Having been the recipients of the Gene People Leadership Symposium 2022, Best Research Partnership Award with the Timothy Syndrome Alliance, Jack has continued to work with the charity over the last three years, and has provided an update on their joint activities.

Since 2019, I've been working with Sophie Muir and the Timothy Syndrome Alliance (UK Charity; TSA) to raise awareness, encourage public engagement, pursue co-produced research, and change healthcare policy. Sophie approached Prof Jeremy Hall and our lab at the Neuroscience and Mental Health Innovation Institute on behalf of a Facebook group for a community of families of children with Timothy Syndrome or *CACNA1C* gene variants. Timothy Syndrome is caused by a pathognomonic G406R protein change in the *CACNA1C* gene, while other variants in the *CACNA1C* gene are less well understood but appear to have pathological phenotypes. These are multi-system, but typically present with autism spectrum disorder, developmental delay, prolonged cardiac QT interval, syndactyly/ hip dysplasia, hypotonia, epilepsy and hypoglycaemia. We began by holding a conference for these families, getting them together for the first time, which included inviting the eponymous Kathryn Timothy over from the US. This led to the launch of the Timothy Syndrome Alliance charity.

From there we have undertaken a co-produced clinical phenotyping research study, listening to concerns from families and formally assessing for clinical features using standardised measures, as well as taking patient cell lines for future iPSC modelling of pathological processes. Part of this work was conducted as a collaboration with Stanford University, and has been recently published in Paediatric Neurology https://doi.org/10.1016/j.pediatrneurol.2022.10.013. We have continued our public conference programme, running a bi-annual joint international Brain Research Conference with global attendance and speakers (https://www.cardiff.ac.uk/news/view/2530644-nhmri-co-hosts-successful-annual-brain-research-conference-with-timothy-syndrome-alliance-to-a-worldwide-audience). We have received a small grant for a public engagement film, which is being co-produced with the TSA, encouraging members of the public to engage with rare disease research. We have been able to influence national NHS policies, including updates to the Genomics England PanelApp and adding *CACNA1C* variants on further standardised genetic testing. We have provided support to patients and local clinical teams, with guidance on the specifics of the disorder given it's rarity. We have updated a broad range of widely used online clinical genetic resources, expanding OMIM, Medline Plus, NORD, Orphanet and Wikipedia. We are currently developing a Scientific Advisory Board, planning our next international conference, and beginning a number of international research collaborations, with the research partnership going from strength to strength.

(Dr Jack Underwood GW4-CAT Fellow, Cohort IV November 2022)

Summer 2025 Update: Further awards for awareness and public engagement

Following on from the success shared in our last article, the collaboration between the Timothy Syndrome Alliance (TSA) and the Neuroscience and Mental Health Innovation Institute (NMHII, Cardiff University) has continued to garner awards, funding and international support. In 2023 we set up a Scientific Advisory Board for TSA, which I chair, leading bi-annual meetings. We held a further global conference on the 23rd of June 2023 (https://timothysyndrome.org/conference/), which with financial support from The Stanley Grundy Foundation and software from Wordly, was live-translated

into 30+ languages for international attendees. I also undertook a number of media interviews, as awareness about *CACNA1C* and Timothy Syndrome spread.

2024 was a landmark year for recognition and support. We were first able to contribute to a successful GW4 Epilepsy Community Development Award, providing PPIE input into the community based across Bristol, Bath, Cardiff and Exeter. In October we were delighted to be successful in a Chan-Zuckerberg Initiative (CZI) Rare As One Cycle 3 grant, providing $800,000 over five years and integration into the Rare As One programme (https://www.cardiff.ac.uk/news/view/2873597-zuckerberg-funding-for-rare-syndrome-research-network). This grant has supercharged growth of the charity, enabling us to hire staff, a research and public engagement officer, contract to develop a research portal, and hold further in person international meetings. Alongside the announcement, we launched our public engagement film, Connections, which after a delayed development through COVID https://www.youtube.com/watch?v=A7MR3Jko17wshowcases how intrinsically linked public engagement is to research impact. Connections has gone on to win a People's Choice Award at the Smiley Charity Film Awards 2025, and is currently in the final round of judging for the Rare by Design Film Festival. For our work we were Highly Commended in the Rare Disease Research UK Inaugural Early Career Researcher Award in PPIE.

Working with a rare disease community has been hugely motivating and led me down a completely different research path to the one I envisaged at the start of my GW4-CAT PhD. As a keen and interested early career researcher I was able to contribute to the development of the charity and the community, who now challenge me with novel and interesting research questions. Success in funding and awards has been an unexpected by-product, and I would encourage any similarly staged early career researcher to consider how they could help rare disease charities. Small contributions can make a big difference, and might just be the start of a rewarding journey.