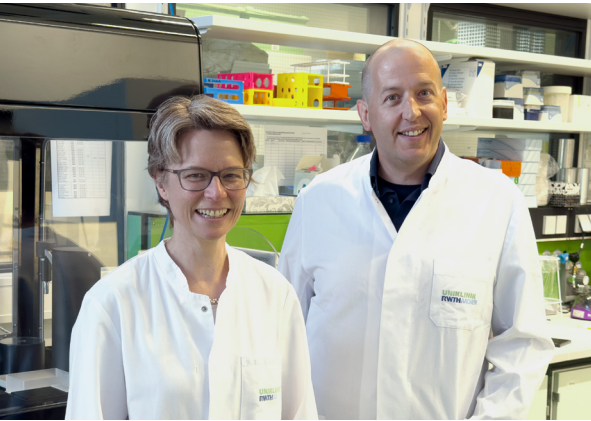


Unlocking personalized medical solutions for chronic neuropathic pain with the Qube 384



Chronic neuropathic pain, a condition affecting up to 8% of the world population, presents a significant challenge in medical treatment due to its complex and often individualized nature.

At Uniklinik RWTH Aachen, a pioneering initiative called Precision²Treat is underway to explore the characteristics of mutated ion channels in people affected by neuropathic pain. Using patients' own sensory neurons derived from induced pluripotent stem cells, the team aims to understand the underlying mechanisms of chronic pain, and they are now using Sophion's Qube 384 solution to investigate therapeutic possibilities.



Angelika Lampert, University Professor, Principal investigator

Ralf Hausmann, Professor, Co-Principal Investigator

Uniklinik RWTH (Rheinisch-Westfälische Technische Hochschule) Aachen is Germany's largest technical university. In the Precision²Treat project, induced pluripotent stem cells (iPSC) derived from the blood of pain patients are used. By differentiating the stem cells into sensory neurons, the team aims to test active substances on the pain patient's own cells to hopefully be able to provide future personalized therapy for those who have so far received inadequate treatment.

In collaboration with Uniklinik RWTH Aachen's neurology department, the Precision²Treat project has amassed a clinical cohort of nearly 300 neuropathic pain patients. These individuals, afflicted with conditions like small fiber neuropathy (SFN) or erythromelalgia (IEM), offer valuable insights into the complexities of chronic pain.

To purchase a high-throughput screening system and fund Precision²Treat, Professor Angelika Lampert from the Institute for Neurophysiology and Professor Ralf Hausmann from the Institute for Clinical Pharmacology received a grant worth €1.7 million from the German Federal Ministry of Education and Research (BMBF).

From trial and error to precision medicine

As reactions to treatment vary widely among people suffering from neuropathic pain, clinical studies have mostly been unsuccessful. Finding a therapy that works often means years of "trial and error" for patients. "Not only is this difficult for the patients, but it's also frustrating for the relationship between the patients and the doctors treating them," explains Ralf Hausmann. "So, we would like to know how drugs work on ion channels and whether there are differences in the unmutated or mutated channels."

Angelika Lampert and Ralf Hausmann's team work on specific ion channels, including two voltage-gated sodium channels. They have seen multiple neuropathic pain patients with a mutation in this ion channel family that alters the way the channel opens and closes. These channels play important roles in initiating action potential in the nerves.

"We're looking for changes induced by genetic variants in the voltage-gated sodium channels Na_v1.7 and Na_v1.8, so we measure their very small electrical current using highly sensitive amplifiers," explains Angelika Lampert. "We normally do this one cell at a time by manual patch clamp electrophysiology with a tiny little glass pipette and then we check if the current flows in the cell and how the current is characterized."

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It's a process that works, but it's also incredibly time consuming. "If you really want to understand the function of a mutation, you need to look at many cells and do many measurements," says Angelika Lampert.

"To speed up the process, we needed higher throughput and the ability to do more recordings at the same time. This was a key reason why we were so interested in a patch clamp robot."

Angelika Lampert

With Precision²Treat, the team is also expanding their investigation beyond single channel mutations or variants. "We have an enormously high number of channels in our nerve fibers and, ideally, we would like to investigate the genetic variants of the patient by including all these ion channels," says Angelika Lampert. "It's almost impossible to do this one channel at a time."

Utilizing the Qube's capabilities

By taking a patient's own cells to derive sensory neurons, which carry the complete genetic code with all the variants of that patient, the team will use the Qube 384 high throughput patch clamp system to see if they can modify the cell's electrophysiological properties by using drugs already on the market. "On the one hand, we are looking for the individual channel when it is expressed in another cell system," says Ralf Hausmann. "And on the other hand, we have the same channel variant expressed in the so-called natural environment of the channel in the patient cells, which includes all other ion channels and maybe additional mutations in these channels."



Founded at Uniklinik RWTH Aachen in 2023, the **Scientific Centre for Neuropathic Pain Aachen (SCN^{AACHEN})** brings together experts in the field. For more information, visit: <https://www.scn-aachen.rwth-aachen.de/>

Expanding treatment – and funding – possibilities

With experience from a previous project funded by the German Federal Ministry for Education and Research (BMBF) that did not include a high throughput automated patch clamp instrument, the team knew this technology would be essential for Precision²Treat. “It also worked in our favor that a funding opportunity came up with BMBF,” highlights Ralf Hausmann. “To get funding for large research equipment is a challenge and a big difference between Industry and Academia.”

Research with a strong link to the clinics and their patients’ treatment

“Having a translational project may make it easier to tap into a larger pool of funding,” explains Angelika Lampert. “With a project like Precision²Treat, a wider pool of funding might be applicable because it’s something that the Industry could also be interested in,” continues Angelika Lampert. “Our project has a basic science foundation and a very strong link to clinics with a direct, relatively concrete vision of how this could lead to a treatment for patients.”

In addition to neurologists, the Precision²Treat research consortium also consists of geneticists, biophysicists, and computer modelers. In contrast to the pharmaceutical industry, the team has detailed phenotyping of all patients along with permission to use their biomaterials for research purposes. “Coordinating our efforts has really helped us make this project a reality – we needed all these specialties under one umbrella,” highlights Ralf Hausmann.

“With Sophion, everything is very professional and straightforward, something we greatly appreciate.”

Angelika Lampert

High throughput screening with Qube 384

The ambition for Precision²Treat project is to show proof of concept. By using iPSC derived sensory neurons on the Qube to screen licensed drugs, the team hopes to identify compounds that are likely to reduce the excitability of the cells.

“The idea is to have a workflow coming from an individual pain patient and to do basic research to understand the biophysical properties of this special variant. The Qube enhances our workflow.”

Ralf Hausmann

“We intend to understand how the biophysical properties could cause the pain symptoms of the patient and then ultimately come to a precision treatment for individualized therapy,” continues Ralf Hausmann.

Facilitating collaborative research

Now with the Qube 384 in place, the team is adapting iPSC cells to the high throughput automated patch clamp system. “This is challenging because it takes about 50 days of culturing for neuronal differentiation and all the sodium channels to be expressed on the cell surface,” explains Angelika Lambert. “And if you do this with neurons, long neurites begin to spread and they must be removed before putting them on the Qube. This can damage the cells, but we have received a lot of help from Sophion, and now we have healthy cells that are working well on our patch clamp system.”



Optimized research workflows with Qube 384

Today the team continues to use manual patch clamp to address specific questions, but the Qube is now giving them more possibilities and enabling them to do the kind of high throughput drug screening that would have been impossible with their previous setup. "Before, we would see a variant of a patient or a certain mutation in the sodium channel that is localized at the voltage sensor, and then we would analyze this specific property with manual patch clamp," explains Ralf Hausmann. "But now we can run a pool of protocols analyzing most of the typical channel properties."

"With Qube, we can do an overall analysis and see what's happening and then maybe later we can focus more precisely on a special feature of the channel or the mutation. It's much faster – you look at the data and decide what your next step will be." Ralf Hausmann

Supporting an optimized research workflow, the Qube enables the team to analyze hundreds of compounds and have the results in just a day or two. "It's much faster – you look at the data and decide what your next step will be," says Ralf Hausmann.

The Aachen team tested the different automated patch clamp systems available, keeping the highly specific needs of the Precision²Treat project top of mind. "The sensory neurons are very large cells and therefore have special requirements such as full Rs compensation for a precise biophysical analysis, and this is available in the Qube," adds Angelika Lampert.



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For more information about Uniklinik RWTH Aachen & the Precision²Treat project, visit: <https://www.ukaachen.de/>

A close partnership with Sophion from the start

The team was also pleased with the installation and the onboarding provided by Sophion. "A team of field engineers and application scientists came to Aachen to set up the Qube," says Ralf Hausmann. "We got an introduction to the system as well as an understanding of how to troubleshoot and get assistance from their subject matter experts. You get the right answer from the right specialist for any question. Plus, they have extensive experience with different cell types and channels, so sometimes you can speed up development just by asking the Sophion team."

The experience has also been collaborative, with the Aachen team excited to share ideas for features and future developments with the Sophion team. "The experience has been highly professional and very friendly," says Angelika Lampert. "When we have new ideas in the project, the Sophion team is always interested in seeing how we can work together to improve the system even more. So, this is a fun aspect of our work together."



Sophion Bioscience is a leading global life science company founded in 2000 by a group of passionate electrophysiologists. We specialize in developing and manufacturing automated patch clamping and cell line solutions. With our complete technical, biological, and application support, we help our partners pioneer ion channel research and drug discovery. Through the continued development of our QPatch Compact, QPatch, and Qube 384 platforms, we offer uncompromised data quality in a user-friendly environment, from assay setup to advanced data analysis. We are headquartered in Denmark and have subsidiaries in the United States, Japan and China. For more information, visit [Sophion.com](https://www.sophion.com)