Institute of Molecular and Cell Biology

2022 was a year that still suffered from the aftermaths of the COVID-19 pandemic, but the pandemic issues paled when Russia started a full-scale war in Ukraine. The war in Ukraine has affected us both economically and mentally, we have faced crises in terms of energy scarcity and inflation, but it is not comparable with suffering of the Ukrainian people. We need to support Ukraine and the Ukrainian people at this extremely difficult time in the fight against the aggressor. *Slava Ukraini!*

Looking back at the activities of our institute in 2022, we could be satisfied with our teaching and research results. **In 2022, the research carried out in the IMCB** was supported by 38 research grants and contracts, including both national and international funding. 8 new research projects were started, out of which 2 are Horizon Europe projects, and 6 are funded by Estonian Research Council (1 postdoctoral MOBJD grant, one Mobilitas Pluss grant, 1 personal starting grant and 3 personal research grants). In this year, we have published 64 scientific papers. Below, I would like to highlight some of the important findings published in 2022.

Chronic wounds pose a major burden to the health care system and account ca 2% of all expenses. The healing of acute wound has been rising into the focus given the current political situation in the world. The research group led by **Associate Prof. Viljar Jaks** has identified two matricellular proteins THBS4 and OLFM4 from the healing mouse livers that were also associated with the liver damage in humans. However, during recent works they identified that these proteins were associated with chronic inflammatory skin pathologies - atopic dermatitis and psoriasis and were also upregulated in healing human wounds. When administered exogenously, these accelerated cutaneous wound heling in vivo in mice. In 2021 the research group characterized the molecular mechanisms activated by THBS4 and in 2022 they reported in Experimental Cell Research (https://pubmed.ncbi.nlm.nih.gov/35337817/) and in Cellular and Molecular Life Sciences (https://pubmed.ncbi.nlm.nih.gov/35218417/) that OLFM4 regulated the behavior of keratinocytes and fibroblasts via a complex network of genes that affect both the migration, proliferation, and inflammatory response.

Maintaining apicobasal cell polarity (ABP) of epithelial cells is crucial for tissue development and homeostasis in multicellular organisms. Whilst previous studies have documented knowledge on the intracellular mechanisms whereby ABP is established, tissue-wide mechanisms were not well explored. The research group led by **Prof. Osamu Shimmi** found that “intercellular alignment of ABP” is indispensable for ABP integrity, epithelial homeostasis, and growth control in *Drosophila* larval wing imaginal disc. Intercellular relay of the status of ABP is regulated by Scribble, a key ABP determinant, and alpha-Catenin, a core component of adherence junctions. Loss of *scribble* leads to regressive loss of ABP in neighbouring WT cells prior to neoplasia formation (https://www.biorxiv.org/content/10.1101/2021.10.11.463906v1, under review). Importantly, a similar

mechanism, published in Frontiers in Cell and developmental Biology, has been shown to be utilized in human cells (https://pubmed.ncbi.nlm.nih.gov/36211469/). These findings open the horizon of intercellular mechanisms of ABP in development of epithelial tissues and human diseases.

The chromatin biology research group led by **Prof. Arnold Kristjuhan** published a paper illuminating the mechanisms how the basal transcription factors cope with chromatin structure when the transcription preinitiation complex is formed. As the first step of gene activation, the basal transcription factors need to gain access to DNA, which is normally packaged into chromatin. During opening of promoter in chromatin, some nucleosomes are disrupted and DNA becomes temporarily accessible either for the assembly of the preinitiation complex, or reassembly of nucleosomes. The study published by *Peil et al*. in the Journal of Biological Chemistry (https://doi.org/10.1016/j.jbc.2022.102369) demonstrates that incorporation of an alternative histone H2A.Z into nucleosomes, or the DNA-binding activity of the TFIID subunit Taf14, tip the balance to favour the assembly of the preinitiation complex. These results help us to understand the basic molecular mechanisms that drive gene expression in eukaryotic cells.

Ribosome research group led by Prof. Jaanus Remme continues to study *E. coli* ribosome biogenesis, functioning and degradation. In 2022 this research group has completed analysis of ribosomal protein metabolism during stationary growth phase. Bacterial ribosomes consist of over 50 different protein and 3 rRNA molecules. When bacteria reach stationary growth phase, most of the ribosomes are decomposed. rRNA is known to be degraded but it is not known what happens to r-proteins. In the paper published by Reier et al. in *mBio*, systematic proteomic analysis has revealed that about 30 r-proteins remain stable while 20 r-proteins are rapidly degraded in concert with rRNA (https://doi.org/10.1128/mbio.01873-22). The degradation of r-proteins and its potential functionality is an intriguing new aspect of r-proteins and their part in cellular systems. In addition, the collaboration between **research groups in Chair of Molecular Biology and Chair of Genetics** revealed an importance of pseudouridines around the anticodon stem-loop in translational fidelity. Unexpectedly, the work published by Jürgenstein et al. in *RNA Biology* (https://doi.org/10.1080/15476286.2022.2121447) revealed that the effect of TruA directed pseudouridines (Ψ) on translational accuracy is markedly variable between bacterial species *Pseudomonas putida*, *P. aeruginosa* and *E. coli*. Ψ's are important mainly for the reading frame maintenance in *E. coli* but not in *P. aeruginosa*.

Biofilm is a sessile life form of microorganism that can severely affect medicine, industry and agriculture. In 2022, the Bacterial Life Forms Group led by **Associate Prof. Riho Teras** ascertained two aspects that help to understand the biofilm formation of the agriculturally beneficial bacterium, *Pseudomonas putida*. First, extracellular peptides, as a structural component of biofilm, positively affect the biofilm of *P. putida*, and second, the vWFa domain of the *P. putida* surface protein LapA (von Willebrand factor A-like domain) is required for peptide-mediated biofilm formation (doi.org/10.3390/microorganisms10030618 , dx.doi.org/10.3390/ijms23115898). It is the first time that the extracellular peptides have been demonstrated to enhance *P. putida* biofilm through the vWFa domain of LapA. Considering the preferred habitat of this bacterium, the surface of plant roots, which is rich in breakdown products of root cells, this work adds essential facts to the colonization of plant roots by plant growth-stimulating bacterium *P. putida*.

Researcher Hedvig Tamman published two research papers in Nature group journals based on her post-doctoral work. With several collaborators, she studied the structure and regulation of bacterial stringent response related proteins. One of the papers reported the first structure of a full-length SpoT protein of *Acinetobacter baumannii*, in charge of down-regulating stringent response and proved that the stability of a core domain of SpoT is important for its regulation and for bacterial viability and virulence (https://doi.org/10.1038/s41589-022-01198-x). The second publication showed how a small fused toxin-antitoxin protein having a similar active site to stringent response proteins is activated upon

bacteriophage attack by a viral capsid protein (https://doi.org/10.1038/s41586-022-05444-z). This activation is toxic for the bacteria and leads to the death of the infected cell. However, by preventing virus maturation, the bacterial population is saved from phage attack. She is continuing studies on the importance of the stringent response in phage defense in the IMCB.

The IMCB provides "white biology" education at all three levels: bachelor's, master's and doctoral. In 2022, 31 bachelor and 19 master degrees were defended at our institute. Also, 9 PhD students successfully defended their theses. In the study year 2022-2023 we have accepted 63 bachelor students, 16 master students, and 6 doctoral students, out of which 2 are industrial doctoral students. Importantly, the latter are the first 2 industrial doctoral students at the University of Tartu within the framework of the new doctoral study program.

In addition to higher education, the institute also contributes to the promotion of education in "white biology" in general education schools.

Genetic workshops are conducted for high school students, and **Mobile Bioclass** visits schools all over Estonia for in-site practical courses. In 2022, **Genetics workshops** hosted 208 high school students from 5 counties in the institute during two weeks. The workshops were funded by the Estonian Research Council and biotechnology companies Solis BioDyne and Bioatlas, special thanks to our students who were the supervisors, especially to Katariina Kordemets and Agnes Vaht, assistant Merle Külaots, engineer Dmitri Lubenets and project manager Teele Eensaar.

Mobile Bioclass travelled quite a lot in Estonia in this year; the end of the COVID-19-pandemic finally favored it. This was possible thanks to the Estonian Research Council, Bioscience Students' Association, special thanks to coordinators Katariina Kordemets and Marcella Laura Polverino, assistant Merle Külaots, professor Ants Kurg.

Career Day for students on May 5th was a big success, we organized it together with other institutes in the faculty for the second time (the first was in 2020). The Day met the expectations of both companies and students and the day will be followed with a Career Event in February 2023.

Biology Olympiads were carried out at state and international level and over two years, in full on-site form again. The state Olympiad was in March in our institute and the International Olympiad was in Armenia, Yerevan, in July. Special thanks to Sulev Kuuse, Karl Jürgenstein, Mari Remm and Ando Vaan, but also many others in our institute.

We are happy that our people have been recognized for several activities. **Science popularization awards** were given to **professor Andres Metspalu** (Tiiu Sild *Lifetime Achievement Award*) for his devoted work in science and long-term systematic work in popularizing science. Andres founded the Estonian Biobank and has introduced gene technology higher education in Estonia as well as introduced genes and DNA topic to public and politicians, and **to a scientific collective coordinated by Sulev Kuuse** for the popularization of science and technology through the printed word.

University honorary decorations were given to **professor Richard Villems** (for being in the university for 100 semesters), gene technology bachelor student and the former president of Biosciences Students' Association **Hannes Ruusmaa** and **Kalle Tihemets** (our IT specialist). **Sulev Kuuse** was recognized for organizing Biology Olympiad.

Signe Värv was awarded the Citizen's Day badge of honor by the Minister of Internal Affairs. This year, 14 people in Estonia were recognized in this special way and all of them were women.

Importantly, our success is also related to our mental and physical health. In 2022 we actively continued the tradition of **various art exhibitions in the Omicum atrium** to boost mental health; we hosted ten exhibitions this year and Sulev Kuuse was the curator to all these exhibitions. Ermo Leuska organized also some **musical events**. In cooperation with the Institute of Computer Sciences, we have initiated science-art cooperation projects. The first event was Anu Kaur's exhibition and Tõnu Kõrvits author's evening organized in cooperation with Kärt Summatavet, and we are planning to join the Tartu Capital of Culture 2024 event series with similar events.

At the 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.

We also shared a sad moment this year as we said goodbye to **professor Ain Heinaru**, the founder of our Institute. We all have our memories connected to Ain, as a colleague or as a student, and I am sure he lives on in all of us and he lives on through his books.

Maia Kivisaar,
Director of the Institute of Molecular and Cell Biology

Annual Conference 2022

Institute of Molecular and Cell Biology
Institute of Genomics
University of Tartu

January 19th - 20th, 2023