IMCB in research and teaching in 2021

One more year with the coronavirus. Thanks to vaccines, the restrictions have not been as extensive this year as in 2020. The work in laboratories has taken place all the time. Although in the spring semester we moved our lectures online and strong safety requirements were applied during the practical courses, in the autumn, we started again with lectures, seminars and practical courses in face-to-face teaching. Unfortunately, due to the emergence of new and very infectious coronavirus variant Omicron, the current annual conference will be held online again. Hopefully, for the last time.

What did the year 2021 bring in addition to the nasty news about coronavirus? Undoubtedly, our teaching and research results were good and we could be satisfied with it.

The Institute of Molecular and Cell Biology (IMCB) is a teaching research institute, which means that we are teaching at all three academic levels – bachelor, master and doctoral levels, in both Estonian and in English. We are coordinating 5 curricula that are fully accredited, and we are also involved in teaching in curricula coordinated by other institutes. In 2021, 31 bachelor and 14 master degrees were defended at our institute. Also, five PhD students (Antti Matvere, Ajai Kumar Pathak, Burak Yelmen, Kairi Raime, and Linda Ongaro) successfully defended their theses in 2021.

Our professors are highly dedicated to teaching, and this has received positive feedback from students. It is a great pleasure to note that in 2021, our colleagues Prof. Maido Remm and research fellow Reidar Andreson were nominated and received annual study award of the University of Tartu.

Our research cowers a broad spectrum of disciplines such as bioinformatics, biochemistry, biotechnology, cell biology, epigenetics, enzymology, developmental biology, molecular biology, genetics, microbiology and microbial genetics, applied and environmental microbiology. In 2021 we published 60 scientific papers. Below, I would like to highlight some of the important findings published in the last year.

On May 13th 2021 **Prof. Angela Ivask** with collaboration partners from the University of South Australia published her work on interactions between human cells and silver nanoparticles in Nature Nanotechnology (https://www.nature.com/articles/s41565-021-00914-3). Nanosilver with applications ranging from hygiene products to biomedicine is one of the most widely used nanomaterials and therefore, inadvertently exposed to humans. The published study showed that the extent to which nanoparticles bound, enter, and chemically transform on or in human white blood cells, is determined by the size and surface properties of silver nanoparticles. Clearly, small size and positive surface charge ensure also high cytotoxicity of nanosilver as evidenced with human T-lymphocytes.

Early testing for toxicity of the new drug candidates in a lifelike setting is paramount for further drug development as most of the failures occur in preclinical testing phase. High throughput testing of new drugs in human livers has been hampered by the lack of an easily scalable, lifelike human liver testing platform that could be readily handled by pipetting robots. In 2021, the somatic stem cell group led by **Associated Prof. Viljar Jaks** completed the design of novel 3D human micro-liver tissue equivalents that could be used in high-throughput drug screening and toxicity applications. This was based on electrospinned collagen mesh prepared in collaboration with Dr. Järvekülg from the

Institute of Physics and in collaboration with prof. Mart Loog's group from the Institute of Technology. In their paper published in Scientific Reports (https://www.nature.com/articles/s41598-021-99659-1) the researches could demonstrate the superiority of their system to the currently used matrigel-based pseudo 3D system for sustaining the specific properties of normal primary human hepatocytes and are currently looking for interested industry partners for further implementation of their system in pharma industry.

Developmental patterning is a fundamental process in animal development and often involves pattern refinement. Whilst various potential mechanisms for pattern refinement have been investigated; the role played by diffusible growth factor signalling remained to be addressed. The research group led by **Prof. Osamu Shimmi** reported in the paper published in Developmental Biology (https://pubmed.ncbi.nlm.nih.gov/34555363/) that cell shape change caused by BMP signal plays a role in the refinement of developmental patterning through forming a mechano-chemical feedback loop, which is crucial for vein patterning in the developing Drosophila wing. These findings are important to understand not only how developmental patterns arise and refine, but also the bioengineering of self-organising systems.

The Chair of Molecular Biology continues the long-standing tradition of studying ribosomal components involved in protein synthesis, initiated in the 1960s by a research group led by Prof. Artur Lind. In 2021, a Renilla-firefly luciferase fusion reporter system, that was developed to investigate the in vitro elongation rate and processivity of ribosomes, was published in Nucleic Acids Research (https://pubmed.ncbi.nlm.nih.gov/33684199/). This system allows to assess the elongation rate and the processivity of ribosomes on different mRNA sequences independently of the initiation and termination steps. As a proof of principle, the synthesis of three protein domains of different lengths and structures was analysed. Using a yeast cell-free translation assay, both the elongation rate and processivity of ribosomes were shown to vary depending on the domain synthesized. This system is attractive to a variety of studies, such as investigation of the correlation between elongation rate and protein folding, mutational analysis of translational machinery and screening for novel translation-inhibiting compounds.

The collaboration between research groups in Chair of Molecular Biology and Chair of Genetics resulted in publishing a paper demonstrating connections between tRNA modifications and mutation frequency in bacteria (https://www.mdpi.com/2076-2607/9/1/25). Pseudouridine synthases TruA or RluA modify U nucleotide in the tRNA anticodon stem loop (ASL), which is important for efficient translation. In this study, an unexpected link between pseudouridines in ASL of tRNAs and mutation frequency was reported. The results demonstrated that the lack of pseudouridylation activity of TruA or RluA elevates mutation frequency in soil bacterium *Pseudomonas putida* by a mechanism that is not clearly associated with error-prone DNA synthesis or malfunctioning of DNA repair functions.

The research of **Associated Prof. Priit Jõers** with collaborators on bumblebee microbiome researches revealed that genus *Fructobacillus* dominated in those individuals who fed on natural biotopes (forest meadows) (https://www.mdpi.com/2075-4450/13/1/98). This is very significant since these bacteria due to their unique metabolism have very important role in detoxification of harmful compounds and resistance to pathogens. This finding points to a problem that colonies living in human-made environments might be more susceptible to colony collapses, a frequent phenomenon observed around the world.

Structural polysaccharides - cellulose and chitin - contain a huge supply of renewable carbon. Their enzyme-mediated valorization offers a green and sustainable alternative to the traditional oil-based industry. Unfortunately, the crystalline structure of cellulose and chitin makes them difficult to degrade for enzymes. The development of optimal enzyme mixtures requires a thorough understanding of the mechanisms of action of individual enzymes. Recently discovered lytic polysaccharide monooxygenases (LPMOs) have secured a place in modern commercial enzyme mixtures. Unfortunately, our current knowledge of the stability and mechanism of these enzymes is incomplete and does not allow them to reach their full potential. The research group led by **Associated**

Prof. Priit Väljamäe has focused on detailed studies of the kinetics of both traditional hydrolytic enzymes and novel LPMOs. In 2021, the research group reported a relationship between the kinetic parameters of LPMO catalysis and the half-life of the enzyme - a crucial determinant of the suitability of LPMOs in industrial applications (https://doi.org/10.1016/j.jbc.2021.101256).

These are just a few examples demonstrating that our institute has a broad competence in molecular biosciences and that in addition to creating new basic knowledge, our results could have future applications in biomedicine, environmental protection and biotechnology. IMCB research groups have close research cooperation with other groups in the institute and the university, as well as with different research institutions in Estonia and abroad. In 2021, the research carried out in the IMCB was supported by 37 research grants and contracts, including both national and international funding. Our people are very active in writing grant applications (25 applications were submitted). Despite intense competition for grants from the Estonian Research Council, our researchers received three personal research grants (Angela Ivask, Priit Väljamäe and Rita Hõrak), one personal starting grant (Mariliis Klaas), one Mobilitas Pluss grant (Hedvig Tamman), and one postdoctoral MOBJD grant (Indrek Teino).

Importantly, our success is also related to our mental and physical health. In 2021 we actively continued the tradition of various art exhibitions in the Omicum atrium to boost mental health. At the very beginning of January 2022, an indoor walking trail was opened in the three research and study buildings of the IMCB and the Institute of Genomics. It is the first indoor trail in the buildings of the Tartu University. Many thanks to the members of the working group who designed and set up the track: Teele Eensaar, Dmitri Lubenets, Karoliina Kruusmaa, Sulev Kuuse, and an artist Ülle Ottokar.

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