First Clinically Validated Predictive Marker for Anthracycline-Based Chemotherapy in High-Risk Breast Cancer Patients

Manfred Schmitt¹, Olaf G. Wilhelm¹*, Rudolf Napieralski¹, Gabriele Schricker¹, Marion Kiechle²

¹Therawis Diagnostics GmbH, Germany
²Department. Ob&Gyn, Technical University of Munich, Germany

Abstract

International guidelines recommend anthracycline-based chemotherapy for high-risk breast cancer patients as the standard-of-care, but not all patients do equally benefit from such a chemotherapy. The novel therascreen® PITX2 RGQ PCR assay is a quantitative in vitro methylation-specific real-time PCR test (qMSP), intended for the determination of the percent methylation ratio (PMR) in the pituitary homeobox 2 (PITX2) promoter 2 expressed by primary breast cancer tumor tissue (FFPE-material). After bisulfite exposure of extracted DNA to distinguish between methylated and unmethylated PITX2 DNA, the percent methylation ratio (PMR) of the PITX2 gene promoter 2 is quantified by qMSP. The PMR obtained does provide information to the treating physician about whether a patient is likely to respond to anthracycline-based chemotherapy. Data will be presented for 205 high-risk lymph node-positive, estrogen receptor-positive, HER2-negative breast cancer patients, treated with adjuvant anthracycline-based chemotherapy. The PITX2 pre-defined cut-off value of PMR = 12 demonstrated a statistically significant differentiation between low- and high-risk breast cancer patient for the primary endpoint DFS, also for patients treated with endocrine therapy in addition to anthracycline-based adjuvant therapy. High-risk lymph node-positive, estrogen-receptor-positive, HER2-negative breast cancer patients, with PITX2 methylation defined as low (PMR≤12), are sufficiently treated with anthracycline-based chemotherapy, irrespective if treated with additional tamoxifen. High-risk lymph node-positive, estrogen receptor-positive, HER2-negative breast cancer patients with PITX2 methylation defined as high (PMR>12) should avoid anthracycline-based chemotherapy. These patients are recommended to switch to other chemotherapy regimens, since with this PITX2-characteristics, the patient has a lower probability to respond to anthracycline-based chemotherapy.

Biography

Olaf G. Wilhelm is founder and Chief Executive Officer of Therawis Pharma GmbH, Munich. He also was co-founder of Wilex Biotechnology GmbH and its Managing Director from October 1, 1997 until April 8, 2001, and has been Chief Executive Officer of WILEX AG since April 9, 2001 since the conversion of the company into a stock market corporation (Wilex AG). Prof. Wilhelm managed two company acquisitions, several international development and commercialization partnerships and listed Wilex AG on the public stock Exchange. In the year 2001, he was appointed Extraordinary Professor of Gynecology at the Technical University of Munich. From 1990 to 1997, he was employed as senior physician for Obstetrics and Gynecological Oncology at the Department of Obstetrics & Gynecology (Frauenklinik) at the Medical School of the university hospital (Klinikum rechts der Isar des Klinikums rechts der Isar) at the Technical University of Munich. While at the Technical University of Munich, he was also a member of the Clinical Research Unit of the Frauenklinik. From 1987 to 1990, he worked as a scientist for Eli Lilly and Company, Indianapolis, Indiana/USA. He received the Midwest Trainee Award of the American Federation for Clinical Research and has authored over 70 publications. He received his MD from the Technical University of Munich. He is a member of the senate of the “Bundeswirtschaftssenat des Bundesverbandes mittelständische Wirtschaft Deutschland e.V.” In 2011, the Technical University of Munich awarded him the title “TUM Entrepreneur of Excellence”.

Oncology and Radiobiology, NAS, Ukraine and postdoctoral studies from Taras Shevchenko National University of Kyiv. Currently she is a professor of the Educational and Scientific Centre “Institute of Biology and Medicine” of Taras Shevchenko National University of Kyiv (Ukraine) and head of the Department of Microbiology and Immunology. Her area of scientific activity include immunomodulation as a component of adjuvant cancer therapy, metabolic polarization of phagocytes in the pathogenesis of inflammatory diseases.
Whole Transcriptome Analysis for Identification of Exercise-Related Markers in Thoroughbred Racing Horse

Byung Wook Cho*, Jeong-Woong Park, Jae-Young Choi, Hyo Gun Lee, Jin Hyeog Oh
Department of Animal Science, College of Nature Resources and Life Science, Pusan National University, Korea

Abstract
Thoroughbred is the main horse breed in the horse racing industry. The horses which record excellent performance are valuable in the aspects of economics and industry. Because of the limitation of the conventional breeding methods, it is needed to develop a reliable system for the selection of stallion stud based on molecular breeding. Therefore we conducted high throughput analysis to discover exercise-related single nucleotide variations (SNVs) and differentially expressed genes (DEGs). We sequenced the whole mRNA from the blood and muscle tissues of six thoroughbred horses before and after exercise. By comparing current horse genome annotation, we identified 32,361 unigene clusters and 189,973 SNVs from the sequence aligned against the horse reference genome. We also identified genes regulated by exercise: 62 up-regulated and 80 down-regulated genes in the blood, and 878 up-regulated and 285 down-regulated genes in the muscle, respectively. In addition to DEGs, we also found differentially expressed alternative splicing forms of AXL, DYNC1, PLEKHG1, and COBLL1 before and after exercise. Overall, our results indicated that exercise stress induces massive gene expression change. Further studies should be focused on the mechanism of exercise-induced change and their relation in excellent performance in racing horses. Our data would be valuable information to develop exercise-related markers in horses and ultimately applied to establish a reliable selection system for producing a better stallion.

Biography
Byung-Wook Cho is the professor in Animal genetics at the Department of animal science of the Pusan National University (PNU) in Korea. He completed a PhD in animal genetic engineering at the Seoul National University (SNU). His research examines the effects of the exercise-related stresses on the muscle in horse. Especially he dedicated his efforts to the development of genetic breeding techniques for Korean domestic horses by comprehensive omics studies and comparative and functional analysis of genes related to the exercise.

Carbohydrate-Based Electrochemical Biosensors for Detection of a Cancer Biomarker in Human Plasma

Laurent Salmon*, Marion Devillers, Lama Ahmad, Hafsia Korri-Youssoufi
Institute of Molecular Chemistry and Materials of Orsay, University of Paris-Saclay, University of Paris-Sud, France

Abstract
Autocrine motility factor (AMF) is a tumor-secreted cytokine that stimulates tumor cell motility in vitro and metastasis in vivo. AMF could be detected in serum or urine of cancer patients with worse prognosis. Reported as a cancer biomarker, AMF secretion into body fluids might be closely related to metastases formation. A first sensitive and specific carbohydrate-based electrochemical biosensor was designed for the detection and quantification of a protein model of AMF, namely phosphoglucose isomerase from rabbit muscle (RmPGI). Indeed, RmPGI displays high homology with AMF and has been shown to have AMF activity. The biosensor was constructed by covalent binding of the enzyme substrate D-fructose 6-phosphate (F6P). Immobilization was achieved on a gold surface electrode following a bottom-up approach through an aminated surface obtained by electrochemical grafting of ethylene diamine and terminal amine polyethylene glycol chain to prevent non-specific interactions. Carbohydrate-protein interactions were quantified in a range of 10 fM to 100 nM. Complex formation was analyzed through monitoring of the redox couple Fe2+/Fe3+ by electrochemical impedance spectroscopy and square wave voltammetry. The F6P-biosensor demonstrates a detection limit of 6.6 fM and high selectivity when compared to other non-specific carbohydrate proteins such as D-glucose-6-phosphate dehydrogenase. Detection of protein in spiked plasma was demonstrated and accuracy of 95% is obtained compared to result obtained in PBS (phosphate buffered saline). A second carbohydrate-based electrochemical biosensor using an enzyme inhibitor as bioreceptor was recently created and evaluated on overexpressed human AMF.

Biography
Laurent Salmon, aged 53, has been working in bioorganic chemistry at the University of Paris-Sud as an Assistant Professor since 1991, and as Full Professor since 2012, in Orsay (France). Several collaborative national and international research projects were initiated and managed by the author led to recognized results by the scientific community, particularly within the area of aldose-ketose isomerases. As a known specialist of enzyme inhibition by phosphosugar and surrogates, Laurent Salmon is the author of 40 publications on the subject, as well as co-author of the deposition of about 20 crystal structures of enzyme–inhibitor complexes.
Serum Free Bilirubin is a Potential Biomarker of Endogenous Antioxidant Capacity of Human Vascular Endothelium

Sabina Passamonti1*, Lovro Ziberna2, Mitja Martelanc3, Mladen Franko1
1University of Trieste, Department of Life Sciences, Italy
2University of Ljubljana, Faculty of Medicine, Institute of Pharmacology and Experimental Toxicology, Slovenia
3University of Nova Gorica, The Laboratory for Environmental Research, Slovenia

Abstract

Bilirubin is a potent endogenous antioxidant with anti-inflammatory and anti-thrombotic effects. It is also in a negative correlation with the risk of cardiovascular disease, such as ischemic heart disease, hypertension, type II diabetes, metabolic syndrome and obesity. In our study, we first proved that bilirubin is not only in the serum, but also endogenously present in the endothelial cells of the vessels, which are crucial in maintaining the normal vascular function. With the development of new HPLC-Thermal Lens Spectroscopy analysis methods, we could quantitatively determine the low levels of bilirubin in endothelial cells. We found that intracellular contents of bilirubin can be increased by induction of genes for its synthesis (evidence that bilirubin is endogenous in endothelium) and/or if the content of bilirubin in the extracellular medium is increased. The intracellular antioxidative ability of bilirubin (EC50 = 11 nM) was also determined, which is in the concentration range of measured free bilirubin in serum (10-15 nM). This means that extracellular and intracellular free bilirubin concentrations are in dynamic equilibrium, providing an accessible biomarker for the assessment of the endothelial oxidative stress status.

Biography

Sabina Passamonti is a biochemist at the University of Trieste. She is the principal investigator of the Laboratory of Molecular Nutrition of the Department of Life Sciences. She studies membrane transport of dietary flavonoids, with special focus of the pigments found in red fruits and wines, i.e. anthocyanins. This study goes in parallel with the investigation of bilirubin transport into cells.

Antibody-Proteases as Highly Informative Biomarkers and Efficient Targets of the Newest Generation

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1Sechenov University, Russia
2Moscow Engineering Physical Institute (MEPhI), Russia
3A.I.Evdokimov Moscow State University of Medicine & Dentistry, Russia
4EPMA, Brussels, EU
5PMC, Washington, DC, USA
6ISPM, Tokyo, Japan
7Center for Autoimmunity Research, John Hopkins University, USA
8Harvard Medical School, MA, USA
9M.M.Shemyakin and Yu.A.Ovchinnikov Institute of Bioorganic Chemistry, Moscow, Russia
10Moscow State University, Russia
11UAB, Birmingham, ALA, USA

Abstract

Introduction and Purpose: Among the translational biomarkers, antibodies (Abs) are the best ones and thus key mediators of inflammatory responses to generate the events. Abs against myelin basic protein/MBP endowing with proteolytic activity (Ab-proteases) are to monitor demyelination at either of the stages. Ab-proteases were found in bronchial asthma (BA), hemophilia; autoimmune myocarditis (AIM) and antithyroid autoAbs.

Outcome: Anti-MBP autoAbs from MS patients and mice with EAE exhibited specific proteolytic cleavage of MBP. The activity of the latter markedly differs between: (i) MS patients and healthy controls; (ii) different clinical MS courses; (iii) EDSS scales of demyelination to correlate with the disability of MS patients to predict the transformations prior to clinical changes.

Ab-mediated proteolysis of MBP results in generating a fixed set of peptides with MW ranged in fixed boundaries to suit common principles of the molecular architectonics of MBP. The sequence-specificity of Ab-proteases demonstrates
five sites of preferential proteolysis to be located within the immunodominant regions of MBP. Two of them falling inside the sequence covering 81-103 peptide and the 82-98 segment as well, with the highest encephalitogenic properties to be attacked by Ab-proteases in MS patients at the most severe (progradient) courses. Meanwhile, sites localized within the frame of 43-68 and 146-170 segments whilst being less immunogenic happened to be EAE inducers very rare and were shown to be attacked by Ab-proteases at moderate (remittent) courses.

The activity of Ab-proteases was first registered at the subclinical stages 1-2 years prior to the clinical illness and demonstrated a variety of sequence specificity to suit the definite stages of the disorder.

Conclusions: The activity of Ab-proteases in combination with the sequence-specificity would confirm a high subclinical and predictive value of the tools (biomarker-related) as applicable for personalized monitoring protocols. Ab-proteases can be programmed and re-programmed to suit the needs of the body metabolism or could be designed for the development of principally new catalysts with no natural counterparts. Further studies on targeted Ab-mediated proteolysis may provide translational tools for predicting demyelination and thus the disability of the MS patients.

Biography

Sergey Suchkov was born in the City of Astrakhan, Russia, in a family of dynasty medical doctors. In 1980, graduated from Astrakhan State Medical University and was awarded with MD. In 1985 maintained his PhD at the I.M. Sechenov Moscow Medical Academy and Institute of Medical Enzymology, Moscow, Russia. In 2001, maintained his Doctor’s Degree at the National Institute of Immunology, Russia. From 1985 through 1987 worked as a Post Doc Research Associate, Institute of Medical Enzymology. From 1987 through 1989 was a Senior Researcher, Koltsov Institute of Developmental Biology, USSR Academy of Sciences. From 1989 through 1995 was being a Head of the Lab of Clinical Immunology, Helmholtz Eye Research Institute in Moscow. From 1995 through 2004 was being a Chairman of the Department for Clinical Immunology, Moscow Clinical Research Institute (MONIKI). In 1993–1996 was an Executive Secretary–Chief of the Editorial Board, Biomedical Science, an international journal published jointly by the USSR Academy of Sciences and the Royal Society of Chemistry, UK.

At present he is the Director, Center for Personalized Medicine, and Professor, Department of Pathology, Sechenov University, Moscow, Russia; Chair, Department of Translational Medicine, National Research Nuclear University MEPhI; Secretary General, United Cultural Convention (UCC), Cambridge, UK. Dr Suchkov is an author of more than 500 publications including 10 patents and more than 10 monographs, handbooks and textbooks published in Russia and USA. A fellow of 10 International Societies and Associations. And a member of International Editorial Boards of 15 journals.

Alpha-1-Microglobulin/Bikunin (AMBp) Protein Corona (PPC) as Biomarker for Early Diagnosis in Non-Small-Cell Lung Carcinomas (NSCLC) Patients: A Case Report

Marina Di Domenico¹,²,³, Daniela Pozzi,⁴ Sara Palchetti,⁴ Luca Digiaccomo,⁴ Rosamaria Iorio⁵, Camilla Siciliano⁵, Federica Pinto⁶, Giuliana Settembre⁷, Matteo Pierdiluca⁴, Mario Santini⁵, Antonio Giordano³,⁷ Alfonso Giovane⁴, Giulio Caracciolo⁴

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Abstract

Nanoparticles are increasingly used in biomedical applications such as imaging, drug delivery and hyperthermic therapies. The surface of this nanoparticles once incubated with biological medium is covered by proteins constituting a shell named “protein corona”. Thus, understanding the interaction of nanomaterials with biological fluids becomes basic for their application. Recently it has been shown that the protein corona composition is critically affected by biological sample originates from the specific disease. This innovative concept takes the name of “personalized protein corona (PPC)”, which represents a promising strategy for personalized medicine. PPC acts a ‘nano-accumulator’ of proteins with affinity for the particle surface. Thus, this approach allows detecting protein alterations as those produced by clinical manifestations of disease even when they are too small to be detected by rutinary blood tests. Non-small–cell lung carcinomas (NSCLC) is the most common type of lung
cancer and it has poor prognosis, because overall survival after 5 years is 20–25% for all stages. Thus, innovative methods for early
detection and proper characterization of NSCLC are an urgent task. To this end, we incubated liposomes nanoparticles
with plasma from humans with histologically proven NSCLC. In this study we report an NSLC case. We have analyzed
the serum before and after incubation with liposome by a HPLC ion trap mass spectrometer. Proteins were identified by
fragments characterization of MS/MS spectra through MASCOT search engine using Swiss-Prot database. We have found
the protein Alpha-1-microglobulin/bikunin (AMBP) enriches the PPC from NSCLC patients thus being a potential
biomarker, in fact this protein has already been proven to be a potential biomarker of prostate and pancreas cancer. We have
identified AMBP both in protein corona and serum. These results suggest that the use of nano particles could be a test able
to provide early cancer detection.

Biography

Marina Di Domenico research interests are Molecular oncology and Translational medicine. The aim of her research
is to develop new valid diagnostic and prognostic tools for epithelial cancers by using innovative 3D–cell culture system
which are favourable to reflect the tumour microenvironment in order to provide a new essential insight for personalized
therapies of cancer. She is member of the International Societies, acting as referees for many International Journals such
as: Oncotarget, Oncoscience, PlosOne, Journal of Cellular Physiology etc. and Member of Editorial Boards for many
International Journal such as: World Journal of Pathology Journal of Cardiovascular Medicine and Cardiology etc., MDD
received national and international research grants and has numerous participations on international congresses as invited
speaker. She has more than 70 international publications in several book chapters, and special issues.

Transforming Precision Medicine in the Middle East

Carlos Malpica
MLP Vision Biotech SL, Spain

Abstract

Middle East countries have invested heavily in adopting state of the art omic technologies to support data generation
pertinent to the development of a new generation preventive medicine. The unique genetic makeup of the local population
requires the development of specific tools.

Real prevention medicine is now possible and commercially available tools are becoming available in the Middle East,
moving beyond research use and providing actionable information to clinicians from a patient in time to prevent the onset
of disease, is made possible by increased knowledge generated about human health using multiple omic tools including
genomics, transcriptomics, proteomics and metabolomics.

The presentation by Valdia Health will also highlight the importance of establishing an educational programme on
Precision Medicine. The first steps into a certified program at Weill Cornell Medical College in Qatar will be outlined.

Biography

Carlos Malpica was trained in Life Sciences at Institut National Agronomique Paris-Grignon and Pasteur Institute in
France. He obtained his PhD in Biotechnology from Paris University. He also holds a diploma from the Spanish Diplomatic
School and an International Executive MBA from IE Business School (Spain).

Dr. Malpica is the CEO of Valdia Health LLC and MLP Vision Biotech SL. He has been actively involved
in promoting worldwide adoption of metabolomics technologies as Global Director of Business Development at Metabolon
Inc. (USA). Past activities include Marketing and Sales Director at Biopolis S.L. (Spain), Research Director at L’Oréal
Group (France), CEO of Kina Biotech S.L. (Spain), Global Business Development Manager at Syngenta (Switzerland),
Head of Business Development Europe at Novartis Seeds (France) and Biotechnology Research Coordinator at the
DANONE Group (France).
Developing a Personalized Treatment Model Based on Molecular Biomarkers and Molecular Imaging in Breast Cancer

Partha Choudhary
Department of Nuclear Medicine, Rajiv Gandhi Cancer Institute & Research Centre Delhi, India

Abstract

Risk stratification in breast cancer can be done with either bio markers or 18F FDG a marker of glucose metabolism demonstrating tumor aggressiveness. The receptor status also plays an important role in predicting outcome as well as have a significant role in personalizing treatment protocols. In vivo receptor imaging has also made an inroad from the bench to the bed side. Hormone positivity has an impact on both treatment planning and prognosis and therefore imaging the ER receptor plays an important role. 18F-FES PET CT helps in resolving diagnostic dilemma and also planning further management. Estrogen is involved in the growth of both normal and cancerous breast tissues and a uniform expression of receptor is an exception rather than a rule. At the same time the expression in primary tumor and the metastatic sites may be different which may further prompt the need for imaging. FES PET-CT scan in combination with FDG PET-CT scan can be used as a problem solving modality in deciding the regimen. Our results point to this and a common rule of thumb could be well differentiated hormone positive tumor with FDG uptake less than FES uptake is unlikely to benefit from cytotoxic chemotherapy and would be an ideal candidate to be treated with hormone or vice versa. In the coming years and in future we hope that the treatment of breast cancer has a very high potential to be personalized based on PET scan (both FDG and FES) and other molecular bio markers giving early and clear indications to the treating oncologist as to where the disease is heading and how the treatment regimen needs to be modified. In this presentation I will discuss how a combination of conventional FDG PET-CT and FES PET-CT along with the receptor status can help in precision management of breast cancer based on our work and literature.

Biography

Partha Choudhury is a Nuclear Medicine Physician by training and has approx. 25 years of experience in Nuclear Oncology. He is currently affiliated to Rajiv Gandhi Cancer Institute & Research Centre with is an internationally acclaimed tertiary level cancer institute located in New-Delhi India. He is currently holding the post of Director in the department. Dr Choudhury received part of his training in St.Vincents Hospital, Sydney, and University of New South Wales, Sydney, Australia and in Germany. He is an avid clinical researcher, and has publications to his credit and has delivered many invited talks in India and abroad.

Mass-Spectra-Based Peak Alignment for Automatic Non-Targeted Metabolic Profiling Analysis for Biomarker Screening in Plant Samples

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1School of Pharmaceutical Sciences, South Central University for Nationalities, China
2College of Pharmacy, Ningxia Medical University, China

Abstract

Non targeted metabolic profiling analysis is a difficult task in a routine investigation because hundreds of chromatographic peaks are eluted within a short time, and the time shift problem is severe across samples. To address these problems, the present work developed an automatic non targeted metabolic profiling analysis (aniTMPA) method. First, peaks from the total ion chromatogram were extracted using modified multiscale Gaussian smoothing method. Then, a novel peak alignment strategy was employed based on the mass spectra and retention times of the peaks in which the maximum mass spectral correlation coefficient path was extracted using a modified dynamic programming method. Moreover, an automatic landmark peak-searching strategy was employed for self-adapting time shift modification. Missing peaks across samples were grouped and registered into the aligned peak list table for final refinement. Finally, the aligned peaks across samples were analyzed using statistical methods to identify potential biomarkers. Mass spectral information on the screened biomarkers could be directly imported into the National Institute of Standards and Technology library to select the candidate compounds. The performance of the TMPA method was evaluated using a complicated plant gas chromatography-mass spectrometry dataset with the aim of identifying biomarkers between the growth and maturation stages of the tested plant.

Biography

Haiyan Fu is an experienced researcher in analytical techniques and chemometric. She has completed her PhD at the age of 27 years from Hunan University. She is associated professor and director of the department of Pharmaceutical analysis at south central university for nationalities. She has authored 78 research papers (58 SCI papers in the international journals).
The Unique Property of Melanin to Dissociate the Water Molecule like Chlorophyll in Plants: Implications in the Assessment and Understanding of Genomic Instability and Warburg Effect in Human Cancer

Arturo Solís Herrera¹*, Sergey Suchkov²
¹Human Photosynthesis® Research Center, Mexico
²Sechenov University, Moscow, Russia

Abstract

Impaired cellular energy metabolism is the defining characteristic of nearly all cancer regardless of cellular or tissue origin. The replacement of respiration by fermentation (glycolysis) can be a symptom of cancer and not the cause. Aerobic glycolysis in cancer cells involves elevated glucose uptake with lactic acid production in the presence of oxygen. Warburg recognized that oxygen consumption is not diminished in tumor cells, instead, respiration is altered because glycolysis persists in the presence of oxygen. The uniqueness of the intrinsic property of melanin to dissociate the water molecule, like chlorophyll in plants, through the dissociation of the water molecule, opens a new era in the current landscape of reactive medicine.

This means that glucose is the universal precursor of any organic matter of the body, but it cannot provide the energy that its own metabolism requires. The necessary energy, defined as everything that produces any change, our body takes from light through water dissociation. In humans is through melanin, in plants by mean of chlorophyll. Biomarkers of photosynthetic activity of human body can be assessed by enzymatic activities of catalase, ascorbate peroxidase, superoxide dismutase; glutathione reductase and glutathione S-transferase. The defects in the generation and distribution of energy are not readily detectable. Pollutants and other stresses can produce symptoms that mimic or conceal damage caused by polluted air, contaminated water, metals, pesticides, fertilizers, herbicides, industrial waste, drugs, etc.

Sodium 4-Phenylbutyrate Ameliorates Particles-Induced Inflammatory Osteolysis by Promoting Macrophage Apoptosis and Inhibiting Inflammatory and Osteoclastogenic Reactions

Guoyin Liu¹,²,³, Yong Zhang¹, Yuansheng Xu¹, Yunfan Ti¹, Jiangning Chen¹, Jianmin Chen¹, Junfeng Zhang³, Jianning Zhao²
¹Bayi Hospital Affiliated to Nanjing University of Chinese Medicine, China
²Jinling Hospital affiliated to the School of Medicine, Nanjing University, China
³School of Life Sciences, Nanjing University, China

Abstract

Macrophages represent both the ‘initiators’ and ‘amplifiers’ of the pathogenetic cascade in inflammatory osteolysis. In this study, we investigated the therapeutic potential of ER-stress protector (PBA) on the inflammatory, osteoclastogenic and apoptotic reactions in cultured macrophages and osteolytic periosteum in particles-induced osteolysis (PIO) animal models. The results demonstrated that apoptosis-related markers, inflammation, and osteoclastogenesis were significantly up-regulated in particles-treated macrophages and osteolytic periosteum tissues. ER-stress protector down-regulated ER chaperone (IRE, Bip, CHOP), and ameliorated particles-induced osteolysis by promoting macrophage apoptosis and inhibiting the inflammatory reactions and osteoclastogenesis. During the apoptotic process, apoptotic regulators, JNK, the mitochondrial and death receptor pathways were all involved in PBA--induced macrophages apoptosis, while the ER stress pathway was not. More importantly, PBA treatment alone was of relative low toxicity and experimental tested safeness in PIO mice. Since the ER chaperone BiP migrates out of the ER into the nucleus (intracellular protein) and to the cell surface (extracellular protein). Thus, BiP conforms to the definition of a true moonlighting protein with two quite distinct roles. Besides the function that focused on preserving or restoring ER function, the BiP has also been implicated in exerting functions that are of immunologic importance, and the discovery of cell surface BiP makes it an innovative concept in biological therapy for inflammatory diseases. Therefore, future studies will need to address the many open questions about the physiological significance of the ER and BiP to improve the overall understanding of how these diseases develop and indicate how they might be treated with pharmacological interventions that modulate ER or BiP on inflammatory diseases.

Biography

Guoyin Liu has completed his Master’s degree from Medical School of Nanjing University. He is the Orthopedic Surgeon of Bayi Hospital Affiliated to Nanjing University of Chinese Medicine. He is also the Secretary and Research Director of Orthopaedics Department. He worked mainly on the immunization therapy and the signaling pathways of apoptosis and inflammation, and has published 2 papers in reputed journals.
Prediction of IPF within 1-2 year with the Early Changes in Quantitative Imaging Patterns Using High Resolution Computed Tomography

GJ Kim1,2, S. S. Weigt3, M. Brown1, R. Huynh, J. A. Belperio1, Y. Shi1, J. Lai1, J. G. Goldin1

1UCLA, David Geffen School of Medicine, University of California at Los Angeles Radiological Science – Los Angeles, CA, USA
2UCLA, Fielding School of Public Health, University of California at Los Angeles Biostatistics – Los Angeles, CA, USA
3UCLA, David Geffen School of Medicine, University of California at Los Angeles Med-Pul Critical Care – Los Angeles, CA, USA

Abstract

Introduction: High resolution computed tomography (HRCT) plays an indispensable role in the diagnosis of Idiopathic Pulmonary Fibrosis (IPF). Due to the short median survival of 2 to 5 years, understanding the chance of progression in the next follow-up of a patient is critical. The aim of this study is to test the predictability of progression in IPF of the near follow-up of a patient using the early quantitative changes in HRCT scans.

Methods: Volumetric anonymized HRCT scans were obtained. Two data sets were collected: a pilot study with 35 subjects in three sequential scans (baseline, 6 and 12 month scans) and validation study involving 157 subjects with clinical information. Quantitative lung fibrosis (QLF) scores were calculated for HRCT scans using an automated system. A log-rank test and Cox regression were used to test a prediction with early changes in QLF.

Results: In the pilot study mean changes in QLF increased by 4.33% at 6 months and 14.83% at 12 months, when the visual assessments changed from stable to worse. Mean QLF changes were -1% for the stable cases during 12 months. Using 4% QLF differences at 6 months in the validation cohort, significant differences in progression were found (p<0.001).

Conclusion: Early changes in a quantitative score from HRCT can predict progression in lung function. A quantitative texture-based score can play a pivotal role for informed and timely management decision for patients with IPF.

Biography

Grace Hyun J. Kim was born in Seoul Korea and moved to Hong Kong for a few years. After finishing her bachelor degree in Ewha Woman's University, she moved to USA. She finished her PhD in biostatistics in 2007 and post-doc training in radiology in 2009 at UCLA. Her research focuses on classification and pattern recognition of therapeutic responses in medical imaging. Dr. Kim developed a robust statistical model for classifying the patterns of interstitial lung disease using mathematical de-noise, which led to quantitative lung fibrosis score (so called QLF). She received grants in prediction of progression idiopathic pulmonary fibrosis using imaging.

Anemia in Kawasaki Disease: Hepcidin as a Potential Biomarker

Ying-Hsien Huang1,2,3, Ho-Chang Kuo1,2

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2Kawasaki Disease Center, Kaohsiung Chang Gung Memorial Hospital, Taiwan
3Department of Pediatrics, Chiayi Chang Gung Memorial Hospital, Chiayi, Taiwan

Abstract

Kawasaki disease (KD) is an autoimmune-like disease and acute childhood vasculitis syndrome that affects various systems but has unknown etiology. In addition to the standard diagnostic criteria, anemia is among the most common clinical features of KD patients and is thought to have a more prolonged duration of active inflammation. In 2001, the discovery of a liver-derived peptide hormone known as hepcidin began revolutionizing our understanding of anemia's relation to a number of inflammatory diseases, including KD. This talk focuses on hepcidin-induced iron deficiency's relation to transient hypoferremia, anemia, and disease outcomes in KD patients and then suggests possible routes of further study.

Biography

Ying-Hsien Huang graduated from Chang Gung University College of Medicine in 2009. He works as visiting staff in Kaohsiung Chang Gung Memorial Hospital since 2009 and as an Associate Professor of Chang Gung University College of Medicine since 2014. He is interested in the fields of biliary atresia, liver fibrosis, and Kawasaki disease and has published many papers in this area. He awarded as Young Investigator's Award in Pediatric Academic Societies & Asian Society for Pediatric Research Joint Meeting in 2008 and Asian Society for the Pediatric Research in 2014.
Bacteriophage-Derived dsRNA of Natural Origin Alters Functional Profile of Rat Microglial Cells Exposed to Hypoxia in vitro: Evaluation of Metabolic and Phenotypic Markers

Yehor Pashkevych¹, Mariia Rudyk², Yevheniia Hurmach², Vitalina Svyatetska², Natalia Senchylo², Dace Pjanova³, Guna Feldmane³, and Larysa Skivka²

¹National University of Kyiv-Mohyla Academy, Kyiv, Ukraine
²Taras Shevchenko National University of Kyiv, Ukraine
³Latvian Biomedical Research and Study Centre, Riga, Latvia

Abstract

Background: Microglial cells (MC) are thought to be major innate immune cells in the central nervous system. Hypoxia can cause pro- and anti-inflammatory MC activation. Toll-like receptors (TLRs) play an important role in the regulation of microglia activity and can skew metabolic profile of resting and activated MC. However, the data concerning the effect of TLR agonists on metabolic profile of MC activated by hypoxia are controversial and sparse. Larifan is a pharmaceutical product containing a heterogeneous population of natural origin double-stranded RNA (dsRNA). This study was aimed to investigate the effect of the treatment with Larifan on functional profile of rat MC exposed to hypoxia in vitro.

Methods: Rat MC were cultured under normoxic (21% O₂) or hypoxic (3% O₂) conditions for 24 h. After this, cells were treated with Larifan (200 µg/mL) for 18 h. To characterize MC functional profile, reactive oxygen species (ROS) generation, phagocytic activity, arginine metabolism as well as CD206 and CD14 expression were examined.

Results: Hypoxic MC were characterized by sharply increased ROS generation, moderately boosted phagocytic activity, arginine metabolism was skewed towards increased arginase activity, CD14+ and CD206+ cell fractions were higher than those in normoxic cells. Treatment MC with Larifan resulted in further increase ROS generation along with the decrease of phagocytic activity that is characteristic for the acquisition of antigen-presenting properties by these cells. The level of CD206 expression was lowered in treated hypoxic MC.

Conclusion: Larifan promotes transition of hypoxic MC to the state of mature pro-inflammatory APC in vitro.

Biography

Yehor Pashkevych is an undergraduate student of National University of Kyiv-Mohyla Academy. He is a member of the research group of undergraduate students, masters and PhD students of National University of Kyiv-Mohyla Academy and Taras Shevchenko National University of Kyiv under the direction of ScD, PhD Larysa Skivka. This research group is engaged in the search for differential markers of functional polarization of tissue phagocytes of various origin, as well as the development of methodological approaches for their re-education in vitro and in vivo.

Association of Vitamin D Receptor and Toll like Receptor Variants with Colon Cancer Risk: A Case Control Study in Egypt

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Abstract

Variants of vitamin D receptor (VDR) and toll like receptors (TLR) have been investigated in relation to colon cancer (CC) susceptibility, however results were always inconsistent. Methods: We examined the association of CC risk with four variants VDR rs2228570 (FokI), VDR rs11568820 (Cdx2) and Asp299Gly (rs4986790) and Asp399Ile (rs4986791) in TLR4. rs11568820 was assessed by allele specific-multiplex polymerase chain reaction, while the other variants were examined by restriction fragment length polymorphism. We evaluated whether any of the associations differed by tumor location or criteria.

Results: The A allele of rs11568820 was associated with decreased risk with adjusted OR = 0.523 (0.344–0.796), p = 0.002, while G allele in Asp299Gly and T allele in Thr399Ile were associated with > 3 fold increased risk of CC with
OR = 3.430 (1.588–7.408), p = 0.002 and OR = 3.290 (1.628–6.648), p = 0.001 respectively. G allele of Asp299Gly was more strongly associated with distal tumors OR = 4.952 (2.171–11.29), p < 0.001 than proximal tumors OR = 2.401 (1.002–5.751), p = 0.043 with almost 2 fold rise in the OR. On the other hand rs11568820 A allele was more associated with proximal tumors OR = 0.574 (0.355–0.926), p = 0.022 than distal tumors OR = 0.400 (0.224–0.712), p = 0.001.

Conclusions: We conclude significant association of VDR rs11568820 (Cdx2) and TLR4 variants with CC, although results should be confirmed in additional studies.

Biography

Ragaa A. Ramadan, PhD is an Assistant Professor in medical Research Institute, Alexandria University, Egypt. She is a chemical pathologist and specialized in molecular diagnostics. Her research focuses on genetic and environmental interactions and tumor phenotypes. Dr. Ramadan has actively done research relating to different tumors with high prevalence in Egypt such as hepatocellular carcinoma, lung cancer and colon cancer.

Post-Translational Modifications of STAT3: Modulators of Androgen-Resistance in Prostate Cancer

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Abstract

“Androgen Escape” is a clinical phase in which tumoral prostatic cells become able to survive and proliferate without circulated androgens. This reflects a more aggressive tumor development form with worse prognosis. Then, cell survival and proliferation can be under control of non-canonical mechanisms and some of these pathways involved the protein STAT3 (Signal Transducer and Activator of Transcription). STAT3 activation can regulate genes expression and subsequently cell proliferation, differentiation and apoptosis. In prostate cancer, androgenic and STAT3 pathways are constitutively activated, cross-talking differently in a hormone-responsive or hormone-refractory tumor [1,2]. Considering this, the aim of our study was to assess the involvement of STAT3 and its post-translational modifications (PTMs) in the androgen escape process in two different human prostate cancer cell lines, LNCaP (androgen-responsive) and PC3 (androgen-refractory). Both cell lines were stimulated by IL-6, EGF and H2O2 to mimic inflammatory and oxidative conditions. The acetylated STAT3 form, expressed in low Gleason Score and in inflammatory process [3], increased after IL-6 treatment in both cell lines. Under the same treatment conditions, in LNCaP there was an overexpression of genes, which inhibit cell proliferation, reflecting LNCaP lower aggressiveness. On the other hand, the glutathionylated STAT3, typical of high Gleason Score and of oxidative conditions [3], was constitutively expressed in PC3 untreated cells and in LNCaP only after H2O2 treatment, indicating a higher aggressiveness of PC3 cells. Therefore, we can speculate a functional role of STAT3 and its PTMs in the “Androgen Escape” trigger.

Biography

Flavia Giamogante is a PhD student in biochemical sciences. She is studying the STAT3 involvement in pathological processes, e.g. prostate cancer, using samples tissue and cellular models. In particular, she is seeking about STAT3 role in androgen-resistance to identify a new prognostic marker and target for pharmacology strategies. Besides, she is focusing on Pdia3 (Protein disulfide-isomerase A3), a known STAT3 interactor, to understand which cellular functions are under STAT3/PDIA3 binding control. She is testing different natural compounds, able to modify PDIA3 and STAT3 activity. In this respect, during her first PhD year, she published an article on different PDIA3 activity modulators.
Assessment and Comparison of Salivary Survivin Biomarker in Oral Leukoplakia, Oral Lichen Planus and Oral Cancer - A Comparative Study

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Abstract

Background: Oral squamous cell carcinoma (OSCC) is the most common malignant tumour of the oral cavity. It is preceded by various potentially malignant conditions like oral leukoplakia and oral lichen planus. Survivin is an inhibitor of apoptosis whose levels have been found increased in oral cancer as well as various potentially malignant conditions. Thus survivin can act as a biomarker and help in early detection of potentially malignant conditions which can prevent its transformation into malignancy.

Aim: To assess and compare the level of total human salivary survivin in Oral Leukoplakia, Oral Lichen Planus, Oral Cancer and Control group.

Methods and Material: A total of 96 subjects were included in the study which were further grouped into 24 in each group. The saliva was analyzed for survivin level among all the four groups. Survivin concentration (pg/ml) was studied in relation to clinical data.

The results were analyzed using Mann-Whitney U test to derive the statistical difference.

Results: The average of levels of survivin in control group was 0.199 pg/ml, in Oral Leukoplakia Group 0.312 pg/ml, in Oral Lichen Planus Group 0.380 pg/ml and in Oral Cancer Group 0.430 pg/ml. A comparison of all these groups revealed statistically significant difference among the groups.

Conclusion: Survivin may not be considered as an independent predictor of the malignant transformation for premalignant lesions but it can be an indicator for an increased risk of malignant transformation.

Biography

Ruchika Garg completed her post-graduation in Oral Medicine and Radiology in June 2017 from Belagayi and prior to that she was in Manipal where she completed her graduation in 2013.

She aspire to make a good carrier as a clinical researcher. She has been recognized multiple times in colleges for various accomplishments and presented various papers and posters in her college as well as in various national conferences and has won awards for the same. Recently three of her scientific papers have been published in international journals.

Specific Platelet microRNA Signature for Dementia with Lewy Bodies as Promising Biomarker

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4Nephrology Service, Hospital Universitari Germans Trias i Pujol, Spain

Abstract

Dementia with Lewy bodies (DLB) shows overlapping features with Alzheimer disease (AD) leading to its misdiagnosis and hindering its adequate treatment. It is well established that microRNAs play an important role in neurodegeneration and they can be found in brain and the central nervous system. Since 30 years ago, the presence of RNA (mRNA and microRNA) in platelets has attracted attention and different mRNA expression patterns have been reported to be altered in human diseases. Our main objective was to identify disease specific mRNA and miRNA biosignatures through the analysis of platelet rich plasma (PRP) obtained from DLB patients (n = 31), AD patients (n = 10) and age-matched control individuals (n = 31).
After isolation of mRNA and miRNA from PRP, we analyzed SNCA and GBA mRNA expression levels in DLB patients and controls by reverse-transcription real time PCR; next generation sequencing was applied for miRNA discovery in the same samples.

22 miRNAs were differentially expressed and selected to be validated by real time qPCR. From those, 9 were considered as potential biomarkers for DLB being evaluated in a group of AD patients and independent groups of control and DLB individuals. Interestingly, miRNAs levels seemed to correlate with clinical symptoms and to correlate inversely with SNCA-mRNA expression in DLB patients.

These results, although replication and follow-up with larger, carefully characterized cohorts are needed, represent an integrated miRNA and mRNA profile in platelet rich plasma that is likely to provide non-invasive biomarkers for the differential diagnosis of DLB versus AD.

Biography

Ana Gámez-Valero obtained her degree in Biotechnology in the University Pablo de Olavide (Seville). During these 4 years, she had the opportunity to study a year in France where she started her research experience in the Histology Department of the medical school (Nîmes). In 2013, she obtained a MSc in Advanced Genetics by the Universidad Autónoma of Barcelona. Since 2015, she is carrying out her PhD project entitled - “Identification of specific biosignatures from plasma samples for differential diagnosis of dementia with Lewy bodies” in the IGTP Institute in Badalona, having already published 4 research articles.

MicroRNA: A Key Player in Oral Tumors Pathogenesis

Ghazaleh Baniebrahimi, Razieh Khanmohammadi

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Abstract

Oral tumors are one of main tumors which could be related with serious health problems worldwide. It has been indicated that several cellular and molecular pathways including genetics and epigenetics mechanisms (e.g. chromosomal alterations, and microRNA) could be anticipated in oral tumors pathogenesis. The recognition of these pathways is found as key steps for better treatment of oral tumor patients. MicroRNAs (miRNAs) are one of important molecules which could be involved in various physiological processes in oral tumors. These molecules are known as short non coding RNAs which are associated with initiation and progression of various diseases such as oral tumors. Multiple lines of evidence showed that various miRNAs (i.e. miR-9, miR-7, miR-21, miR-31, miR-15a and miR-16-1) via targeting various cellular and molecular pathways such as epidermal growth factor receptor (EGFR), MAPK, Akt, ERK, Jak/STAT, and PTEN could be involved in oral tumors pathogenesis. Here, we summarized various miRNAs which have critical roles in oral tumors pathogenesis. Moreover, we highlighted the utilization of various miRNAs as diagnostic and therapeutic biomarkers for patients with oral tumors.

Biography

Ghazaleh Baniebrahimi is assistant professor at department of pediatric dentistry, school of dentistry, Tehran University of Medical Sciences, Tehran, Iran. Ghazaleh was born in Tehran, on 29 March 1987. She graduated from school of dentistry in the Shahid Beheshti University of Medical Sciences on 20 September 2012 (For DDS degree), and from the Isfahan University of Medical Sciences for MSc in Pediatric Dentistry on 21 September 2015.
Diagnosis of Oral Tumors in Children

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Abstract

Oral tumors are known as one of rare tumors which are associated with serious problems in infant and children. Multiple lines of evidence revealed that various cellular and molecular mechanisms involved in oral tumor pathogenesis which identification of them could provide effective therapeutic approaches for treatment children with oral tumors. Early detection is one of key steps in management of oral tumors which could contribute to improve clinical outcomes and better treatment of infant with oral tumors. Despite of easy accession of the oral cavity, oral tumors (malign/benign) are diagnosed in advance stages. Several studies indicated that various approaches such as imaging techniques (i.e. MRI, PET, SPECT, and CT), and utilization of various chemical, genetics, and epigenetic biomarkers (i.e. E-cadherin, CCND1, BRAF, NOTCH1, VEGFA, S100, CD1a and microRNAs) could be employed for early detection of oral tumors. They showed that utilization of various diagnostic approaches could contribute to better management of oral tumors patients. Here, we summarized various diagnostic approaches including various imaging techniques and utilization of various biomarkers for monitoring children with oral tumors.

Biography

Razieh Khanmohammadi is assistant professor at department of pediatric dentistry, school of dentistry, Tehran University of Medical Sciences, Tehran, Iran. Razieh was born in Tehran, on 25 April 1986. She graduated from school of dentistry in the Tehran University of Medical Sciences on 21 September 2011 (For DDS degree), and from the Mashhad University of Medical Sciences for MSc in Pediatric Dentistry on 21 September 2014.

Interleukin-4 Receptor as a Cancer Prognosis Biomarker and Therapeutic Target

Sri Murugan Poongkvithai Vadevoo, Gowri Rangaswamy Gunasekaran, Guruprasath Padmanaban, Lianhua Chi, Byungheon Lee

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Abstract

There are two types of interleukin-4 receptor (IL-4R). Type I IL-4R, a heterodimer of IL-4Ra and IL-2RyC, is expressed on cells of hematopoietic origin such as T cells and B cells. In contrast, type II IL-4R, a heterodimer of IL-4Ra and IL-13Ra1 is commonly up-regulated in many types of cancer cells including breast cancer and head and neck cancer. Interaction of IL-4 and IL-4R up-regulates anti-apoptotic proteins such as Bcl-xL in tumor cells. In this study, we examined the co-relationship between IL-4R expression and prognosis of patients. In breast cancer patients, high expression levels of IL-13Ra1 subunit of IL-4R was correlated with low overall survival (OS) and disease-free survival (DFS) compared to negative or low expression of IL-13Ra1. However, in oral squamous cell carcinoma patients, high IL-13Ra1 expression was correlated with increased DFS and cancer-specific survival, while high expression of 13Ra1 was correlated with a lower DFS. Next, we tested the feasibility of IL-4R as a therapeutic target IL-4RPep-1 (IL-4 receptor-targeting peptide-1), CRKRLDRNC, bound to H226 lung tumor cells that over-express IL4R, while little binding was observed in H460 lung tumor cells that express IL-4R at low levels. When injected intravenously into nude mice bearing a subcutaneous H226 tumor, Cy7.5 near-infrared fluorescence dye-conjugated IL-4RPep-1 selectively homed to tumor. IL-4RPep-1-labeled liposomes containing doxorubicin showed more efficient anti-tumor growth activity than untargeted liposomes. These findings suggest that IL-4R is a promising cancer prognosis biomarker and also therapeutic target for the treatment of cancer.

Biography

Byungheon Lee is currently a Professor in Department of Biochemistry and Cell Biology, School of Medicine, Kyungpook National University (KNU). He received his B.S. from School of Medicine, KNU in 1989 and his PhD in Biochemistry from KNU in 1995. He is currently a member of American Association for Cancer Research. He has published over 70 peer-reviewed papers, 3 book chapters, and 1 review article. He also filed 50 domestic and international patents. His main research interest is the discovery of tissue-specific homing peptides using phage display and their applications to molecular imaging and targeted drug delivery to cancer.
Elevated Circulating MicroRNA-486-3p and -145 Levels in Hereditary Hemorrhagic Telangiectasia Patients with Cerebral Arteriovenous Malformations: Potential Biomarkers

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Abstract

Hereditary Hemorrhagic Telangiectasia (HHT) is a rare, autosomal dominant, genetic disorder that leads to abnormal vasculature. Approximately 50% of HHT patients have arteriovenous malformations, direct connections between arteries and veins without intervening capillary beds, in the brain, lung, or liver. Cerebral AVMs (CAVMs) can spontaneously develop and lead to sudden morbidity and mortality. Our objective was to profile and characterize circulating microRNAs (miRs) in HHT patients with untreated CAVMs to identify a CAVM biomarker.

Four clinically confirmed HHT patients with untreated CAVMs, 4 clinically confirmed HHT patients without CAVMs and 4 healthy controls were recruited. 4 ml of peripheral blood was collected for plasma isolation. Total RNA was purified from plasma and miR profiling was conducted with a human miR array analysis. Select dysregulated miRs were validated with RT-qPCR and compared to HHT patients without CAVMs and healthy controls.

Of the 384 miRs screened, 49 dysregulated miRs were identified. Select miRs (MiRs-28, -145, -152, -486-3p and -500) were validated with RT-qPCR. MiR-145 (p=0.03) levels were significantly higher compared to HHT patients without CAVMs and significantly lower compared to healthy controls. Mir-486-3p (p=0.04) levels were significantly higher compared to HHT patients without CAVMs and healthy controls.

Our results show that circulating miR-145 and 486-3p, known brain specific miRs, are elevated in HHT patients with untreated CAVMs. These miRs represent candidate biomarkers for the detection of clinically significant CAVMs. The potential utilization of circulating miR biomarkers will provide a rapid, inexpensive, safe, and relatively non-invasive screening test for the diagnosis of CAVMs in HHT patients.

Biography

Anthony Cannavicci is a Master’s student at the University of Toronto studying epigenetic regulation in Hereditary Hemorrhagic Telangiectasia (HHT). Anthony successfully completed an undergraduate degree in Molecular Biology and Genetics at York University. He is currently a co-chair to the charitable organization HHT Canada. He was awarded Best Clinical Poster Presentation and a Young Investigator Travel Award at the 12th International HHT Scientific Conference. Anthony Cannavicci currently resides in Toronto, Canada and is fulfilling his passion in studying and advancing the field of HHT research.
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