

Novel small molecule modulation of PIEZO1 channels

Tools:
SyncroPatch 384

Dr. Jacob Kinsella
featured by Nanion Technologies



Jacob Kinsella completed his PhD at the University of Leeds, UK, studying mechanical activation of PIEZO1. During his PhD, Jacob spent two months at Nanion working with the SyncroPatch 384. Jacob recently completed his PhD and is currently taking some time out to travel and invest in his pastimes such as hiking, climbing and camping.

Introduction

There are a number of ion channels which are mechanically activated and play a vital role in sensing mechanical forces in various cell types. One type of mechano-activated ion channel is PIEZO1, a cation channel activated by mechanical force. Dysfunction of PIEZO1 has been associated with numerous pathophysiological states, including generalized lymphatic dysplasia, varicose vein disease, and hereditary xerocytosis. Therefore, PIEZO1 is a potential therapeutic target and finding ways to study such mechanosensitive channels using high throughput techniques is critical for drug discovery.

Jacob has a background in medicinal chemistry, completing his first degree at the University of Manchester, following which he undertook his PhD at the University of Leeds under the supervision of Prof. David Beech investigating analogues of Yoda1 to activate PIEZO1. As part of Nanion's continued commitment to academic research and supporting young researchers, Jacob was invited to spend some time at Nanion to optimize the PIEZO1 assay and supplement his PhD thesis.

Jacob enjoying some time with Nanion colleagues on the terrace. During Jacob's time at Nanion's headquarters, he enjoyed socializing with friends and colleagues on Nanion's roof terrace, pictured here with Markus and Tom.

Can you give us a brief summary of your PhD?

"The aim of my PhD project was to identify novel structurally unique inhibitors of the PIEZO1 mechanosensitive ion channel."

What brought you to Nanion?

"Professor David Beech has had a longstanding and highly successful collaboration with Nanion who has long shown a great interest in PIEZO1. The successful mechanical activation of the PIEZO1 channel with the SyncroPatch 384 marked a fantastic milestone in the automated patch-clamp field and inspired the idea that a slightly modified protocol may be used to screen a small library of compounds. After a brief discussion, Nanion kindly offered to host me in their Munich office to develop the proposed assay and flesh out my thesis."

What was your project at Nanion?

"My project was to further optimize the automated mechano-patch-clamp assay developed by Nanion with a focus on increasing its response rate to a level sufficient for testing a medium-sized library of small molecules."



"My colleagues at Nanion were some of the most welcoming and friendliest people I've ever had the pleasure to work with."

Dr. Jacob Kinsella, University of Leeds

Was your project work at Nanion related to your PhD?

"I was very fortunate that the project at Nanion was directly related to my PhD project. The work conducted at Nanion contributed significantly to my project's strategic development and greatly influenced the overall quality of the thesis than I initially imagined it would. I was able to publish the work in the British Journal of Pharmacology ([Improved PIEZO1 agonism through 4-benzoic acid modification of Yoda1](#)) and travel to San Diego and present a poster at the Biophysical Society Annual Meeting which I thoroughly enjoyed."

Which instruments did you use at Nanion?

"My work was conducted entirely on the newest iteration of the SyncroPatch 384 which was an absolute pleasure to work with. We were able to take advantage of the adjustable pipette speed of the SyncroPatch 384 and position the pipette very close to the cell which meant that we could obtain high mechanical forces at the cell and reproducibly activate PIEZO1. What is more, we could repetitively pipette up and down close to the cell and saw effects on the PIEZO1 response. This procedure became known unofficially as 'cell massage' at Nanion."

Did your project at Nanion accelerate your PhD project?

"Absolutely! The SyncroPatch 384 afforded me the ability to test 60 inhibitors against the PIEZO1 channel. While this is possible with the conventional manual patch-clamp technique, using the SyncroPatch 384 was significantly less time-consuming saving me months of work. The data generated from the SyncroPatch 384 allowed me to select promising compounds before testing them in orthogonal assays."

What was your best moment during your time at Nanion?

"Aside from frequently raiding the stocks of apfelschorle, Haribo and Kinder, I would say that it was creating lasting friendships. My colleagues at Nanion were some of the most welcoming and friendliest people I've ever had the pleasure to work with. An honorable mention to the very regular parties. It was through these that I developed my newfound love for English beers, particularly Augustiner."

