

# German-Russian Forum Biotechnology



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German-Russian Forum Biotechnology  
Abstracts

## **MATHEMATICAL MODEL OF THE AUXIN METABOLISM IN SHOOTS OF *ARABIDOPSIS THALIANA* L**

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Indole-3-acetic acid (IAA) is physiologically active in the form of the free acid, but can also be found in conjugated forms in plant tissues. IAA can be degraded and redundant pathways lead to its synthesis. Auxin participates in regulation of cell differentiation in development of embryo, leaves, vascular tissue, fruit, primary and lateral root and in controlling apical dominance and tropisms. The regulation of the IAA metabolism (synthesis, conjugation and degradations) is enough complex and may explain in some aspects how this simple substance is able to influence such diverse processes. Mathematical modeling of IAA metabolic gene network can help reveal the main factors

governing this complex process. To reach this aim, we first reconstructed a gene network of auxin biosynthesis, conjugation degradation by annotating experimental data from 107 published papers into GeneNet computer system. This gene network after reduction was input into converter to generate the mathematical model of auxin metabolism. We have reconstructed the gene network and develop the mathematical model of auxin metabolism in arabidopsis shoots. The model allows to reproduce some phenomenological and molecular-genetic aspects of the auxin role in the plant development.

## BIOTECHNOLOGY OF ANTI-INFECTIVE MEDICINES FOR FARM ANIMALS

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The presentation is focused on biotechnology of anti-infective medicines for farm animals produced by the company “Diafarm”. Pharmacologic properties of medicines, their advantages and areas of application are described. “**Vestine**” is an IFN inducer. “Vestine” is an etiotropic antiviral agent for urgent prophylaxy and effective therapy of diseases in various vertebrates: mammals, poultry, and fish. The preparation is able to suppress viruses of different families and to prevent secondary infections. “Vestine” induces immunoadjuvant and growth stimulating effects when it is simultaneously used with antibacterial and antiviral vaccines.

“**Polyribonate**” is a high polimerous RNA from baker’s yeast. RNA content is not less than 80 per cent. The preparation is free from cell wall components and proteins. Polyribonate is an immune

stimulator. It has a positive effect on hemopoiesis. It has radioprotective, antimutagenic and antistressory effects. The preparation can be used to overcome immunodeficiency states including those which result from infectious and surgical diseases and radiation effects. Polyribonate has an adjuvant effect when it is used in combination with vaccines. Polyribonate is practically non-toxic. It causes no allergic reactions and has no mutagenic and teratogenic toxic effects.

“**Provest**” is an interferonogen of a prolonged effect for urgent prophylaxy of viral diseases.

“**Endoglukin**” is an enzyme based on endonuclease. It has a marked antiviral effect and inhibits propagation of different viruses by hydrolyzing viral nucleic acids. “Endoglukin” stimulates the development of bee colonies during the spring-summer season.

## BIO-COMPOSITES WITH GRAIN BY-PRODUCT

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In recent years, a special concern has been manifested towards “green composites”. Some of the effort has been introduced based on the use of new waste sources, with the aim to obtain biologically active compounds which can be applied in different fields and applications. These natural lignocellulosic cereal residues (by-products) are compatible with the environment and could provide the sources for specialty chemicals. Grain by-products are an annually renewable fibre and is available in abundant volume through out the world. According to April 2009 the world and EU-27 production of grain by-products are as:

husk, barley husk and coconut shell are waste product of food processing from grain and have sufficient fibre value (cellulose and starch). Grain by-products content about 35% to 65 % structural materials which is equivalent to common natural fibre as well as wood fibre. So proper utilization of those waste materials will provide cheap engineering materials as well as help to waste management. The quality, fibre contents and chemical composition of cereal by-products depend on the grain collection process from the field and on food processing process. Grain by-products have defined in terms of fibre morphology, size, chemical

Fibre's Name	Main source	EU-27 (Million tons)	World (Million tons)
Wheat husk	EU-27, China, India, Russia, USA and Ukraine	37.5	170.5
Barley husk	EU-27, China, Russia, and Ukraine	16.4	38.5
Rye husk	EU-27, Russia, Belarus and Ukraine	2.3	4.4
Coconut Shell	India, Indonesia, Philippines, Thailand, Sri Lanka and Africa	-	9.2

The use of the cereal residues or by-products as a filler or reinforcement in the production of plastic composites alleviate the shortage of wood resources and can have the potential to start a natural fibre industry in countries where there are little wood resources left. The composite industries are looking into alternative low cost lignocellulosic sources, which can decrease overall manufacturing costs and increase properties of the materials.

Wood fibre is the most widely used lignocellulosic natural fibre for reinforcing plastics. The demand of wood plastic composites (WPC) is increasing steadily with new application window in North America as well as Europe. Considering economic and ecology, wood fibre plastic established itself as standard material but unfortunately raw wood fibre price increased 25% to 30% compared to last year price. Therefore, scientist from all over the world are searching new source which could be the proper alternative of wood fibre. According to source and availability, grain by-products are getting interest in the region of Asia, Europe and North America. The abundance of grain by-product is eco-friendly, available, cheap and which is complicated in term of cell geometry, morphology and chemical composition. It also has created an environmental issue such as fouling and attraction of pests. Grain by-products i.e. wheat husk, rye

compositions and thermal properties prior to composites preparation. The main aim of this research was to study the potential of grain by-products as reinforcements for thermoplastics as an alternative or together with wood fibres.

Grain by-products reinforced poly propylene composites were fabricated using a high speed mixer followed by injection moulding with 40% of fibre load. To characterize the composites materials, mechanical properties, viscoelastic properties, water absorption properties and morphology were studied. Coupling agent (MA) has been used to increase the better interaction between grain by-products and polymer matrix. The grain by-product -polymer matrix adhesion and interaction of the composites was studied by scanning electron microscope.

The tensile, flexural and charpy impact strength of all grain by-products composites were found better than those of wood fibre composite and wood fibre composites showed lower water absorption property than grain by-product composites. The addition of coupling agent (MAH-PP) in all grain by-products composites increased almost all mechanical properties 30 to 50% except modulus properties. The mould viscosity and melt flow rate of grain by-product composites found to be comparable or better than soft wood fibre composites.



## BIO-COMPOSITES BASED ON WOOD- AND OTHER NATURAL FIBERS

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Polymer composites reinforced with wood flour or other natural fibers show increasing growth rates worldwide and numerous applications in many branches of industry. There is a steady interest to find new fields for their usage. Good mechanical properties combined with relatively low specific gravity are a good basis for new applications. New materials should not only fulfill technical but also ecological demands.

Wood particles are being used as filler or as reinforcement elements, and their ratio can vary within a wide range from 10 – 90 %. Depending on the application of the composite, wood can be added as powder, sawdust, chips or fibers to the polymer matrix. The breakthrough with wood composites (WPC's) in the market started in the USA and Japan.

Composites with plant fibers are widely used in the automotive industry. Hemp, flax, jute, sisal, cotton, coconut, abaca are the currently used fibers for the production of parts in the European vehicle industry. The balance between mechanical properties and cost is the basis of success. The automotive industry is a sensitive indicator of these requirements. However, the increasing acceptance by this industry demonstrates that natural fiber reinforced polymers have become mature materials.

Identifying optimal properties and the process parameters of bio-based composites is an ever increasing demand. Optimal conditions for production are claimed, especially production time reduction and minimized thermal damage of the natural fiber. Weather resistance, resistance to ecological influences, UV-radiation of and humidity content as well as the biological decomposition are required to be optimal in regard of the planned application.

To improve their properties many companies offer a continuously growing number of additives and auxiliary supplies. Coupling agents improve the fi-

ber/matrix adhesion. Lubricants increase the throughput and improve the surface properties of the products. Colorants increase the UV-resistance and lead to more attractive product variations. Fungicides prevent a biological decomposition, which could also be of importance in composites, especially with a higher proportion of natural fibers, for instance wood.

The foaming of composites is gaining in importance and more often flame-retardants are applied.

Several basic production technologies are applied:

Compression molding and extrusion are standard processes for the manufacture of products made of fiber reinforced plastics.

A typical example is the by Cincinnati Milacron developed conical twin screw extruder TimberEx TC96 with an output of 1100-1300kg/hour. With the longer length of the screw the extruder is able to de-vitalize the humidity of the wood. The L/D proportion was adjusted with regard to the use of other natural fibers. -

Cincinnati Extrusion Fiberex® allows to use fiber contents between 50% and 90%. The required end-product defines the best mix of material types and fiber share.

Etlinger's low-pressure "srm" series compression molding machine can be used for the manufacture of palettes as well as for products for garden and playgrounds. Special shut off nozzles allow for processing a range of plastics to be processed contain soft PVC, PE, PP, PS, ABS, PA as well plastics, mineral or wood powder filled compounds. Low pressure means: Mold cavity pressures ranging from 50 to 250 bar.

To use natural, renewable material fibers is of utmost importance in Europe. Advantages such as lower density and lower prices compared to conventional glass fiber composites contribute to an increasing interest in these new materials.

## INVOLVEMENT OF DOPAMINERGIC GENES IN MECHANISMS OF REPEATED AGGRESSION IN MALE MICE

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It is generally recognized that recurrent aggression can be the result of various psychiatric disorders. The sensory contact model allows the aggressive type of behavior to be formed as a result of repeated experience of victories in daily agonistic interactions in male mice.

It has been experimentally demonstrated that positive fighting experience changes many forms of individual and social behaviors. Abnormal aggression, hyperkinetic and stereotypic reactions, hyperactivity, hostility, decreased emotionality, disturbances in social recognition, pronounced anxiety as well as activation of brain dopaminergic systems in different brain areas were found in the winners. The mRNA levels of the *Th*, *Dat1*, *Sncα* and *Bdnf* genes that may possibly be associated with repeated aggression were analyzed in the ventral tegmental area of the midbrain (VTA) in male mice that had each won 20 daily encounters in succession and a group of animals that had the same winning track record followed by a no-fight period for 14 days. Repeated positive fighting experience enhances the expression of the *Th*, *Dat1* and *Sncα* genes

in comparison with the control. The expression of the *Th* and *Dat1* genes stays enhanced for a long time. Significant positive correlations were found between *Th* and *Dat1* mRNA levels in the VTA, which suggests a close relationship between dopamine synthesis and inactivation. Data obtained provide evidence that the *Th* and *Dat1* genes are part of feedback mechanism in regulation of dopamine metabolism. Significant positive correlations were found between the level of aggression and *Th* and *Sncα* mRNA levels in victorious male mice. It is discussed that *Th*, *Dat1* and *Sncα* genes in the VTA are involved in the mechanisms of aggressive pathology developing in mice under long experience of aggression. Some data allow suggesting involvement of other genes into mechanisms of repeated aggression. Our behavioral approach may be useful for the study of brain molecular mechanisms of affective disorders.

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## FERMENTATION OF NON-WOODY RAW MATERIALS

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The paper presents results of research into fermentative power of grain crops straw, oats husk, biomass of *Miscanthus sinensis*, and products of their chemical processing. Biomass of *Miscanthus sinensis* was supplied by Institute of Cytology & Genetics SB RAS in 2008. The industrial fermentative complex *Cel-*

*loLux-A* was used as a biocatalyst. A comparison of hydrolyzability of 12 substrates allowed us to reveal certain regularities of the dependence of fermentative power upon a sort of cellulose-containing feedstock and method of its chemical preprocessing.

## NEW WATERSOLUBLE PHTHALOCYANINES AS REAGENTS FOR PHOTODYNAMIC THERAPY

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At present time phthalocyanines (Pc) containing metal ions Zn(II) and Al(III) are used as photosensitizers in photodynamic therapy (PDT) of malignancies and other diseases. As reactive groups, phthalocyanines and their metal complexes have the advantage of high molar absorptivity, resistance to chemical and photochemical degradation, long lifetimes with high quantum yields, absorption and emission at 600–700 nm. Absorption in this region makes them sensitive to the light, which can penetrate deep into living tissues. However, Pcs have a propensity to form aggregates due to molecular stacking. This results in low quantum yields and limits their solubility in aqueous media. The solubility of Pcs could be increased by introducing short charged moieties in peripheral positions.

One of main questions in the investigation of these compounds is the influence of peripheral water-solubilizing groups on the photo-physical properties of the Pc dyes. Therefore, this work was devoted to the study of the spectroscopic and photo-physical parameters, which are crucial for determining the feasibility of using new Pc's derivatives in PDT. We examined Al(III) and Zn(II) Pc- metallocomplexes having eight small charged substituents. Quantum yield of singlet oxygen generation, fluorescence and absorption spectra, fluorescence lifetimes were reported and related to the structure of substituents.

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## MOLECULAR MODELING TECHNOLOGIES IN DRUG DISCOVERY

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Molecular modeling aims at reducing the experimental workflow and guiding the drug discovery process towards tangible deliverables. Despite the accuracy of the current molecular modeling approaches is not sufficient enough to compete with the experiment, the progress in this field goes on, a lot of novel methods and software tools appear regularly. With this respect MolTech Ltd has developed two core technologies for the drug discovery process: Lead Finder — an extra precision molecular docking software suitable for robust protein-ligand binding energy estimations and virtual ligand screening, and a Target Finder — a database of more than 1000 experimentally validated therapeutic targets with annotated pharmacological involvement and full-atomic structure for modeling purposes. The accuracy of ligand docking with Lead Finder was assessed on a public set of 407 structures, which included almost all published test sets of the following programs: FlexX, Glide SP, Glide XP, Gold, LigandFit, MolDock, and Surflex. RMSD of 2 Å or

less was observed for 80-96% of the structures in the test sets (80.0% on the Glide XP and FlexX test sets, 96.0% on the Surflex and MolDock test sets). The predicted values of the free energy of protein-ligand binding were benchmarked against a set of experimentally measured binding energies for 330 diverse protein-ligand complexes yielding RMSD of 1.50 kcal/mol. Using the Lead Finder docking engine and the Target Finder as a source of therapeutic targets, we were able to model *in silico* the polypharmacology of kinase inhibitors, and even discovered a novel chemical scaffold of tyrosine kinase inhibitors, which was experimentally validated by Chem-Bridge Corp. Application of Target Finder aided in deciphering the molecular mechanism of action of an innovative Russian drug Ingavirin. The on-going applications of Lead Finder and Target Finder include the search for novel therapeutic targets of well known compounds (including approved drugs and nutritional) and the design of innovative drugs.

## NATURAL EFFECTIVE COSMETICS STIMULATING BASAL CELL DIVISION FOR PROTECTING SKIN FROM AGING AND ABNORMAL STATES

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The presentation is focused on new solutions found by Scientific Cosmetological Company for protecting skin from aging and abnormal states, such as cellulite and skin stretching (striae). The main approach is to compensate both haemodynamic failure (lack of nourishing substances) and hormonal failure which are the basic skin aging factors. The cosmetics developed include ingredients of vegetal and animal origin, which contain hormones, hormone-similar substances and cells development factors, thus stimulating division of basal (lower) cells of epidermis (the upper layer of the skin). Basal cells of epidermis are similar to stem cells by the following parameters:

- division of these cellular structures results in cell substance that forms an epidermis;

- they are able to multiple and permanent division;

- They can act as a basis for developing special cells involved in cell transformation into the horny scale.

Thus practical application of the stem cell unique properties has been achieved without cells abstraction and genetic modifying. The cosmetics developed do not have any compounds blocking cells division, such as biocide preservative additives. All ingredients have been tested on cell test-systems and allowable concentrations of the ingredients have been found. The products are neutral (pH  $7.0 \pm 0.2$ ).

## MICROSATELLITE MAPPING OF GENES FOR INFLORESCENCE ARCHITECTURE IN WHEAT (*T. aestivum*) AND RYE (*S. cereale*)

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The wheat and rye spike normally bears one spikelet per rachis node, and the appearance of supernumerary spikelets (SS) is rare. The loci responsible for the 'multirow spike' or MRS trait in wheat, and the 'monstrosum spike' trait in rye were mapped by genotyping F<sub>2</sub> populations with microsatellite markers. Both MRS and the 'monstrosum' trait are under the control of a recessive allele at a single locus. The *Mrs1* locus is located on chromosome 2DS, co-segregating with the microsatellite locus *Xwmc453*. Along with the main contribution of the *mrs* gene, the effects of minor genes that modify expression and stability of the MRS trait were detected. The placing of flanking mi-

cro-satellite loci into chromosome deletion bin 2DS-5 (FL 0.47–1.0) delimited the physical location of *Mrs1* to the distal half of chromosome arm 2DS, within the gene rich region 2S0.8. The *Mo1* locus maps about 10 cM from the centromere on chromosome arm 2RS. The similar effect on phenotype of *mo1* and *mrs1*, together with their presence in regions of conserved synteny suggest that they may well be members of an orthologous set of *Triticeae* genes governing spike branching. The practical importance of the MRS spike is that it produces more spikelets per spike, and thereby enhances the sink capacity of wheat, which is believed to limit the yield potential of the crop.

## CONSERVATION OF RARE AND ENDANGERED SPECIES OF SIBERIAN PLANTS USING BIOTECHNOLOGY METHODS

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Among 4544 plant species of Siberian flora the list of threatened and protected plants includes about 400 species.

Tissue culture techniques and biotechnological approaches serve as a crisis management tool for conserving species that are critically endangered and are on the verge of extinction. Although species conservation is achieved most effectively through the management of wild populations and natural habitats (*in situ* conservation), *ex situ* techniques can be used to complement *in situ* methods and in some cases may be the only option for rare species.

The goal of our work is to develop the methodology for plant genetic conservation of Siberian flora.

The first step is the study of genetic variation in rare species. Until recently isoenzymes and storage proteins were the main tool available for such studies, but in last two decades, DNA-based techniques for examining the relationships of plants to each other at various levels have become widely available. Information gained from these studies can then be incorpo-

rated into management strategies for conservation.

The second step is regeneration and propagation of identified plants by *in vitro* cell and tissue culture methods. Since cells in culture, during dedifferentiation and growth, divide mitotically, clonal fidelity of regenerated plants should be expected. Instead, a great number of observations have demonstrated that the occurrence of genetic variation in cultured cells and plants originated *in vitro* by adventitious regeneration (via organogenesis and/or via somatic embryogenesis) is the rule rather than the exception. Therefore the next indispensable step is to control by DNA markers the genetic integrity of *in vitro* propagated clones because plantlets derived from *in vitro* culture can exhibit somaclonal variation which is often heritable and results in stable genetic changes. Verified clones are included in collection *in vitro* cultures.

The work was financed by the grant on the Integration project of SB RAS and grant on the Program of Presidium RAS "Biodiversity"



## USING THE COMPUTER-BASED IMAGE PROCESSING TECHNIQUE IN GENETIC ANALYSIS OF LEAF HAIRINESS IN WHEAT TRITICUM AESTIVUM L.

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Leaf hairiness in wheat is of great importance for protection from pests and for adaptation to environmental factors. For example, this trait is characteristic of a number of drought resistant wheat cultivars referred to the steppe ecological group. Study of the features of leaf hairiness morphology and identification the corresponding genes will allow to obtain varieties resistant to hard climatic conditions and certain pests. To identify the genes responsible for the leaf hairiness, mass analysis of a great number of plants belonging to different hybrid populations is needed, accompanying with a laborious manual job.

Furthermore, a more accurate description of the morphological properties of the trait for correct determination of phenotypic classes is timely. Using of new computer-based technologies for descriptions of quantitative characteristics of leaf hairiness is the important step in this direction. In the course of the work, we used the LHDetect program for determining the degree of leaf hairiness and its morphologi-

cal properties on the basis of its microscope image processing.

The suggested method appeared to be the effective approach for a large scale analysis of leaf hairiness morphological peculiarities in individual plants. For example in according with genotyping this approach can be useful to quantitative trait loci (QTL) mapping.

In this study we detailed analysis of hairiness in wheat as a complex feature. For two different cultivars with similar leaf hairiness was shown differences. The disjoining of hairiness trait in F<sub>2</sub> generation hybrids was studied for several combinations of parents. This allowed us to qualitatively estimated the possible number of genes that may control the hairiness trait in different cultivars. It was shown that this trait for several cultivars is polygenic.

The work was supported by RAS Program 2 «Origin and evolution of biosphere» and Scientific School HIII-2447.2008.4.

## IDENTIFICATION OF THE NEW GENE *Ha2*, DETERMINING ENDOSPERM TEXTURE OF BREAD WHEAT GRAIN, INTROGRESSED FROM *AEGILOPS SPELTOIDES* Tausch

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Endosperm texture is the most important trait of wheat grain determining its end-use purposes. It reflects a linking strength between the two main grain components - starch granules and protein inclusions. The bread-making flour is manufactured from the grain of cultivars with hard texture of endosperm. The main genetic determinant of this trait is a locus situated in 5DS chromosome which responsible for biosynthesis of two proteins – puroindolines (PinA и PinB) and grain softness protein (Gsp-1). Mutations in the two first proteins result in hard grain texture. No other such genes have been found in wheat genome until now.

In this work, the new homoeologous gene determining the soft endosperm structure is described introgressed from *Aegilops speltoides* Tausch., a wild diploid cereal which is considered to be a possible progenitor of B genome of bread wheat. The gene was discovered in the winter line 84/98<sup>w</sup> from “Arsenal” collection developed by Dr. I. Lapochkina with co-workers in the Institute of Agriculture of Non-Chernozem Regions of Russia (Nemchinovka, Moscow re-

gion). The collection was obtained by direct crossing of spring wheat cultivar “Rodina” with a specimen of *Ae. speltoides*. The maternal cultivar has a hard type of endosperm texture and the winter line with introgression – a soft type.

The winter habit and speltoid awned spike of the line proved the introgression to be non-homoeologous, 5S instead of 5A chromosome. 5S chromosome from the line 84/98<sup>w</sup> was introduced through monosomic analysis into genotypes of two additional bread wheat cultivars Saratovskaya 29 and Diamant 2 with hard type of endosperm. This also led to the softness of endosperm texture. The association of grain hardness with virtuousness – another endosperm trait characterizing milling properties of grain was also investigated.

Therefore, the species *Aegilops speltoides* is a carrier of the dominant allele of the locus determining endosperm structure which is homoeologous to the locus situated in 5DS chromosome of bread wheat. It is suggested the designation *Ha2* to this gene.

## BIOTECHNOLOGICAL APPROACH FOR OPTIMIZATION OF PLAGUE VACCINE PRODUCTION

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The *Y. pestis* EV line NIIEG strain has been successfully used as a human and animal live plague vaccine in Russia and the CIS countries. Thus far, this vaccine is the only preparation licensed for prophylaxis of plague. However, reference sub-cultures of the vaccine strains grown in a standard bacteriological medium at 28°C during large-scale manufacturing of the vaccine provided a specific immunity in no more than in 50% of outbred mice vaccinated. Another biotechnological problem is an optimization of growth conditions for providing both a high bacteriological yield and desired antigen composition of the vaccine preparation. For this propose, the bacteria of the reference vaccine strain was cultured in the medium simulating the mammalian extracellular conditions developed by us earlier (Feodorova, Golova, 2005). We obtained at least a 3.7-4.2-fold increase in the cell biomass in comparison with the same vaccine strain grown at routine conditions. Moreover, these growth conditions provided a consecutive generation of the antibodies in immunised mice with enhanced protec-

tive activity resulting in a survival of 80-90% of the animals against experimental plague after challenge with the wild-type *Y. pestis* 231 strain. Parallel immunisation experiments with the vaccine prepared by using standard bacteriological media provided not more than 45% survival rate. Despite enhanced protection, no antibodies to the *Y. pestis* major antigens such as F1, Ymt or Pla were detected in immunoblotting using antisera from mice taken at one day prior to challenge. Nevertheless, a protective potential correlated with the presence in the murine antisera antibodies to a single immunodominant protein with mol. wt  $48.4 \pm 2$  kDa, likely, synthesised by the *Y. pestis* at early stage of plague infection providing a development of the extracellular resistance to phagocytosis within the host organism. Thus, optimised growth conditions developed in this study provided both increased yield of a microbial biomass and desired expression of the protective antigens leading to the improvement of vaccine protective potential.

## COMPLEX COMPUTATIONAL ANALYSIS IN UGENE BIOINFORMATICS SUITE.

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The cross-platform open-source system UGENE is aimed to integrate popular and specific bioinformatics algorithms within a single visual application environment. Acceleration and simplification of biomolecular data processing act as key features of the environment, ensured by a rich set of components.

*Visual components:* The core component of the visual interface of UGENE is **Workflow Designer**, destined for construction of computational diagrams (workflows) from the predefined set of visual algorithmic blocks or data sources in easy drag-and-drop manner. Operating with these blocks, molecular biologists can create complex and reusable visualized computational workflows, ready for execution on local workstations or on computer clusters as well. The key idea of Workflow Designer is to make the process of automation of routine tasks as simple as it's possible and make it available for non-programmers.

Rich palette of views and charts and their adjusting capabilities enables user to reach high visualization level. Highly-interactive user interface is provided by various pop-ups, visual hints, setup forms.

*Optimized algorithms:* Incorporated to UGENE are optimized versions of the original algorithms for modern architectures taking advantages of multithreading both for multi-core CPUs. Already implemented are SIMD optimizations for Intel and IBM CELL platforms, showing 1-2 orders of magnitude

performance improvement. Currently MPI version for HMMER3 destined for run on computer clusters is under development. With the next version UGENE will also add GPU based version of HMMER2 algorithm.

*Progressive integration:* Since its first release in June 2008 UGENE is updated monthly, accruing base of integrated algorithms and their versions, accompanied by relevant tests. Current version v1.4 UGENE codebase incorporates about 20 different plugins, each of them representing one of popular bioinformatics algorithms or methods. These include multiple alignment tools, Smith-Waterman algorithm implementation, HMMER2 tools, repeats and ORF analysis, restriction enzymes markup, 3D structure analysis, search for transcription factor binding sites, integration with web databases like BLAST and CDD.

*Conclusion:* Integrated softwaresuite is designed and implemented to solve the problems such as incompatibility and disconnection of different information sources and methods of analysis, lack of adjustability to contemporary computational resources, wide availability.

*Availability:* UGENE is written with open-source QT4 C++ multiplatform library and QtScript scripting language, licensed by GPL v.2. It is available for most of the popular platforms like Linux, Windows, MacOS X. UGENE is also included into Ubuntu and Fedora Linux distributions. Software and source code are available at <http://ugene.unipro.ru/download.html>

## THE ROLE OF $\delta$ OAT GENE IN PROLINE ACCUMULATION AND STRESS RESPONSE IN PLANTS

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Accumulation of proline (Pro) is a way to increase tolerance to various abiotic stresses in plants. Pro is mainly synthesised in the cytosol from glutamate via pyrroline-5-carboxylate (P5C) by the sequential action of P5C synthetase (P5CS) and P5C reductase (P5CR). There is also evidence for a pathway of Pro synthesis from ornithine (Orn), and Orn- $\delta$ -aminotransferase ( $\delta$ OAT) has been implicated in this pathway. The aim of present study is to investigate the role of  $\delta$ OAT in the proline accumulation and the stress tolerance of plants. In order to investigate the effect of changed OAT gene expression, the transgenic *Nicotiana tabacum*  $\delta$ OAT overexpressing plants and  $\delta$ OAT antisense suppressed plants have been made. It was shown that  $\delta$ OAT overexpression in transgenic tobacco plants did not yield significant increase in proline level under either normal or NaCl-induced stress conditions. However measurements of shoot and root biomass showed that the constitutive overexpression of the

OAT enzyme increases the growth performance of the transgenic plants under 300 mM NaCl condition. It allows us to assume that  $\delta$ OAT does not contribute to proline biosynthesis but involved in NaCl and osmotic stress responses. In order to investigate the transcriptional control of plant  $\delta$ OAT gene, the set of reporter genetic constructs has been made. Including the translation initiation codon, the regions of 5'-upstream sequences of Arabidopsis promoter (1850 bp, 1300 bp and 450 bp) were fused to GUS reporter gene. GUS expression in transgenic plants carrying the fusion constructs will be investigated under normal and different stress growth conditions to reveal the pattern of transcriptional control and its relation to stress tolerance.

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## BIOTECHNOLOGY APPLICATION IN ANIMAL BREEDING

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The main biotechnological methods in animal breeding including the development of transgenic animals are based on the cellular technologies in reproduction and DNA technology applications. The transgenesis-based methods for breeding acceleration and the increase of quantity of the animal production had not overcome the experimental stage yet. In our work we investigated the transgenic rabbits for the changes in organ-specific spectra of gene expression in comparison with control animals and found that the changes were similar to those observed after the treatment of non-transgenic rabbits with ionizing radiation. The applications of cellular technologies in farm animal reproduction are complicated by the number of unpredictable population effects. Positive correlations between cytogenetic anomaly frequency in cells of peripheral blood of embryo donor cows and the number of washed away embryos were revealed. Allele distribution of some genes in generation born after embryo transplantation, essentially differed from those typical for parent animals (for example, Aberdeen Angus). DNA technology applied to mark the polymorphism of various genome elements, with the aim to search for the main loci of the quantitative traits (QTL) and gene-candidates of the control of trait efficiency, as well as for research in the field of functional genetics and for diagnostics of infectious agents. The analysis of polymorphisms of various of genome elements allowed to reveal of breed-specific gene pool characteristics, to estimate the breed consolidation, and also to find the genotype combination which were targets of action of factors of artificial and natural selections. An analysis of allele frequencies in cattle generations revealed an increase of frequencies of some alleles of genes participating in oxidative stress protection. This phenomenon may reflect the selection against the ac-

tion of biotic and abiotic factors of ecological stress. Search for QTL, for example, of cattle milk productivity, showed their variability in relation to both the genotype background and environment factors. It was revealed that in some species (e.g., rice) the chromosome segments, in which the resistance-associated QTLs were localized, covered ca. 52 % of genome and were enriched with genes coding the proteins participating in protection against ROS. A number of gene-candidates for the control of animal productivity traits were observed, however, their allele distribution differentiated the breeds, which distinguished by productivity, but not the animals from one breed with different expression of productivity traits. Use of the DNA microarray technologies allowed to carry out simultaneously the analyze of nucleotide sequences of the many genes and to estimate the profiles of their transcription. These methods had special importance to search for the “critical” genes for the development of different phenotypes. Comparison of organ-specific profiles of gene expression in liver and kidneys of pigs showed the differences between them corresponded to known organ-specific physiological functions, and also the histological features (in particular, in kidneys the dynactin expression, which participates in the cytokinesis control, was much higher than in polyploid liver). A new area of research with the aid of DNA technologies is the search for the genes, polymorphism of which determines the quality of the end animal production, irrespective of its quantity. For example, genotypes in kappa-casein in cattle determined the possibility to obtain the hard cheese, calpastatin - postlethal tenderness of meat and a number of others. Apparently, DNA technologies remains the most perspective direction in the development of biotechnology of farm animal species.

## **BIOTECHNOLOGICAL METHODS IN TESTING POTATO RESISTANCE TO BACTERIAL PATHOGEN**

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The study based on the use of in vitro potato plants and suspension cultivars showed participation of peroxidases loosely linked with cell wall in formation of potato protection mechanisms under exposure to bacterial pathogen. There were revealed regularities of activation of molecules of peroxidases under study or their synthesis de novo depending on the potato species ability to demonstrate resistance to pathogen. For the first time there were justified two strategies of potato cells protection from pathogen. One of them

is inherent to resistance genotypes and is connected with rapid and drastic activation of peroxidases which existed prior to infection; the other is characteristic for susceptible genotypes and is due to synthesis of the enzyme molecules de novo at later stages of infection. Thus, the results acquired prove the possibility of use of biotechnological methods in plant testing for resistance to pathogens at early stages of plants development.

## **ANDCell AND ANDNanobiotech: ASSOCIATIVE NETWORK DISCOVERY SYSTEMS IN SYSTEMS BIOLOGY AND NANOBIO TECHNOLOGY.**

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Computational systems (ANDCell and ANDNanobiotech) for automated extraction of knowledge from scientific texts (PubMed abstracts) and databases were developed. The ANDCell is targeted on the reconstruction of semantic associative networks in systems biology (molecular genetic interactions, gene regulation events, catalytic processes, proteolysis, polymorphic gene – disease associations, etc.). The ANDNanobiotech is targeted on nanobiotechnology (drug-delivery systems, labeling, diagnostics, treatment, microfluidics, implants, grafts, biosensors among others.). Information is extracted with the aid of original text-mining technology. The ANDCell database contains about 5 millions of facts, the ANDNanobiotech database contains about 1,5 millions of facts. The ANDVisio program provides the access to the databases and the representation of the results in a graphic form of reconstructed associative networks.

The vertices of such networks are the molecular genetic objects (genes, proteins, microRNAs, metabolites, cellular components), diseases, processes, nanomaterials and nanobioconstructs while the edges between the vertices represent various types of associations. For molecular interactions and associations, data on the cell types and organisms are represented. The systems provide a user's friendly interface implemented links to the molecular-genetic databases and the articles from which information was extracted. The developed systems may be useful for resolving a wide range of tasks in biology, biomedicine and biotechnology.

*Availability:* The ANDCell and ANDNanobiotech systems are available at request to the authors. Work was supported in part by Government contract FASI № 01.647.11.2013, SB RAS interdisciplinary integration grant №111.



## **ENT-KAURENOIC ACID OXIDASE GENES IN COMMON WHEAT: CLONING, MAPPING AND EXPRESSION ANALYSIS**

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*Ent*-kaurenoic acid oxidase (KAO) catalysis three steps in the gibberellin (GA) biosynthesis pathway, which yields a large hormone family effecting plant growth and development. In the current study, we performed partial gene cloning and comparative structural and mapping analysis among three homoeologous *Kao* genes in bread wheat (*Triticum aestivum* L.). Molecular-marker based precise mapping demonstrated that the *Kao* loci map to the distal ends of the chromosome arms 7AS, 4AL and 7DS, corresponding to the 7BS/4AL translocation region. It was found that

exonic sequences of the three homoeologues differ from each other mainly by silent mutations, and each homoeologue is functional. Furthermore, expression of *Kao* mRNA in wheat seedlings was investigated and compared between genotypes carrying distinct alleles at a GA-sensitive dwarfing locus, and it was concluded that regulatory-target gene relationships may exist between the chromosome 7DS *Rht* gene originating from German cultivar 'Prinz' and the *Kao* gene in wheat.

## MAINTAINING THE VIABILITY OF PROBIOTICS IN FOODS FOR A LONG TIME AND DELIVERING PROBIOTICS TO THE COLON THROUGH THE ACID BARRIER OF THE STOMACH

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The presentation is focused on advantages of solutions found by the company “Dia-Vesta” to the problem of maintaining the viability of probiotics in foods for a long time and delivering probiotics to the colon through the acid barrier of the stomach. The most commonly used technology for maintaining the viability of probiotics is lyophilization, or the vacuum freeze-drying. It helps to increase storage time of probiotics up to 6-12 months. However, their therapeutic effect is rather weak because of the following reasons. First of all, around 25% of probiotic bacteria population is destroyed in the process of lyophilization. Secondly, proliferating activity of remaining bacteria is reduced, as they are not able to generate colonies in the colon.

An alternative technology to be discussed in this presentation is micro-encapsulation. The company “Dia-Vesta” applies two ways of micro-encapsulation. In both ways a microcapsule includes fructooligosaccharides, the natural dietary fibers. They are natural food substrate for probiotic bacteria.

Fructooligosaccharides induce high activity of probiotic bacteria from the time of their activation, increase rate of probiotics reproduction and raise effectiveness of dysbacteriosis correction. A microcapsule also includes vitamins and prebiotics that maintain biological properties of probiotics for a long period, including the time necessary to reach the colon.

The company “Dia-Vesta” applies micro-encapsulation to manufacture 7 kinds of wafers and 5 kinds of muesli bars. Wafers with probiotics have been clinically tested at 3 hospitals of Novosibirsk (Russia). The results are the following:

- Dysbacteriosis has been cured or significantly reduced
- No allergic reactions occurred
- Carbohydrate metabolism and digestive tract functioning are improved significantly.

Most importantly, for children with gastroduodenal pathologies and dysbacteriosis wafers were recommended as one of the ways of treatment.

## EXPRESSION OF $\Delta 9$ DESATURASE GENE FROM *CYANOBACTERIUM SYNECHOCYSTIS SP. PCC 6803* RESULTED IN IMPROVEMENT BOTH OF COLD AND *PHYTOPHTHORA INFESTANS* RESISTANCE IN TRANSGENIC POTATO PLANTS

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It is known that capacity to resist against the influence both abiotic and biotic stresses is dealt with the activity of lipid desaturase enzymes, which catalyze double bond introduction into the aliphatic chain of fatty acids.  $\Delta 9$  desaturase catalyzes the first double bond introduction into the aliphatic chain of oleic acid.

The results of many researches exhibited that the increase in unsaturated fatty acids in the membrane lipids of plants could result in improved resistance both to low temperatures and pathogen attacks.

Several transgenic lines expressing  $\Delta 9$ desaturase gene from cyanobacterium *Synechocystis sp.PCC 6803* were obtained for potato cultivar Zhucov's Jubilee. Lines 5 and 6 contained native gene  $\Delta 9$ -desaturase, lines 7 and 8 contained a combined gene:  $\Delta 9$  + a reporter lichenase gene LicBM3 from *Clostridium thermocellum*.

The capacity for these transgenic plants to survive during 6-month growing at +8C° and to resist against infection with *Phytophthora infestans* pathogen in vitro and in vivo was investigated.

After the cold stress 27,9% plants of the initial cultivar Zhucov' Jubilee left alive. In transgenic lines 5 and 6 with the native  $\Delta 9$  gene, 92,8 and 90,0% plants survived, in transgenic lines 7 and 8 with the combined gene  $\Delta 9$ -LicBM3, the shares of survived plants were 100,0 and 85,1% correspondingly.

On the 8<sup>th</sup> day after inoculation with *Phytophthora infestans* zoospores in vitro, the indices of pathogen resistance were 8,0 and 7,8 in lines 5 and 6; they were 7,0 and 8,0 - in lines 7 and 8. The index of the initial cultivar resistance was 5,2. In the green house on the 8<sup>th</sup> day after artificial infection, the indices of pathogen resistance were: 8,6 and 8,2 in lines 5 and 6; 7,0 and 7,0 – in lines 7 and 8. At the same time, the index of the initial cultivar resistance was 5,2. In the field (against the natural infectious background), pathogen resistance was estimated during harvesting. The indices of line 5 and 6 resistance were 5,0 and 7,0. They were 9,0 and 7,0 in lines 7 and 8. The index of the initial cultivar resistance was 4,5. Also, we observed 2-days delay in infective symptom appearing in all the transgenic lines comparing with the initial cultivar and standard-cultivars. The high indices of pathogen resistance on the 8<sup>th</sup> day after artificial infection allowed us to attribute these transgenic lines 6, 7 and 8 to the forms with high field resistance.

So, incorporation of  $\Delta 9$ -desaturase gene from cyanobacterium *Synechocystis sp.PCC 6803* allowed us to obtain potato forms characterized of improved resistance both to low temperatures and *Phytophthora infestans* attacks.

## MRI: FROM CHEMISTRY TO BIOLOGY AND MEDICINE

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Nuclear magnetic resonance imaging (MRI) has become one of the most powerful tools in modern medical diagnostics. At the same time, the potential applications of magnetic resonance techniques in biology and medicine are clearly not exhausted, as evidenced by the impressive developments reported recently in the field of biomedical research. While the MRI applications being developed in the MR microimaging group at ITC SB RAS mostly deal with chemistry, they nevertheless have direct relevance to applications in environment protection, agriculture, food industry, and even biomedical research. Furthermore, our research is being extended to the biocatalytic technology, and the most recent efforts aim at the sensitivity enhancement strategies with potential applications in the field of molecular imaging. In the presentation, examples of the MRI studies performed at ITC will be paralleled by the relevant literature examples in other fields including biomedical research. Contrast agents are widely used in MRI diagnostics to enhance image contrast. Paramagnetic contrast agents are equally useful in other applications such as heavy metal removal in bioreactors for wastewater remediation. Our studies of supported catalysts preparation are based on the MRI visualization of the distribution and transport of paramagnetic metal ions. Over the years, powerful MRI tools have been developed for the visualization and quantification of the flow of liquids. Biomedical practice relies heavily on this possibility in fluid flow studies such as angiography. Other published examples include xylem and phloem fluid flow in intact plants, rheological properties of fluids ranging from polymer melts to food processing, etc. Our studies address flow of liquids, gases and granular solids in porous media

and model reactors. Diffusion imaging is extensively used in biomedical MRI applications, for instance to reveal brain architecture by tracing fiber tract orientation. MRI can be used as a non-invasive temperature sensor, with applications for real-time monitoring of, e.g., tumor thermotherapy. Certain chemicals with high sensitivity of NMR properties to temperature are being developed to advance such studies. In our practice, we have developed an MRI approach to monitor spatial temperature distribution in an operating catalytic reactor. Dynamic functional imaging, a vast field of biomedical MRI, is applied in our research to study processes in functioning chemical reactors. One of the recent trends is the MRI of bioreactors based on the use of immobilized biofilms. Our recent results address the structure and function of a biocatalytic reactor with a packed bed of biocatalyst for heterogeneous enzymatic biocatalysis. Yet, the ultimate power of the MRI technique is the chemical specificity provided through the spectroscopic modality of NMR. This is currently used in biomedical practice to follow biochemical transformations of individual molecules in a living organism and represents the basis for the non-invasive molecular imaging, which brings together molecular and cell biology with the state-of-the-art imaging and is being developed for the characterization of biological processes at the cellular and molecular level. The low intrinsic sensitivity of NMR hinders the development of this field, but various signal enhancement strategies are being currently developed [1] for such applications.

[1] L.-S. Bouchard, S.R. Burt, M.S. Anwar, K.V. Kovtunov, I.V. Koptug, A. Pines. *Science*, 319, 442-445 (2008).

## HETEROGENEOUS BIOCATALYSTS FOR PROCESSING OF RENEWABLE RESOURCES TO COMMERCIALLY RELEVANT FOOD SWEETENERS (STARCH TREACLE, SYRUPS)

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The highly stable heterogeneous catalysts with desirable enzymatic activity serve as a basis for the up-to-date biotechnologies of processing of renewable resources (potato, corn, beetroot) to commercially relevant sweeteners for food industry – starch treacle, glucose-fructose syrup, invert sugar syrup. The immobilization of enzymatic active substances, in particular enzymes, cell compartments and whole non-growing microorganisms on/inside inorganic supports is the profitable approach to prepare commercially attractive heterogeneous biocatalysts.

### I. Immobilization by adsorption on carbon-containing supports

**Biocatalyst for starch saccharification.** Biocatalyst “Glucoamylase on Sibunit” was prepared by adsorption of Glucoawamorin<sup>®</sup> on mesoporous carbon support Sibunit<sup>®</sup>. Under industrial conditions of hydrolysis of dextrin (32 wt%) at 60°C, the inactivation half-time of the biocatalyst exceeded 350 h. The process of starch saccharification (hydrolysis of dextrin) was carried out in high productive vortex reactors which were designed specially to overcome diffusion restrictions of enzymatic reactions and to eliminate stagnant zones and stream jets inside biocatalyst bed. The total productivity of biocatalyst “Glucoamylase on Sibunit” was estimated as ca. 5 tons of glucose per 1 kg.

**Biocatalyst for sucrose inversion.** Biocatalyst “Invertase-active autolysate on Sapropel” was prepared by adsorption of bakers’ yeast autolysate on macroporous carbon-mineral supports produced by carbonization of

lake’s sapropel. The biocatalysts retain completely its invertase activity ca. 50-100 U/g for several months of periodic sucrose inversion at 50°C.

### II. Immobilization by entrapment inside SiO<sub>2</sub>-xerogel

A peculiar method of immobilization of whole non-growing microorganisms by entrapment inside silica xerogel is rather simple and universal. The prepared heterogeneous biocatalysts have good properties – high enzymatic activity and operational stability.

**Biocatalyst for glucose isomerization.** The biocatalysts with glucose isomerase activity were prepared by entrapment of harvested biomass of producer strain, in particular *Arthrobacter nicotianae*, inside SiO<sub>2</sub>-xerogel. The optimal composition of biocatalysts was following, in dry wt% of constituents: bacteria biomass/SiO<sub>2</sub>/Co<sub>x</sub>O<sub>y</sub> = 10–15/50–60/20–40. The inactivation half-life time of the biocatalyst is more than 500 h of continuous isomerization of monosaccharide syrup (~44 wt% ) at 65±5°C.

**Biocatalysts for sucrose inversion.** The biocatalysts with invertase activity were prepared by entrapment of biomass of pressed bakers’ yeast into SiO<sub>2</sub>-xerogel. The optimal composition of biocatalysts is following, in dry wt% of constituents: yeast biomass/SiO<sub>2</sub> = 50–80/20-50. The invertase activities run up to 600 U/g. The inactivation half-life time of the biocatalyst is more than 200 h of inversion of sucrose syrup (~20 wt% ) at 50°C.

## BIOTECHNOLOGICAL PRODUCTION OF ECOLOGICALLY PURE RAW MATERIAL OF VALUABLE MEDICINAL PLANT

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The maintaining of high demands in plant-based medicines and increasing deficit of medicinal raw material, explicable by uncontrollable harvesting of valuable and endangered plants, dictate the necessity of applications of biotechnology for the production ecologically unpolluted plant raw material. Skullcap (*Scutellaria baicalensis* Georgi) is one of the endangered medicinal plants. The value of skullcap is determined by wide spectrum of pharmacological activity of flavones synthesized in roots. It is proved that main flavones of skullcap roots (baicalein, wogonin and their glucuronides) possess of effective antihypertensive, antimicrobial, cerebroprotective and cytostatic activities. The area of skullcap is sufficiently limited and in natural biocenose plants propagate only via seeds. Introduction of skullcap is very difficult. Roots of skullcap have been applied in official and traditional medicine, mainly in Russia, China and Japan. The scientists from Research Institute of TSC of Siberian Department of RAMS have been worked out skullcap flavones-based medicines for long time. But last time this work is significantly limited by lack of medicinal raw material.

Root culture of skullcap has been established following sterile seedlings infection with wild strain of soil agrobacterium (*Agrobacterium rhizogenes*) in IPP RAS for compensation natural plant material. Skullcap in vitro cultured roots (so called hairy roots) have been grown under strictly controllable condi-

tions for 10 years. The quantitative flavones content in root culture is 3 times lower than in roots of intact plant, but total productivity of skullcap hairy roots is similar with intact roots because of fast growth and possibility to grow all the year round.

Antioxidant activity of cultured root extracts was the similar with activity of intact roots. Test of pharmacologically activity of cultured roots extracts with laboratory animals in RIP has showed that extracts of roots in vitro express cerebroprotective and anxiolytic effect analogous medicines form roots intact plants. Besides extracts of cultured in vitro roots of skullcap as well as extracts of roots intact plants normalize the processes of blood-building of laboratory animals. The results obtained indicate perspectives of biotechnological way of production valuable and ecologically absolute pure medicinal material and also about real possibility using for compensation of deficit traditional raw material.

The implementation of this biotechnological method requires a creation of specialized bioreactor for skullcap large scale cultivation. Scale up production of plant biomass let provide medicinal and food industry with necessary amount of ecologically pure plant material of new type. At the same time large scale cultivation of skullcap roots shall promote to save of plant in nature that has been included in Red date book.

## DEVELOPMENT OF A NEW STRATEGY FOR THE REVEALING OF CERTAIN SINGLE-NUCLEOTIDE MUTATIONS IN THE PRESENCE OF DIFFERENT SINGLE NUCLEOTIDE POLYMORPH SUBSTITUTIONS IN HIV GENOME

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The goal of this project is the elaboration of the universal approach for the simultaneous revealing of point mutations in the presence of single nucleotide polymorph substitutions in the *pol* gene of HIV-1, which determine resistance of the virus to antiretroviral drugs.

Analysis of the certain region of HIV-1 genome is carried out using Stanford University HIV drug resistance database and the data of testing HIV strains from blood of 184 patients treated or not treated with antiretroviral drugs. We took into account the list of the mostly used antiretroviral drugs leading to drug resistance and the fact that subtype A is the most epidemically significant in Russia. Therefore, to develop a test-system for revealing mutations of drug resistance to protease inhibitors, we chose codons 32, 46, 50, 54, 82, 84, and 90 in *pol* gene coding for HIV-1 protease, which are the most substantial for the revealing in medical practice. To reveal the single-nucleotide substitutions in HIV-1 *pol* gene, we use ligation of oligonucleotide tandems (mini-probes) on nylon DNA chips, with an analyzed DNA being the template. We elaborated the computer algorithm for designing mini

probes, which allows one to choose the oligonucleotide tandem having maximum discriminating ability in the revealing of single nucleotide substitutions. Oligonucleotide mini-probes, both three-component oligonucleotide tandems and two-component bridged tandems (cross-linked with a non-nucleotide spacer), were designed and synthesized taking into account single-nucleotide substitutions, which are responsible or not for drug resistance. We also synthesized the model DNA fragments bearing codons 32, 46, 50, 54, 82, 84, and 90, which contain single mutations leading to drug resistance. We demonstrated the opportunity of solid-phase ligation of the chosen mini-probes on the synthetic templates. Polymorphism in DNA templates and mini-probes structure was not shown to prevent ligation of tandems. The revealing of the biotin-containing ligation products was performed by colorimetric method using streptavidine/alkaline phosphatase conjugate and chromogenic substrates. The results obtained at this stage are the basis for the development of test-systems for revealing mutant HIV-1 strains resistant to antiretroviral drugs.

## AUXIN REGULATED ROOT PATTERNING: THE MATHEMATICAL MODEL AND KEY GENETIC MECHANISMS

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The flow of auxin across plant cells plays the extensive role in regulating patterns of cell growth, divisions and fates in development and under treatments. Auxin active transport is regulated by efflux and influx carrier proteins (PIN, PGP, Aux/LAX families) that asymmetrically localized on cell membranes. In plant roots, carrier-mediated auxin flows form maxima of auxin concentration in (1) root apical meristem where it is necessary for stem cell niche maintenance; (2) protophloem cells of basal meristem that predetermines initiation of lateral root; (3) in collar region where initiation of adventitious roots takes place. We developed a mathematical model where auxin distribution is studied in 2D tissue of initially unspecialized cells. Following processes are considered: auxin flow from the shoot; auxin active transport and diffusion; genetic regulation by auxin of carriers expression; degradation of auxin; regulation of cell division and growth. In the model solutions, we observed formation of auxin maxima in positions (1)-(3) and analyzed changes in auxin distribution in series of numerical experiments on simulation of root treatments. We also observed patterning near maximum (1) where functional zones could be distinguished in positional information, that auxin had formed. The model predicts that the prevalence of lateral or adventitious roots that determines two types of plant root architecture (taproot or fibrous) may be based on dif-

ferent efficiency of inhibition by auxin the rates of its own transport. The proposed model can be developed for investigation of the effects of different treatments on root growth (such as water deficit, salt and phosphorus stress, changes in temperatures etc).

The next point was to analyze the possible mechanisms of auxin effect on its carriers expression. It is known that primary auxin response is mediated by transcription factors of ARF family and PIN1 gene expression is regulated through this mechanism (Vieten et al., 2005). In *A. thaliana* it is counted 22 ARF genes, some of them are activators and the others are inhibitors. We analyzed ARF's promoter sequences of *A. thaliana* and found that all activators haven't TATA-boxes in their regulatory regions, whereas inhibitors have. Thus, all ARF-activators have a lower basal level of expression than ARF-inhibitors. This information will be used for the model extension.

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Reference:

Vieten A, Vanneste S, Wisniewska J Benková E, Benjamins R et al. (2005) Functional redundancy of PIN proteins is accompanied by auxindependent cross-regulation of PIN expression. *Development*. 132(20): 4521-4531.



## MULTIPLE ANTIGENIC PEPTIDES CONTAINING TICK-BORNE FLAVIVIRUS FUSION PEPTIDE

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Tick-borne flaviviruses (tick-borne encephalitis virus, Omsk hemorrhagic fever virus, Powassan virus and mosquito-borne West Nile virus persisting in natural populations of Russia) possess variable genome RNA and viral proteins. To reveal numerous flavivirus quasispecies in wild populations and clinical specimens universal detection system is required. One of the most conserved fragment of the flavivirus surface glycoprotein E is fusion peptide (98-113 amino acids) responsible for the virus penetration into host cells. The aim of present work was to analyze immune response after administration of synthetic peptides containing flavivirus conserved fusion peptide and different T-helper epitopes.

Peptides FA4T5

DRGWGNHCGLFGKGSIFTSLGKAVHQVFVKK (98-113 aa of tick-borne flavivirus E protein, FT, 431-440 aa DEN4 E protein, VKK) and FA4T4 DRGW-

GNHCGLFGKGSIGITVNPIVTEKDSPVNIKK (98-113 aa of tick-borne flavivirus E protein, G, 352-368 aa DEN2 E protein, KK) had been synthesized in Keck Biotechnology Resource Center (New Haven, USA) and were attached to lysines as tetravalent multiple antigenic peptides. Direct ELISA with immobilized MAPs using polyester plates and nitrocellulose filters allowed us to reveal monoclonal and polyclonal antibodies against E protein of the tick-borne encephalitis virus, West Nile virus and Denge 1 virus. However, indirect ELISA with immobilized antibodies against different flaviviruses and subsequent binding with MAPs was unsuccessful due to sterical obstacles. Monoclonal antibodies binding with MAPs and, consequently, having their epitope near the fusion peptide inhibit hemagglutination and can neutralize the tick-borne encephalitis virus, but not Powassan virus.

## BIOTECHNOLOGY OF DIETARY SUPPLEMENTS AND HEPATITIS A VACCINE PRODUCED BY VECTOR-BIALGAM CJSC

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The presentation is focused on biotechnology of dietary supplements and hepatitis A vaccine developed by Vector-BiAlgam CJSC. The composition, pharmacologic properties, advantages, methodology and areas of application of products are described.

“**Ecoflor**” is a unique complex of bifidobacteria and lactic acid bacteria immobilized on enterosorbent “SUMS-1”. It helps to increase significantly the viability of probiotics while reaching the colon through the acid barrier of the stomach.

“**Trilact**” is an active complex of lactic acid bacteria that includes the most effective strains *L.acidophilus*, *L.casei* and *L.plantarum*.

“**Bifidum 791 BAG**” is an active complex of bifidobacteria. The composition of this dietary

supplement includes the most effective strains of bifidobacteria *B.bifidum* and *B.longum*. Furthermore, it includes new perspective strain *B.bifidum791BAG* specially developed and patented by Vector-BiAlgam CJSC.

“**Bifidokefir**” is a usual kefir enriched by live and active bifidobacteria.

“**Bifacil**” is a new cultured milk product that contains a unique complex of bifidobacteria and lactic acid bacteria.

The vaccine “**HEP-A-in-VAC**” is the first Russian vaccine for Hepatitis A prophylaxis (dosages are designed both for children and adults). The vaccine has been clinically tested, registered and included into National Russian Register of Pharmaceuticals.

## USING BIOTECHNOLOGY IN FORESTRY AND WOOD-PROCESSING INDUSTRY

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The collection of mycelium cultures containing, mainly, siberian isolates of wood-attacking (basidiomycetes) and wood-staining (ascomycetes) fungi is maintained at the Institute of Forest. It consists of active wood-destroying strains, producers of bioactive substances, cultivated edible mushrooms, phytopathogens, blue stain fungi. The collection makes it possible to carry on the studies as follows: (a) cultivation of fungi to obtain edible fruit bodies and bioactive metabolites (enzymes, vitamins, antibiotics, anticancer substances etc.), (b) utilization of wood waste through bioconversion, (c) assessment of wood antiseptic efficiency.

The studies carried on at the Institute are principally focused at (a) bioconversion of softwood by

wood-destroying fungi and (b) cultivating mycelium of medicinal xylophagous fungi in liquid media and sawdust substrates. It was found that the water extract of greater celandine stimulated fungal decomposition of softwood appreciably. Possibility of using the products of solid state cultivation of wood-attacking fungi on pine sawdust as organic manure or sorbent of heavy metal ions is examined. The supplement of mycocompost (the partly delignified pine wood) to forest soil was shown not to inhibit the activity of soil microorganisms but increase their number and rate of mineralization process. Laboratory cultivation of *Inonotus obliquus* Pilat (tshaga) siberian isolates in liquid media and sawdust substrates was mastered.

## RESEARCH AREAS OF THE SIBERIAN INSTITUTE OF PHYSIOLOGY AND BIOCHEMISTRY OF PLANTS OF SIBERIAN BRANCH OF RAS

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In Siberian institute of Physiology and biochemistry of Plants of Siberian Branch of RAS carry out researches in several directions:

1. Protection of rare and endangered species of Cisbaikal region.

2. Creation of transgenic plants with rapid biomass accumulation for pulp and biofuel production.

3. Elaboration of micropropagation methods of local planted fruit, ornamental and wood plants.

We also elaborate utilization methods of plant and cattle residues, fertilization of soil and production of ecologically pure product based on EM technology.

These researches consider specialities of local continental climat.

## CORRELATIONS OF QUANTITATIVE CHARACTERS OF YELLOW-SEEDED *IN VITRO* PROPAGATED LINES OF *BRASSICA NAPUS* L.

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All cultivars of *B. napus* currently grown in Russia are black-seeded. The development of yellow-seeded forms has been proposed as a means to improve the quality of the canola meal. Yellow seeds of summer rapeseed may have more oil and protein than black seeds. Meal from light-pigmented genotypes of rapeseed may have lower fibre content than meal from their dark-pigmented counterparts.

In order to accelerate breeding process of the most valuable forms, *in vitro* propagation was used. This method made it possible to develop new high yielding lines of summer rapeseed.

Results of the correlation analysis carried out during 2005-2007 of components of summer rapeseed seed production have shown that the structure of correlation of the initial inbred lines and cultivars, despite of their different origin, differed much less, than

of initial inbred forms and somaclons (fig). Changes in correlation are caused by changes of genetic structure of somaclonal lines. The path coefficient analysis also has revealed modifications in correlation between quantitative characters of inbred lines and somaclons of *B. napus*.

Differences of correlations between quantitative characters point at changes which occur in plant genome *in vitro* culture. The main cause of the inherited variability induced by factors of cultivation *in vitro* at free cell division, we consider absence of a complex of regulating factors of the whole organism which controlling systems of a reparation. Mutagen effect of components of a nutrient medium and toxic metabolites of the cultivated tissue is amplified by absence of the control of an intact organism and generate appearance of somaclonal variations.

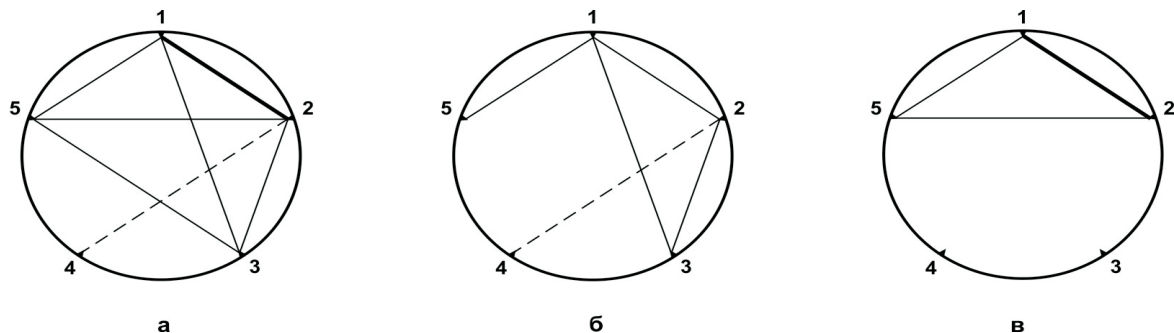


Fig. Correlation between quantitative characters of cultivars (a), inbred lines (b), and somaclons (c) of *B. napus*: 1 - seed yield per plant, 2 - number of pods per plant, 3 - number of seeds per pod, 4 - weight of 1000 seeds, 5 - height of plant

## HAPLOTYPE ANALYSIS IN MULTIPLE CROSSES OF BARLEY (HORDEUM VULGARE L.) TO IDENTIFY A QTL GENE

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More than 20 mapping segregating populations were developed for barley worldwide and scored for variation of important phenotypic traits ([www.grain-gene.com](http://www.grain-gene.com)). The accumulated data inspired some attempts to summarize the information about the QTL locations and hypothesize the potential hotspots in the barley genome that may affect agronomically important traits (Tinker et al., 1996). However, the number and locations of QTL reported for agronomic traits in different barley mapping populations vary from cross to cross dropping possible targets for marker-assisted selection.

One of the problem in comparing barley genetic maps and particularly QTL locations, is the lack of common markers on the different maps (Thomas, 2003). On other hand, barley crosses differ each other by a set of segregating loci. As a result, the same QTL being mapped, for example, in the double haploids population from barley genotypes in the Steptoe/Morex cross may not be detectable in mapping populations of other barley genotypes (e.g. Barke/Morex cross), simply because there is no polymorphism between Barke and Morex for the particular chromosome regions affecting the trait. Besides, environments of different geographical regions where the barley mapping populations were scored for QTL analysis may also affect the QTL abundance reported in publications. Thus, there is a logical need to combine at least the most cited barley mapping populations as one

panel within the same experiment to analyze genetic variation of some important agronomic traits exposed under similar environmental conditions.

To do that we are going to integrate the conventional QTL mapping approach with haplotype analysis of parents in multiple crosses of barley. The seeds of ~ 1500 double haploid (DH) and recombinant inbred lines (RILs) of the thirteen barley mapping populations developed worldwide and kindly provided by their authors were reproduced at the Vavilov Institute in summer 2008 and currently available for the field trials, phenotyping and QTL mapping. On other hand current barley genomic effort yielded large amounts of EST-derived markers (Varshney et al., 2007; Ros-toks et al., 2006; Stein et al., 2007). The genome location of the markers is known. Thus, working with the representative series of barley mapping populations scored for polymorphism with the large common set of the EST-derived markers there is an opportunity to answer the question: what is the DNA polymorphism that exists in one barley cross and does not exist in other in such way that the presence/absence of that polymorphism is associated with the QTL appearance?

Summarizing, we are intended to perform haplotype analysis in multiple barley crosses to reveal the genetic polymorphism between the parental lines that systematically causes a QTL appearance in a series of the mapping populations.

## MAPPING OF QTLs ASSOCIATED WITH THE IMPORTANT AGRONOMIC TRAITS USING RECOMBINANT SUBSTITUTION DIHAPLOID LINES SARATOVSKAYA 29 (JANETZKIS PROBAT 4D)

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High yield and good bread-making quality of grain are the main agronomic characteristics of wheat cultivar. Both of them have a complicate polygenic inheritance and are influenced by environment. The modern approach of dissecting such traits on more simple genetic components consists in genotyping and further phenotyping sets of recombinant inbred lines obtained from crossing of two cultivars with certain characteristics. Different kinds of DNA molecular markers are used for this purpose and SSR markers are the most convenient. One shortcoming of this powerful method consists in masking of the effects of some loci involved into genetic control of quantitative trait with others.

In this work, the new kind of genetic material was used for the mapping of quantitative trait loci (QTL) responsible for such important traits as grain yield and physical properties of dough. The set of intervarietal substitution lines Saratovskaya 29 (Janetzki Probat), (S29(JP)) of bread wheat was used for identification of chromosomes carrying the genetic factors responsible for this two traits. The donor of chromosomes is a high-yield cultivar while the recipient is a low-yield one but having outstanding technological properties of grain. The chromosome 4D was detected as “critical” for certain components of productivity as well as

for variability for physical properties of dough. The set of 107 recombinant dihaploid lines were developed on the base of this substitution line using haploids produced after maize pollination of F<sub>1</sub> hybrids between S29 and S29(JP) substitution line.

Microsatellite marker based genotyping revealed that the substitution line ‘S29’ (‘YP’ 4D) carries an additional fragment ‘YP’ on chromosome 7A extending from the locus *Xgwm0060* on the short arm to *Xgwm0748* on the long arm. Mapping in the DH lines was performed using both chromosome 4D and chromosome 7A microsatellite markers. The chromosome 4D linkage map carried 14 microsatellite loci, whereas that for 7A comprised five microsatellite loci and in addition four major genes, controlling anthocyanin pigmentation on different plant organs.

Phenotyping of these lines after field sowing in Novosibirsk was accomplished for such quantitative traits as plant height, number of tillers, productivity of main spike, productivity of secondary spikes, whole plant productivity, 1000 grains weight, flour strength, dough tenacity and extensibility. Two main QTLs were identified on 4DL and 7AS chromosomes which were associated with those yield components of donor cultivar JP which differ it from the low-yield recipient S29.

## **POLYVALENT BACTERIOPHAGES AS A PREPARATION BASE FOR THE TREATMENT OF URINARY TRACT INFECTIONS**

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Polyvalent bacteriophages as a preparation base for the treatment of urinary tract infections. Urinary Tract Infections (UTIs) are prevalent infection diseases in ambulatory and in hospital practice worldwide. Non-complicated UTIs are major diseases of woman in childbearing age. More than 95% of non-complicated UTIs are caused by single agent. More often they are gram-negative enterobacteria, mainly *Escherichia coli* (70-95%). *Klebsiella* spp., *Proteus mirabilis*, and other gramnegative pathogenic bacteria are founded rarer. A part of grampositive microorganisms is no great. The increasing prevalence of infections caused by antibiotic-resistant bacteria makes the empirical treatment of UTIs more difficult. One of the important factors contributing to these high resistance rates might be high antibiotic use. Antibacterial properties

of phages were assessed earlier on, but unfortunately the mechanism was not well defined, leading to trial failures. Currently, we are witnessing a renaissance of phage research. Now we understand some features of phage efficacy. Extensive research and searching has been conducted on the development of a phage collection against typical and individual pathogens. Particular interest targets on polyvalent phages caused *Escherichia coli*, *Klebsiella* sp., *Proteus* sp. lysis. Several such DNA containing pages have been found. Phage therapies on the base of the bacteriophages are efficient, highly specific, and relatively cost-effective.

This work was partly supported by the Russian Academy of Science, program "Fundamental science for medicine" project # 32.



## NANOCOMPOSITES ON THE BASIS OF TITANIUM DIOXIDE NANOPARTICLES BEARING DNA FRAGMENTS AND ANTIBIOTIC BLEOMYCIN A5

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The goal of the work is the design of antisense nanocomposites consisting of nanoparticles providing the penetration into cells, oligonucleotides aimed to the definite nucleic acids (NA), and reactive groups capable of damaging NA with the formation of direct breaks. We used nanoparticles of titanium dioxide (TiO<sub>2</sub>) for they were known to penetrate into cells. Anticancer glycopeptide antibiotic bleomycin A5 (Blm) was used as the reactive group capable of damaging the single- and double-stranded DNA with the formation of the direct breaks and alkali-labile sites. According to their structure, the proposed nanocomposites should have unique cumulative properties: they should penetrate into cells due to TiO<sub>2</sub>-nanoparticles, find a definite NA responsible for viral, hereditary, or oncological diseases due to the given sequence of an oligonucleotide, and damage this NA due to the Blm residue. For the first time, we elaborated the approach to the preparation of nanocomposites TiO<sub>2</sub>-Blm consisting of nanoparticles and antibiotic bleomycin. Im-

mobilization of Blm onto nanoparticles of titanium dioxide was shown to occur almost quantitatively under the definite conditions. It was demonstrated that the Blm residue in the prepared nanocomposites TiO<sub>2</sub>-Blm preserved its ability to destroy target nucleic acids making the direct breaks and alkali-labile sites. The bleomycin-containing oligonucleotides (Blm-oligo) were immobilized onto TiO<sub>2</sub>-nanoparticles giving nanocomposites TiO<sub>2</sub>-Blm-oligo. Another type of nanocomposites, TiO<sub>2</sub>-PL•Blm-oligo, was prepared due to the electrostatic interaction of positively charged amino groups of polylysine in nanocomposite TiO<sub>2</sub>-PL and negatively charged phosphate groups of oligonucleotide in Blm-oligo. This type of the interaction was studied on the model system TiO<sub>2</sub>-PL and oligonucleotide. The designed nanocomposites were shown to penetrate into cells. Thus, they can be considered as prospective reagents for the action on nucleic acids inside cells.

## GAS-VORTEX BIOREACTORS APPLYING FOR DIFFERENT PROCESSES IN BIOTECHNOLOGY AND APPLICATIONS.

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A gas-vortex bioreactor is a unique device of a new generation that has no analogues in the world. The bioreactor surpasses all known types of bioreactors by characteristics. Culture is mixed by producing a three-dimensional movement of the "rotational vortical ring" type (a quasi-stationary flow with axial countercurrent flow) in a liquid medium. The movement is generated by aerating gas vortex resulting from the pressure difference above the suspension surface and the airflow frictional force on the suspension surface. The aerating gas vortex is formed by the centrifugal activator mounted at the upper part of the vessel above the level of the cell suspension. The gas vortex bioreactor executes gentle and efficient mixing without foaming, water hammers, cavitation, high-turbulent and stagnant zones. Application areas of a gas-vortex bioreactor are the following.

**Substitution of the roller technologies** by industrial gas-vortex technology for manufacture of vaccines and other medical substances. When making vaccines and other medicinal preparations the method for cultivation of sensible types of cells and microorganisms in roller bottles is applied. This method does not provide standard terms in separate roller bottles by pH, concentration of cells, air exchange. Roller technologies are non-technological, labour-intensive, expensive and unsafe. It is expedient to apply gas-vortex bioreactors in the processes of vaccines and other medicinal preparations manufacture using sensible types of cells and microorganisms.

**Biotechnological small factories for fodder sugar production from grain raw materials** with

use of gas-vortex bioreactors and rotary-pulsating dispersants. A technology for production of easy-digestible carbohydrates from corn raw materials (wheat, rye, barley, triticale, etc.) including grain forage has been developed. The carbohydrate fodder addition (CFA) obtained from wheat contains 25-29% of sugar, 16 amino acids, 7 vitamins and starch-splitting enzymes ( $\alpha$ - and glucoamylases) improving animals alimentary process. The quantity of milk with the 3.5% fattiness has been increased on 9.96% while making investigation. CFA has been obtained while examining the technology in breeding factory "Irmen" (the best agricultural factory in Russia in 2007). The general physiological state of the animals has been improved as well.

**Liquid wastes of poultry and hog-breeding plants and farms.** The technology provides efficient utilization of liquid wastes of poultry and hog-breeding plants and farms resulting in production of biofuel. At the moment, utilization of such wastes is carried out in a cascade of expensive facilities or in air-tight tanks. These technologies require long periods of treatment of wastes and produce small volume of biogas. Novel technology allows to reduce treatment time used to process bio wastes in tanks and to increase biofuel production rate. The technology is simple, environment friendly and cost saving, it accelerates microbiological decomposition of wastes. Furthermore the rotor and pulse dispergator mince biowastes and sterilize them. Utilization of wastes involves using of pure lines of microorganisms which are processors of wastes.

## BIOTECHNOLOGY FOR DEVELOPMENT OF RESISTANT WHEAT GENOTYPES

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One of the approaches in modern plant biotechnology is using of the mapping data of genes and genomes for direct introgression of valuable agricultural traits into recipient genotypes. *Triticum timopheevii* and other wild common wheat relatives are regularly involved in selection process as donors for creation of new forms of wheat with improved properties.

The following researches were conducted for more effective utilization of the donor species *T. timopheevii* in biotechnological wheat programs:

1. Construction of molecular-genetic maps for *T. timopheevii* by using microsatellite (SSR) markers.
2. Identification of chromosomal regions associated with powdery mildew, leaf and stem rust and spot blotch resistances in *Triticum aestivum* x *T. timopheevii* introgression lines by means of SSR-genotyping.
3. Mapping of genes for leaf rust resistance (*Lr* genes).
4. Application of marker assisted selection for development of 'near-isogenic' lines of common wheat resistant to different pathogens.

These works provide new insight into fungal diseases resistance and utilization of the data in disease management strategies.

## TRANSGENIC PLANTS WITH A MODIFIED LEVEL OF EXTRACELLULAR RIBONUCLEASE ACTIVITY AS A NEW GENETIC MODEL

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Extracellular S-like RNases of plants are endoribonucleases with no absolute substrate base specificity that are found in apoplastic compartment. Their expression is associated with senescence, phosphate starvation and wounding, but the nature of their function is largely unknown. It was previously shown that transgenic tobacco plants with high level of bovine RNase activity in apoplast were characterized by lower accumulation of a viral antigen and delayed symptoms when inoculated by tobacco mosaic virus (TMV). Taking into account this fact and the fact that wounding is one of the major ways of viral invasion, we have suggested that wound-inducible extracellular RNases could be used to protect plants at the viral infection onset. However, the role of plant ribonucleases in the mechanism of antiviral protection has not been studied yet.

The objective of this research concerns investigation of the functional role of plant wound-inducible extracellular RNases in the mechanism of defense against viruses. For this purpose, we planned to obtain model tobacco plants with modified activity of certain wound-inducible extracellular RNases and to analyse their resistance against TMV.

In order to obtain plants with increased activity of a wound-inducible RNase we obtained tobacco plants expressing *ZRNaseII* gene of *Zinnia elegans*. In the host plant, ZRNaseII is not detected in intact leaves and is induced in response to wounding. The transgenic plants were characterized by a high level

of RNase activity in apoplast. Activity gel assay also revealed the presence of an additional RNase in the transgenic plants.

To obtain plants with decreased level of wound-induced RNase we transformed tobacco plants with genetic construction bearing a dsRNA suppressor of the tobacco RNase gene *Nk1*. This RNase is particularly interesting as it is induced either by wounding or by virus inoculation. Activity gel assay showed lack of one of proteins with RNase activity compared to control plants.

Thus, we obtained tobacco plants with either increased or decreased levels of extracellular RNase activity and these plants can be used as a model to study the functional roles of apoplastic RNases.

Under normal conditions the expression of introduced genetic constructions had no visible effect on the growth and development of the transgenic plants. We have obtained some preliminary data concerning resistance of the plants bearing ZRNaseII gene against TMV infection. These data agree with our hypothesis on the role of wound-inducible ribonucleases in plant antiviral defense mechanisms.

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## **SYNTHESIS AND SUBSTRATE PROPERTIES OF NANOCOMPOSITES CONSISTING OF TITANIUM DIOXIDE NANOPARTICLES AND DEOXYNUCLEOSIDE TRIPHOSPHATES**

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Design of antiviral drugs on the basis of deoxynucleoside triphosphate analogs capable of penetrating through the cell membrane is an important problem. Nanocomposites consisting of titanium dioxide nanoparticles and immobilized derivatives of deoxynucleoside triphosphates analogs can be used to solve this problem. Titanium dioxide nanoparticles with the size of 2-5 nm are known to easily penetrate into cells. So, they can be used as a “carrier” for the transportation of immobilized ligands into eucaryotic cells. The goal of the present work is the investigation of the substrate properties of deoxynucleoside triphosphates

(dNTPs) immobilized onto TiO<sub>2</sub>-nanoparticles in the elongation reaction with Taq polymerase. dNTPs were bound to nanoparticles containing the immobilized polylysine residues. Nanocomposites TiO<sub>2</sub>-PL-dNTP as well as TiO<sub>2</sub>-PL(Ac)-dNTP with blocked amino groups were used in the polymerase reaction. It was demonstrated that the immobilized dNTPs in the prepared nanocomposites are the substrates for Taq Polymerase. In addition, the influence of TiO<sub>2</sub> nanocomposites (with or without polylysine residues) on elongation reaction was studied in this work.

## TGP (Transgene Promoters): A DATABASE OF BIOTECHNOLOGICALLY IMPORTANT PLANT GENE PROMOTERS

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One of the most important problems when planning a genetic engineering experiment is to ensure the adequate pattern for transgene transcription. A database containing annotated published data on the promoters operating in plant cells with a certain specificity and activity may be used for solving this problem. Such specialized databases are yet absent.

We have developed the database on promoters (TGP), collecting the information on plant promoter sequences with experimentally verified specific transcription patterns including general, tissue-, stage-, and stress-specific activities. The database was constructed on the SRS platform and consists of three cross-linked parts: gene description (TGP\_GENE), promoter description (TGP\_PROMOTER), and corresponding experimental promoter sequences (TGP\_SEQUENCE).

The TGP\_GENE database compiles the information about the genes whose promoters are offered for the transgene design. Each entry of this database contains gene and product names as well as the name of organism and its taxonomic classification. There is description of the functional activity of the gene in various organs and tissues as well as its changes during ontogenesis. The entry for a gene also contains cross-references to the TGP\_PROMOTER and TGP\_SEQUENCE as well as references to the literature source wherefrom the information about this gene was extracted.

The TGP\_PROMOTER database accumulates information about functionally active promoters and its deletion mutants described in annotated scientific sources. The deletion mutants of promoters display different specificities and transcription activities. Annotation of these data increases essentially the suc-

cess rate in selecting the desirable promoter variant. Each entry of the TGP\_PROMOTER database contains information about the promoter location relative to the start of transcription or translation, reference to EMBL, location of the sequence given in the corresponding EMBL entry as well as the information about specific features of the genetic construct. There is information about reporter gene; stage of development, organs and tissues of the transgenic plant where the promoter was studied. The database contains the names of inducers that change the activity level of the promoter in question, the concentration of inducers, and their action time. The database provides quantitative information about the expression and induction levels of the promoter. The entry for a promoter contains cross-references to the TGP\_GENE and TGP\_SEQUENCE as well as references to the literature source wherefrom the information about this promoter was extracted.

SRS tools allow for indexing the fields of databases and search by the fields via a system of adequate queries. This provides a possibility to select promoters with the required properties including the origin, dimensions, and appropriate stress-, tissue-, and stage-specific activities for different experimental tasks. On demand, the user may retrieve the nucleotide sequence of the desired promoter as well as characteristics of the initial gene. TGP is aimed to provide information for experiments on transgenic plants and may be useful for either basic research in molecular biology or biotechnology.

The database is available at <http://www.mgs.bionet.nsc.ru/mgs/dbases/tgp/>

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## PREDICTION OF THE REGULATION PATHWAYS OF THE *ESCHERICHIA COLI* *DPS* GENE EXPRESSION UNDER STRESS CONDITIONS

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Progress in sequencing of the genomes from different organisms raised the problem of rapid functional decoding of their genetic programs. One possible approach could be based on computer analysis of potential regulatory regions of the genes and experimental verification of the predicted pathways. This approach was used to reconstruct the pathways of the *E. coli dps* gene regulation. In order to develop genosensor derived from the *dps* promoter, a reporter gene encoding an intermediate stability variant of green fluorescent protein (*gfp-vaa*) was exploited. The constructed plasmid *pDps-gfp* was used for transformation of *E. coli* cells. The sensitivities of the resulting cells *E. coli/pDps-gfp* were assayed in the model experiments with various external toxic stimuli. The sensor cells *E. coli/pDps-gfp* responded to oxidative stress (H<sub>2</sub>O<sub>2</sub>), protein damaging (phenol), exposure to heavy metal ions (Cd<sup>2+</sup>). However, the mechanisms underlying the responses are known only for oxidative stress. This

prompted us to seek potential transcriptional factor binding sites (TFBSs) in the regulatory region of *dps* by the SITECON method, which allows recognition of conservative physicochemical and conformational TFBS features. The high recognition level estimated by type II error (false positive) was demonstrated for 12 TFBS. We applied these data to reconstruction of the structure of the *E. coli dps* promoter and prediction of its regulation pathways under stress conditions. Detection of the great number of potential sites for TFs for oxidative agents and global regulators of metabolic processes, supports our assumption that genosensor derived from promoter of *E. coli dps* gene could be a multifunctional sensor.

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## NEW METHODS FOR CONTROLLING THE NUMBER OF NEMATODES, THE PARASITES OF PLANTS AND ANIMALS

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The presentation is focused on new methods developed by the company “Global Vendor” for controlling the number of nematodes, the parasites of plants and animals. The most widespread technology used at present for fighting zoonematodes and fitonematodes is application of chemical poisons of neuroparalytic action that kill the most part of parasites. However, this technology has many disadvantages. To begin with, such poisons are also toxic for animals / plants and can significantly weaken the immune system of an animal. Secondly, nematodes develop resistance rapidly towards the toxins and therefore it is necessary to increase a dosage of a poison or change it. The last but not least nematode adults lay eggs that get with fecal masses into the soil and develop into larvae. When an animal eats the grass or drinks the

water, it also receives the larvae of nematodes and becomes ill again. Thus the poisons currently used for protecting animals do not protect from reinfestation (revermination).

The new approach developed by the company “Global Venfor” is fighting the nematodes in fecal masses and in the soil thus destroying the larvae and breaking the cycle of vermination (parasitosis development). Consequently, the number of nematodes in an animal is reduced and the adult parasites die after finishing their life cycle. The methodology is based on application of predacious fungi. They are natural enemies of the parasites. Microbiological drugs have been developed that are non-toxic and ecologically safe for animals and plants, and for the environment.



## PHARMACOLOGICAL PROPERTIES OF *Scutellariae baicalensis* Georg. EXTRACT, RECEIVED FROM HAIRY ROOT CULTURES

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**The most significant therapeutic effects of Scullcap (*Hairy root extract Scutellariae baicalensis* Georg.) preparations are cerebroprotective action and stimulation of a damaged by chemotherapy of malignant tumours hematopoiesis. (V.I.Litvinenko at al., 2007). By this reason it was investigated the extract from Scullcap *in vitro* cultured roots (so called *hairy roots*) received from IPP RAS. The activity of Scullcap extract (ES) was estimate by parameters of higher nervous activity at development of conditioned reflexes elaboration and reproduction at high psychoemotional loadings, under hypoxic conditions and at the infringements of memory caused by scopolamine introduction, and also on hematotoxicity and genotoxicity indices after antitumor agent paclitaxel administration.**

Experiments was performed in mice CBA/CaLac lines and Wistar mail rats. Paclitaxel in mice administrated once inter peritoneum - 40,0 mg/kg, to rats – intravenously – 5,0 mg/kg. ES in all experiments administrated in a doze of 40 mg/kg *per os* within 5 days before experiments. In hematopoiesis parameters study standard hematological methods used. Cytogenetic infringements estimated by Ford modified method. The account of genic mutations spent by means of the test somatic mosaic on *Dr.melanogaster*.

Paclitaxel administration lead to decrease marrow cells amount, development reticulocytopenia neutropenia and lymphocytopenia and increase of genic mutations. ES administration lead to increasing of the general cells amount in marrow. The quantity of erythrocytes during all period of research was increased. In peripheral blood it was observed increasing of leukocytes quantity, due to increase of the neutrophiles and lymphocytes content, and as increase in quantity reticulocytes during all period of research is noted. Except for that, it was marked expressed genoprotective effect (decrease in quantity of aberrations and the general number damaged metaphase plates). In the test of somatic mosaic on *Dr.melanogaster* decrease in number of mutant spots female *Dr.melanogaster* has been shown.

It was observed improvement of conditioned-reflex activity, conditioned reflex elaboration enhancement due to decrease of neurotic and freezing reaction amount. ES administration lead to improvement of elaboration and stability under hypoxic trauma. ES reduced amnesic and dissociating action of scopolamine on memory processes.

Thus, ES received from «hairy root» cultures of *Scutellariae baicalensis* Georg. on the basic parameters by it activity are close to activity of the extract received from a plant.

## ENGINEERING OF BROAD SPECTRUM RESISTANCE TO VIRAL INFECTIONS IN TRANSGENIC PLANTS: INDUCIBLE EXPRESSION OF EXTRACELLULAR RIBONUCLEASE

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Viruses are particularly fast evolving pathogens, so they are capable of overcoming natural and engineered virus resistance. This is why engineering of virus resistance has become a testing area for new transgenic approaches.

It was suggested that introduction of RNase-encoding genes could be used to protect plants against various pathogens. Most plant viruses have single-stranded RNA genomes but virus reproduction includes formation of double-stranded RNA molecules.

Vectors, bearing extracellular pancreatic ribonuclease from *Bos taurus* and RNS1-like extracellular ribonuclease gene of *Zinnia elegans* (ZRNaseII), were constructed. Both vectors bear ribonuclease genes under the control of 2'-promoter of the mannopine synthase gene from Ti-plasmid of *A. tumefaciens*. It was shown that the promoter confers developmental and tissue-specific expression, and wound and plant growth hormone inducibility that we need for genes providing resistance to pathogens.

Transgenic tobacco plants, bearing these constructs, were created and it was shown that the transgenic plants have higher level of ribonuclease activity in leaf extracts than control plants. We have shown that the transgenic plants exhibited a significantly higher level of protection against the virus infection than the control non-transformed plants. The protection was

evidenced by the absence (or significant delay) of the appearance of typical mosaic symptoms and the retarded accumulation of infectious virus and viral antigen. These results demonstrate that modulation of extracellular ribonuclease expression can be efficiently used in promoting protection against viral diseases. In general, if the virus concentration in the inoculum was low or medium (0.01-0.1 µg/ml), transgenic plants were characterized by the absence or considerable delay of virus accumulation and appearance of disease symptoms, at higher TMV concentrations in inoculum (10 µg/ml), the differences between the control and transgenic plants were negligible in the later stages of infection (14-28 DAI). Transgenic expression of the secretory RNase is likely to enhance the intrinsic mechanisms of plant antiviral defense based on plant extracellular RNases (e.g., *Nicotiana tabacum* RNase NE). Taken together, all these results demonstrate that the pathogen-targeted resistance strategy can be effectively employed in conferring resistance to viral diseases of crops.

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## PHOTO-CATALYTIC AIR PURIFICATION SYSTEMS: EXPERIENCE AND OUTLOOK OF RAPID AND COMPLETE AIR DISINFECTION IN HUMAN PRESENCE

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Air disinfection in human presence is an urgent task for a wide variety of human activities ranging from medicine to food production. The focus of the report is a new multi-module approach to effective deep and complete indoor-air disinfection in human presence. The experimental and statistical data will be demonstrated confirming high efficiency of the photocatalytic air-cleaners developed by the company "Airservice". Basing on photo-catalysis, the air-cleaners combine effectively a polypropylene filter, an electrostatic filter, photocatalytic and adsorptive

filters. A polypropylene filter and prefilter are used for air cleaning off the coarse dust. An electrostatic filter is used for filtering air off the fine dust and aerosol. A photocatalytic filter is designed for biological and molecular pollution control. It destructs pollutants into harmless mineral substances, water and carbon dioxide. An adsorptive filter prevents breakthrough of molecular pollutants in high concentrations. More technical details and market applications will be provided in the presentation.

## DEVELOPMENT OF PROTOTYPES OF PROPHYLACTIC PREPARATIONS AGAINST ZOOGENOUS INFECTIONS BY MEANS OF PHOTODYNAMIC INACTIVATION OF BACTERIAL CELLS

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In almost countries of former Soviet Union, agricultural animals is vaccinating by attenuated alive vaccines against dangerous infections. In USA and Europe, alive vaccines are not applying, because of high level of residual virulence, possible reversion of attenuated strains and also because of significant re-actogenicity of initials strains. That is why inactivated (killed) vaccines are widely used. But, nevertheless, killed vaccines possesses by lower efficiency, because thermal processing (heating at the temperature of 80<sup>o</sup>C -100<sup>o</sup>C) causes destruction of thermolabile antigens. At the same time, formalin and alcohol induce fast coagulation of proteins of cytoplasm, phenols produce inactivation of respiratory ferments, and acetone initiates essential drying of cells.

Recent achievements in the field of microbiology and biotechnology open perspective ways for development of new modern prophylactic preparations. One of the promising techniques is a method of soft inactivation of bacteria by low-intensity laser irradiation in the presence of photosensitizers (dyes).

Authors have suggested new set-up for bacteria photoinactivations (RUS patent N 20088125317 from 25.06.2008)

Proposed devise is performed on the base of standard plane-table for immune- ferment analysis with removable stripes. Each microcavity of plane-table is

supplied by individual light source of low-coherent irradiation, i.e. light emitting diode (LED). Wavelength of used light is 630 nm, bandwidth of spectrum is 10 nm. Power of radiation of each source can be varied in a wide range: from 0.2 mW to 1 mW.

Four types of bacterial cells *Escherichia coli communis*, *Pseudomonas aeruginosa*, *Francisella tularensis* 15 NIIEG, *Brucella abortus* 19 BA has been selected as the objects for investigations.

Described set-up for photoinactivation of bacterial suspension by dynamic low-coherent optical speckles in the presence of photosensitizers allows:

- 1) To obtain preparative quantity of inactivated bacterial cells, which keep their initial antigen structure of cellular membranes. Total amount of bacterial suspension, which can be obtained during one session of photoprocessing, is about 20 ml. This quantity of cells is enough to carry out whole range of biochemical, genetic microbiological and other investigations.
- 2) To carry out bacteriological work in sterile conditions.
- 3) To vary parameters of illumination with purpose of optimization of regime of photoprocessing.
- 4) To conduct photoprocessing of bacterial cells in anaerostat, thermostat and other units with limited volumes.

## ESTIMATION OF TOXICITY OF BACTERIAL PREPARATION BY SPECKLE-MICROSCOPY

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Essential changes in the system of blood microcirculation may show up at the infection diseases of human and animals. The alternations of characteristics and structure of blood flow carry important pathogenic and diagnostic information. Investigation of variations of blood flow using the method of biotesting may serve the basis of screening of bacterial preparations, and investigating of toxic effects. At present time, toxicity of prophylactic preparations is usually determined using laboratory animals, performing the intraperitoneum and subcutaneous injection. Testing preparation is considered as non-toxic one if any local or general reactions are not observed on the animals during 7 days. Authors of this presentation defined the level of toxicity of bacterial preparations *in vivo* on white rats by methods of speckle-microscopy. Vaccine strains of *Francisella tularensis* 15 NIIEG, *Brucella abortus* 19 BA have been applied on the mesentery of animals. Changes of blood flow have been observed in single isolated blood microvessel during 40 minutes after the application of preparations.

Experimental set-up is mounted on the base of conventional microscope Biolam (LOMO, St-Petersburg, Russia), in which additional source of coherent light – He-Ne laser (power 1 mW, wavelength 630 nm) - has been introduced. This device has been utilized for estimation of toxic effects of testing preparations, which have made on the base of bacterial suspension.

As experimental investigations shown, alternations of character of blood flow have been detected immediately after the application of suspension of bacteria of *F. tularensis* 15 NIIEG on the mesentery

of white rat. Velocity of blood flow in microvessels reduced approximately in 15 times after the application of preparation. Sometime, complete stop of blood circulation in isolated vessel has been recorded. But, approximately in a 5 minutes after the application, blood flow acquired the regular character, which remains slower in comparison with a norm (i.e. in intact vessel). Then velocity of blood flow relieved up to initial level approximately in 10 minutes after the application of preparation.

Application of suspension of cells *B. abortus* 19 BA caused constriction of capillaries. In this case, velocity of blood flow increased in 5 times, because of essential reduction of diameter of the vessel. Velocity of blood constantly reduced in time after the application of preparation. But, blood flow completely recovered up to its normal level in 5-7 minutes after the application of preparation.

Performed experiments allow to formulate following conclusions: (i) suggested method of biotesting opens a new way to record visually the effect of influence of suspension of bacterial cells on capillaries of white rat mesentery *in vivo*; (ii) toxicity of preparation lies in the range of norm, because the disorders of microcirculation carry the reversible character: blood flow is completely normalized in 10 minutes after the application of preparation; (iii) definition of toxicity by method of biotesting using speckle-microscopy allows to carry out reliable estimation of effects, caused by preparations, during relatively short time (approximately, in 10-15 minutes).

## **SOME ASPECTS OF THE WORKING OUT OF *IN VITRO* SELECTIVE MEDIA FOR FIBER FLAX (*LINUM USITATISSIMUM* L.)**

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Flax (*Linum usitatissimum* L.) as fiber and oil crop is cultivated in different countries, including Russia and Germany. Climatic and soil conditions in flax production zone are very different. One of the breeding tasks is creation of stable yield varieties. It means good stability of plant in different conditions. Traditional methods of breeding on the population and organism's level could be added with biotechnological methods.

Selection on the cell level for flax can be effective for looking for resistant forms to abiotic and biotic stress factors. There are some of them: temperature (low, high and fluctuating regime), drought (osmotic stress), salinity, deficit and surplus of metals, pH, herbicides. Using of toxic extract from pathogenic fungi's can be working out to selection of resistant cells.

For practical use of different selective factors the stage of object developing and the origin of initial material would be taking into account. Cells on the stages

of callii initialization, its morphogenesis, shoot developing possess different resistance to stress factors.

High temperature treatment of callii in our experiments resulted the following parameters: +38°C duration till 18 hours. In stage of callii morphogenesis and shoot forming stress pressing would be lower. Salinity in selective media for callii could be in range of till 60 mM NaCl, then for shooting – lower. Resistant cells could be selected in that conditions. Aluminum ions could be used as selective factor in concentration till 200 mg/l in callii stage and in lower concentration in stage of shooting. Toxic water extract of *Colletotrichum lini* could be used in media in range of 20-50 mg/l in dependence of stage and type of initial material.

Working out new *in vitro* systems for selection to environmental stress factors for flax can be resulted not only practical outputs as new forms, but theoretical approaches in metabolite pathways of the crop.

## ULTRASOUND EXTRACTION OF GLYCANES FROM *LINUM USITATISSIMUM* L.

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Earlier the glycanes were used only as subsidiary components and they are considered as independent biologically active substance due to the discovery of new properties. Antihypoxic, antitumoral, antiviral, antimicrobial, sorption, antiatherosclerotic properties of plant polysaccharides were detected.

One of the widely known and accessible sources of polysaccharides is flax seed (*Linum usitatissimum* L.) which are used both as a drug in herbal medicine and as valuable food plant raw material. Flax seed-coat contains  $\approx 10\%$  mucilage. Flax seed slime has coating and emollient properties decreases local irritant action of different substances. It is taken to lessen the irritation in case of inflammatory and ulcerous processes on the mucous membrane, especially in the gastrointestinal tract. Flax glycanes are prospective prebiotics. Prebiotic action of polysaccharides is connected with following factors: the increase of the number and activity of bifido- and lactobacteria, optimization of intestinal motility, increase of calcium, magnesium and other metal absorption, decrease of the level of cholesterol and triglycerides, prevention of intestines cancer. Besides polysaccharides of flax can be used as water-retaining and binding agents in bakery production, rendering, thus, protective action on the digestive system.

In the paper presented the ultrasonic extraction of polysaccharides from flax seed was carried out. Water extracts of polysaccharides were obtained at a room temperature with the help of ultrasonic dispersant IKASONIC U50; the ratio raw materials : extraction solvent 1:10 (wt). Optimal parameters of ultrasonic

treatment were determined using the dependences of viscosity of polysaccharides solutions obtained and the mass of solid residue on ultrasonic intensity and time of treatment. IR Fourier-spectroscopy was used for the identification and confirmation of structure of the glycanes obtained. IR-spectra of polysaccharides of flax seeds obtained by traditional infusion were compared to the spectra of glycanes obtained by ultrasonic extraction at optimal parameters of the process (intensity –  $276 \text{ W/sm}^2$  and duration 16 minutes).

The analysis of the spectra obtained shows that the chosen optimal parameters of ultrasonic treatment do not considerably change the structure of flax polysaccharides. The spectra contain all the peaks corresponding the functional groups of flax polysaccharides. The peak correlating the carboxyl group oscillation is especially distinct that allows attributing the polysaccharides to polyuronides.

Thus, the ultrasonic treatment were revealed to considerably increase the affectivity of polysaccharides of *Linum usitatissimum* L. extraction and to reduces the time of the process from 24 hours to several minutes without causing glycanes destruction. The analyses conducted prove that the use of ultrasonic treatment does not result in the qualitative change of fraction composition of glycane extracts but allows obtaining the extracts more homogeneous by composition. The polysaccharides extracted from flax seeds have no unpleasant odour, they improve the structure of the product, they are non-toxic, promising prebiotics and can be used as components of functional food-stuffs.

## APPLICATION OF BIOTECHNOLOGICAL APPROACHES TO SCIENTIFIC RESEARCH AND INNOVATIONS

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Biotechnological methods and approaches are used in the Institute for a number of purposes. Primarily they are applied for acquisition of callus and suspension cultivars for scientific objectives. Clonal micropropagation is used to produce planting stock of decorative and heat-loving plants. This method is widely applied in many countries to produce a number of agricultural, arboreal and decorative plants. It has a variety of advantages as compared to standard methods. In the Institute it is intensely used to create a "test-tube" plant collection grown in isolated cultivar. The method is based on cultivating of a small part of the plant or one seed on artificial nutrient medium containing mineral salts, sugar, vitamins and growth regulators, with artificial illumination and temperature controlled and complete absence of bacteria, fungi and insects. Under such conditions plants propagate all year round, and one explantate may produce thousands and hundreds of thousands of tiny plants. Biotechnological methods are widely used to preserve rare plants of Pribaikal'ye threatened with extinction. For this purpose there were created a seed bank of such plants, live collections of plants growing in the ground, test-tube collections. Plants are grown for re-introduction into disturbed populations and into habitats of vanished populations. There are created demonstrative plantations on the sites of educational excursions for schoolchildren, students and tourists.

In 2005 a bank of rare and endemic Pribaikal'ye plants was started; it currently comprises seeds of

the following plants: oxytrope trifoliolate, oxytrope Popov, oxytrope Peshkova, oxytrope tragacanth, Hedyarum Zunduk, Urals licorise, dwarf lily, Pennsylvanian lily, uniflorous tulip. The bank is replenished with seeds of other rare plants of Pribaikal'ye. The seeds are kept at  $-70^{\circ}$  C. They are subjected to complex investigation. We have developed a method of acquisition from the seeds of plants ready to be planted into the ground.

In co-operation with SSC "Vector" and Institute of Chemical Biology and Fundamental Medicine SD RAS there was developed a candidate edible vaccine against HIV and hepatitis "B" with the help of genetic engineering and biotechnological methods. It was accomplished by genetic transformation of tomato plants by TBI-HBs gene encoding synthesis of antigenic proteins of HIV-1 and HBV. Emergence of adequate mucous and overall immune response of tested animals.

It is planned to obtain transgenic plants for medical and technical purposes.

To ensure ration security of Russia there will be created resistant and highly productive agricultural cultivars based on investigation of the following mechanisms: a) genetic and physiological-biochemical regulation of cells metabolism; b) intra-cellular integration of genomes into general genetic system; c) transfer of genes into cellular organelles; d) phyto-immunology.



## THE EFFECTS OF ALLELIC VARIATION OF BOVINE CYTOKINE GENES ON SUSCEPTIBILITY TO INFECTIOUS DISEASES

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Identification of agricultural animal's genome loci responsible for the susceptibility/resistance to infectious diseases is an emerging area of basic and applied researches in agricultural science. This approach promises to provide an efficient tool for improving livestock genetic background in respect of the animal infectious diseases control by improving selection practice. This challenge is particularly important in control of viral diseases for which efficient treatment is still unavailable and which seriously affect production and have great economic impact. One of the examples of such diseases is the infection caused by bovine leukemia virus (BLV) in dairy cattle. In some countries, particularly in Russia, this virus affects a significant portion of cattle livestock. From the other hand, it is well known that different cattle breeds have extremely contrast susceptibility to this infection. Therefore, there are strong reasons to believe that genetic background of the breed plays an important role in the development of the predisposition to this condition.

Data on the existence of the significant association of several candidate genes with this infection were obtained. The list of the candidate genes includes monocyte differentiation antigen CD14 gene, tumor necrosis factor TNF $\alpha$  gene, tumor necrosis factor receptor TNF1R gene, chemokine GRO1 gene, stro-

mal cell-derived factor SDF1 gene and macrophage migration inhibitory factor MIF gene. The frequencies of the single nucleotide polymorphism (SNP) markers located in some of these genes differed significantly both in affected and non-affected animals in one herd and between herds with different prevalence of the infection. Considerable diversity also exists between different breeds. Interestingly, the pure elite representatives of some most popular dairy breeds in Russia have a high prevalence of haplotypes associated with the infection. For example, G to A substitution in the first intron of the TNF- $\alpha$  gene, was detected in black-spotted cattle. The occurrence frequency of the variant A of this polymorphism was significantly higher among the BLV carriers and animals at the terminal stage of leucosis than in the healthy controls. These data provide a strong support that analyzed genome loci may be involved in determination of predisposition to chronic leukemia virus infection in cattle. Further confirmation of this result will lead to significant insight into molecular-biological mechanisms of virus-host interaction in case of this infection.

This research was supported by International Science and Technology Center Grant 1883 and Russian Foundation for Basic Research Grant 03-04-48569.

## EXPERIMENTAL STUDY OF PREDICTED REGULATION PATHWAYS OF *E. COLI/pYFI-GFP* GENOSENSOR UNDER OXIDATIVE STRESS

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The *Escherichia coli yfiA* gene encodes structure of protein pY (RaiA) which is known to stabilize ribosome structure and take a part in regulating translation elongation under stress conditions. Microarray data indicate that *yfiA* is sensitive to various external impacts including oxidative stress. Previously, we have shown existence of independent promoter of this gene and recognized a putative regulatory region of *yfiA*, stretching from the end of the *ectD* gene to the ATG codon of *yfiA*. We have constructed the *E.coli/pYfi-gfp* genosensor where that region was fused with the *gfp* reporter gene. This genosensor responded to various stresses including oxidative one but the processes mediating these responses were unknown. Based on that data analysis we have concluded that the promoter regulation is of complex nature. *In silico* analysis of the promoter structure revealed about 20 different transcription factors potential binding sites. Specifi-

cally, high reliability of the prediction with regard to type II error probability was shown for the binding sites of the MarA, IscR, MetJ, PurR, and SoxS transcription factors, directly or indirectly involving in response to oxidative stress. Using this data we predicted regulation pathways of the gene under oxidative stress. Encoding regions of IscR, MarA and SoxS transcription factors were cloned and corresponding proteins were expressed and purified. EMSA method has shown that SoxS and IscR are capable of binding to the *yfiA* promoter. Thus we have revealed the *yfiA* gene is positive regulated by IscR and SoxS transcriptional factors during oxidative stress.

This work was supported by the RFBR, project 08-04-01008; Program of the RAS on molecular and cell biology, No. 10.7; Programs of the SB RAS, Nos. 107 and 119; and grant for scientific schools No. NSh-2447.2008.4.

## INTERACTION OF TiO<sub>2</sub> NANOPARTICLES WITH INFLUENZA VIRUS VIRIONS

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The effective deactivation of infectious agents plays an important part in prevention of their spreading and epidemic expansion. The important task is the search of highly effective and harmless for humans remedies and applications modes for vira and bacteria destruction. This work deals with the investigation of interaction of TiO<sub>2</sub> nanoparticles with the virions of influenza virus A/Aichi/2/68 (H3N2). As a virus source the allantoic liquor with the virus concentration of 9,5 lg TCD<sub>50</sub>/ml. The viability of virus has been investigated on the MDCK cell culture and detection of viral RNA using PCR. The changes of morphology of viral particles were studied using negative contrasting electron microscopy (JEM 1400).

The incubation of the virions with TiO<sub>2</sub> nanoparticles (mean size 5 nm) resulted in damage of virions' envelope after 30-60 minutes and full destruction of virions after 3-5 hours. The viability of virus in presence of TiO<sub>2</sub> nanoparticles depends upon the concen-


tration ratio and duration of incubation period. The full inactivation of influenza virus with 6,5 lg TCD<sub>50</sub>/ml was achieved at the TiO<sub>2</sub> nanoparticles concentration of 2-7 mg/ml. The inactivating action of TiO<sub>2</sub> nanoparticles was more marked on light rather the in dark. This could be attributed to photo-catalytic properties of TiO<sub>2</sub> nanoparticles.


Thus, the results of our investigation demonstrate the direct inactivating and damaging effect of TiO<sub>2</sub> nanoparticles on the influenza virus, which allows us to say about the possibility of usage of this type of nanoparticles for deactivation of influenza virus in various conditions.


This work has been supported by Federal Scientific and Technical Program under direction of "Living Systems" (The State Contract No 02.512. 11.2081), the Program of Ministry of Education and Science (registration No 2.1.1/5642) and the Grant of Russian Foundation of Basic Research 08-04-01045-a.




German-Russian Forum Biotechnology  
German Company Profiles


<b>Surname</b>	<b>Angersbach, Dr.</b>
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Profile of the Institution	The company Biotronix GmbH is focused on the monitoring systems for the bio- and pharmaceutical industry, which are critical for ensuring compliance with regulatory requirements and product safety. The main areas of application are fermentations and production based on bacterial cultures. Potential customers with „bacteria cells, bacterial fermentation“ background are pharmacy companies, food industry and R&D institutions.
Work Topics	<p>The goal of biotronix GmbH is to create a new technological platform to monitoring the status of cells in biotechnological processes and cell research. The main development of biotronix is the patented electro-optical technology and device <b>EloTrace®</b>. EloTrace is the world's first commercial measurement unit for continuous electro-optical monitoring of bacterial parameters <i>in vivo</i>. The level of electro-optical parameters is closely linked to the actual physiological state of bacterial cells, so that dynamic changes in cell activity and regulatory processes will be determined during cultivation processes in real time. EloTrace is an automatic measurement tool which combines all necessary functions of probe sampling and probe preparation with electrooptical measurements in as yet unseen quality. Areas of application are: bacterial fermentations, in particular protein expression, starter cultures, bio-fuels, vaccines, quality assurance, etc.</p> <p>Other biotronix-products:  <b>EloCheck:</b> inline / online photometer for continous recording of optical density of cell suspensions.</p> <p><b>EloFerm:</b> Single- and multi-channeled fermentation units with optimal cost-performance ratio.</p>

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Profile of the Institution	<p>A professorship entitled „Polymer and Recycling Technology” was cofounded jointly by 29 industry and trade companies of the region. This position was created in 1994 with the goal of preserving and expanding the expertise in the field of polymer development, processing, analysis and recycling. After five years of successful work, the state of Hesse has taken over the funding of the chair. Additionally the association “Innovation Centre for Polymer and Recycling Technology” is closely connected with the professorship. This member organization is mainly funded by midsize industrial businesses but also by private individuals. The Professorship is also member of the “Scientific Circle of Polymer Technology” (WAK) which is joined by the leading polymer chairs of German Universities.</p>
Work Topics	<p>Biocomposites</p> <ul style="list-style-type: none"> <li>• High-strength composites</li> <li>• Microfoamed biopolymers and biocomposites</li> <li>• Innovative polymer blends from renewable raw Materials</li> </ul> <p>Thermoplastics</p> <ul style="list-style-type: none"> <li>• Selfreinforced gradient thermoplastics</li> <li>• Microcellular foams</li> <li>• Influence of coupled hygrothermalmechanical load Recycling</li> <li>• Odour detection and reduction</li> <li>• Quality management in the field of ,recycling of thermoplastic polymers and thermosets</li> <li>• Technical expertise Fibre-Reinforced Plastics</li> <li>• Experimental identification of temperature and moisture dependent interphase effects</li> <li>• Optimisation of glass, carbon and natural fibres and their composite properties</li> </ul>

<b>Surname</b>	<b>Börner</b>
Name	Andreas
Institution	Leibniz-Institut für Pflanzengenetik und Kulturpflanzenforschung (IPK) Corrensstraße 3 • D-06466 Gatersleben
Logo of the Institution	 The logo of the Leibniz Institute of Plant Genetics and Crop Plant Research (IPK) Gatersleben. It features a stylized green plant icon to the left of the text 'IPK' in a bold, green, sans-serif font, with 'GATERSLEBEN' in a smaller, green, sans-serif font below it.
Contact Information	Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), Corrensstrasse 3, D-06466 Gatersleben <a href="http://www.ipk-gatersleben.de">http://www.ipk-gatersleben.de</a>
Profile of the Institution	The objective of the Leibniz Institute of Plant Genetics and Crop Plant Research (IPK) is to carry out basic and applied research on crop plants with a special emphasis on genetics. An outstanding feature of the IPK is its multidisciplinary research on the extensive collection of plant genetic resources preserved in its germplasm collection (the Genebank). Research results are of interest to plant breeders, agriculture and other branches of the economy including the pharmaceutical sector.
Work Topics	Major research areas are: Crop plant diversity Plant genome dynamics Integrative biology of plant performance



<b>Surname</b>	<b>Bubenheim</b>
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Profile of the Institution	<p>The Institute of Technical Biocatalysis is part of the Hamburg University of Technology. Since December 2004 Prof. Dr. rer. nat. Andreas Liese is head of the institute. The main research field covers technical and fundamental aspects of the application of whole cells and isolated enzymes in biocatalysis and environmental biotechnology.</p> <p>At the institute process engineers, biotechnologists, chemists and microbiologists interact in an unique interdisciplinary way in the laboratories that are equipped with state-of-the-art equipment for research and education.</p> <p>The Institute of Technical Biocatalysis takes part in different educational programs. We are actively involved in several B.Sc. and M.Sc. programs in Chemical Engineering, General Engineering Science and Bioprocess Engineering as well as in the education of BTA and CTA applicants. The unique „Kinderforscher“ program motivates school children for science and technology and offers children the possibility to do experiments in the labs of the Technical University.</p>
Work Topics	<ul style="list-style-type: none"> <li>• Asymmetric synthesis</li> <li>• Redox reactions</li> <li>• C-C bond formations</li> <li>• C-N bond cleavage</li> <li>• Enzymatic conversion of natural products</li> <li>• Solvent free biocatalysis</li> <li>• Biocatalytic polymerization</li> <li>• Process engineering</li> </ul>

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Profile of the Institution	<p>Leipzig University (“Alma Mater Lipsiensis”) is one of the oldest and most renowned university of Germany, celebrating this year its 600 years anniversary. Famous students of Leipzig University were:</p> <p>Georg Agricola, Ulrich von Hutten, Thomas Müntzer, Gottfried Wilhelm Leibniz, Gotthold Ephraim Lessing, Johann Wolfgang Goethe, Robert Schumann, Richard Wagner, Friedrich Nietzsche, Erich Kästner and Carl Friedrich von Weizsäcker</p> <p>The Leipzig University Medical School was founded in 1415 and is the second oldest medical faculty in Germany. It is one of the largest research institutions in the region and is closely linked to other research institutes, such as the Max-Planck-Institute for Human Cognitive and Brain Sciences, the Fraunhofer Institute for Cell Therapy and Immunology, the Leibniz Institute for Surface Modification. The research of the Leipzig University Medical School focuses on Neuroscience, Endocrinology, Immunology and Molecular Oncology.</p> <p>The Leipzig University Hospital comprises 28 clinical and 5 research departments. Over 3.000 medical and other employees treat over 350.000 patients per year. The hospital is the second largest employer in the city of Leipzig and hosts the largest blood transfusion center of all universities in Germany.</p> <p>The Department of Abdominal, Thoracic, Vascular and Transplant Surgery (Director: Prof. Dr. Sven Jonas) is the regional center for organ transplantation in the state of Saxony and one of the most successful German centers for liver transplantation.</p> <p><a href="http://www.uni-leipzig.de/welt/eng/index.html#02">http://www.uni-leipzig.de/welt/eng/index.html#02</a>  <a href="http://www.uniklinikum-leipzig.de/">http://www.uniklinikum-leipzig.de/</a></p>

## Work Topics

*1. Oncogenesis and Cancer Prevention*

Gastrointestinal tumors, in particular colorectal tumors, are the most common malignant diseases in the industrialized countries. We have discovered about 15 years ago a new type of cell adhesion molecule, LI-cadherin. This molecule became a differentiation marker for gastrointestinal adenocarcinomas and appears to be involved tumorigenesis since it is ectopically expressed in very early cellular changes (intestinal metaplasia) that can ultimately develop into adenocarcinomas. We have unraveled the molecular and genomic structure of LI-cadherin and its kidney-specific paralogue, Ksp-cadherin, analyzed their phylogenetic origin, studied the expression of LI-cadherin during embryogenesis as well as in healthy and malignant tissues and published numerous papers on these subjects in international scientific journals. We have generated LI-cadherin knockout mice and are currently constructing additional genetically modified animal models in order to reveal the molecular and cellular changes that ultimately lead to gastrointestinal malignant tumors. This project has been supported by the Deutsche Forschungsgemeinschaft (DFG), the Volkswagen Foundation, the German Academic Exchange Service (DAAD) and the Interdisciplinary Center for Clinical Research Leipzig (IZKF).


More recently we have begun to study the effect of nutrients on the gastrointestinal system and in particular their oncogenetic potential. These studies rely on various cell culture systems and the animal models. The ultimate goal of this project is to identify components in the human nutrition that either increase the risk for gastrointestinal tumors or have the potential to protect us against malignant diseases. This knowledge should ultimately help the food industry to avoid nutrients with negative health effects and to increase the fraction of beneficial components.

*2. Endocytosis-based cellular uptake of DNA and RNA*

Over the recent years Prof. Christine Lang (Technical University Berlin) and I have developed and validated a proprietary two-stage screening system to optimize the endocytosis-based cellular delivery of nucleic acids and other macromolecules/nanoparticles with therapeutic potential. In the first stage a large number of compounds is screened in Berlin for their potential to enhance the transfection efficiency of yeast, the best studied eukaryotic cellular model. Active compounds are then tested in the second stage in my laboratory for their ability to enhance the endocytosis-based uptake of vector DNA into human cell lines. We have already identified and patented a number of small molecules that induce in combination a 7-fold higher cellular uptake of DNA via endocytosis than the best previously known transfection enhancer. Currently we are screening a very large chemical bank of natural compounds of an industrial partner in order to identify even more potent transfection enhancer. This project has been supported by the German Federal Ministry of Education and Research (BMBF).

*3. Impact of heterotypic interactions of PrP on TSE pathogenesis*

The cellular prion-related protein (PrP<sup>C</sup>) is an endogenous vertebrate protein highly expressed in the central nervous system and on thrombocytes. Scrapie disease of cheep, variant Creutzfeld-Jacob disease of humans, bovine transmissible spongiform encephalitis (bTSE or BSE) are infectious diseases transmitted by aggregates ("Prions") of a conformational variant of PrP, called PrP<sup>Scrapie</sup> or PrP<sup>Sc</sup>. Whereas many research projects have addressed the pathogenesis of prion diseases, little is still known about the physiological function of PrP<sup>C</sup>. We have discovered that PrP<sup>C</sup> binds via its too highly basic lysine clusters to the kringle repeats of plasminogen and t-PA and enhances the t-PA mediated plasminogen activation. However, PrP<sup>C</sup> turned out to be also a substrate of plasmin and is cleaved at K110 and R151. The released N-terminal fragment PrP23-110 is even more potent in stimulating the t-PA mediated plasminogen activation. Two promising candidates for prion disease therapy, pentosan polyphosphate and HM2602 are further enhancing the effect of PrP<sup>C</sup> on plasminogen activation. Since t-PA and plasminogen are present in liquor and PrP<sup>C</sup> highly expressed on neural cells, we propose that PrP<sup>C</sup> is involved in the regulation of proteolytic activity in the brain and thus potentially important for regeneration and remodeling. Moreover, since the plasmin cleavage products of PrP<sup>C</sup> are not able to be converted into PrP<sup>Sc</sup> an activation of plasmin may interfere with TSE pathogenesis. TSE and in particular BSE can be transmitted orally by ingestion and intestinal uptake of infectious prion particles in the nutrient (i.e. food stuff prepared from infected animals). We recently discovered that

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Profile of the Institution	<p>The East-West-Science Centre was established as an initiative of the University of Kassel in 1992 to pave the way and intensify the co-operation in research and educational fields with universities and research and development organizations in Central and Eastern Europe. Since 2003 the East-West-Science Centre has been advising all universities in Hessen and has developed initiatives which strengthen the international research and development network which concentrates on Central and Eastern Europe.</p> <p>The aim of the East-West-Science Centre is to support the scientific exchange with Central and Eastern European countries as well as to convey information on the landscape in science and technology in each of these countries. The Centre provides a forum for discussions between scientists from East and West, supports the transfer of sustainable technologies and provides consultancy, technical support, and information.</p> <p>Website: <a href="http://www.owwz.de">www.owwz.de</a></p>

## Work Topics

The East-West-Science Centre is coordinator in the German-Russian Network for scientific cooperations between Germany and Russia in Biotechnology.

### German-Russian Cooperation Network Biotechnology

Biotechnology is one of the fastest and strongest growing industrial sectors of the world economy. Russian and German co-operation in this field is one of the main areas within the dynamic economic relations between both countries.

The German-Russian Co-operation Network Biotechnology will support collaboration between German and Russian research institutes and industry. The Network is part of the Agreement of Strategic Co-operation signed by the Federal Ministries of Research and Education of both sides.

The Network is funded on the German side by the Ministry of Science and Education (BMBF), the federal States of Brandenburg and Hessen as well as the Russian Federal Ministry of Science and Education.

Main goal is to develop an effective and sustainable transfer system for co-operation between German and Russian science institutions and small and medium sized enterprises. The Network was established in April 2005.

As promising areas for co-operation with Russian scientific institutions and enterprises have been determined:

- Genomics and Proteomics
- Pharmaceutics and Medical Engineering
- Agriculture and Food Biotechnology
- Bioinformatics
- Molecular Biology

### **Services**

Specific country information on biotechnology in R&D

Processing of co-operation proposals

Partner-Matching

Monitoring of the co-operation process


Individual project consultation concerning funding programmes, application, contracts and financial support

Special Workshops

Data bases and Internet information



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Profile of the Institution	<p>The Institute for Biochemistry investigates transport processes across physiologic barriers like blood-brain-membranes and lung surfactants discovering the molecular phenomena. Applied research in medical technology is involved.</p> <p>The small enterprise marcotech trades nanomaterials and provides services in settlement and management of international projects focused on nanotechnology.</p> <p>The network HiNanoAnalytics consisting of 20 partners offers collaboration in nano(bio)analytics, biomedical research and nanotechnology. Furthermore, the network provides options of international cooperation and the exchange of scientists and graduate students. The University of Muenster, marcotech and the Center for Nanotechnology are partners within the HiNanoAnalytics.</p>
Work Topics	Development of biomaterials, especially on the base of hydrogels; organization and management of international joint projects, market analysis, and marketing supports

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Profile of the Institution	<p>The AG Bioinformatics and Medical Informatics is member of the Technical Faculty of the University Bielefeld. This faculty includes workgroups of Biotechnology, Bioinformatics and Computer Science. The faculty is responsible for different Bachelor and Master courses in Biotechnology, Genome Informatics, Cognitive Science and Computer Science. The University Bielefeld is one of the youngest universities in Germany and was founded during the 60ties of the last century. Today the university has nearly 20000 students.</p>
Work Topics	<p>The AG Bioinformatics and Medical Informatics is responsible for the application of methods and concepts of computer science for Medicine and Molecular Biology. The main topics for education and research are: database implementation, database integration, implementation of molecular data warehouses, modeling and simulation of metabolic processes, parallel computing, visualization and the implementation of medical expert systems.</p>

**Surname**

**Holl**

Name

Peter

Institution

Sartorius-Stedim Biotech

Logo of the Institution



Contact Information

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Profile of the Institution

A profile of Sartorius Stedim Biotech  
 Sartorius Stedim Biotech is a leading provider of cutting-edge equipment and services for the development, quality assurance and production processes of the biopharmaceutical industry. Its integrated solutions covering fermentation, filtration, purification, fluid management and lab technologies are supporting the biopharmaceutical industry around the world to develop and produce drugs safely, timely and economically. Headquartered in Aubagne, France, Sartorius Stedim Biotech is listed on the Eurolist of Euronext Paris. With its own manufacturing and R&D sites in Europe, North America and Asia and a global network of sales companies, Sartorius Stedim Biotech enjoys a worldwide presence. Its key manufacturing and R&D site is in Germany. The company employs over 2,300 people, and in 2008 generated sales revenue of 368.0 million euros.

Work Topics

For next generation processes, Sartorius Stedim Biotech focuses on single-use technologies and value-added services to meet the rapidly changing technology requirements of the industry it serves. Strongly rooted in the scientific community and closely allied with customers and technology partners, the company is dedicated to its philosophy of turning science into solutions. on a daily basis.



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Profile of the Institution	<p>EML Research is a private research institute focussing on Information Technology and its applications. The main aim is to develop innovative information processing systems that combine highly sophisticated technology with optimum user-friendliness. At present there are three research groups at EML Research, working in the fields of bioinformatics, databases for scientific applications, and computational linguistics. <u><a href="#">Scientific Databases and Visualization Group</a></u> focuses on research and development in the area of scientific databases and the visualization of scientific data. <u><a href="#">The Molecular and Cellular Modeling Group</a></u> works on the development and application of computer-aided methods to predict and simulate biomolecular interactions. The focus is on proteins and our computational approaches are mostly based on the three-dimensional structures of macromolecules. Techniques cover a wide spectrum from interactive, web-based visualization tools to molecular and Brownian dynamics simulations. <u><a href="#">The Natural Language Processing (NLP) Group</a></u> develops software facilitating the multimodal dialogue between users and machines, applying both statistical and symbolic methods. The group's research focus lies on the semantics and pragmatics of discourse.</p>
Work Topics	Data Mining Information Retrieval Explorative Search Bio-Curation Data integration Reaction kinetics Molecular Dynamics Protein-Protein-Interaction Multi-modal and statistical speech generation Discourse Processing Text- and Web-Mining Knowledge Acquisition Ontology Learning

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Profile of the Institution	<p>Abacus Analytical Systems GmbH is a leading supplier of cutting-edge equipment for the development, quality assurance and production processes of the biotechnology industry for laboratory and industrial applications. Closely allied with technology partners, Abacus is dedicated to provide only the best solutions available in the market.</p> <p>Our partners are well known companies, the leaders in different branches of biotechnology-related production:</p> <ul style="list-style-type: none"> <li>• <b>Applikon Biotechnology</b> – full spectrum of bioreactors and fermenters, high quality sensors and Cell separation devices. The first and only in the world microbioreactor, suitable for use in <b>Nanobiotechnology</b> (biotherapy, antitumor vaccine production) – Micro24.</li> <li>• <b>Dionex</b> – the most innovative company in Ion Chromatography and Rapid High Performance Liquid Chromatography systems; the best choice for each laboratory to work with; huge amount of ready to use applications are available.</li> <li>• <b>Avestin</b> - High-Pressure Homogenizers. Those devices are suitable to be used in <b>Nanobiotechnology</b>: AVESTIN®'s high pressure homogenizers are used all over the world for liposome research and production. Only EmulsiFlex homogenizers offer the combination of high pressure homogenization, high pressure membrane filtration or a combined, homogenization/filtration process.</li> <li>• <b>Armen Instrument</b> – Flash Chromatography, Preparative HPLC, Industrial HPLC, CPC, Industrial CPC.</li> <li>• <b>Syngene Ltd, Synbiosis Ltd</b> - Genomic and Proteomic Gel Documentation (Gel Doc) Systems. Gel documentation (gel doc) and image analysis systems for DNA and protein gels. Chemiluminescence and fluorescence systems for Western blots and probes. Proteomics hardware and software for 2D gel electrophoresis (2DGE).</li> </ul>


## Work Topics

### **Applikon's product line**

Applikon Biotechnology is a privately owned Dutch company whose purpose is to develop, manufacture and supply on-line process analyzers and bioreactor systems for both research and production use. Starting in 1973 Applikon has grown from a small sized company supplying laboratory instrumentation to a dynamic worldwide enterprise capable of supplying a broad and diverse line of bioreactor systems.

Qualified manufacturing partners ensure that only products made to the highest standards will be delivered to our customers. Applikon's product line benefits:

1. Functional completeness of Applikon's product line and the variety of the operating modes: the compatible versions of software, the family of controllers, autoclavable, SIP, CIP and single-used bioreactors.
2. Wide range of vessels volumes: from several milliliters to thousands of liters.
3. Well thought-out strategy of investment protection throughout customer company lifetime.
4. First and only in the world cassette microbioreactor, suitable to be used in Nanobiotechnology: A fermentation and cell culture system using specialized single use 24-reactor cassettes providing individual control and monitoring of reactor conditions.
5. Opening to collaboration with cutting-edge scientific and production bodies: Over the years Applikon has developed close cooperative relationships with a variety of academic institutes in order to have access to relevant know-how and bioprocess development.

<b>Surname</b>	<b>Wandrowski</b>
Name	Annette
Institution	ZukunftsAgentur Brandenburg GmbH
Logo of the Institution	 <b>Brandenburg Economic Development Board</b>
Contact Information	ZukunftsAgentur Brandenburg GmbH RegionalCenter Nordost-Brandenburg Alfred-Nobel-Str. 1, Haus 26 16225 Eberswalde  Fon: +49 3334 59414 Mobil: +49 173 6255936 Fax: +49 3334 59411  E-Mail: <a href="mailto:annette.wandrowski@zab-brandenburg.de">annette.wandrowski@zab-brandenburg.de</a>  Web: <a href="http://www.zab-brandenburg.de">www.zab-brandenburg.de</a> Web: <a href="http://www.businesslocationcenter.de">www.businesslocationcenter.de</a>
Profile of the Institution	<b>Brandenburg Economic Development Board GmbH – Your partner for business development</b>  The Brandenburg Economic Development Board GmbH (ZAB) is the main contact point for all issues relating to business settlements, innovative medium-sized companies and technology-oriented start-up firms. ZAB is Brandenburg's central contact for inquiries concerning innovation and (external) business promotion as well as energy, technology transfer and cluster management.  <b>One-stop business support</b>  ZAB functions as a one-stop agency dealing with individual clients on a project-to-project basis. The RegionalCenters offer clients on-the-spot consultation service. ZAB works as a "Partner for the Future" together with the InvestitionsBank des Landes Brandenburg (ILB) and BC Brandenburg Capital GmbH. This partnership ensures fast and specific advice on regional, central and EU funding as well as all aspects of finance.  <b>Capital region Berlin-Brandenburg</b>  ZAB cooperates closely with funding agencies in Berlin. Together with Berlin Partner GmbH, ZAB commercialises the business and science location Berlin-Brandenburg.

## Work Topics

### **Our Services – Your Success**

#### **Target Groups**

The Brandenburg Economic Development Board supports and accompanies projects of

- Domestic and foreign investors
- Companies in Brandenburg
- Innovative and technology-oriented start-up firms
- Company networks.

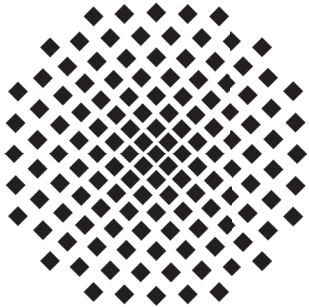
#### **Our activities**

- Together with its partner organisations in Berlin, ZAB commercialises the economic and scientific location Berlin-Brandenburg.
- The ZAB-team “International Business” supports external economic activities, like business travels, cooperation meetings and EU-projects.
- ZAB is a competent service agency regarding the development of business, innovation and technology.
- ZAB supports the technology transfer between science and businesses.
- ZAB organises business promotion projects in the sector of innovation and technology, for the European Union, different federal departments, et al.
- The business support association “pro brandenburg e. V.” links up ZAB with Brandenburg’s entrepreneurs.

#### **Our areas of expertise**

ZAB-experts are specialised in the following future and growth fields

- Industry, in particular automotive, synthetics, chemicals, paper, metal working, wood processing and optics
- Logistics and aeronautics / transport technology
- Media, information / communications technology and geographic information industry
- Biotechnology / life sciences
- Energy and biomass fuels

<b>Surname</b>	<b>Zakhartsev</b>
Name	Maksim
Institution	Institut für Bioverfahrenstechnik (IBVT), Universität Stuttgart
Logo of the Institution	
Contact Information	<p><b>Institut für Bioverfahrenstechnik</b> Prof. Dr.-Ing. Dr. h.c. Matthias Reuss (reuss@ibvt.uni-stuttgart.de)</p> <p>Allmandring 31 70569 Stuttgart Deutschland</p> <p>Sekretariat Renate Moser (secret@ibvt.uni-stuttgart.de)</p> <p>Tel. + 49 - 7 11 - 6 85 - 64574 Fax. + 49 - 7 11 - 6 85 - 65164</p>
Profile of the Institution	<p>Biochemical engineering has two central domains: (i) processing of biological materials and (ii) processing using biological agents as living cells, enzymes or antibodies. Biochemical engineering is an interdisciplinary field: (i) it requires an integrated knowledge of governing biological properties and principles as well as (ii) of chemical engineering methodology and strategies. To work at the forefront and to be successful captures the latest, best informations and technologies from both areas and accomplishes new synthesis for bioprocess design, operation, analysis and optimisation. Classic topics of biochemical engineering are design and analysis of bioreactors, biomass production in cell cultures, instrumentation and control of bioprocesses, and bioproduct recovery, while recent developments are metabolic engineering and biosystems technology.</p>
Work Topics	<ul style="list-style-type: none"><li>- Metabolic Engineering and Systems Biology</li><li>- Modelling of Bioreactors</li><li>- Biocatalyses and Enzyme technology</li><li>- integrative bioprocess development</li><li>- Bioproduct downstream processing</li></ul>

German-Russian Forum Biotechnology  
Russian Company Profiles

<b>Company</b>	<b>Airservice</b>
Ownership	Co. Ltd.
Full names of company representatives	1. Philipp K. Sabelfeld, 2. Denis S. Lokhov
Positions of participants	1. Director of marketing (Marketing Executive). 2. Chief Developer
Mailing address	Russia, 630559, the Novosibirsk Region, Koltsovo, Technoparkovaya 1
Telephone, fax, e-mail	+7 (383) 306-15-98, +7 (383) 306-16-40, info@sibairservice.ru
Industry	Air-cleaning and filtration industry
Description	Airservice is an innovative manufacturing company, which develops and produces high performance systems of deep air purification based on photo-catalysis.
Brief history / Achievements	We do research on advanced techniques of air purification and disinfection, as well as on filtering materials in close cooperation with research institutes and private companies. The result of this long-term research is presented by unique air purification module system called "Tion" developed by our experts. It allows coping efficiently with any tasks on indoor air purification and disinfection.



<b>Company</b>	<b>DIAFARM Ltd</b>
Ownership	Private
Full names of company representatives	1) Mr. Goloushkin Grigory 2) Mr. Alikin Yuri
Positions of participants	1) Director 2) Head of Biological and Technical Control Unit
Mailing address	Russia, 633010, the Novosibirsk Region, Berdsk, p/o box 112
Telephone, fax, e-mail	Tel.: +7 (38341) 5-80-74, +7 (38341) 5-80-82, +7 (38341) 5-80-91 Fax: +7 (38341) 5-80-88 E-mail: alikiny@mail.ru
Industry	Biotechnology industry
Description	Manufacture of antiviral pluripotential medicines for people and animals.
Brief history	The company was established in 1996. Since that time it manufactures antiviral medicine "Ridostine" designed for protection from and treatment of around 280 viruses, including flue viruses and acute respiratory viral infections. Since 2001 "Ridostine" is produced in a form of ointment. Since 2004 the company manufactures "Ridostine-suppositories". Since 1996 the company also produces veterinary antiviral medicines "Endoglukin" (the unique medicine for viruses of bees), "Vestine", immunomodulators "Polyribonate" and "Provest" (since 2007).

<b>Company</b>	<b>Dia-Vesta Ltd.</b>
Ownership	100 % individuals
Full names of company representatives	Ms. Khomicheva Svetlana
Positions of participants	Director
Mailing address	Russia, 630559, the Novosibirsk Region, Koltsovo, Technoparkovaya, 1, office 144
Telephone, fax, e-mail	+7 (383) 306-19-17, ick@rttn.ru svet778@mail.ru
Industry	Manufacture of dietary and functional foods, healthy foods.
Description	Sugarless vitaminized wafers, biscuits, muesli bars and jams made of natural vegetable components (embryonic wheat flakes, cereals, fruits, berries, topinambour etc.). The foods contain vitamins A, B1, B2, E, PP, C and microelements K, Ca, Mg, P, Fe, Mn, I, Se, Cr, Zn. Wafers and muesli bars are enriched with probiotics and prebiotics. The foods are designed for people with diabetes, cardiovascular and digestive tract diseases and for everybody who keeps fit.

<b>Company</b>	<b>Global Vendor Ltd.</b>
Ownership	Limited Company
Full names of company representatives	1) Mr. Kirill Stafichuk 2) Mr. Alexander Sviridenko
Positions of participants	1) Director 2) Chief technologist
Mailing address	Russia, 630559, the Novosibirsk Region, Koltsovo, Technoparkovaya, 1, office 111
Telephone, fax, e-mail	+7 (383) 306-20-13 Mobile phone +7 913 915 01 74 stafichuk@yandex.ru
Industry	Agriculture and veterinary
Description	Microbiological drugs based on predacious fungi for controlling zooparasites and plant parasites. The products are active towards larvae and adults of nematodes.
Brief history / Achievements	2006 Year of establishment. 2007 A prototype sample was manufactured. 2007-2008 Trials on plants were conducted 2009 Trials on animals will be made in cooperation with the Institute of Experimental Veterinary of Siberian Branch of Russian Academy of Agricultural Sciences

<b>Company</b>	<b>PBSoft</b>
Ownership	Co. Ltd.
Full names of company representatives	Vladimir A. Ivanisenko
Positions of participants	Director
Mailing address	10 Lavrentyev Ave, Novosibirsk, 630090, Russia
Telephone, fax, e-mail	tel: +7 (383) 333 29 71 fax: +7 (383) 333 12 78 e-mail: info@pbiosoft.ru www: www.pbiosoft.com
Industry	Bioinformatics software development.
Description	Development of the innovative software tools directed toward the resolving of biomedical and biotechnological tasks.
Brief history / Achievements	We developed Associative Network Discovery (AND) System for the automated extraction of knowledge about molecular-genetic interactions in cell from scientific literature and databases using text-mining and data-mining approaches. The PBSoft company is the winner in a nomination "Perspective business" in the First Siberian Venture Fairs, 2007, Russia In 2008 PBSoft became a member of the German/Russian Virtual Network of Bioinformatics "Computational Systems Biology"

<b>Company</b>	<b>Sayany JSC</b>
Ownership	Joint Stock Company
Full names of company representatives	<ol style="list-style-type: none"> <li>1. Max Zainullin</li> <li>2. Yuriy Ramazanov</li> <li>3. Michael Harichko</li> </ol>
Positions of participants	<ol style="list-style-type: none"> <li>1. CEO: Chief Executive Officer</li> <li>2. CSO: Chief Scientific Officer</li> <li>3. CMO: Chief Marketing Officer</li> </ol>
Mailing address	sayany@bioreactor.ru
Telephone, fax, e-mail	<p>+7 (383) 3062640            Contact person: Michael Harichko</p>
Industry	Biotechnology, agriculture, oil&gas-industry
Description	<p>Sayany holds the patent for the gas-vortex bioreactor construction and the action principal. We produce BIOREACTORS for different applications, mostly in biotechnology and agriculture. The scale of these bioreactors begins from 1 litre (for stem cells) and goes to 3000 litres and above in BioGas and Starch Hydrolysis applications.</p>
Brief history	<p>The company “Sayany” was established in 1994. Gas-vortex bioreactor has been patented in US, Japan, Europe and Russia. The invention is considered to be one of the most significant in the area of High Tech and Innovation. It was awarded the first and second prize medals at the number of international exhibitions and fairs.</p>

<b>Company</b>	<b>Scientific Cosmetological Company Ltd.</b>
Ownership	100% individuals
Full names of company representatives	Mr. Detsina Anatoly
Positions of participants	Director
Mailing address	Russia, 630559, the Novosibirsk Region, Koltsovo, Technoparkovaya, 1, office 143
Telephone, fax, e-mail	+7 (383) 306-17-01 scicosmetSOC@online.nsk.su
Industry	Manufacture of natural innovative cosmetics and balneological means
Description	New cosmetics made of natural ingredients and stimulating basal cell division. The products are designed for protecting skin from aging and abnormal states such as cellulite and skin stretching (striae). The main innovation is application of stem cell unique properties without cells abstraction and genetic modifying.
Brief history	The company has been established in 2008. By now it has won the competition within "Start - 2009" program organized by the Russian Foundation for Small Knowledge-Intensive Companies Support.

<b>Company</b>	<b>Vector-BiAlgam CJSC</b>
Ownership	Close Joint-Stock Company
Full names of company representatives	1) Mr. Nikulin Leonid 2) Mr. Molokeev Alexey
Positions of participants	1) General Director 2) Operational and technology director
Mailing address	Russia, 630559, the Novosibirsk Region, Koltsovo, p/o box 149
Telephone, fax, e-mail	+7 (383) 336-75-01 office@bialgam.ru
Industry	Production of pharmaceuticals and cultured milk foods
Description	The products of the company - the only Russian vaccine for Hepatitis A prophylaxis (dosages are designed both for children and adults); - probiotic drugs with liquid concentrates of bifidobacteria: “Bifidum 791 BAG”, “Trilact” and «Ecoflor»; - active starter cultures of bifidobacteria and lactic acid bacteria; - cultured milk foods “Bifidokefir”, “Bifacil” and “Bifatonic”.
Brief history / Achievements	Vector-BiAlgam CJSC was established in 2003. The primal activity of the company is development and production of dietary supplements, medical, preventive and immunobiological drugs. The company was awarded several diplomas of different trade fairs.

## German-Russian Forum Biotechnology List of Participants

Name	Organization
Akberdin Ilya	Institute of Cytology & Genetics, SB RAS, Novosibirsk, Russia
Alikin Yuri	DIAFARM Ltd
Afonnikov Dmitry	Institute of Cytology & Genetics, SB RAS, Novosibirsk, Russia
Angersbach Alexander	biotronix GmbH
Angersbach Natalia	biotronix GmbH
Baikov Konstantin	Institute of Soil Science and Agrochemistry, SB RAS. Novosibirsk
Balzi Elisabetta	European Commission DG Research, Biotechnologies, Agriculture and Food
Beklemishev Anatoly	Institute of Biochemistry, SB RAMS, Novosibirsk, Russia
Börner Andreas	Leibniz-Istitut für Pflanzengenetik und Kulturpflanzenforschung
Bubenheim Paul	Hamburg University of Technology
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Cottam John	Abacus Analytical Systems GmbH
Deineko Elena	Institute of Cytology & Genetics, SB RAS, Novosibirsk, Russia



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Goloushkin Grigory	DIAFARM Ltd
Gusseva Anastasya	Research Institute of Pharmacology, SB RAMS, Tomsk, Russia
Harichko Michael	Sayany JSC
Heinrich Lothar	University of Münster
Hofstaedt Ralf	University of Bielefeld, Germany
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Khomicheva Svetlana	Dia-Vesta Ltd.

Kirsanova Svetlana	ВНИИКХ РАСХН Russian Academy of Agricultural Sciences All-Russian Potato Research Institute by A.G. Lorkh
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Nikulin Leonid	Vector-BiAlgam CJSC
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Pashenova N.V.	V.N. Sukachev Institute of Forest, SB RAS, Krasnoyarsk, Russia

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Stafichuk Kirill	Global Vendor Ltd.
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Zimmermann Hans	Abacus Analytical Systems GmbH





