Longer, Better, Cheaper: Revolutionizing Drug Screening

A central objective of the ASMENA project is developing new screening methods for ion channels. Ion channels are membrane proteins which regulate the flow of ions in and out of all biological cells. They are key to a number of processes which involve rapid changes in cells. For example, ion channels are an important part of the nervous system, and are also involved in processes such as muscle contractions, T-cell activation, and pancreatic beta-cell insulin release.

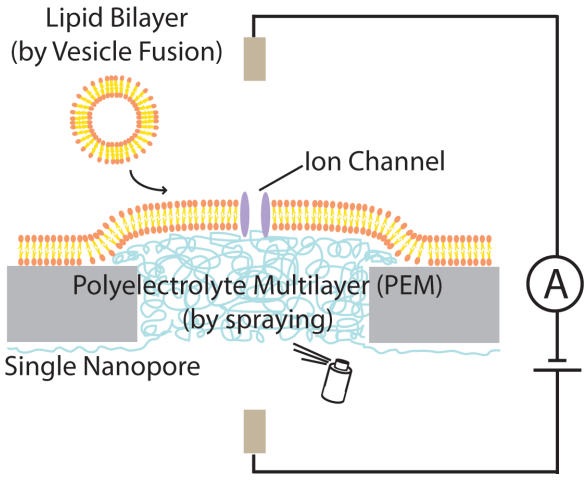
The study of ion channels traditionally involve voltage clamp electrophysiology, first and foremost the so-called patch clamp technique. The patch clamp method is a very powerful approach, since it directly measures transmembrane signalling. However, the need for highly trained specialists for its usage and its low throughput hamper an efficient use in industries. ***Kaori Sugihara***, a Ph.D. student at the Laboratory of Biosensors and Bioelectronics at ETH Zürich, explains,

– The patch clamp technique allows the study of single or multiple ion channels in cells. The problem with the conventional system is that it has a very short lifespan. It's there for two or three hours, and then it's gone. Thus, creating a system with a longer lifespan was my first priority. Another problem with the conventional system is that it's too labor intensive. So, making the system easier to fabricate was the second thing I had to address. In other words, my mission was to make the system high-throughput by improving those two points.

Kaori Sugihara at ETH Zürich, Switzerland, is working on creating a new platform for the study of ion channels, a type of membrane protein of great importance to drug development.

In recent years, advances have been made in how to form lipid bilayers (or membranes) on substrates through self-assembly. Being able to create such bilayers – incorporating ion channels – on top of a sensor chip integrated with voltage-clamp recording and label free array sensing, would represent a revolutionizing technique for the study of ion channels. Kaori explains how her system was created:

– I used a silicone chip with holes inside, and sprayed that chip with charged polymers to fill the holes. Then, a lipid bilayer was assembled over the surface, with a pore-forming peptide incorporated into the bilayer.



The patch clamp technique requires the electrode (a micropipette) to be attached to the cell membrane manually. In Kaori's system, measurements are made through holes in the chip, with no need for manual attachment of electrodes. The polymers can be sprayed onto the chip using robots, making it easier to scale up the measurement platform and thereby increasing throughput.

– The injected lipids self-assemble into a lipid bilayer, which also makes for higher throughput, she says. Self-assembly means that the components – in this case the injected lipids – form an organized structure, a membrane, due to specific, local interactions between the components themselves, with no extermal direction.

Whereas the conventional system has a lifespan of two to three hours, her system has a lifespan of two to three weeks. Further challenges remain however. Being able to integrate the right kinds of membrane proteins – the ones most interesting for drug screening – while preserving the integrity of the proteins as well as the bilayer, is one such challenge. Will Kaori continue within the same area of research after finishing her Ph.D.?

– I don't know about the exact same area, but I'm interested in the field of biomedical research itself. I chose this project among several offered to me. It sounded very interesting, and indeed it is – I have learned a lot. The possibility of working closely with other research groups all over Europe as well as with industrial partners was something that really attracted me to this project, and it has proven very valuable.

Kaori says she is not sure of whether she wants to stay in academia or head for a job within the industry after she finishes. However, she says the ASMENA project has permanently affected the way she wants to do research in the future:

– The most interesting part for me has been the collaboration with the industrial partners. It was very beneficial to hear what they had to say over the course of the project. When you are in academia, you are surrounded by people who are mainly oriented by their specific research interest, and often that means they are focused on fundamental research. On the other hand, the industrial partners need to find specific solutions fast and are focused on what is truly needed *right now*. Their point of view let me realize another style of doing research. I definately believe in the importance of working closely with industrial partners to find the right research topics.

ASMENA *is part of the EU Seventh Research Framework Programme (FP7). Over three years, the consortium consisting of 15 partners in 7 countries aims to develop new platforms for drug screening and analytical profiling base on in vitro measurements of functional and conformational changes in membrane proteins. Such tools will allow standard profiling and screning also against membrane protein targets that can currently not be screened in these ways. They will shorten the time and cost involved in drug lead development by increasing predictability as well as contribute to fundamental understanding of structure-function relationships of membrane proteins.*

The partners of the consortium are world leading experts on surface functionaliztion, membrane self-assembly, biosensing, membrane protein functional measurements and commercialization of the same. Now, their complementary competences can be put together on the European level to create a timely breakthrough in the area.