RUSSIAN GERMAN FORUM
BIOECONOMY AND BIOMEDICINE

Russian–German Forum Bioeconomics and Biomedicine

15-18 November 2015

Program & Abstracts

Pushchino-Moscow
2015

MOSCOW
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ФЕДЕРАЛЬНЫЙ
ИССЛЕДОВАТЕЛЬСКИЙ ЦЕНТР
«ФУНДАМЕНТАЛЬНЫЕ ОСНОВЫ
БИОТЕХНОЛОГИИ»
РОССИЙСКОЙ АКАДЕМИИ НАУК

Deutsches Wissenschafts- und
Innovationshaus – Moskau

Deutschland
Land der Ideen

Institute of Theoretical and Experimental Biophysics of the Russian Academy of Sciences
Moscow Region Development Corporation
German Embassy Moscow
German House for Research and Innovation (DWIH) Moscow

Russian-German Forum «Bioeconomy and Biomedicine»

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Pushchino - Moscow

RUSSIAN GERMAN FORUM
BIOECONOMY AND BIOMEDICINE

http://rgbioforum2015.ru/

With the participation:
Branch of Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences
Pushchino Research Center of the Russian Academy of Sciences
Federal State Institution «Federal Research Centre «Fundamentals of Biotechnology» of the Russian Academy of Sciences
The Russian Technology Platform «BioTech 2030»
Russian National Contact Point «Biotechnology»
Biotechnology Department Lomonosov Moscow State University
Russian National Contact Point «Environment and Climate Change»
The Ministry of Investment and Innovation of the Moscow region
Pushchino Municipal Administration

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NOVEMBER 15, SUNDAY

"TZARGRAD" HOTEL

Arrival and Registration of participants

NOVEMBER 16, MONDAY

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09.30 – 10.00 **REGISTRATION OF THE PARTICIPANTS**

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Mikhail Rusakov, Embassy of the Federal Republic of Germany in the Russian Federation
Representative of the Federal Agency of the Scientific Organization
Representative of the Ministry of Investment and Innovation of the Moscow region

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SECTION "BIOECONOMY". *Small conference hall*
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MECHANISMS OF NEURONAL SURVIVAL IN STROKE

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[1]ICB RAS, Pushchino, Russia. [2]University of Hamburg, Germany. [3]University of Wurzburg, Germany. [4]Catholic University of Leuven, Belgium

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[1]Institute of Applied Medical Engineering, Helmholtz Institute Aachen, RWTH Aachen University, Germany. [2]Institute for Textile Engineering, RWTH Aachen University, Germany

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[1]Institute of theoretical and experimental biophysics at RAS, Pushchino, Russia. [2]Pushchino State Natural Sciences Institute, Pushchino, Russia. [3]Bakulev Scientific center for cardio-vascular surgery, Moscow, Russia. [4]Central Institute for Traumatology and orthopedics, Moscow, Russia. [5]Moscow state university of medicine and dentistry, Moscow, Russia

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[1]Institute of Theoretical and Experimental Biophysics RAS. [2]Institute of Biochemistry and Physiology of Microorganisms RAS. [3]Institute of Protein Research RAS. [4]Institute of Cell Biophysics RAS, Moscow region, Pushchino

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[1]Institute of Theoretical and Experimental Biophysics of the Russian Academy of Sciences, Pushchino, Russia. [2]School of Systems Biology, George Mason University, Manassas, VA 20110. [3]National Center for Biodefense and Infectious Diseases, George Mason University, Manassas, VA 20110

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Chair of Analytical Chemistry & Institute of Hydrochemistry, Technical University of Munich, Germany

RESEARCH CENTRE OF MEDICAL TECHNOLOGY AND BIOTECHNOLOGY (FZMB GMBH)
Miethe P., Ponomarev I.
Research Centre of Medical Technology and Biotechnology, Bad Langensalza, Germany

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Preclinical Study Centre, LLC

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Institute of Problems of Chemical Physics RAS, Chernogolovka, Russia

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G.K. Skryabin Institute of Biochemistry and Physiology of Microorganisms, Russian Academy of Sciences, Pushchino, Russia

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“Biotechnologies of Pushchino”, Limited Liability Company, Pushchino, Russia

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G.K. Skryabin Institute of Biochemistry and Physiology of Microorganisms, Russian Academy of Sciences

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[1]Center for Ecological Research and BioResources Development. [2]G.K. Skryabin Institute of Biochemistry and Physiology of Microorganisms, Russian Academy of Sciences. [3]Potok-Inter Ltd.

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[1]Central Research Institute of Epidemiology, Moscow Russia. [2]Rostov Research Institute of Biotechnology, Academy of Biology and Biotechnology, Southern Federal University, Rostov-na-Donu, Russia

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[1]NATIV Ltd. Moscow, Russia. [2]Institute of Protein Research, Pushchino, Russia. [3]Vivacell Biotechnology GmbH (Germany)

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University of Applied Sciences Ostwestfalen-Lippe, Germany

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[1]Institute of Theoretical and Experimental Biophysics Russian Academy of Sciences. [2]Institute of Cell Biophysics Russian Academy of Sciences, Pushchino, Russia

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Moderator: Vadim Sharov

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Pushchino State Institute of Natural Sciences, Russia

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Sharov V. I., Vetrova A. A.
Pushchino State Institute of Natural Sciences, Russia

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[1]Pushchino State Institute of Natural Sciences, Russia. [2]Moscow State Forest University, Russia

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G.K. Skryabin Institute of Biochemistry and Physiology of microorganisms RAS, Russia

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Moderators: Vadim Sharov (Russia) and Anna Urumyan (Germany)

November 17, Tuesday

CONFERENCE «COOPERATION BETWEEN RUSSIA AND GERMANY IN BIOECONOMY. EXPERIENCE IN THE IMPLEMENTATION OF RESEARCH PROJECTS IN THE FIELD OF BIOTECHNOLOGY INDUSTRY»

Venue: Moscow, German Embassy Moscow, Mosfilmovskaya street, 56

09.30 – 10.00 **REGISTRATION**

10.00 – 10.40 **GREETINGS:**
Wolfgang Dik, German Embassy Moscow
Iliya Kazeev, Federal Ministry of Education and Science, Moscow, Russia
Vladimir Popov, Director of Research Center of Biotechnology RAS, Moscow, Russia
Martin Krispin, German Houses of Research and Innovation (DWIH), Moscow, Russia

11.00 – 11.30 **STRUCTURE OF JOINT INDUSTRIAL AND ACADEMIC COOPERATION IN THE FIELD OF BIOECONOMY IN GERMANY**
Manfred Kircher, Chairman of the Advisory Board, Cluster Industrial Biotechnology CLIB2021, Düsseldorf, Germany

11.30 – 12.00 **THE CURRENT SITUATION OF THE BIOTECHNOLOGICAL AND BIO-ECONOMIC DEVELOPMENT IN RUSSIA**
Vladimir Popov, Director of Research Center of Biotechnology RAS, Moscow, Russia

12.00 – 13.00 **Panel discussion:**
TECHNOLOGY TRANSFER FROM ACADEMIC RESEARCH INTO INDUSTRIAL REALITY IN THE FIELD OF BIOECONOMY. SUCCESS STORIES, PROSPECTS AND CHALLENGES

Moderators:
Manfred Kircher, Chairman of the Advisory Board, Cluster Industrial Biotechnology CLIB2021, Düsseldorf, Germany
Arkady Sinitsyn, Research Center of Biotechnology RAS, Moscow, Russia

German participants:
Ulrich Schwaneberg, RWTH Aachen, Germany
Wolfgang Liebl, TU München, Germany
Timo Johannes Koch, Pfeifer & Langen GmbH, Köln, Germany
David Schönauer, SeSam-Biotech GmbH, Aachen, Germany

Russian participants:
Arkady Sinitsyn, Research Center of Biotechnology RAS, Moscow, Russia
Ivan Zorov, Research Center of Biotechnology RAS, Moscow, Russia
Mikhail Beburov, Research Institute for Genetics and Selection of Industrial Microorganisms, Moscow, Russia
Sergey Yarotsky, Research Institute for Genetics and Selection of Industrial Microorganisms, Moscow, Russia

13.00 – 14.00 *LUNCH*

PRESENTATIONS OF THE REPRESENTATIVES OF THE FEDERAL STATES AND EXAMPLES OF THE IMPLEMENTATION OF BIOTECHNOLOGY IN THE INDUSTRY IN NORTH RHINE-WESTPHALIA, THURINGIA AND LOWER SAXONY

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Dieter Bryniok, Hochschule Hamm-Lippstadt
14.30 – 15.00 THURINGIA, **Guzel Shaikhullina**, Moscow, Russia
Igor Ponomarev (FZMB GmbH), Bad Langensalza, Germany
15.00 – 15.30 LOWER SAXONY, **Anna Urumyan**, Moscow, Russia
Alexander Kel (geneXplain GmbH), Wolfenbüttel, Germany

15.30 – 16.00 *COFFEE-BREAK*

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16.00 – 16.20 **PROGRAMS OF THE GERMAN MINISTRY OF EDUCATION AND RESEARCH (BMBF)**
Dr. Jens Schiffers, Research Centre Jülich, Jülich, Germany
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Irina Kuklina, International Centre for Innovations in Science, Technology and Education (ICISTE), Moscow, Russia
16.40 – 17.00 **INTERNATIONAL COOPERATION AND INNOVATION – THE VIEW FROM FASIE**
Olga Levchenko, Fund for Assistance to Small Innovative Enterprises (FASIE), Moscow, Russia
17.00 – 17.20 **CO-FUNDING MECHANISMS OF RUSSIAN-EUROPEAN S&T COOPERATION**
Richard Burger, Research & Innovation Counsellor
Head - Science & Technology Section
Delegation of the European Union to the Russian Federation Research and Innovation Counsellor Delegation of the European Union to the Russian Federation Commission, Moscow, Russia
17.20 – 17.40 **FUNDING POSSIBILITIES OF THE GERMAN HOUSE FOR RESEARCH AND INNOVATION (DWIH)**
Martin Krispin, German House for Research and Innovation (DWIH), Moscow
17.40 – 17.50 **GERMAN RESEARCH FOUNDATION AND ITS PROGRAMS**
Jörn Achterberg, German Research Foundation (DFG), Moscow

18.00 – 20.00 **RECEPTION HOSTED BY WOLFGANG DIK, HEAD OF THE DEPARTMENT OF SCIENCE AND ECONOMY OF THE GERMAN EMBASSY.**

November 18, Wednesday

PERSONAL MEETINGS AND NEGOTIATIONS
Venue: Pushchino, Moscow

SCHOOL-CONFERENCE FOR YOUNG SCIENTISTS "RUSSIAN-GERMAN BIOTECH-2015"
Venue: Pushchino, Branch of Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, prospect Nauki, 6

DEPARTURE OF PARTICIPANTS

ABSTRACT COLLECTION

SECTION "BIOMEDICINE"

MECHANISMS OF NEURONAL SURVIVAL IN STROKE

Zinchenko V. P.[1], Magnus T.[2], Kleinschnitz C.[3], De Meyer S.[4]
[1]ICB RAS, Pushchino, Russia.
[2]University of Hamburg, Germany.
[3]University of Wurzburg, Germany.
[4]Catholic University of Leuven, Belgium.

Despite the devastating nature of ischemic stroke, affecting millions of people each year, current treatment options are remarkably limited. Development of better and safer therapies is strongly hampered by the lack of knowledge on the precise pathogenic mechanisms underlying stroke. In recent years IL-10, one of the most central anti-inflammatory cytokines, have been implicated in the modification of neuronal activity and activation of protective pathways. Previously we show that intravenous administration of IL-10 significantly reduces infarct area. In a rat hippocampal neuronal cell model IL-10 prevented the development of posthypoxic hyperexcitability and protected GABAergic neurons from death. The goal of this project is to understand the role of anti-inflammatory processes in neuronal survival and to use the knowledge of IL-10 signaling cascades to increase it beneficial effects, for the treatment of cerebral ischemia. We will show that IL-10 increases resistance of neurons against hypoxia. We will determine the signaling cascades induced by IL-10 that protect cell from hypoxic injuries. These intracellular signaling experiments will provide new insights into the molecular mechanisms of anti-inflammatory treatment in neurons, helping to design future treatment targets. We plan to design new drugs against these targets to block or stimulate some of these pathways. We will develop IL-10 nanobodies - small single domain antibodies derived from camelid heavy chain antibodies that effectively imitate or potentiate the function of human IL-10. All experiments will necessarily be done by at least two groups often even by all four. Transgenic mice will be sent from Hamburg and Leuven to the other partners, treatments from Moscow and Leuven will be tested by the advanced readout techniques in Wurzburg or Hamburg, positive results will be reproduced at least in three laboratories, and information will be quickly distributed between the partners.

TEXTILE REINFORCED TISSUE-ENGINEERED IMPLANTS

Frese J.[1], Moreira R.[1], Wolf F.[1], Mela P.[1], Thiebes L.[1], Kurtenbach K.[2], Gesche V. N.[2], Jockenhoevel S.[1,2]
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Textile-based solutions are an indispensable part of our daily life and not only limited to fashion and clothing. Therefore, it is not surprising that they play a key role in the medical field of implantology. A closer look at the anatomy and biomechanics lead to the hypothesis that the human body is a textile product as biomechanical properties are mainly defined by fibre structures, like e.g. collagen bundles, elastic fibres, fibrin fibres, fibrous cartilage, and ligament etc.

Driven by the development of biocompatible materials, textile engineering applications are increasingly gaining in importance especially in the field of regenerative medicine and tissue engineering. Tissue engineering approaches are being investigated to construct living autologous implantable structures which have a post-implantation capacity for growth and remodelling. The design strategies are typically based on the seeding of a scaffold material with suitable source of living cells in an appropriate three-dimensional configuration, which is subsequently, conditioned using various external stimuli, including biochemical or mechanical factors.

Our work is focusing on the development of autologous implants, by combining textile-based scaffolds with an autologous fibrin cell carrier material. Fibrin represents an ideal scaffold to the rapid synthesis of autologous tissue-engineered constructs, as it can be isolated from a patient's blood sample. Fibrin gel offers

immediate high cell seeding efficiency, a homogenous cell distribution by gelation entrapment and has a degradation rate that can be controlled by protease inhibitors. Although it seems to be an ideal scaffold material, fibrin alone possesses inadequate mechanical properties to withstand implantation in the vascular system. Therefore, textile reinforcement is inevitable, as it allows the combination of the ideal properties of fibrin with textile structure. Textile reinforcement of cell seeded fibrin gel not only provides the needed mechanical stability, but also anisotropic behaviour and the possibility of controlling the organization of the newly synthesized extracellular matrix. We could successfully demonstrate the ability of different textile technologies to create cardiovascular and respiratory prosthesis such as vascular grafts, heart valves and biologised stents.

TISSUE-ENGINEERED IMPLANTS FOR CARDIO-VASCULAR SURGARY, TRAUMATOLOGY AND ORTHOPEDICS

Akatov V. S.[1,2], Fadeeva I. S.[1,2], Fadeev R. S.[1,2], Senotov A. S.[1], Muratov R. M.[3], Lekishvili M. V.[4], Guriev V. V.[5]

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[2]Pushchino State Natural Sciences Institute, Pushchino, Russia.
[3]Bakulev Scientific center for cardio-vascular surgary, Moscow, Russia.
[4]Central Institute for Traumatology and orthopedics, Moscow, Russia.
[5]Moscow state university of medicine and dentistry, Moscow, Russia.

Tissue-engineering implants based on biomaterials are widely used for reconstructive cardiovascular surgery, traumatology, orthopedics, maxillofacial surgery. Some modification of these materials is required to provide regenerative and reconstructive properties taking into account understanding the mechanisms of body reaction against implanted materials, mechanisms of tissue regeneration stimulated by implants.

In the laboratory of tissue engineering at ITEB RAS the mechanisms of calcification of biomaterials for cardiovascular surgery are studied and new technologies are developed for suppressing the pathological calcification of these biomaterials, to improve their functionality. Some of these technologies were introduced into the process of heart valve allograft modification in Bakulev Center of Cardiovascular Surgery.

Laboratory of Tissue Engineering at ITEB RAS develops also new biomaterials for traumatology and orthopedics, and studies effects of these biomaterials on the regeneration of bone, tendons and ligaments in laboratory animals. These biomaterials are developed in cooperation with Moscow centers of traumatology and orthopedics.

OBTAINING OF HYDROLYSATES FROM CARTILAGE TISSUE BIOPOLYMERS AND VITAMIN MINERAL COMPLEX TO PREVENT AND TREAT JOINT DISEASES

Nikolaeva T. I.[1], Molchanov M. V.[1], Laurinavichus K. S.[2], Sova V. V.[3], Kaptsov V. V.[4], Shekhovtsov P. V.[1]

[1]Institute of Theoretical and Experimental Biophysics RAS.
[2]Institute of Biochemistry and Physiology of Microorganisms RAS.
[3]Institute of Protein Research RAS.
[4]Institute of Cell Biophysics RAS; Moscow region, Pushchino.

Joint arthritides and arthroses, destructions of intervertebral cartilage are widely spread chronic diseases. As degradation of connective tissue occurs, the disorders of musculoskeletal system are hardly treated by pharmacologic drugs. One of the problems of efficient search of preparations may be solved by development of the nutraceuticals derived from animals' and hydrobionts' tissues components. Provided that the preparations have biopharmaceutical effect on joints. Connective tissue formation arises from the substances that predominantly are orally administered in the form of nutrition. Complete set of biopolymers can be obtained from analogous tissues of farm animals. The basic structural elements of the cartilage tissue are collagen proteins and proteoglycans. Bioavailability of these biopolymers for absorption by human body is high after hydrolysis to the extent of amino acids peptides and glycosaminoglycans' fragments. These low

molecular components enter into blood-vascular system then into cells, they participate in the biosynthesis of macromolecules and in the formation of tissue matrix.

During diseases changes occur in all joints first of all in the hyaline cartilage. Thinning, separation and loss of elasticity of collagen fibrils take place. This is why we chosen material for study hyaline cartilages on the 1st stage of research. The cartilages were derived from the tracheae of bovine animals and pigs. As a rule, sets of enzymes, but not separate proteases, are used for the hydrolysis of proteins that are contained on the connective tissues. These enzymes have specific effect destroying certain links in the proteins. We used the following sets of enzymes: protepsin, phytopain, himopsin, papain, pancreatin, collagenase. We demonstrated that the highest extent of hydrolysis is observed under the effect of phytopain with the following conditions: pH 6,0, T=55 °C, 10% of phytopain, time of hydrolysis is 3 hours. The analysis of qualitative composition of the hydrolysates was studied by the methods of nuclear magnetic resonance (NMR) and mass spectrometry. Signals of peptides that contain 10 to 50 amino-acid residues are identified in NMR spectra. The results of mass spectrometry demonstrate the presence of peptides having molecular weight 2000 - 4000 D and also fragments of hyaluronic acid and chondroitin-4-sulphate of molecular weight 80 - 1000 D.

As a result of enzymatic hydrolysis we made the basic composition of the nutraceuticals containing low molecular elements of matrix of the hyaline cartilage. Oral administration of these nutrients stimulates disordered during diseases biosynthesis of matrix macromolecules in cells. The efficiency of nutraceuticals increases if they contain vitamins, micro- and macroelements. We assembled the composition of them for activation of the enzymes that catalyze the process of collagen fibrils and proteoglycans' formation. Such composition of substances is contained in marine algae fucus manufactured by LLC "Native" (Town of Pushchino, Moscow region). On the base of fucus and other vegetable components we obtained additional set of vitamins and minerals applicable to the basic one.

NANOAEROSOLIZED DRUGS AND INSECTICIDES

Morozov V. N.[1,3], Kanev I. L.[1], Mikheev A. Y.[1], Shlyapnikova E. A.[1], Shlyapnikov Y. M.[1], Nwabueze A. O.[2,3], Propst C. N.[2,3], van Hoek M. L.[2,3]

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Many commercial devices for treatment of asthma, tuberculosis and other lung diseases with drug aerosols have been developed. However, all inhalers and nebulizers produce micron-sized drug particles which poorly penetrate into the alveolar region. Recently we have developed a new technology for generation of nanoaerosol particles (NAPs) from biological molecules (antibiotics, proteins) with complete retention of their structural and functional properties. The technology has been tested in treatment of mice infected with pulmonary tularemia. It was found that inhalation of levofloxacin NAPs saved most infected mice if the antibiotic was packed into liposomes before atomization.

In this report the benefits and drawbacks of the new drug form will be discussed. Atomization of a substance into NAPs changes its chemical and physical properties as well as its pharmacodynamics and therapeutic effects. First, unlike the oral application when drug is first subjected to destruction in the stomach and then in the liver inhaled drug quickly penetrate into blood stream and reach other organs without being subjected to proteolysis and hydrolysis. Second, substantial reduction in the working doses is expected in terms of mg/kg, since the drug NAPs are delivered to the infection site and since the number of particles per number of the lung cells may provide a new basis for dosing. It is not excluded, however, that the direct exposure to a highly concentrated drug solution in the area where drug particle landed may produce unusual side effects.

To study potential side effects of nanoaersolized drugs fruit flies (*Drosophila melanogaster*) were employed as an inexpensive biological model. We showed that exposure of the flies to imidacloprid (IMI) NAPs resulted in their rapid knockdown (T_{50}=88 ± 14 min at 22 °C and T_{50} = 36± 2 min at 33 °C). It was demonstrated that the concentration dependence of T_{50} follows the Haber rule, CxT_{50}=const., and that only the IMI NAPs with the diameter below 300 nm contributed to the fly poisoning. Doses inducing knockdown in flies upon oral application were experimentally determined and compared with the doses upon exposure to IMI NAPs. Two models were developed to calculate NAPs doses. First one assumes that IMI NAPs are

deposited from all the air volume from which oxygen was consumed. In the second model NAPs deposition is calculated by comparing diffusion of oxygen and NAPs in the fly tracheas. It was found that the tracheal deposition resulting in the knockdown is ~ 1/100 of the oral dose according to the first model and ~ 1/100,000 according to the second model.

Experimental data thus indicate that IMI NAPs quickly penetrate fly nervous cells through the breathing system causing knockdown. Shown here ability of non-volatile insecticide NAPs to be highly effective in killing insects might find applications in the green houses and vegetable storage facilities.

BIO-ISPIRED TOOLS BASED ON SELF-ASSEMBLED HYBRID NANOSTRUCTURES IN BIONANOTECHNOLOGY

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The development of nanotechnological tools based on bio-inspired nanostructured materials for the delivery of anti-infective, anti-cancer and diagnostic agents is a pivotal goal to solve challenges in several areas of biotechnology. The available technologies to design and fabricate nanostructures with controlled composition and architectures are often not green and expensive nor scalable and usually limited in dimension and require multiple step processes. The presentation will demonstrate a simple and bio-inspired nanofabrication approach based on directed self-assembly of organic-inorganic hybrid materials as green, cost-effective and powerful tool for manufacturing well-defined architectures. These are designed with nanometres precision to control bio-interfaces interactions at different dimensions and length scales. The key concept is to use self-assembled soft-matter systems (block copolymer, biopolymer, Dendrimers) linked with in-situ inorganic components (Au, Ag, Fe_3O_4 ...) to generate bulk quantity of quality multifunctional nanostructured hybrid materials. These are controlled by composition, shape and size imposed during the fabrication process to obtain hybrid nanostructures for wide range of biotechnology applications. The main advantage of the in-situ preparation is that the size and size distribution of the inorganic components are well controlled inside the soft-matter systems. These will facilitate novel collective properties and provide active building blocks for constructing novel multifunctional materials with cost-effectiveness and superior quality in broad spectrum of vital applications in biotechnology, nanomedicine and public health.

RAPID QUANTIFICATION OF PATHOGENS, BIOTOXINS AND SMALL MOLECULES BY FLOW-BASED CHEMILUMINESCENCE MICROARRAYS

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Microarray technology is an emerging field in analytical chemistry and a powerful analytical tool for the simultaneous detection of multiple analytes in a single sample. A microarray consists of a defined matrix of reaction fields on a supporting material. Biochemically selective receptors like antibodies, DNA or aptamers are deposited by microdispensing and immobilized on a surface by physical or chemical interactions. The generated spots have diameters in the micrometer range. Hundreds or more bioanalytical reactions can be performed on an area of one square centimeter. The reaction on each spot is traceable back by knowing the position of each selective receptor. The multi-analyte method by means of analytical microarrays became a frontier research topic in analytical chemistry due to the possibility of generating multiple sets of quantitative data for different analyte classes in a short time.

Applications are in the field of pharmaceuticals, toxins, allergens, proteins, and (pathogenic) microorganisms and viruses. Multi-analyte quantitative methods are important if a panel of analytes should be quantified. For many different analytes, critical values in food and water safety are defined. Forensics, diagnostics and biosecurity are other fields in analytical chemistry for multiplex analysis. Small organic molecules, proteins, microorganisms, and viruses are quantified by microarray immunoassays (MIAs). Nucleic acids of microorganisms, viruses, or eukaryotic cells are analyzed by nucleic acid amplification tests (NAATs) on DNA microarrays. For multiplex measurement, hybridization assays on DNA microarrays are performed.

In our research institution is developed the flow-based chemiluminescence microarray analysis platform MCR 3. Pathogens, proteotoxins and small molecules are quantified rapidly with high sensitivity by DNA and antibody microarrays [1]. Following applications are presented in the lecture: Antibiotics in milk, biotoxins in food samples, zoonotic pathogens in slaughtered pigs, hygiene control of food and water by quantification of pathogenic microorganisms and viruses.

[1] Seidel, M. and Niessner, R., Chemiluminescence microarrays: a critical review. Analytical and Bioanalytical Chemistry 2014,406, 5589–5612.

RESEARCH CENTRE OF MEDICAL TECHNOLOGY AND BIOTECHNOLOGY (fzmb GmbH)

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The *fzmb GmbH* is a private non profit research company for medical technology and biotechnology. It has 110 fellows in the 4 departments, Animal clinics (horse, cow, companion animal), Diagnostics (veterinary, food control), Biotechnology (antibodies, recombinant proteins, cartilage cell culture) and Bio-instruments (Immunoassay analyzer, near infrared spectroscopy NIR, ion mobility spectroscopy IMS).

The mission of the company is to provide research services for small and medium size companies (SMEs). The major FZMB research and development areas are: 1) immunology and antibody technology; 2) arthritis and cartilage regeneration; 3) gas (IMS) and food analytics (NIR)

In the field of *antibody technology* the fzmb has a complete horizontal technology portfolio which comprises antibody generation, characterisation, immobilisation and various applications in biological assays (immunoassays) and down stream processing (affinity chromatography, magnetic bead separation). The fzmb has been working many years together with Russian research partners to develop new antibodies and innovative immunological methods - in particular for “point of care testing”.

Currently the fzmb GmbH and the RCMDT Research Center for Molecular Diagnostics and Therapy use a Joint German-Russian funding competition of the Federal Ministry of Education and Research (BMBF) and the Russian Foundation for Assistance to Small Innovative Enterprises (FASIE) in the area of applied, industry-related, innovative research and development. In this joint project (project number: 01DJ14011A) “The development of highly sensitive recombinant antibodies for the establishment of rapid tests based on the 3-D-immunofiltration for the detection of toxins” we jointly develop a new method for *in vitro* generation of monoclonal antibodies. The partner combine their expertise in genetic engineering (RCMDT), Cell biology (FZMB) and testkit production (Senova GmbH) to generate a novel antibody based rapid test kit for the detection of microbial toxins.

In the field of *arthritis and cartilage regeneration* the fzmb has developed a method to produce 3D-scaffold-free cartilage transplants (SFCT). Cartilage constructs produced by SFCT-technology provide promising opportunities to restore cartilage defects in humans and horses. In addition, SFCT-technology presents a new suitable and promising approach to reduce and replace animal testing that can be used in different fields of interest such as pharmacological screenings in frame in vitro arthrosis research.

In the scope of the «Trilateral Partnerships» programme funded by the Volkswagen Foundation, together with Ukrainian (Institute for Genetic and Regenerative Medicine, Kiev) and Russian (Baltic Federal University of Immanuel Kant, Kaliningrad) colleagues we want to apply our SFCT-technology for regeneration of ligaments and tendons.

In the area for *IMS and NIR* the fzmb is involved in several joint product developments with industrial partners aiming to provide portable devices for on spot testing of voitals substances (IMS) and foodstuff composition (NIR).

SITE MANAGEMENT ORGANIZATIONS IN NON-CLINICAL STUDIES

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Biopharmaceuticals industry imperatives demands a systematic approach to preclinical research that starts with predefined objectives and emphasizes processes, systems, and process control based on quality risk management. Centralized management of business and operational functions intended to control the quality and performance of work from the very beginning of the planning phase, usage entire quality metrics relating to preclinical research safety, risk, and conduct standards, generalized for the group of Investigational Sites allows to maintain required level of quality of study results, reduces data bias, monitoring and management burdens while facilitating trial supply and documentation. The survey is aimed to provide a summary of the modern market situation, SMO definitions and Preclinical Study Centre roles and responsibilities within the Pushchino Scientific Center and the biotechnological regional innovation cluster network.

NITROSYL NON HEME PROTEINS MIMETICS AS NEW AGENTS FOR CANCER CHEMOTHERAPY

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The search for new approaches to the development of effective and non-toxic prodrugs based on metal coordination compounds has been performed intensely in leading laboratories world-wide.

It is known that nitrosyl iron complexes are intermediates in the decomposition of proteins and formation of S-nitrosothiols, which are catalyzed by the iron, and are reservoirs and transporters of nitric oxide (NO) *in vivo*. Based on these data, methods for synthesis and investigation of properties (X-ray analysis, IR-, EPR, Mössbauer spectroscopy, SQUID magnetometry and amperometry (NO donating activity)) of nitrosyl [2Fe-2S] and [1Fe-2S] ferredoxins mimetics have been developed, with the aim to use them as NO donors in the in the treatment of NO-chemotherapy of oncological diseases. High anticancer activity *in vitro* and *in vivo* has been first shown for a series of binuclear tetranitrosyl iron complexes. Functional sulfur-containing ligands in such complexes are reversible inhibitors for synthesis of cellular DNA, and they suppress the growth of tumors of various genesis, while the NO group, being the second component of the hybrid complex, is a key signal molecule that controls the tumor growth. All studied binuclear tetranitrosyl iron complexes were shown to be inductors of apoptosis in tumor cells. High anticancer activity of some nitrosyl iron complexes was detected on mice's transplantable tumors.

A water-soluble мononuclear dinitrosyl iron complexes (DNICs) with thiourea and Nethylthiourea have been synthesized and studied for the first time. They were shown to be less toxic (almost ten times) than the anticancer agents of the platinum group – *cis*-platin and satraplatin – studied earlier, their activity being the same. HeLa cells have been shown to be much more sensitive to DNICs than MCF7 cells, a response similar to that observed for the platinum complexes. The mechanisms of the cytotoxic effect of the nitrosyl complexes, as well as the reduced sensitivity of MCF7 cells to the effects of the NO donor of this class, should be examined additionally.

AMINONITROXYL PLATINUM COMPLEXES AS ANTITUMOR COMPOUNDS

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Platinum based drugs have long history of successful cure of a number of cancers, but their clinical use is restricted because of severe side effects and resistance (intrinsic or acquired) of tumors to these drugs. We have synthesized a series of aminonitroxyl tetravalent platinum complexes of common structure $Pt(IV)(NH_3)(R{\bullet}NH_2)Y_2Cl_2$, where R is a nitroxyl radical and Y is an axial ligand, and studied their effects on tumor cells of several lines. The axial ligands of synthesized complexes are the residues of fatty acids of different lengths. These ligands can change lipophilicity of the complexes which is important for their ability to penetrate into cells. The nitroxyl radical moiety was introduced into the platinum complexes because it is

known that nitroxyl radicals possess antioxidant properties. Since reactive oxygen species generation and oxidative stress were observed in cells and organs of animals exposed to platinum based drugs, the antioxidant nitroxyl moiety could confer less toxicity.

It was found that introduction of nitroxyl radical to structure of Pt(IV) complexes drastically decreased the cytotoxicity of resulting compounds. Placing fatty acids at axial positions of tetravalent platinum complexes allowed us to obtain complexes that possess cytotoxicity exceeding that of original Pt(IV) componds. Cellular accumulation of aminonitroxyl Pt(IV) complexes depends on structures of their axial ligands. The direct nitroxyl derivatives of Pt(IV) complexes have the slowest accumulation rates, while complexes with modified axial ligands exhibite higher rates of cellular accumulation.

In experiments with pulse exposure, the aminonitroxyl Pt(IV) complexes have been shown to develop their cytotoxic effect much slower compared to cisplatin. Thus, despite high cellular accumulation rates, aminonitroxyl Pt(IV) complexes compounds require an additional time to reach their high cytotoxicity. This suggest that the Pt(IV) complexes are prodrugs that have to be reduced to active Pt(II) derivatives to exert their antitumor activity.

Antitumor effects of aminonitroxyl Pt(IV) complexes is compared to that of cisplatin, but aminonitroxyl complexes are several fold less toxic to animals. In experiments with combination therapy of model animal tumors a synergistic action of aminonitroxyl Pt(IV) complexes and cyclophosphamide or cisplatin was observed, resulting in high survival rates of tumor bearing animals.

HYDROXYLATION OF STEROIDS BY FILAMENTOUS FUNGI AS A PLATFORM FOR PRODUCTION OF HIGH-VALUED PHARMACEUTICAL INTERMEDIATES

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Hydroxylation is one of the most important reactions of steroid functionalization. Steroids of pregnane or androstane series with hydroxyl functions at positions 11α/β or 14α are widely used as anti-inflammatory, immunosuppressive, anabolic and contraceptive agents; 7α/β-hydroxyderivatives of bile acids are known for their therapeutic action against many human diseases.

Microbial catalysis is an effective tool for steroid hydroxylation which allows generation of the compounds which may be difficult to obtain by conventional synthetic methods. Hydroxylase activity towards steroids is widespread among the fungi. However, practical realization of steroid hydroxylation bioprocesses by fungi is often restricted by insufficient selectivity because of some side reactions in whole-cell catalysis. In this regard the search of new highly efficient biocatalysts capable of selective steroid hydroxylation is of importance.

In this work we used experimental screening in order to reveal novel strain candidates with target steroid hydroxylase activity. More than 300 fungal strains of different taxonomy were tested on their capability to catalyze regio- and stereospecific hydroxylation of 3-keto- and 3α/β-hydroxy-steroids of adrostane, pregnane and cholane series with optimization of processes by the most active strains.

The representatives of *Gongronella*, *Scopulariopsis*, *Epicoccum*, and *Curvularia* genera have been revealed as the most promising biocatalysts for steroid 11β-hydroxylation of cortexolone, deoxycorticosterone and their acetylated derivatives. The presence of 17-acetyl group was shown to facilitate further selectivity of 11β-hydroxylation. The strains of *C. lunata* VKM F-644 and *G. butleri* VKM F-1033 expressed maximal target activity. Original procedures for protoplasts obtaining, mutagenesis and mutant strain selection of *C. lunata* allowed obtaining of a stable mutant M4 with increased 11β-hydroxylase activity that provided over 90% of 11β-hydroxylated derivatives under optimized conditions. *C. lunata* M4 mutant strain was also revealed as the most effective biocatalyst of 14α-hydroxylation towards steroids of androstane series. The maximal yield of 14α-OH derivative (up to 80%) was obtained at the incubation of *C. lunata* M4 strain with 9α-hydroxy-androstendione. Another strain, - *Aspergillus ochraceus* was shown to be the most effective biocatalyst for 11α-hydroxylation of androstendione (AD); yield of 11α-OH-AD exceeded 95%.

The capability of pregnenolone transformation to 11α-hydroxyprogesterone with 3β-OH group oxidation, $\Delta^5 \rightarrow \Delta^4$-izomerization and 11α-hydroxylation combination in one biotechnological stage was revealed for *Rhizopus stolonifer* VKM F-401, as well as for three strains of *Aspergillus* genus with its maximal level in

Aspergillus niger VKM F-212. 11α-Hydroxyprogesterone was accumulated as major product yielding up to 70% under the optimized conditions.

With the exception of few experimental works, lithocholic (LCA) and deoxycholic (DCA) acids have not been strongly investigated as a substrates for bioconversion by fungi. We firstly revealed the formation of 7α/β-hydroxylated derivatives for 34 tested fungal strains of different taxonomy. Under the optimized conditions, the yield of 7β-OH-derivatives: ursodeoxycholic (UDCA) and ursocholic (UCA) acids reached 90% during LCA and DCA transformation by *Gibberella zeae* VKM F-2600 and *Fusarium merismoides* VKM F-2310 strains, correspondingly.

The results confirm that experimental screening is still a powerful tool for the discovery of novel active biocatalysts. Fungal strains are capable of effective regio- and stereoselective hydroxylating of different types of natural and synthetic steroid substrates of both pregnane and androstane series, as well as bile acids. The results might be suitable for preparative-scale exploitation of the selected fungal strains for production of high-valued hydroxylated intermediates for pharmaceutical industry.

"INNOVATION BRIDGE NORTH RHINE-WESTPHALIA – RUSSIA": ENHANCING COOPERATION IN RESEARCH AND INNOVATION

Paveliev S.
ZENIT GmbH – Centre for Innovation and Technology in NRW

ZENIT GmbH is the innovation agency of the German State of North Rhine-Westphalia (NRW). ZENIT paves the way and helps clients from across the globe gain a foothold in one of Europe's leading regions. On behalf of the EU, national and regional bodies, ZENIT provides innovation related services for the benefit of companies, as well as universities and research institutions.

Russia is regarded as a strategic partner of NRW in R&D, innovation and business. The long term project "Innovation Bridge NRW – Russia" enables a cost-neutral access to a broad range of ZENIT's services for Russian companies, universities and research institutes. Services include: initiation and support of research and innovation partnerships; customized advisory on regional, national and international funding and financing instruments; establishment of technology and know-how transfer; organisation of conferences and delegation visits; provision of information on markets, infrastructure and innovation related measures.

COMPOSITION FOR TREATMENT OF ACUTE AND CHRONIC HEPATIC ENCEPHALOPATHY

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Definition: Hepatic encephalopathy (HE)-brain dysfunction determined by liver insufficiency to filter out gut ammonia and related toxins.

The aim: Development of combined preparations, which may be used as pharmaceutical compositions or as dietary supplements, which enable to prevent, delay or relief the neurocognitive and metabolic disorders, related to HE, liver, brain, vascular system, etc. dysfunction.

Current state: Most common therapeutic options are directed towards the treatment of precipitating factors and reduction of circulating ammonia («ammonia lowering strategies»-ALS), rather than on correction of the deterioration in the brain, liver, vascular system, etc. or on supportive therapy. ALS are used over last 50 years and are based on trapping of ammonia (L-ornitine-L-aspartate) or of ammonia and adaptively accumulated L- glutamine (L-ornitine-phenylacetate). More than 55 years ago W. McDermott, evaluating the efficacy of existing treatment options, based on amino acids therapy, wrote*: it should not be expected that this will prove to be a universal panacea not should be expected than any one administered substance could effectively reverse all the derangements...*

New offered approaches in the therapy of HE so cold «counteracting or neuroprotective strategies» are based on application of the inhibitors or antagonists of multiple proteins, attacked by ammonia or other toxins. Systemic application of them might have side effects.

Results: The etiology of HE is multifactorial and very complex and to address this issue the multi target therapy should be developed. Our strategy is focused on the development of group of medical preparations, representing complex formulations of compounds, having multiple functions and combined synergistic action on different targets, which are affected in the process of HE development. Based on animal study were run out preliminary treatment with different dosage of 45 patients (1 week treatment and 1 month treatment periods and 1 month follow up period), which have liver cirrhosis of viral etiology and hepatic encephalopathy. The study was performed on the basis of informed consent. We have Russian patent, PCT application and the License for the production of dietary supplements.

Conclusions: No adverse events were observed in both study groups. The results of this trial show that oral administration of claimed composition is safe, well tolerated and effective. It resulted in significant decrease in ammonia concentration with concomitant rise in CFF-test values and reduction of AAT activity and do not have rebound effect (the rise in ammonia concentration and fall of CFF values) after cessation of patients treatment, due to the fact that therapeutic effect is preserved during one month post treatment period.

SECTION "BIOECONOMY"

REFINEMENT OF LIQUID AGRICULTURAL SLURRY OR DIGESTATE

Drs. Hans J. P. Freiherr v.
Donop – Vapora group B.V. The Netherlands and Germany

"Waste does not exist, only wasted resources"

That is the vision and ethical basis of VAPORA, an international West- European technical consulting company in Germany and The Netherlands. We don´t develop and trade technology but analyze, evaluate existing or new methods or technical solutions and arrange them in a operating process chain.

Intensive livestock breading and importing fodder increase the problems of liquid "waste". The main objective is to prevent over-fertilization and longtime consequences to agricultural soil.

Most important is to understand: what is the real situation of customers, on which resources they have access and which are the main problems with slurry, digestate or sewage sludge.

To prepare good decisions on customer's side, we know and advise how to refine this "waste" into useable secondary products or renewable resources. That needs time to analyze and report his "reality" and his objectives and preselect technologies for economical solutions.

Working together with governmental organizations like Energy Agency North-Rhine-Westphalia (NRW) at the cluster for "biomass conversion and energy research" at Düsseldorf and the NRW-Ministry of Environment & Agriculture, early we get knowledge about new technologies and methods.

We evaluate those technologies, how to use and to shorten the "time to market". We benchmark the potential of these technologies to be combined with other ones and how to be part of a complete process chain from "waste" to renewable resources.

An optimal solution in refining liquid "waste" is to extract the water content out of the contaminated liquor, to save organic minerals, destroy hormones and pharmaceutic elements and clean the water into environmental friendly osmotic water to be dumped in rivers. The dry solid content can be used as an energetic source to make offgrid heat and power.

There are 20 up to 30 different technologies to be implemented. But which combination will solve customer´s problems and what will come as close as possible to his economic intent?

So we are transmission belts between R&D- / production companies and customers need, but staying at customer´s side, which normally has no detailed knowledge or experiences of possible approaches. We have the focus on the total process chain and no reduced look on isolated modules. So we reduce the risks in decisions.

Summary:

The VAPORA advisors analyze customers need /objectives, evaluate and arrange adequate technologies, how to separate liquid/dry content, to clean the water content of liquid "waste" from agriculture and/or municipal sewage, to recycle and refine the fertilization elements as ammonium, phosphate and potash to secondary products. The dry solid content can be used for energy production to feed burning, pyrolysis or steam installations.

THE NEW UNIVERSITY OF APPLIED SCIENCES HAMM-LIPPSTADT: THRIVING FOR EXCELLENCE IN TEACHING AND SCIENCE

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The University of Applied Sciences was founded in 2009. Today, it comprises 4.500 students studying in fourteen different Bachelor and five Master degree programs at two locations - the cities of Hamm and Lippstadt. Currently, the University is staffed with 77 Professors, 65 Research Associates and 94 administrative and technical employees. The University is still in its planned growth phase, aiming for employing 120 Professors and 120 additional staff in its final state in a few years.

The University is headed by its President Prof. Klaus Zeppenfeld and its Vice-President Karl-Heinz Sandknoop. The University currently has four departments (two in Hamm and two in Lippstadt) and comprises brand new Buildings and state-of-the art laboratories.

Bachelor and Master Degree programs include: "*Energy Engineering and Resource Optimization, Biomedical Engineering, Technical Management and Marketing, Intelligent Systems Design, Sports and Health Care Engineering, Product and Asset Management, Applied Biomedical Engineering, Mechatronics, Industrial Engineering with Business Studies, Computational Visualistics und Design, Material Design – Bionics and Photonics, Social Media and Communication Informatics,* and *Business and Systems Engineering*.

In 2015 the following Bachelor and Master Degree programs were newly introduced: *Environmental Monitoring and Forensic Chemistry, Intercultural Industrial and Organizational Psychology, Biomedical Management and Marketing, Business Administration, Industrial Engineering and Design*, and *Technical Entrepreneurship and Innovation.*

This broad orientation of study programs is supported by central functions like the *Center for Knowledge Management*, the *Center for Teaching Management* and a (planned) *Center for Research Management*. Additionally, essential administrative support is provided by the functions of *Academic and Student Affairs, Organization and Service*, and *Finances, Research and Human Resources*.

Whereas the Universities' initial years were characterized by focusing on excellence in teaching, now new efforts are made to thrive in science and technology. These efforts include establishing links to basic and industrial research institutions and companies as well as directing independent and strong sciences programs within the University. Examples of such research programs relating to Bioindustry, Bioresources and Biotechnology include the MOST- (*Model-based process control of biogas facilities*) Project directed by Prof. Dr. Dieter Bryniok, and the LEUKAEMIA- (*Microchip for differential diagnosis of leukaemia*) Project directed by Prof. Dr. Lara Tickenbrock.

The infrastructure to initiating additional, innovate Biotech programs is established.

INTEGRATION OF VKM IBPM RAS IN EUROPEAN AND GLOBAL INFORMATION SYSTEMS

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Brief presentation of the main projects and infrastructures in microbial culture collections information systems: MINE, MSDN -> CABRI -> EBRCN -> StrainInfo -> GBRCN, EMbaRC -> WDCM, MIRRI. Participation of the Russian culture collections. Data communication with biomedicine, pharmacology, agriculture, brewing, with food and vine production – information problems and possible solutions in MIRRI-ERIC.

MICROBIAL RESOURCES, DATA AND SERVICES OF VKM OFFERRED FOR BIOTECHNOLOGY

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The expanding network of culture collections seeks to provide a widening spectrum of biomaterials and associated information to meet the growing demands of modern biotechnology.

The All-Russian Collection of Microoganisms (VKM) located at the G. K. Skryabin Institute of Biochemistry and Physiology of Microorganisms (Pushchino, Moscow region) is one of the largest Russian collections in the area of non-medical microbiology. It hosts nearly 20,000 cultures of bacteria (including actinobacteria), archaea, filamentous fungi and yeasts isolated from various environments of different geography, and contains many strains of biotechnological interest. The VKM sub-collection of fungi from low-temperature habitats is the largest one among those "coming in from the cold" and currently includes nearly 750 strains (more than 140 species). Screening conducted among fungi and bacteria from low-temperature habitats revealed several strains of potential medical interest. VKM also offers services such as supply and deposition of cultures, including deposition for patent purposes according the requirements of the Budapest Treaty and deposition of newly described taxa. Scientific services mostly focus on identification,

sharing expertise as well as training. Recent activities of VKM emphasize the development of information resources at VKM (including the DataBase "Microbial Application Properties") as well as integration of the currently dispersed microbial collections in Russia into a common virtual network.

NEXT GENERATION IN PROBIOTICS

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On the market there is a large number of probiotics, which contain live beneficial microorganisms intended for the restoration of violated intestinal biocenosis. Current probiotics are obtained by laboratory cultivation on nutrient media. However, bacteria living in nature are greatly different by the properties from the cultures grown in ''classic'' laboratory conditions. The dominant lifestyle of bacteria in the natural environment is biofilm. Biofilm is a stress-tolerant community of microorganisms held together by intercellular junctions and a self-produced extracellular matrix, which forms on the surface of objects of the environment and the tissues of living organisms. We proposed that biofilm probiotics had advantage over the marketed planktonic ones. One can suppose that biofilm-driven gene expression might make the probiotics bacteria harmful for health. Three responses can be given as a counterclaim. First, the resident microbiota of the human and animal body grows in a biofilm. Second, according to our study the traditional health-giving foods Natto (similar to Pepoke of Myanmar, Chungkukjang and Doenjang of Korea, Sufu or Furu of China and Thua nao of Thailand, soya beans fermented by terrestrial bacilli), which Japanese consume for hundreds of years, include fermenting bacteria in a biofilm. Third, our experiments on animals (mice, dogs, poultry, aquaculture fish) and human volunteers show that the biofilm bacteria are not only harmless but health beneficial. So the results of our studies indicate the possibility of bacterial biofilm growing technology application for the development of veterinary/medical probiotic preparations and products of functional nutrition.

PREBIOTIC PRODUCTS BASED ON ALGAE FUCUS AS A MEANS OF PREVENTION OF COLORECTAL CANCER

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Chronical intestinal inflammation provoked by dysbiosis in genetically susceptible individuals is an important factor related to carcinogenesis. One of mechanism of normal gut microbiota formation is fucose-contained oligosaccharides of mother's milk and gut mucins which are a feed for bacterial symbionts and a part of innate immunity. Source of fucose-contained polysaccharides in food could be the kelp. These polysaccharides could be prebiotic for bifido- and lactobacteria, the group of bacteria whose quantity is reduced during the development of inflammatory bowel disease and colorectal cancer. The Russian company NATIV and German VivaCell Biotechnology GmbH together under a project supported by FASIE and BMBF, engaged in the development of functional food - beverages from Fucus algae for the prevention of colorectal cancer. NATIV Ltd. is developing of their production technology, while VivaCell Biotechnology GmbH is examining on the safety of food components and evaluation of their anti inflammatory properties.

FOOD SAFETY

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Substandard food products are the cause of high morbidity and mortality in the general population, but especially among people with weakened immune systems, children and the elderly. The number of food-borne diseases is increasing due to changes in farming practices; livestock intensive technologies aimed at maximum reduction of production costs; increase in the proportion of meat and poultry products in the diet; expansion of food distribution systems; the emergence of new types of products that may contain little-known pathogens; the emergence of new hazardous for people zoonotic infections; expansion of the range of diseases caused by microbial, parasitic or chemical contamination of food; a significant increase in the number of people who are more susceptible to microbial contamination of food. Emergency situations caused by substandard food, dictate the need for countries to take all measures to reduce the scope of their possible severe consequences for health, the economy and society as a whole.

The Proposed Developments:

(1) New biofungicides Cellobiosolipids (CBL) - natural detergent compounds able to effectively inhibit the growth of a wide variety of plant pathogenic fungi. CBL can be used in greenhouses, in store houses to improve the preservation of fruit and vegetables, as well as at small enterprises of dairy and meat industry as a gelling agent, biodegradable detergents, and as agents able to reduce ice formation in refrigerators. They are non-toxic, easily utilized by microorganisms, thermostable and stable at storage. The CBL preparations are safe for animals and humans, they do not jeopardize the soil microflora and do not adversely impact on the environment. They can be produced as solutions or sprays for the treatment of plants and /or fruits and vegetables; in the form of powder, CBS microbiological preparations (yeast strains-producers) can be applied directly to soil or to treat the harvest. Advantages: An easy and cheap production as well as simple, not requiring expensive equipment, method of application. At present it is planned to study the possibility of optimizing the yield of CBL using cheap nutrients depending on the geographical region, e.g. biodiesel wastes, sugarcane wastes, food and soap industry wastes that contain vegetable oils, and others.

(2) “Potok” Technology to provide safety conditions of production, transportation and storage of food. This innovative energy-saving technology “Potok” is used for the decontamination of air in enclosed spaces. The technology provides a consistent, controlled, 100% efficient inactivation of viruses and microorganisms in the treated air stream. The technology has proven its absolute effectiveness in a variety of conditions ranging from space stations to hospitals, food production facilities, greenhouses and vehicles. The technology can be used to provide food safety in such cases as: Growing of fruits and vegetables under conditions with the controlled air flow; transportation and storage of food in the controlled air environment to prevent its damage and decay and thus to provide longer shelf life; preparation, packing and packaging of food in the required “clean” environment with the controlled air conditions (according to ISO and GMP).

“USEFUL SUN” STRATEGY FOR PHOTOBIOMODULATION IN MEDICINE AND AGRO-BIOTECHNOLOGY

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This project focuses on the development of nanoparticle containing light-converting materials (LCM) and the further of experimental validation our priority approach - strategies “useful sun” (Khramov et al., 2010; Gapeev et al., 2012). Such LCM absorb shortwave (including UV) components of solar radiation and convert it into orange-red (OR) and infrared (IR) light. In our studies , it was found that the strategy of “useful sun” in comparison with the strategy of “safe sun” (to block UV only) provides the following benefits for the man and

animals: a) increases physical performance of athletes at bench tests by 9%, b) speed up the rate of 40-100% of the regenerative processes of tissues and organs of human and animal without conceding a laser and LED technology photobiomodulation, c) increases by 50% the physical performance of animals (swimming test),in particular, with the improvement of morphological and functional characteristics of the myocardium, g) improves recovery retinal of rabbit after laser burn, d) protects the blood cells (in vivo and in vitro) from the damaging effect of genotoxic factors of physical and chemical nature.

DEVELOPMENT AND PRODUCTION OF ENZYMES FOR THE SELECTIVE AND EFFICIENT DEGRADATION OF PLANT BIOMASS

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Plant biomass represents an attractive, abundant and sustainable resource that can supply a variety of products for direct usage or for chemical or fermentative production processes in industry. In particular the polysaccharides of plant cell walls, cellulose and various types of hemicelluloses are interesting raw materials for applications in industrial biotechnology. To this end, enzymes involved in plant cell wall polysaccharide decomposition represent important biocatalysts that allow the efficient saccharification of (hemi)celluloses while simultaneously operating under relatively mild conditions. To be of the best possible value for environmentally friendly industrial production processes, such enzymes (i) must perform the desired catalytical function as efficiently as possible, and (ii) must be available in sufficient amounts at an affordable price. In collaboration with partners from Russian research institutions (Prof. Dr. A. Sinitsyn, INBI RAS; Prof. Dr. S. Yarotsky, Genetika) our group is working on both of these aspects. On one hand, we are developing an enzyme toolbox containing enzymes, in particular from anaerobic thermophilic bacteria, which have a broad range of different substrate and cleavage specificities with respect to hemicellulose polysaccharides. Such enzymes are useful for plant biomass degradation processes and can also be used to generate specific oligosaccharides from hemicelluloses, for example xyloglucan, for applications such as food or feed additives or neutraceuticals. On the other hand, we are working on the establishment and improvement of microbial host organisms for the efficient high-level production of selected enzymes for (hemi)cellulose degradation.

STRUCTURE OF JOINT INDUSTRIAL AND ACADEMIC COOPERATION IN THE FIELD OF BIOECONOMY IN GERMANY

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CLIB2021 Cluster Industrial Biotechnology e.V.

In our understanding the Bio-Economy encompasses the production of materials, chemicals and energy. It addresses all fields of our daily life: Food and feed (e.g. supplements), equipment (plastics), machinery (lubricants), consumer care (cosmetics, detergents), medicine (implants, drugs), mobility (fuel), energy (biogas) and more.

Academic Science

The transformation of the industrial feedstock base (which is predominantly biomass plus carbon sources from recyling) asks for new technologies in preprocessing raw materials, transformation into intermediates and finally producing consumer products. In providing the science basis for these technologies academic institutions play the key role in fundamental and applied research and - equally important - education of young scientists. The Technical Universities Aachen (RWTH) and Munich (TUM), to name just these two because they are joining this conference, are active in basic research on using sustainable feedstock and concerning education the University of Hohenheim implemented shortly its Bioeconomy Master Program.

Technology Transfer

Applying scientific results in industrial reality needs technology transfer. In Germany early cooperation of academic institutions and industry (SME and big industry) is one of the preferred models. All universities run offices for licensing technologies ready to be applied. Forming R&D partnerships with German and international institutions is another activity. In addition these offices offer support in raising public and private

funds – not only for R&D projects but also for spinning out start-ups as a way of technology transfer. One of the latter examples is SeSam Biotech, a spin-off from Jacobs Bremen University.

Cluster

Another model of technology generation and technology transfer are clusters comprising all bioeconomy stakeholders. Because mostly industry-oriented clusters help to identify new business options not only for individual companies but whole sectors; thus supporting the realization of bioeconomy value chains. Examples for bioeconomy clusters in Germany are IBB Netzwerk (Munich) focusing on Bavaria, the Bioeconomy Cluster in Leuna centered on its pilot plant about chemicals from woody biomass and CLIB2021 (Duesseldorf) which is oriented to chemical industries.

International Partnering

Bioeconomy value chains have a global dimension - both concerning raw materials and products. The focus of clusters goes therefore beyond Germany. Bavaria is part of a partnering program along the river Danube, the Leuna cluster just signed the 3BI initiative with Dutch, French and British organisations. CLIB2021 founded together with the leading chemical EU-regions in Flanders (Belgium) and The Netherlands the Bio-Innovation Growth Cluster BIG-C and works since many years in strategic partnerships with Brazil, Canada, Malaysia and last not least Russia. Especially Russia with its long tradition in bioprocessing science and industrial practice is seen as a most promising partner on the way into the bioeconomy.

PUSHING THE GLOBAL BIOECONOMY NEEDS INTERNATIONAL TECHNOLOGY TRANSFER

Dr. Manfred Kircher

Chairman of the Advisory Board. CLIB2021. Germany

Abstract

Industrial demand for more cost-efficient processes, innovative products and feedstock-flexibility as well as the societal driver of climate protection is pushing the bioeconomy – the vision of an industry based predominantly on renewable raw materials.

In fact, already today the bioeconomy makes up 17% of the European GDP and its expansion seems just to be a technological challenge - with industrial biotechnology key in producing food, feed, fuel and fibers from renewable carbon sources. Industry and academia are pushing the just emerging synthetic biotechnology, improving continuous processes, cutting downstream processing cost and integrating biotechnological and synthetic process steps.

However, beyond such technological topics more challenges appear on the horizon: i) renewable carbon sources will gain value when substituting fossil feedstock more and more, ii) biomass producing regions will become more relevant for industrial production and iii) the bioeconomy value chains ask for cross-sectorial cooperation of agro- and silvicultural enterprises, biorefineries, energy and chemical industries as well as the consumer sector.

This presentation will present drivers and challenges of the emerging bioeconomy as well as its impact on global value chains. Finally it will discuss CLIB2021 as a successful model of cross-sectorial partnering and Chinese-German cooperation opportunities.

Biography

Dr. Manfred Kircher is Chairman of the Advisory Board of CLIB2021 (Cluster Industrial Biotechnology.V.) - a non-profit organization of more than 100 members from industry, SME, academia and investors in Europe, Russia, North-America, China and South-East Asia.

Manfred Kircher brings along more than 30 years of business experience in industrial biotechnology in R&D, production and financing at Evonik (Germany), Fermas (Slovakia) and Burrill&Company (USA). He has a proven track record in moderating Open Innovation Platforms, building Project Consortia and Industrial Cluster and is advisor to private enterprises and public bioeconomy programs.

In 2014 he founded KADIB, a bioeconomy advisory company (www.kadib.de). He has been awarded with a honorary professorship of the Michurinsk State Agrarian University (Russia). Manfred Kircher is biologist by training (Goethe-University; Frankfurt, Germany).

UTILIZATION OF NATURAL RAW MATERIALS FOR THE FERMENTATIVE PRODUCTION OF FINE CHEMICALS ESPECIALLY NATURAL AROMA CHEMICALS

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After a short introduction of our university some examples of processes developed by the author in the past will be presented.

1) The fermentative production of vanillin, the most important flavouring substance, from ferulic acid. Ferulic acid is an abundant phenolic phytochemical found in plant cell wall components such as arabinoxylans as covalent side chains and as a monomer of lignin. In a fed-batch fermentation process, an *Amycolatopsis sp.* is able to convert ferulic acid in high yields into vanillin. Within 32 hours 11.5 g L^{-1} vanillin can be obtained.

2) The production of short chain carboxylic acids, like Butyric acid, Propionic acid, Isobutyric acid, 2-Methylbutyric acid, Isovaleric acid by oxidation of the corresponding alcohols with *Gluconobacter sp.*.These carboxylic acids are important flavour compounds when applied in trace amounts for flavouring of different types of foods. In this biotransformation process high product concentration in the range of over 80 – 90 g L^{-1} within three to four days.

3) The microbial production of Guaiacol and 4-Vinylguaiacol by *Bacillus sp*. is an actual project. Both substances are important smoke-flavours. We have obtained product concentrations of more than 6 g L^{-1} within less than a day.

Interest for cooperation is in the area of utilization of natural raw materials for the production of fine chemicals, especially natural aroma chemicals. This includes the valorisation of waste materials of food processing as a substrate. These can include oily, fatty or waxy materials, which should be modified by bacterial, yeast and mould cultures.

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