10TH LIFE SCIENCE SYMPOSIUM

SAILING AWAY FROM ONE-SIZE-FITS-ALL:

TECHNOLOGICAL DEVELOPMENTS IN PERSONALISED MEDICINE

REVIEW BOOKLET

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CORPUS CONGRESS CENTRE
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TIMO VAN REEUWIJK

Chairman of the Symposium Committee

Dear reader,

I hope all of you enjoyed the 10th Life Science Symposium, on *Technological Developments in Personalised Medicine*! The day was filled with a great deal of science and technology that may have us sailing away from one-size-fits-all, and towards the use of personalised medicine. I personally learned a lot during the symposium, the talks opened my mind to what Life Sciences may contribute to personalised medicine, while also engaging in critical thinking about the way it should be implemented and the desirability of large-scale application. And I think you felt similar! The amount of engagement the audience had during the talks and the discussion really blew me away.

We, as the symposium committee, are very proud of the way the day turned out, and are very grateful for having had the opportunity to welcome you. We are glad to see that so many people attended, including many LIFE members, but also people from different studies, and academic staff. We want to thank all thirteen speakers and discussion participants for taking valuable time out of their day to share their knowledge with the attendees. We also want to thank Sander and Roxanne for their amazing work as chairman and chairwoman, as their enthusiasm really inspired the crowd to participate in lively discussions. For the support in funding of the symposium, we thank our sponsors for being there and showing interest in helping us exciting the attendees about science. The members of our board of recommendation also had very valuable insights in who to ask and what to do, for which we also want to thank them.

This review contains summaries of the talks by our speakers and many pictures of the day. I hope that you may be reminded of some interesting fact you learned or get inspired to look up a speaker you missed the talk of. Enjoy!

SANDER VAN KASTEREN & ROXANNE KIELTYKA

Co-chairs of the Symposium

Sander van Kasteren and Roxanne Kieltyka are professor and associate professor at the Leiden Institute of Chemistry: Van Kasteren in the field of chemical immunology, and Kieltyka in supramolecular chemistry. Both are teachers of the Life Science and Technology bachelor's and/or master's degree in Leiden and have high affinity with its students.

"The students did a stellar job! From arranging a world-class lineup, to a super-professional organisation of the conference itself. Simply amazing." - Sander van Kasteren

PROF. DR. HENK-JAN GUCHELAAR

Professor in Clinical Pharmacy, Leiden University Medical Centre

Henk-Jan Guchelaar is professor Clinical Pharmacy at both the Leiden University Medical Centre (LUMC) and the institute Leiden Academic Centre for Drug Research (LACDR). Furthermore, Guchelaar is the program leader of the research program 'Personalised Therapeutics' which aims to optimise drug treatment of patients by personalising the drug selection and dosage based on the patient's genetics.

Guchelaar had the honour of opening the symposium with the first talk of the day and really lived up to the expectations. He explained that different people have different responses to the same drug (dosage) which is largely due to genetic variations between humans and introduced a patient called "Bob" to the principle of personalised medicine to the audience. During his comprehensive, yet easy to understand, introduction some historical developments were pointed out. These enabled the field of personalised medicine to emerge, such as DNA sequencing techniques that became more and more accessible and affordable.

In the second part of his talk, Guchelaar talked about 'actionable genes' and genetic tests that general practitioners can use to improve their patients' treatment. His research makes use of pre-emptive pharmacogenetics (PGx) testing which can help limit adverse drug reactions and lower medical costs as well. Guchelaar intrigued the audience with a passport that encompasses a complete set of clinically actionable genes (variant alleles) that can be used to personalise and improve drug therapies for 49 commonly prescribed drugs.

Before bringing this talk to a close, Guchelaar answered some sharp questions from the audience and was happy to mention that such passports can already be employed by general practitioners and hospitals. Of course, Guchelaar also took part in the panel discussion later that day where he reminded us all that personalised medicine won't be gone tomorrow and is here to stay.

PROF. DR. DIEDERIK GOMMERS

Professor in Intensive Care Medicine, Erasmus Medical Centre

Diederik Gommers is a Dutch medical doctor specialised in intensive care. Currently, he is an intensivist at the academic hospital Erasmus MC in Rotterdam. Gommers obtained his title Doctor of Medicine at the Erasmus MC, and did his PhD here on 'Factors affecting surfactant responsiveness'. Gommers has been and is currently part of different committees and advisory boards. During the COVID crisis in the Netherlands, Gommers was part of the Outbreak Management Team.

Gommers started his talk by explaining what currently happens on the ICU. He explained that the first step is to take blood samples and culture the cells, and with this information antibiotics will be given. This process is not very ‘personal’ as for example dosing is not taken into account. Gommers mentioned that it would be good to make the treatment of patients on the ICU more personal. It was no surprise that the example of corona patients was given. Some

corona patients on the ICU suffered from acute respiratory distress syndrome (ARDS). The cause of this ARDS was explained by the massive inflammatory response of the host during the infection. However, this inflammatory response was different for different patients. It would be useless to treat all these patients in the same way. During COVID a lot of data from different patients was obtained. This data could be used in prediction models. These models could for example be useful in finding parameters that indicate that a patient can be discharged from the ICU. This could help solve the capacity issue of the ICU that we encountered during the pandemic. What was very interesting was that Gommers mentioned a hospital in Canada that is completely digitalized. A patient is constantly observed with 22 monitors. All the data obtained can be used in prediction models.

PROF. DR. CHRISTINE MUMMERY

Professor in Developmental Biology, Leiden University Medical Centre

Christine Mummery is a professor in Developmental Biology at Leiden University Medical Centre. Her current research concerns modelling cardiovascular diseases using stem cells from patients and developing organ-on-chip models of multiple organs for safety pharmacology and potential disease and drug targets. The development of these models plays an important role in the field of personalised medicine, opening up the possibility to find personalised treatments using organs-on-a-chip.

Understanding the origins and mechanisms of action of diseases is key to finding new effective drugs. The widely used cell assay and animal assay do not give us this insight, because there is simply too little data on human physiology and the large amount of data from mice is not always applicable to humans. Prof. dr. Christine Mummery, an expert in developmental biology, explained that this insight can be gained by developing microphysiological systems from stem cells in the form of organoids. These organoids are microtissues and are used to model diseases. For example, the cause of a heart disease is discovered by the formation of a mini heart. This mini heart is analysed, after which the cause and an appropriate treatment are determined. With the use of organs on a chip, the interrelationships between diseases can be determined and effective medicines for chronic diseases can be found more quickly.

Mummery shared that she is currently conducting her own research on modelling a blood vessel disease. In this study, they are looking for the connection between the appearance of spots on the face and nosebleeds, which patients experience as symptoms of this disease. Organs-on-a-chip make it possible to develop medicines for these rare diseases and identify drugs for trial. Organs-on-a-chip therefore play a key role in personalised medicine.

"Fantastically well organised meeting on an important subject: the committee put together a great line-up of speakers, all of whom enjoyed the symposium as much as the students." - **Christine Mummery**

PROF. DR. MARIANNE BOENINK

Professor in Ethics of Healthcare, Radboud University Medical Centre

Marianne Boenink works at the Radboud University Medical Centre as a professor in Ethics of Healthcare. She analyses visions of the future of medicine, like 'personalised medicine' or 'smart healthcare'. How do such visions shift ideas about health, disease and good care? She also investigates the social and ethical implications of specific innovations. Her field of research is of utmost importance when considering how personalised medicine will be established in our lives.

Personalised medicine can exist in many forms and ways, from your doctor listening to your concerns at the doctor's office, to therapeutics customised to your genetic information. The road taken to get to where we are today in personalised healthcare has been a long one, and it hasn't always been simple and straightforward. Questions about priorities concerning personalised medicine have arisen, but so far the end has seemed to justify the means. But is this indeed the case? What other values are affected and what effect does this have on health(care)? Marianne Boenink gave an introduction into the ethics of personalised medicine and tried to answer these questions for us.

Over the last decades, personalised medicine has evolved. The tackling of these ever complex technologies, gave rise to different societal and ethical concerns. Boenink discussed three contemporary challenges during her talk: data-sharing and privacy, bias and injustice, and datafication and limits.

As for the first concern, the question was mostly about who should be allowed to access what data, when, and under which conditions. The second challenge is that using these data sources and technologies, could create or even reinforce injustice within our society. The last challenge regards the boundaries of personalised medicine. Where do we draw the line between biological (dys)functioning, and the more

subjective 'well being'? Most European healthcare systems are grounded on that the same risk of illness is shared by everyone, and therefore, healthcare costs should also be equally distributed. Personalised medicine could potentially disrupt these systems and therefore more thought and discussion is needed in order to fully grasp what lies ahead.

PANEL DISCUSSION

Esther Thole, Prof. dr. Marianne Boenink, Prof. dr. Henk-Jan Guchelaar, Dr. Pauline Evers, Mr. Dr. Corrette Ploem.

Since personalised medicine is such a new and controversial topic, it is important to open up the discussion on the ethics and possibilities of personalised medicine. The following panel discussion includes input from the attendees through both a Mentimeter to visualise the general opinion and through questions from the crowd.

The discussion was moderated by Esther Thole, who is a freelance science journalist specialised in chemistry of living systems and is currently also editor-in-chief of chemistry trade journal C2W. Corrette Ploem, who is an associate professor in Health Law at Amsterdam University Medical Centre, was part of the panel since she is specialised in the legal aspects of new technologies. The patient interests were represented by Pauline Evers, who is a patient advocate at the Dutch Federation of Cancer patients' organisations. Marianne Boenink and Henk-Jan Guchelaar also took part in the panel discussion as experts on the ethics of healthcare and clinical pharmacy.

Thole opened the discussion with questions on data-sharing: *"Would you be willing to share your health data with companies for the*

improvement of personalised medicine?", where Thole, the experts and the attendees also explored this question with regards to scientists instead of companies. The consequences of this data-sharing were brought up as well. *"Could this data, after sharing, be misused? And how could this misuse be prevented?"*

From here the discussion shifted towards *"Would you want to know in advance if you'll develop a disease? Does this differ for curable versus incurable diseases? How to deal with problems following pre-diagnosis, such as overscreening? Are these decisions solely your responsibility, or do they affect your family as well?"*.

A large number of opinions and questions were given by the attendees, which the panel members were eager to discuss. Many interesting thoughts were shared, and the panel discussion developed into an interactive and refreshing conversation between the panel and the audience.

"Moderating a panel discussion with open-minded scientists is always a pleasure, but when you have an audience as engaging and active as we did during the LST symposium, it really becomes a dynamic experience that is interesting to everyone present. Thanks again for letting me participate in the program." - **Esther Thole**

"As a panelmember I enjoyed the lifely discussion with the audience on the ethical and juridical aspects of personalised medicine. It's so good and important to see that LST-students are interested in these problems and are willing to think along. The questions they posed reinspire me for my own research." - **Corrette Ploem**

DR. IR. CHRIS CALLEWAERT

Senior Postdoctoral Research Fellow of the Research Foundation Flanders at Ghent University, Belgium

Chris Callewaert is a senior postdoctoral research fellow of the Research Foundation Flanders (FWO) at Ghent University, Belgium. He studies the skin microbiome and metabolome in health and disease. He is a pioneer in skin microbiome transplantation and skin bacteriotherapy to solve body odour.

Callewaert explained that body odour is mainly produced by bacteria feeding on a certain type of sweat, that from the apocrine sweat glands. As there are many people with smelly armpits, Callewaert started to look into the armpit microbiome of these people, to find out what is the cause of this smell. When comparing people that have more body malodour with people that smell less, he found out that corynebacteria are more prevalent on the skin of people with more malodour, while staphylococci are more prevalent on people that smell better. Furthermore, a more diverse skin microbiome seems to cause more malodour.

A way for people to have a better body odour is for them to stop using anti-perspirant, as this kills many of the bacteria on the skin, while the most resilient bacteria survive. These resilient bacteria are predominantly corynebacteria, causing malodour. The use of deodorant has a significantly less negative effect on the selection towards corynebacteria, though it is still there.

Callewaert, or Dr. Armpit, developed a method for studying armpit microbiome transplants. In a study where one twin had bad armpit odour, and the other twin had better smelling armpits, he was successful in transferring the microbiome of the better smelling twin to the other, making odour better (by introducing more staphylococci, as opposed to corynebacteria that were present before). These findings suggest that armpit microbiome treatment is possible. Currently, Dr. Armpit is working on a start-up company that may one day sell bacterial armpit sprays to improve your microbiome!

"What I noticed the most is the enthusiastic, open-minded and critical-thinking audience I encountered in Leiden. I received a lot of questions after my talk and had many meaningful interactions with the audience during the breaks and reception. The organisation of the symposium was subliminal and an absolute example of how a conference should be organised. Overall, a great experience!"

- Chris Callewaert

DR. ALBERT VAN HELL

Medical Lead Cell & Gene Therapy at Novartis Oncology

Albert van Hell is the Medical Lead Cell & Gene Therapy at Novartis Oncology. Novartis Oncology is a global healthcare company based in Switzerland, that develops innovative medicines for the needs of patients worldwide. The Cell & Gene Therapy department focusses on reimagining medicine through cell and gene therapy, and Van Hell works on CAR T-cell therapy.

CAR T-cell therapy can be used to treat different cancer types. In CAR T-cell therapy the patient's own immune cells are used. CAR stands for *chimeric antigen receptor* and consists of an extracellular and an intracellular part. The intracellular part of the receptor activates the T-lymphocyte to proliferate and eliminate the target cell (tumor cell). The extracellular part binds the antigen CD19 that is only present on the target cell.

The first step is to take the T cells from the patient. These T cells will be cultured and the CAR is implemented in the cells. The CAR T-cells are then given back to the patient. The first patients that were treated with CAR T-cells had to go to the ICU. It turned out that the reason was cytokine release syndrome. Because of the strange cells entering the body there was a burst of cytokines released by macrophages. This problem can be solved by giving cytokine inhibitors to patients. The CAR T-cell therapy showed a 80% relapse free response. However, CAR T-cell therapy is very expensive because it is so personal. Therefore, the therapy is currently only used as a last resort when all other therapies failed.

"A nice programme and the great organisation made it a valuable symposium!" - **Albert van Hell**

DR. MARTA ARTOLA

Assistant Professor in Chemical Biology, Leiden University

Marta Artola is an assistant professor of Chemical Biology at the Leiden Institute of Chemistry. She combines organic chemistry, chemical biology and biochemistry aiming to develop inhibitor and degrader libraries, activity-based probes and enzymatic substrates for glycoprocessing enzymes that reach solutions for unmet medical needs in terms of target validation, drug discovery and diagnostics. This science has the possibility to make a big impact on personalised medicine as the amount of unmet needs expands rapidly when medicine is treated on a more personal basis.

On the day of the symposium, Artola was one of the speakers of the parallel sessions, but nonetheless she was able to draw a wide audience with her talk on rational and development design of glucosidase inhibitors. For some people without a background in chemistry, the presentation was not easy to follow from time to time, although Artola did have a clear outline throughout her presentation. She started by explaining the mechanisms of α-glucosidases and β-glucosidases and she gave designs of irreversible inhibitors of these enzymes which render the glucosidases suppressed.

After showing some *in vivo* test results and making the link with diseases like Pompe, Artola also explained how reversible inhibitors can be designed and synthesised. These inhibitors promise to have important applications in the treatment of diseases like Gauche and diabetes and could even be used in the biofuels industry. With her presentation, Artola underlined the importance of biochemistry and gave the audience a wonderful insight in her multidisciplinary work.

"The Life Science Symposium was a real success: an inspirational event perfectly organised by students. The Corpus Museum at the core of the Leiden Bio Science Park was the perfect location to bring together exceptional researchers, doctors and speakers working on the field of personalised medicine. The exceptional quality of the sessions was reflected by the enormous interest and participation of the attendees, which led to very interesting scientific and ethical discussions."

- Marta Artola

PROF. DR. HOLGER FRÖHLICH

Professor in AI & Data Science at Fraunhofer SCAI, University of Bohn

Holger Fröhlich is the Head of Artifical Intelligence & Data Science, and Deputy Head of the Department of Bioinformatics at the Fraunhofer Institute for Algorithms and Scientific Computing (SCAI). He is responsible for a newly formed artificial intelligence and data science team that focuses on precision medicine and early drug discovery.

Fröhlich started his talk going back to the beginning of computer science – Alan Turing, 'the father of computer science' and the computation theory used to crack Enigma in World War II. Turing

thought about artificial intelligence, and how human-like, intelligent behaviour can be defined, and thereby came up with the Turing Test. Since then interest in this subject has evolved, and the subject of machine learning has evolved.

Machine learning is a subfield of artificial intelligence and entails the ability to learn without specifically being programmed. Within machine learning there are many possibilities, categorised as 'unsupervised', 'supervised' and 'reinforcement'. Machine learning can be highly useful in the medical field, as it can for instance predict drug responses of never before seen patients. Thereby, instead of designing medicine for the average patient, it can help design medicine for instance Alzheimer and Parkinson patients based on their genome, environmental data and population health data. Today however, personalised healthcare is still more a vision than a reality, because a lot of really sensitive data is needed and the AI models are not yet ready for clinical routines.

"I can only repeat that I really enjoyed the meeting, that it was absolutely professional organised, and that everybody in the organising committee did a fanatastic job. I also really liked the lot of smart questions from the audience and the nice conversations afterwards, including the ones during our dinner." - Holger Fröhlich

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DR. WILLEMIJN VADER

Chief Executive officer at VitroScan B.V.

Willemijn Vader is the CEO of VitroScan based at the Leiden Bio Science Park. VitroScan is a spinout company of Ocello, now Crown Biosciences, who were also present during the symposium. After a successful seed stage with Proof of Concept, VitroScan is seeking funding for the development, certification, and clinical validation of its proprietary tumour testing platform as a service to Health Care and Pharma for treatment decision support in oncology.

VitroScan tests biopsies from patients, by observing the tissues in small wells. Their tests are predictive of the efficacy of certain drugs, that may be used for treatment of the specific tumour that is being tested. The effect of the drug is observed using image analysis of the growth of the tumours in the wells.

For use as personalised medicine, VitroScan couples a score to the responsiveness of the tumours to standard of care drugs, and can also test the responsiveness to non-standard of care drugs. The ability to select specific treatments that work for the specific tumour can greatly reduce expenses in healthcare and increase the possibility of a good clinical outcome for the patient. The technology may also be used by pharma companies, for selecting the right subjects for clinical trials in the testing of new treatments.

The company is making progress in finding partnerships for its market launch, as both the pharma industry and health care sector have unmet needs for the technology that VitroScan is developing.

"Nice programme, I'm impressed by the attendance and the amazing organisation." - **Willemijn Vader**

PROF. DR. JOHN VAN DER OOST

Professor in Microbiology at Wageningen University & Research

John van der Oost is a professor in Microbiology at the Wageningen University & Research. He is considered a pioneer in the CRISPR revolution for his fundamental work on unravelling the mechanism of CRISPR- mediated genome editing. CRISPR-Cas systems are being used by many research groups worldwide, for applications that range from fundamental research to biotechnology, and even to revolutionary treatments of some human genetic diseases, including personalised medicine.

CRISPR-Cas evolved from an adaptive defence system in archaea and bacteria into a powerful tool for genomic research. After a crash course in CRISPR-Cas explaining the general mechanism of the technique, John van der Oost provided insight into how CRISPR-Cas has revolutionised gene editing. The growing diversity of the CRISPR-Cas systems results in many applications of this technique. Because CRISPR RNA-guided nucleases can target both complementary DNA and RNA, precise genome editing and precise gene therapy are possible. Clinical trials of natural and synthetic Cas nucleases to cure genetic diseases are currently on-going, with great promise for specific, personalised applications. Because the ex vivo studies are successful, more and more in vivo experiments are currently underway.

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The Board of Recommendation advices the committee on speakers, sponsors and general affairs. The board consists of eleven members, either related to the city or university of Leiden or Delft, or with a profession in the Life Sciences.

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The symposium committee who organised this edition of the Life Science Symposium consists of the following students:

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Marc van der Toorn	*General Affairs and Support*

From left to right: Heleen Peeters, Talitha den Bok, Marc van der Toorn, Raquel Schoenmakers, Timo van Reeuwijk, Rose Vossen, Sjoerd Ronken, Celine Jilesen.

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SPEAKERS

Prof. dr. Henk-Jan Guchelaar
Prof. dr. Diederik Gommers
Prof. dr. Christine Mummery
Prof. dr. Marianne Boenink
Esther Thole
Dr. Pauline Evers
Mr. dr. Corrette Ploem
Dr. ir. Chris Callewaert
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