Editorial: Special Issue on 'Chemical Biology of Membranes and Signaling'

Howard Riezman

Chemical biology is a discipline that is clearly on the rise. It is also a research area that is quite vast with a large number of chemical approaches to a wide range of physiological problems. Rather than trying to define the breadth of chemical biology in this issue I have chosen to focus our attention on membranes and cellular signaling events where membranes are clearly involved. Membranes are an important topic for chemical biology because other approaches, such as molecular biology and genetics, are not capable of dealing with the great diversity of membrane components, in particular the lipids.[1] Another shortcoming of genetics is that most often mutations are not conditional and the physiological system can adapt to the changes. Small molecule intervention can help alleviate this problem and the ability to follow and perturb events with increased spatial and temporal resolution is an important feature of chemical biology approaches.

Eleven years ago we started the National Centre for Competence in Research (NCCR) in Chemical Biology with ambitious goals.[2] Many of these have been achieved and we believe that we have enriched the base and reputation of chemical biology in the Lemanic region, stemming both from our own results, our interdisciplinary spirit, but also through collaborations with scientists outside of the NCCR. Many of the problems that the NCCR Chemical Biology focused on concern membranes and how they impact cellular signaling, which is another reason why this subject has been chosen for this issue. Presented in this issue are three articles from the NCCR Chemical Biology and four from people who have collaborated with us.

One of the signature accomplishments of the NCCR has been the development of the first in class, fluorescent probes (FlipperTR®) that can measure membrane tension in biological membranes *in situ*. The development of these probes for the scientific community is described in the contribution from ***Assies et al.*** (this issue). This is a long success story of our NCCR and one that has blossomed from a singular idea to a vast array of applications. It is also a good example of how chemical biology can contribute in a much simpler and broader way than genetically engineered approaches to the same problem. As mentioned above another issue of using genetics is the lack of temporal resolution. A contribution from my research group highlights our efforts of use caged, isotope-labeled lipids that are targeted subcellularly to examine lipid homeostasis with increased spatial and temporal resolution (***Simon et al.,*** this issue). The Flipper probes are not the only sensors that are available and there are very many important considerations to be taken when using them and similar probes. A very forward-looking contribution from ***Loewith et al.*** addresses these issues (this issue). It is not just important to trace and measure, but also to be able to perturb and control lipids, which is nicely illustrated by the work from Trauner and his colleagues summarized here (***Trauner and Moorstein***, this issue). In another contribution ***Aguilera-Romero and Muñiz*** (this issue) are able to follow the transport of proteins as they enter into the secretory pathway and have determined that ceramides play an important role in protein sorting during this process. To understand how this works and to be able to comprehend the physics behind membranes and their perturbations, molecular dynamic simulations are a very useful tool as outlined by ***Srinivasan and Vanni*** (this issue). Finally, membranes are also the source for substrates that regulate the most important signaling pathways controlling cell growth and crucial for our understanding of health and disease, in particular cancer. ***Borsari and Wymann*** take us through an historical journey of the development of inhibitors of phospholipid kinases that are promising new therapeutic leads. The ACCESS facility of the NCCR Chemical (EPFL and UNIGE) is here to help you if you are looking for small molecule approaches for your projects.

The NCCR Chemical Biology is proud to have accomplished or been accessory to these success stories and we hope that our interdisciplinary spirit lives on well beyond our official ending at the end of November 2022.

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[1] T. Harayama, H. Riezman, *Nat. Rev. Mol. Cell Biol.* **2018**, *19*, 281, https://doi.org/10.1038/nrm.2017.138.
[2] a) J. Montenegro, C. Gehin, E. K. Bang, A. Fin, D. A. Doval, H. Riezman, N. Sakai, S. Matile, *CHIMIA* **2011**, *65*, 853, https://doi.org/10.2533/chimia.2011.853; b) M. Takahashi-Umebayashi, L. Pineau, T. Hannich, A. Zumbuehl, D. A. Doval, S. Matile, C. Heinis, G. Turcatti, R. Loewith, A. Roux, L. Reymond, K. Johnsson, H. Riezman, *CHIMIA* **2011**, *65*, 849, https://doi.org/10.2533/chimia.2011.849.

Cover image: In this issue we will see novel tools to measure membrane properties (Flipper probes), manipulate membranes (photoswitchable lipids) and analyse membrane lipid homeostasis with increase spatial and temporal resolution. Molecular Dynamics Simulation image of a membrane was provided by Stefano Vanni. Other images were taken from articles in this issue contributed by Stefan Matile, Dirk Trauner, Howard Riezman.

The Editorial Board of CHIMIA warmly thanks Professor Howard Riezman for organising this issue on 'Chemical Biology of Membranes and Signaling' to highlight some of the impressive results achieved in the National Centre for Competence in Research (NCCR) in Chemical Biology, directly and with collaborators.