Faculty of Science and Engineering (FSE)

Profile report: Advanced In Vitro Models for Alternative Drug Testing (Geavanceerde In Vitro Modellen voor Alternatieve Drug Testing)
- Discipline: Organ-on-a-Chip; Drug Screening; Toxicology; Microfluidics
- Level: tenure-track Assistant professor
- Fte: Full time (1,0)

1. Scientific discipline

The use of 3D cell and tissue models are expected to improve the predictive power of *in vitro* drug tests, and provide a more direct translational route to drug development. More effective implementation of these models can be realized through the application of approaches originating in cell biology, materials science and bioengineering. In vitro drug toxicological testing in particular stands to benefit from these advances.

2. Vacancy

This position has been opened by the Board of the Faculty (EMK/gl/16/00282) and will be embedded in the Groningen Research Institute of Pharmacy (GRIP), basic unit Pharmaceutical Analysis. The position falls within the framework of 'Career Paths in Science 3' ('Bèta's in Banen 3'). Please see link below for criteria and conditions.

3. Selection committee (BAC)

Prof. dr. H.W. (Erik) Frijlink, Director of GRIP, chair
Prof. dr. M. (Martina) Schmidt, Deputy Director of Pharmacy Education
Prof. dr. E.M.J. (Sabeth) Verpoorte, Chair of Analytical Chemistry and Pharmaceutical Analysis (GRIP, basic unit *Pharmaceutical Analysis*)
Prof. dr. P. (Peter) Olinga, Associate Professor in Translational Biopharmaceutics (GRIP, basic unit *Pharmaceutical Technology and Biopharmacy*)
Prof.dr. A. (Albert) van den Berg (University of Twente), Professor of Miniaturized Systems for Biochemical Analysis
Prof.dr. F.G.M. (Frans) Russel (Radboud University Nijmegen), Chair of Pharmacology and Toxicology
Student member: To be determined

Advisors: H.IJ. (Henk) Haagsma (HR)

4. Research area

Newly-developed drug attrition rates continue to be appallingly high, with failures often related to a lack of efficacy and safety. In fact, a leading cause for post-market drug withdrawal continues to be the shortage of accurate toxicological data acquired during the drug development process. Two-dimensional cell-based culture techniques are still widely employed in compound screening, lead optimization and drug candidate selection. However, it is generally recognized that the predictive power of cell-based drug tests benefits from the use of cell phenotypes which are

more directly related to the *in vivo* situation in man. Supporting advances in drug discovery are new analytical technologies for better high-throughput or high-content screening of cell response, as well as new approaches to genetically engineer the cells used. Three-dimensional (3D) cell cultures, including spheroids/organoids and precision-cut tissue slices, provide biological models which can recreate more physiologically relevant human organ architecture and function. The incorporation of 3D cultures into microenvironments which have been precisely engineered using micro- and nanofluidic technologies (organ-on-a-chip) enhances their in vivo-like response, through the mechanical stimulation of cells and the introduction of flow for constant nutrient supply and waste removal. More sophisticated monitoring of incubation parameters and metabolite production is also made possible through integration of micro-analytical function, as well as ensuring better interfacing with sophisticated imaging instrumentation.
Recreating *in vitro* the effects of a toxic compound on (human) cells or tissue remains particularly difficult, however, as the processes involved are varied and complex. This places a high demand on any given biological model if it is to properly emulate a toxicological event or events. This is particularly true when one considers that drug toxicity *in vivo* can be due to both acute or chronic, repeated exposures. Addressing the toxicological challenge in drug development requires an interdisciplinary approach, with input from pharmacology, cell biology, materials science and bioengineering.
GRIP provides the ideal environment for this new position in *Advanced In Vitro Models for Alternative Drug Testing*, given the wide breadth of expertise within the institute with respect to disease models, pharmacology, and organ-on-a-chip.

5. Embedding: institute (and base unit)

Pharmaceutical research at the GRIP is multidisciplinary and assumes a central position within the Life Sciences. It bridges clinical and biomedical sciences on the one hand, and chemistry, mathematics (statistics) and physics on the other. The interaction between the pharmaceutical sciences with these fundamental and clinical sciences offers excellent opportunities for cutting-edge research. The GRIP in Groningen is positioned within the FSE, and is physically located within the University Medical Centre Groningen (UMCG) of the Faculty of Medical Sciences (FMS). In other words, GRIP is ideally positioned to benefit from co-operations between both faculties.

GRIP consists of the following research units (with their chairpersons):
Analytical Biochemistry (Prof. dr. R.P.H. Bischoff)
Chemical and Pharmaceutical Biology (Prof. dr. W.J. Quax)
Drug Design (Prof. dr. A. Dömling)
Pharmaceutical Analysis (Prof. dr. E.M.J. Verpoorte)
Pharmaceutical Technology & Biopharmacy (Prof. dr. H.W. Frijlink)
Pharmacokinetics, Toxicology and Targeting (Prof. dr. K. Poelstra)
PharmacoTherapy, -Epidemiology & -Economics (Prof. dr. B. Wilffert)
Molecular Pharmacology (Prof. dr. M. Schmidt)

The research associated with this position will be embedded in the unit Pharmaceutical Analysis (PA). The PA research unit focuses on analytical chemistry as it relates to the pharmaceutical, (medical) biological and life sciences. Over the past decade, the Pharmaceutical Analysis unit has focused on the use of micro- and nanotechnologies for the development of smaller, faster lab-on-a-chip systems for bioanalytical purposes and improved *in vitro* systems based on cell and tissue microculture for drug screening. The Verpoorte group has had substantial funding recently for organ-on-a-chip work (four EU projects, one national project), focusing on the development of a bioartificial liver, early diagnosis of cardiovascular disease (target organ: endothelium), and a modular microfluidic gastrointestinal system for drug and food screening. The GRIP provides a unique opportunity to leverage the organ-on-a-chip and nanotechnologies in the Pharmaceutical Analysis basic unit for realizing and implementing advanced *in vitro* systems for drug screening. To do so effectively, however, requires the addition of a researcher with experience and knowledge in both the organ-on-a-chip and drug-screening/toxicology fields. The candidate will add to GRIP expertise with respect to disease models for understanding the pathophysiology of disease (e.g. lung disease, liver disease, neurodegenerative disease) so as to develop appropriate therapeutic interventions. Importantly, the candidate will be able, through close collaboration with pharmacology and (pre)clinical specialists, to enhance available *in vitro* models and develop new approaches by implementing cutting-edge technologies together with the latest advances in cells and materials.
Within GRIP, there will be close collaboration with the units of *Pharmacokinetics, Toxicology & Targeting* and *Pharmaceutical Technology & Biopharmacy*. The candidate will also participate in the interfaculty research institute Groningen University Institute for Drug Exploration (GUIDE) via collaboration in the research program Medicinal Chemistry and Bioanalysis.

6. Local and (inter)national position

Local position

This research complements very well a new Chair of Precision Pharmacy within GRIP, as well as increasing efforts within the UMCG and GUIDE, towards personalized medicine. Collaboration with stem cell researchers and other preclinical researchers will enable fast translation of new tools to more clinical settings. The new position will reinforce toxicological research within GRIP. The successful candidate will also be able to profit from bioengineering and biomaterials know-how at the Kolff Institute (UMCG), as well as a wealth of fundamental adjacent knowledge within the FSE. Furthermore, the candidate will be able to benefit from well-established GRIP collaborations with pharmaceutical industry to develop advanced *in vitro models* which are directly relevant for drug development.

Dutch/International context

Organ-on-a-chip technology is developing at a very rapid pace worldwide, in part as a response to a general need to rethink the drug development process. In The Netherlands, the focus to date has been mostly on the development of technology for human organ and disease models, and regenerative medicine. This is the

perspective represented by the national Human Organ and Disease Model Technologies Institute (hDMT, www.hdmt.technology). The emphasis on drug screening and development for applied organ-on-a-chip technology as proposed for this position is thus complementary to already-existing national efforts in this field. (Inter)nationally, the positioning of a microfluidics group (and rapid chip-prototyping lab) within a pharmacy/pharmacological environment imparts a unique advantage to GRIP with respect to fast translation of organ-chips to drug testing applications. Validation of organ-chip models will be facilitated, and the optimization of organ models for toxicology undertaken.

In the Netherlands, a bachelor and master program in Pharmacy is offered by the Universities of Groningen, Utrecht and Leiden. Toxicology is a vital part of the drug development process, but also in the daily practice of pharmacists. Pharmacists are the main consultants for toxicological issues of drugs. Therefore, education and research in toxicology is a key component of the bachelor and master programs in Pharmacy at the University of Groningen.

7. Expected contributions to research

The Tenure Track candidate is expected to extend and establish his/her research programme in the field of Advanced In Vitro Models for Alternative Drug Testing. The research should be competitive on a worldwide level and lead to publications in top journals. Obtaining substantial external funding for PhD projects is crucial. Supervision of PhD students is an important part of the research activities. The research is expected to strengthen existing GRIP efforts to enhance interdisciplinary research encompassing organs-on-a-chip and drug development, also within the context of GRIP's position within GUIDE.

8. Expected contributions to teaching

The candidate will contribute to the Bachelor teaching programs of Pharmacy and of Life Sciences & Technology. She/he will also participate in the Master teaching programs, Pharmacy and Medical Pharmaceutical Sciences, and the Top Master program, Medical & Pharmaceutical Drug Innovation. The candidate will contribute especially to subjects related to toxicology, such as Metabolism & Toxicology, Reproductive Toxicology and Molecular Toxicology. Coaching and supervision of bachelor, master and PhD students are also an essential part of the undergraduate teaching program. The candidate will also be actively involved in the development of new courses and/or revision of existing toxicology courses.

9. Expected contributions to the organization

The candidate is expected to have an active interest in, and to provide a positive contribution to, the management and organizational tasks of GRIP. At the level of the FSE, the candidate will contribute to the organization of the faculty, for example by participating in working groups and committees, in the fields of teaching, research and management. The candidate will also be expected to participate in relevant national and international organizations.