



**21st European
Biotechnology Congress**

October 11-12, 2018 | Moscow, Russia

Keynote Forum

Day 1

Euro Biotechnology 2018

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Vladimir P Torchilin

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Next step in drug delivery: Getting inside cells and to individual organelles

There are already some means to deliver drugs inside cells bypassing the lysosomal degradation. Thus, coupling of cell-penetrating peptides (CPP) to various molecules, including peptides and proteins, or even to nanoparticles, such as liposomes, dramatically facilitates their intracellular delivery. Similar effect could be achieved using phage coat fusion proteins purified from the phages selected for their specificity towards certain target cells as was shown with liposome-loaded anticancer drugs. The combination of targeted delivery of drug-loaded nanopreparations to target cells and their subsequent delivery inside cells might still further improve the efficiency of therapy. Intracellular drug delivery with subsequent organelle targeting opens new opportunities in overcoming problems associated with multiple pathologies including lysosomal storage diseases and multidrug resistance (MDR) tumors. Delivery of deficient enzymes for the treatment of lysosomal diseases evidently requires specific targeting of lysosomes, while facilitating apoptotic cell death in MDR tumor would require targeting of mitochondria or lysosomes. Thus, next generation drug delivery systems should be able to target individual organelles inside cells. Clearly, this challenge will require some novel approaches in engineering multifunctional nanomedicines, capable of accumulating in the target tissue, penetrating inside cells, bypassing lysosomes, and bringing pharmaceuticals to individual organelles. Examples of specific targeting of pharmaceutical nanocarriers loaded with pharmaceutical agents to lysosomes and mitochondria in cells illustrate the benefits of this new approach.

Biography

Vladimir P Torchilin PhD DSc, is a University Distinguished Professor of Pharmaceutical Sciences and Director, Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University, Boston. His interests include drug delivery and targeting, nanomedicine, multifunctional and stimuli-sensitive pharmaceutical nanocarriers, biomedical polymers, experimental cancer therapy. He has published more than 400 original papers, more than 150 reviews and book chapters, wrote and edited 12 books, and hold more than 40 patents. Google Scholar shows more than 55,000 citations of his papers with H-index of 105. He is Editor-in-Chief of *Current Drug Discovery Technologies*, *Drug Delivery*, and *OpenNano*. Co-Editor of *Current Pharmaceutical Biotechnology* and on the Editorial Boards of many other journals. He received more than \$30M from the governmental and industrial sources in research funding. He has multiple honors and awards and in 2011, Times Higher Education ranked him number 2 among top world scientists in pharmacology for the period of 2000-2010.

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Personalized and Precision Medicine (PPM) as a model of healthcare services of the newest generation to be promoted via translational applications and biodesign resources

A new systems approach to diseased states and wellness result in a new branch in the healthcare services, namely, personalized medicine (PM). To achieve the implementation of PM concept into the daily practice including clinical cardiology, it is necessary to create a fundamentally new strategy based upon the subclinical recognition of bioindicators (biopredictors and biomarkers) of hidden abnormalities long before the disease clinically manifests itself. Each decision-maker values the impact of their decision to use PM on their own budget and well-being, which may not necessarily be optimal for society as a whole. It would be extremely useful to integrate data harvesting from different databanks for applications such as prediction and personalization of further treatment to thus provide more tailored measures for the patients and persons-at-risk resulting in improved outcomes whilst securing the healthy state and wellness, reduced adverse events, and more cost effective use of health care resources. One of the most advanced areas in cardiology is atherosclerosis, cardiovascular and coronary disorders as well as in myocarditis. A lack of medical guidelines has been identified by the majority of responders as the predominant barrier for adoption, indicating a need for the development of best practices and guidelines to support the implementation of PM into the daily practice of cardiologists! Implementation of PM requires a lot before the current model “physician-patient” could be gradually displaced by a new model “medical advisor-healthy person-at-risk”. This is the reason for developing global sci-entific, clinical, social, and educational projects in the area of PM to elicit the content of the new branch.

Recent Publications

1. T A Bodrova, D S Kostyushev, E N Antonova, Sh. Slavin, D A Gnatenko, M O Bocharova, M Legg, P Pozzilli and S V Suchkov (2012) Introduction into PPPM as a new paradigm of public health service: an integrative view. EPMA Journal 3(16):3-16.
2. I A Sadkovsky, O Golubnitschaja, M A Mandrik, M A Studne-va, H Abe, H Schroeder, E N Antono-va, F Betsou, T A Bodrova, K Payne and S V Suchkov (2014) PPPM (predictive, preventive and personal-ized medicine) as a new model of the na-tional and international healthcare services and thus a promising strategy to prevent a disease: from basics to practice. International Journal of Clinical Medicine 5:855-870.
3. Zemskov V M, Alekseev A A, Gnatenko D A, Kozlova M N, Shishkina N S, Zemskov A M, Zhegalova I V, Bleykh-man D A, Bahov N I and Suchkov S V (2016) Overexpression of nitric oxide syn-thase re-stores circulating angiogenic cell function in patients with coronary artery dis-ease: implications for autologous cell therapy for myocardial infarction. The Journal of the American Heart Association 5:1-18.
4. Zemskov A, Zemskov V, Zemskova V, Buch T, Chernova L, Bleykhman D, Marshall T, Abe H, Zhegalova I, Barach P and Suchkov S (2017) A stepwise screening protocol to secure the module-based treat-ment for managing immunopathology. In-ternational Journal of Information Research and Review 4(1):3507-3510.

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Biography

Sergey Suchkov graduated from Astrakhan State Medical University and was awarded with MD and maintained his PhD and Doctor's degree. He was working for Helmholtz Eye Research Institute and Moscow Regional Clinical Research Institute. He was a Secretary-in-Chief of the Editorial Board, *Biomedical Science*, an international journal published jointly by the USSR Academy of Sciences and the Royal Society of Chemistry, UK. Currently, he is a Director of Center for Personalized Medicine, Sechenov University; Chair of the Department for Translational Medicine, Moscow Engineering Physics University and Secretary General of United Cultural Convention, Cambridge, UK. He is a Member of the New York Academy of Sciences; American Chemical Society; American Heart Association; AMEE, Dundee, UK; EPMA, Brussels, EU; PMC, Washington, DC, USA and ISPM, Tokyo, Japan.

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Igor L Katkov

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Stopping biological time: Science and art of biostabilization

Biostabilization (a.k.a. biopreservation) is a process that leads to cessation of the basic chemical and biological reactions so the biosamples can be pooled and stored (biobanked) for long time. There are 5 basic ways of achieving long-term storage, which ALL essentially lead to vitrification of cells, namely: slow freezing (SF), equilibrium vitrification (E-VF), kinetic vitrification (K-VF), freeze-drying (lyophilization) and vacuum/air flow drying at temperatures above 0°C (xeropreservation). Different combinations of the 5 basic biopreservation technologies such a preliminary drying before cryogenic slow freezing or vitrification is also possible. Author will discuss a phase diagram that shows all 5 basic ways of biostabilization and will discuss pros and cons of all approaches. A special emphasis will be put on the kinetic vitrification as it does not require the high concentrations of (or does not need at all) potentially toxic and osmotically damaging exogenous permeable intracellular vitrificants (also called cryoprotectants). Author will also present KrioBlast-2, a pilot version of the KrioBlast™ platform for cryopreservation by K-VF. Preliminary experiments on K-VF of human pluripotent stem cells and spermatozoa, which showed an equally excellent (80-90% of the untreated control) will be also discussed. A more advanced version KrioBlast-3 will be discussed in the concurrent presentation.

Recent Publications

1. Katkov II, Bolyukh A F, Chernetsov O A, Dudin P I et al. (2012) Kinetic Vitrification of Spermatozoa of Vertebrates: What Can We Learn from Nature? In: Current Frontiers in Cryobiology, Eds: I I Katkov. DOI: 10.5772/34784.
2. Katkov II (2014) Stopping biological clocks: The science and art of biopreservation. BioProcess International 12(4):42-52.
3. Katkov II, Bolyukh V F and Sukhikh G T (2017) KrioBlast™ as a new technology of hyper-fast cryopreservation of cells and tissues, Part I. Thermodynamic aspects and potential applications in reproductive and regenerative medicine. Bulletin of Experimental Biology and Medicine 164:230-235.

Biography

Igor L Katkov is a trained biophysicist with 30+ years of experience in cryobiology and cryogenic engineering. His last years of research have been focused on the fundamental aspects of kinetic vitrification (K-VF) as well on designing the practical system for K-VF KrioBlast™ (in cooperation with V F Bolyukh). Currently, the Head of the Laboratory of the Amorphous state at the Belgorod National Research University BelSU, Russia. He has recently accepted a Professor level position as the Head of the Laboratory of Cryobiology at the V I Kulakov Research Center of Obstetrics, Gynecology and Perinatology (RCGOP), Moscow, Russia and Chief Scientific Officer of Celltronix, San Diego, CA, USA.

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Antibodies with functionality as a new generation of translational tools to monitor, to predict and to prevent demyelination

Antibodies against myelin basic protein/MBP endowed with proteolytic activity (Ab-proteases with functionality) is of great value to monitor demyelination to illustrate the evolution of multiple sclerosis (MS). Anti-MBP auto-Abs from MS patients and mice with EAE exhibited specific proteolytic cleavage of MBP which, in turn, markedly differed between: MS patients and healthy controls; different clinical MS courses and; EDSS scales of demyelination to correlate with the disability of MS patients to predict the transformation prior to changes of the clinical course. Ab-mediated proteolysis of MBP was shown to be sequence-specific whilst demonstrating five sites of preferential proteolysis to be located within the immunodominant regions of MBP and to fall inside into 5 sequences fixed. Some of the latter (with the highest encephalitogenic properties) were proved to act as a specific inducer of EAE and to be attacked by the MBP-targeted Ab-proteases in MS patients with the most severe (progradient) clinical courses. The other ones whilst being less immunogenic happened to be EAE inducers very rare but were shown to be attacked by Ab-proteases in MS patients with moderate (remission-type) clinical courses. The activity of Ab-proteases was first registered at the subclinical stages 1-2 years prior to the clinical illness. About 24% of the direct MS-related relatives were seropositive for low-active Ab-proteases from which 22% of the seropositive relatives established were being monitored for 2 years whilst demonstrating a stable growth of the Ab-associated proteolytic activity. Moreover, some of the low-active Ab-proteases in persons at MS-related risks (at subclinical stages of MS), and primary clinical and MRT manifestations observed were coincided with the activity to have its mid-level reached. Registration in the evolution of highly immunogenic Ab-proteases would illustrate either risks of transformation of subclinical stages into clinical ones, or risks of exacerbations to develop. The activity of Ab-proteases in combination with the sequence-specificity would confirm a high subclinical and predictive (translational) value of the tools as applicable for personalized monitoring protocols. Ab-proteases can be programmed and re-programmed to suit the needs of the body metabolism or could be designed for the development of principally new catalysts with no natural counterparts. Further studies on targeted Ab-mediated proteolysis may provide a translational tool for predicting demyelination and thus the disability of the MS patients.

Biography

Sergey Suchkov graduated from Astrakhan State Medical University and was awarded with MD and maintained his PhD and Doctor's degree. He was working for Helmholtz Eye Research Institute and Moscow Regional Clinical Research Institute. He was a Secretary-in-Chief of the Editorial Board, *Biomedical Science*, an international journal published jointly by the USSR Academy of Sciences and the Royal Society of Chemistry, UK. Currently, he is a Director of Center for Personalized Medicine, Sechenov University; Chair of the Department for Translational Medicine, Moscow Engineering Physics University and Secretary General of United Cultural Convention, Cambridge, UK. He is a Member of the New York Academy of Sciences; American Chemical Society; American Heart Association; AMEE, Dundee, UK; EPMA, Brussels, EU; PMC, Washington, DC, USA and ISPM, Tokyo, Japan.

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KrioBlast™-3 - a three module system for efficient cryopreservation of unfreezable cells

As we have stated before, there are 5 basic ways of achieving long-term storage, which ALL essentially lead to vitrification of cells, namely: slow freezing (SF), equilibrium vitrification (E-VF), kinetic vitrification (K-VF), freeze-drying (lyophilization), and *in vacuo* San Diego vacuum/air flow drying at temperatures above 0°C (xeropreservation). Previously, we presented KrioBlast-2, a pilot version of the KrioBlast™ platform for cryopreservation by kinetic (very fast) vitrification. One of the major advantages of K-VF over the existing approach for vitrification (E-VF) is that K-VF does not need the high concentrations of potentially toxic and intracellular vitrificants (also called: cryoprotectants, which is not exactly correct in this case) such as DMSO, ethylene glycol, dimethyl sulfoxide. The pilot experiments on human pluripotent stem cells and spermatozoa, which showed an equally excellent (80-90% of the untreated control), were presented. The other key advantage of K-VF is its universality so the system is equally suitable for any kind of cells and tissues as soon as the characteristic thermal time of the system, which basically depends on the geometry of the cryo container with the sample, is sufficiently short. In this presentation, we will present the future development, the industrial three module system KrioBlast-3 that comprises 1) the cooling chamber for hyperfast cooling, 2) the intermediate module for shipment or long term storage in liquid nitrogen, and 3) the rewarming module. The second module has two port sites for the cooling and the rewarming modules so the system resembles a space station. All operations of cooling, storage/shipment, and warming are done without any contact of the sample with the ambient environment. The specific cryo containers for K-VF, namely VitriPlate™, VitriComb™, and VitriScan™ for vitrification of cells in suspension, packed in straws, and attached to surface in multiwell systems respectively are also discussed.

Recent Publications

1. Merino O, Sanchez R, Risopatron J, Isachenko E, Katkov II, et al. (2011) Cryoprotectant-free vitrification of fish (*Oncorhynchus mykiss*) spermatozoa: first report. *Andrologia* DOI: 10.1111/j.1439-0272.2011.01196.x.
2. Katkov II, Bolyukh A F, Chernetsov O A, Dudin P I et al. (2012) Kinetic Vitrification of Spermatozoa of Vertebrates: What Can We Learn from Nature? In: *Current Frontiers in Cryobiology*, Eds: I I Katkov. DOI: 10.5772/34784.
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Igor I Katkov is a trained biophysicist with 30+ years of experience in cryobiology and cryogenic engineering. His last years of research have been focused on the fundamental aspects of kinetic vitrification (K-VF) as well on designing the practical system for K-VF KrioBlast™ (in cooperation with V F Bolyukh). Currently, the Head of the Laboratory of the Amorphous state at the Belgorod National Research University BelSU, Russia. He has recently accepted a Professor level position as the Head of the Laboratory of Cryobiology at the V I Kulakov Research Center of Obstetrics, Gynecology and Perinatology (RCGOP), Moscow, Russia and Chief Scientific Officer of Celltronix, San Diego, CA, USA.

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