

The NCCR TransCure: An Incubator for Interdisciplinary Research

Valentina Rossetti and Hugues Abriel*

Abstract: The National Center of Competence in Research (NCCR) TransCure, funded by the Swiss National Science Foundation and the University of Bern, was active from 2010 to 2022. It provided unique research and educational framework in the membrane transporter and ion channel field. Thanks to an interdisciplinary approach comprising physiology, structural biology, and chemistry, in parallel to a rich offering in complementary areas such as education and technology transfer, the network achieved outstanding scientific results and contributed to the education of young scientists. In this review, we present the main features and milestones of the NCCR TransCure.

Keywords: Drug discovery · Education and training · Interdisciplinarity

1. Introduction

“From gene to drug” – with this ambitious goal, the National Center of Competence in Research (NCCR) TransCure was launched in 2010 as a joint effort of Swiss scientists determined to tackle major challenges of membrane transporter and ion channel research. The focus has been put on several major human diseases by investigating the structure, function, biology, and pathophysiological roles of strategically important transport proteins, with the ultimate scope of developing new therapeutic drugs. The choice of these protein transporter targets was motivated by the following factors: potential relevance in disease mechanisms, paucity of information regarding the biochemical structures and druggability, and specific expertise of the participating research groups for a class of transport proteins. To this end, the NCCR TransCure chose a unique interdisciplinary approach that combined three major disciplines, referred to as *TransCure Trias*: physiology, structural biology, and chemistry.

The NCCR TransCure, funded by the Swiss National Science Foundation (SNSF) and the University of Bern (the home institution), was established in 2010 by an initiative of Matthias Hediger, a pioneer in transporter physiology, who conceived the idea of an interdisciplinary effort combining physiology, structural biology and chemistry, to address disease-relevant aspects of transporter biology. Hugues Abriel, an established expert in ion channel physiology, succeeded Matthias Hediger as director of the network in 2015, while Jean-Louis Reymond, active in the field of computational drug discovery, acted as deputy director throughout the 12 years. The NCCR TransCure counted about 80 to 100 members each year, belonging to, on average, 18 research groups affiliated to the Universities of Bern, Zurich, Lausanne, Basel (till 2021, replaced then by EPFL Lausanne), and ETH Zürich. The research activity was organized through a project portfolio that was streamlined over 12 years, according to the outcomes and the advice of the SNSF review panel. In the last phase (2018–2022), the portfolio consisted of eight projects and one screening, profiling and analytical facility (SPAF). Despite being a Swiss-based network, it was embedded in the international scientific community through numerous collaborations worldwide, networking activity at scientific events, and participation in European re-

search programs such as the COFUND – IFP TransCure. Thanks to the latter initiative, a Marie Skłodowska-Curie Action of the European Union, we could attract 21 advanced researchers over 5 years coming from 13 different countries. A major contribution to the international visibility was also the co-organization of the biannual Biomedical Transporters Conferences, established by Matthias Hediger. These events attracted about 200 participants from around the world each time and have been excellent opportunities for interdisciplinary scientific exchange.

In the following sections of this review, we present some of the significant scientific achievements of the 12 years long NCCR TransCure endeavor. Moreover, we will outline its impact through the activities performed in the framework of the 4 non-scientific fields: education and training, knowledge and technology transfer (KTT), equal opportunities, and communication. Fig. 1 provides a visual summary of the main NCCR TransCure traits.

2. The Scientific Impact

The interdisciplinary nature of the network enabled collaborative projects that would not have taken place otherwise and led to important advances in the field of transporters and ion channels. For example, the collaboration of structural biologists (Locher group, ETHZ) and chemists (Altmann group, ETHZ) enabled the first structure of a human multidrug transporter, ABCG2, to be obtained using cryo-EM technologies.^[1] Further studies of this col-



Fig. 1. This word cloud is based on the answers of leading Principal Investigators (PIs) when asked to indicate five words that best represent the NCCR TransCure network and activity.

*Correspondence: Prof. H. Abriel, E-mail: hugues.abriel@unibe.ch
Institute of Biochemistry and Molecular Medicine, University of Bern,
Bühlstrasse 28, CH-3012 Bern, Switzerland

laboration revealed unique insight into the interaction of ABCG2 and small molecules.^[2]

Similarly, new potent inhibitors of the calcium channel TRPV6 were developed using a new ligand-based virtual screening method developed by the Reymond group from the University of Bern.^[3] Here again, cryo-EM technologies demonstrated how and where these small molecules bind to TRPV6.^[4] In a recent paper, in collaboration with the company Vifor Pharma, the group of Dutzler (University of Zürich), described the cryo-EM structure of the iron transporter ferroportin in complex with a new drug (vamifeport – VIT-2763) that is currently in development to treat hemoglobinopathies such as beta-thalassemia and sickle cell disease.^[5] Finally, one of the major translational impacts of these 12-year-long research activities has been establishing a spin-off company (Synendos Therapeutics AG^[6]) that is benefiting from NCCR TransCure findings of the Gertsch group (University of Bern). This company aims to develop novel therapeutic approaches based on newly discovered selective endocannabinoid reuptake inhibitors.^[7] These new drugs target symptoms associated with anxiety, mood, and stress-related disorders.

3. Achievements in the Management Areas

3.1 Training the Next Generation of Scientists

The NCCR TransCure PhD students and postdoctoral researchers have been key players in achieving the results mentioned above. Besides their work on the projects, they could profit from a gapless interdisciplinary educational offer and several network events such as retreats (Fig. 2), symposia, and seminar series. One aspect of the training consisted in teaching specific skills through specialized courses. These mostly approached theories and methods related to the disciplines of the TransCure trias, such as crystallography, cryo-EM, imaging of neurons, electrophysiology-based techniques, and drug discovery. Some other courses provided insights into transversal topics, such as the analysis of datasets, population-based studies, and animal models in pre-clinical research. Besides the scientific training *per se*, the goal was also to foster the search for innovative solutions and critical thinking when approaching controversial topics – as in the case of animal experimentation. In that framework, the courses involved not only experts in veterinary services, animal facilities, and animal welfare but also activists of animal protection associations. It is then rewarding to learn about the impact of the educational effort. For example, in 2020, Christiane Albrecht (NCCR TransCure principal investigator) was awarded a grant from the Swiss 3R Centre for her innovative system to study the materno-foetal interface following the 3Rs principle (Replacement, Reduction, and Refinement). A further major contribution of the NCCR TransCure in the field of education is the role played in re-establishing the

pharmacy curriculum at the University of Bern. In this framework, the collaboration between the medical school and chemistry was instrumental in the re-organization process.

3.2 Sowing the Seeds for Translation

On the way to drug discovery, proper intellectual property (IP) management is crucial. We hence provided regular training opportunities in the field of patents and IP rights thanks to the collaboration with the Federal Institute of Intellectual Property. Moreover, the NCCR TransCure joined in 2016 the ‘bench2biz’ consortium^[8] (previously named ‘SwissCompanyMaker’) and has co-organized since then a series of workshops for academic entrepreneurs. The bench2biz is a Swiss-wide joint initiative of several NCCRs that supports researchers with early-stage ideas on their path towards the commercialization of their product. Several participating teams successfully entered the Swiss start-up ecosystem in the last few years.

The NCCR TransCure fellows had the opportunity for direct contact with industry thanks to a long-lasting collaboration with the Novartis Institutes for BioMedical Research (NIBR), which encompassed educational and scientific aspects. PhD students and postdocs could join the exclusive ‘Drug Discovery and Development Project Simulation’ course and workshops with NIBR scientists. Furthermore, within the framework of the open innovation and academic collaboration program of NIBR, the fellows could work at the FASTLab facilities, free of charge, for the high-throughput screening of compounds. This was not only a clear added value for the advancement of the projects but also a unique training opportunity for the fellows.

A major success of the NCCR TransCure in the field of KTT is finally the launch of the spin-off mentioned above, Synendos Therapeutics, incorporated in 2019 and co-funded by Jürg Gertsch (NCCR TransCure PI) and Andrea Chicca (NCCR TransCure Alumni and current CEO). The scientific knowledge on which Synendos was founded resulted from the NCCR TransCure collaboration between the Gertsch and Reymond groups. This work led to the discovery of a compound that has been further developed and is now a promising treatment for stress-related neuropsychiatric disorders.

3.3 Outside the Ivory Tower

Another aspect of the training program concerned soft skills. On the one hand, we organized courses provided by professionals to train communication, leadership, and social skills, prepare for the job market and improve new media use. Also, the NCCR TransCure staff could benefit from such training: thanks to a film-making course, we set up a self-made video gallery to illustrate scientific projects and document events. On the other hand, we involved the researchers in organizing outreach initiatives with



Fig. 2. Group pictures at the third (2013, Murten) and final retreat (Bern, 2022). The NCCR TransCure network met every year at annual retreats, that always provided the framework for scientific discussions, project presentations, poster sessions and social events.

the public, such as open days for kids, the Night of Research of the University of Bern, and public thematic events. Despite initial hesitation, the NCCR TransCure scientists found their engagement in outreach events rewarding. Discovering new ways of conveying scientific content, answering children's curiosity, and illustrating the impact of research on society – are only a few of the many positive outcomes of these outreach events. A major project in this field has been the realization of the 'Vitaport – what our body transports' exhibition, in collaboration with the School of Design of Bern, in the summer of 2022 (see also the dedicated article in this issue, p. 1063). Researchers and design students developed objects, texts, and information graphics organized as a temporary learning and artistic path, installed in the Bernese Elfenu Park for two months. The thematic stations of the path combined scientific panels and artistic objects and focused on the iron and amino acid transport and the endocannabinoid system. Moreover, we organized accompanying events at the Botanical Garden of Bern to deepen some of the Vitaport topics.

3.4 Plugging the Leaky Pipeline

Besides acquiring various skills, the next generation of scientists cannot miss the goal of achieving equal opportunities in the research environment. This long path requires time, endurance, and capillary work at various levels of the academic system. The NCCR TransCure elaborated a series of measures to provide global support to women in science, such as flexible working hours, the possibility to work in home office, and mentoring opportunities. We also offered financial contributions for childcare costs to fellows not eligible for this kind of support through the Swiss National Science Foundation. Further financial support was provided through the annual 'NCCR TransCure Young Scientists Award' to outstanding projects of NCCR TransCure fellows. An additional field of action aimed to raise awareness and foster a culture of gender equality in the network and the scientific community. We organized topic-specific woman scientist symposia and paid particular attention to the choice of gender-balanced speaker panels at events. We launched a series of yearly career pathway lectures given by female role models and encouraged fellows to participate in gender equality initiatives at local universities. Finally, the directorate, together with the delegate for Gender Equality (Christine Peinelt), strived to encourage applications of women researchers to open positions, to increase the number of female principal investigators in the network, and to promote gender equality at the Faculty of Medicine of the University of Bern.

4. Beyond the NCCR TransCure

A major challenge for NCCRs is ensuring the network's sustainability beyond its lifetime. The efforts and results obtained in terms of scientific output, collaborations, and structural measures need to be channeled into solutions that benefit the scientific community and society in the long term.

The NCCR TransCure legacy consists of three pillars:

- The profiling of the Institute of Biochemistry and Molecular Medicine (IBMM) of the University of Bern as a leading Swiss group of experts in the field of membrane transport and ion channel research. The NCCR TransCure structural measures allowed for the reshaping of the IBMM through the creation of several new professorship positions and for the acquisition of cryo-EM state-of-the-art equipment located at the newly created Bernese branch of the Dubochet Center of Imaging.
- The continuation of the activity of the Screening, Profiling, and Analytical Facility at the University of Bern. The SPAF was initially set up to provide basic technologies related to transporter assays in the context of identifying small molecules that target specific transporters. Over the years, it has become a facility for different groups at the University of Bern interested in bioanalytical questions related to drug discov-

ery and/or drug action *in vivo*. The SPAF is well integrated with other facilities related to metabolomics and analytics and plays an important cornerstone in the emerging lipidomics and LC-MS/MS community in Bern, but also nationally and internationally.

- The establishment of a new section of the umbrella network 'Life Science Switzerland (LS2)' entitled 'Ion Channels and Membrane Transporters'.^[9] This new section was launched in February 2022 as a 'merger' of the NCCRs TransCure and Kidney.CH, who share, at least in part, their interest in membrane transporters. The LS2 framework is ideal for providing a long-term perspective on the collaborations initiated with the NCCRs. As declared on the LS2 website, this section "*aims to keep this multidisciplinary community alive beyond the NCCRs lifetime and to foster collaboration within its members. We envisage fruitful networking with other LS2 sections. Furthermore, we aim to develop it into a reference cluster of Swiss scientists working on the physiology, cell biology, biochemistry, biophysics, structural biology, and pharmacology of ion channels and membrane transporters.*"

5. The Unique NCCR Experience

Behind the scenes of the NCCR TransCure research activity, research managers and administrative coordinators supported the management and development of the whole network operationally. NCCRs are indeed also a place where professionals of the so-called third space can apply their expertise, consolidate and expand their competencies. They support research networks and institutions in various fields, such as reporting, grant management, and fundraising, strategy development, event organization, and communication. In the variegated NCCR universe, third space professionals cover an important bridge function between fellows, principal investigators and governing bodies, and they take care of the collaboration with funding institutions and external partners. Often, they initiate cooperation with other NCCRs to organize events, courses, or larger initiatives, such as the cross-NCCRs #NCCRWomen campaign^[10] or the above-mentioned bench2biz workshop series. This kind of collaboration recently increased – despite the pandemic. In the last months of the NCCR TransCure activity, we were pleased to see how active NCCRs, including those of the last series, were teaming up in several management areas to give rise to new joint initiatives benefiting their researchers, the scientific community, and the lay public.

The scientific progress, its impact on society, the development of interdisciplinary collaborations, and the steps towards a better academic environment characterizing the NCCR TransCure journey showed us clearly the importance of long-term funding schemes such as NCCRs. Unique in their genre, in the Swiss academic landscapes, they offer an incredibly large set of possibilities to generate new knowledge and expand collaborations in many different directions. We wish all the current NCCR networks a fruitful lifetime leading to breakthrough discoveries and sustainable achievements, and we hope that there will be in the future further NCCR series to tackle the challenges of the coming decades.

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