Multidisciplinary activity in Latvia and beyond

Professors Ivars Kalvins and Maija Dambrova form part of a team in Latvia that contributes research to a wide range of scientific fields and activities. Below, they discuss the aims of their work, successes of projects and some upcoming events.

You both work at the leading Baltic regional centre for drug discovery. Which areas of drug discovery do you focus on?

IK: The Latvian Institute of Organic Synthesis (LIOS) performs research in the fields of chemistry, pharmacy, pharmacology, biology and other natural sciences. The scientific activity of LIOS contributes to biomedicine, medical technologies, biopharmacy and biotechnologies. LIOS possesses the resources to discover candidate drugs and chemical biology tools against a variety of targets, with some notable areas of success. These are: anticancer agents, cardiovascular diseases, central nervous system active compounds and anti-infectives.

MD: The researchers at LIOS are very keen to exploit novel and exciting drug targets by designing novel drug candidate molecules. From the time of its creation, the quality and impact of the research performed here has been extraordinary. Today, LIOS is proud to be an inventor of 18 original medicines and more than 70 manufacturing processes of active pharmaceutical ingredients.

Why has the Institute chosen to focus on these areas?

IK: LIOS was established in 1957 to develop new small molecules as medicines and pesticides. From the time of its creation, the quality and impact of the research performed here has been extraordinary. Today, LIOS is proud to be an inventor of 18 original medicines and more than 70 manufacturing processes of active pharmaceutical ingredients.

MD: The researchers at LIOS are very keen to exploit novel and exciting drug targets by designing novel drug candidate molecules. The mission of LIOS is to contribute to scientific progress and enhancing quality of life by innovative synergy of academic achievements in organic chemistry and pharmacology with competent applied research in medicinal chemistry.

In 2013, LIOS started work on the InnovaBalt project, with the aim of strengthening the institute’s multidisciplinary research capabilities, management of intellectual property and human resources. Can you briefly share any of its success stories?

IK&M: The InnovaBalt project has essentially improved the capacity of LIOS. Our cooperation with partnering organisations has resulted in new and successful projects in Horizon 2020, involvement in the Marie-Sklodowska-Curie Innovative Training Network INTEGRATE, and individual fellowship in ‘Virus-DNP-NMR’.

Dr Kristaps Jaudzems has been awarded a fellowship in collaboration with InnovaBalt’s strategic partner Centre de RMN à Très Hauts Champs, Ecole Normale Supérieure de Lyon, France. It is the first and – up to now – only Marie Skłodowska-Curie Individual fellowship in Horizon 2020 that has been granted to a scientist from Latvia.

LIOS is also the leading partner in the BioPharmAlliance cluster, which includes all leading institutions of Latvia. These institutions are participants of the BallScan cluster, where activities are coordinated with partners from Baltic and Northern countries, Russia and Poland. The InnovaBalt project has improved the capacity of LIOS, and this has been essential for the successful implementation of these projects, and more besides.

LIOS organised and delivered the Drug Discovery conference in August 2015. Can you tell us more about the event?

IK: The Drug Discovery conference was organised in Riga and involved around 300 participants from 25 countries (a third of whom were from foreign countries, while two-thirds were from Latvian research institutes, universities and industries). The work of the conference was organised in parallel sections, so it was possible to present 69 lectures, 42 of which were delivered by researchers we invited from abroad. The conference covered topics starting from organic synthesis and medicinal chemistry through to biological and pharmacological applications of novel ligands. The event opened up opportunities to transfer knowledge at an international level, provided possibilities to discuss further collaboration and significantly increased the visibility of LIOS.

MD: It has been recognised as the largest academic conference in Latvia – in the field of medicinal chemistry and drug discovery – for 25 years. Many existing contacts between research groups of LIOS and academic and industrial partners from abroad were strengthened, while many were newly formed during the conference. The remarkable scale of the event was made possible through the funding of the InnovaBalt project.

Do you have any other conferences or events coming up in the future?

IK: The InnovaBalt project will participate in the organisation of the Balticum Organicum Syntheticum, which will take place in Riga, Latvia, from 3-6 July 2016. This is the Ninth International Conference on Organic Synthesis, and this year participants will enjoy four days of organic chemistry and a unique cultural, linguistic and social experience!

The main aims of this conference are twofold. First, to convey the excitement of synthetic organic chemistry as practiced in industry and universities worldwide. Second, to promote the interactions between chemists of the Baltic with other countries in order to create links, collaborations, common research projects in academic and industrial settings.

Registration for the event starts in January 2016.
The Latvian Institute of Organic Synthesis, a target driven research institution that combines excellence in science with expertise in preclinical investigations of novel innovative drug discovery, has developed its flagship project – InnovaBalt. The project’s activities substantially contribute to the institution’s development and advanced approaches research in a wide range of disciplines from organic chemistry to pharmacology and chemical biology.

Since 2010, the Institute has ramped up its activities and declared a mission to combine the findings from its novel academic research practices with applied research to ensure that its activities are not only innovative, but impactful. In doing so, LIOS is fast becoming a highly regarded European-level research centre of excellence that is both contributing many scientific discoveries and improving the quality of life of both Latvians and people further abroad.

INNOVABALT: ONE PROJECT ENABLING OTHERS

Although LIOS is currently involved in many projects (with many more scheduled to commence in the near future), the beginning of the InnovaBalt project signalled a huge step forward for the Institute. The project, which began in 2013, aims to strengthen the Institute’s multidisciplinary research capacities, management of intellectual property and human resources.

At a cost of €5.2 million (€4.7 million of which was provided by the European Commission), it is the largest EU Seventh Framework Programme (FP7) project in Latvian history and, in its brief existence, boasts many success stories.

In synergising the project with different EU Structural Fund activities, alongside coordinating the European Regional

HEALTH SHOULD BE CONSIDERED REAL WEALTH

Professor Ivars Kalvins was a finalist for the European Inventor Award 2015. He was nominated in the category of ‘Lifetime Achievement’ for his invention of meldonium – an efficient drug for the treatment of heart disease. International Innovation spoke to Kalvins about his thoughts on being named as a finalist. Here’s what he had to say:

“I am pleased that the inventions carried out in Latvia have been recognised at the European level. For me, it is of particular importance that the nomination was in the category of lifetime achievement. It is important to realise that this high assessment is not just related to my individual work, because today, the best results in research are achieved by team efforts.

I would like to apply this recognition to the systematic and target-orientated work performed in LIOS. As I was the first scientist from Latvia to be nominated for this prestigious award, the experience of the process has been invaluable. I would like to stress that, in comparison with other researchers in different countries, we are working with insufficient state funding and limited industry support.

My greatest wish is that people are able to live a healthy life and with my work I have tried to promote that idea. I believe Mahatma Gandhi said it best: ‘It is health that is real wealth and not pieces of gold or silver’.”

Read more about Kalvins’ remarkable achievement here: http://bit.ly/IvarKalvins
INNOVABALT

OBJECTIVE
To become a European-level research centre of excellence that successfully merges achievements of innovative academic research in organic chemistry and pharmacology with competence in applied research of medicinal chemistry, thus, contributing to the development of science in Latvia and quality of life of society.

PARTNERS
50 leading European research centres

FUNDING
EU Seventh Framework Programme (FP7) – contract no 316419

CONTACT
Professor Ivars Kalvins
Project coordinator
Latvian Institute of Organic Synthesis (LIOS)
Aizkraukles street 21
Riga, LV-1006
Latvia
T +371 67014874
E kalvins@osi.lv

Professor Maija Dambrova
Project Manager
T +371 67014881
E md@biomed.lu.lv

www.innovabalt.eu
www.osi.lv/en

IVARS KALVINS has his Habilitation in Chemistry and has been working at LIOS since 1969. He has been Director of LIOS since 2013 and Chairman of its Scientific Board since 2015. He is the inventor of anti-ischemic drug Mildronate, new Mildronate-containing pharmaceutical products (Capicor, MildronateGL, Neomildronate), immunostimulator Leakadine and anticancer drug Belinostat. He is also Full Member and Member of the Senate of Latvian Academy of Sciences, and Member of the European Academy of Sciences and Arts in Salzburg. He has been awarded the D H Grindelis and S Hiller medals, the WIPO Award and the Golden Medal.

MAJA DAMBROVA graduated from the Faculty of Chemistry at University of Latvia, where she also defended an MSc in Biology. She earned her PhD in Pharmaceutical Biosciences from Uppsala University, Sweden, and holds an MBA from Riga International School of Economics and Business Administration. Since 2001, she has been the Head of the Laboratory of Pharmaceutical Pharmacology at LIOS and is currently InnovaBalt’s Project Manager. She is also Full Member of the Latvian Academy of Sciences. She has been awarded D H Grindelis and S Hiller medals, and the L’Oréal Latvian Fellowship ‘For Women in Science’ with the support of the Latvian National Commission for UNESCO and the Latvian Academy of Sciences.

Development Fund, LIOS has created several other projects that assist in meeting the goals of InnovaBalt. Project Coordinator, Professor Ivars Kalvins explains: “We have established other programmes to help develop our research infrastructure for research activities related to biomedicine, drug discovery and pharmacy – and to contribute to the development of research potential in Latvia”.

ACQUIRING EQUIPMENT, AIDING DISCOVERY
One major objective of InnovaBalt is to acquire equipment that enables researchers to perform innovative drug development investigations applicable to many diseases, including cancer and cardiovascular disease. Thus far, the project has helped LIOS acquire a computer cluster to improve molecular modelling, an in vivo imaging system and a measurement system that uses light scattering to detail a wide range of characteristics of nanoparticles. InnovaBalt has also helped the Institute establish an X-ray crystallography group and with the recruitment of its researchers.

Technological acquisitions and developments such as these are driving LIOS’s mission to be at the pinnacle of basic and applied research and innovation, as InnovaBalt’s Project Manager, Professor Maija Dambrova explains: “The in vivo Fluorescence Emission Computed 3D Tomography system we obtained enables significantly improved pharmacological studies. In vivo imaging provides possibilities to gather optical information from whole organisms, including information about the location and activity of the molecules/processes present in the image”.

WORKING ACROSS BORDERS
In addition to what InnovaBalt has enabled in terms of financing other projects and providing new technologies, the team at LIOS works continuously to ensure collaboration across European borders. The benefits of these practices have already contributed to the socioeconomic development of the Baltic region, but interacting with partnering organisations has resulted in new project applications and publications, too.

For now – and for the future – LIOS’ exchange of skills and knowledge helps the Institute gain deserved recognition in the European research area.

FIVE MULTIDISCIPLINARY APPROACHES TO DRUG DISCOVERY

In addition to the InnovaBalt project, LIOS has several other ongoing projects. Some of these are connected with the development of new antibacterial drugs. Antimicrobial resistance is a serious public health threat and despite the strong need for new antimicrobials, very few new, effective antibiotics have been brought to the market in the last few decades. To address this and other significant public health challenges, there are several European Commission-funded projects that LIOS is currently involved with or will be implementing in 2016.

NABARSI – an FP7 project where five institutions are collaborating to find new chemical entities with antibacterial efficacy in an animal model of multidrug-resistant bacterial infection. It is hoped that this approach will enable the discovery of broad-spectrum antibacterials.

ENABLE – an Innovative Medicines Initiative project working to advance the development of potential antibiotics against Gram-negative bacteria. The project includes 32 partner organisations that are collaborating to develop attractive candidates for testing in the clinic, bringing the possibility of new antibiotics to treat Gram-negative infections one step closer to patients.

INTEGRATE – a Horizon 2020 project that trains Early Stage Researchers in the discovery and preclinical validation of novel antibacterial agents.

PELICO – one of two new Horizon 2020 projects LIOS will begin implementing in 2016. The project is targeted to the know-how exchange between partners to facilitate the design, synthesis and application of peptide analogous possessing photo-controlled biological activities.

BATCure – a second project due to start in 2016. It will advance the development of new therapeutic options for a group of rare lysosomal diseases. There are currently no curative treatments in the clinic for any type of these diseases. The consortium will follow a novel integrated strategy to identify specific gene and small molecule treatments for three generic types of Batten disease.

In all of these projects, the multidisciplinary approach between the partners of consortiums – which LIOS is facilitating – is the key to their success.