Rare genetic diseases often suffer from a lack of understanding of its pathophysiology. In case of central nervous system (CNS) diseases such as MCOPS12, malfunctioning of processes in the brain lead to the observed disease symptoms. Thanks to the pioneering work by Shinya Yamanaka and co-workers on generating **human induced pluripotent stem cells (iPSCs)** and subsequent differentiation to almost any cell type of the human body, it became possible to "create" patient specific disease models some years ago.

This complex but pivotal work has been successfully carried out by **Prof. Taylor´s research group** at the University of Basel. Since the functional cellular consequences of mutations in the *RARB* gene that cause MCOPS12 still remain unclear, it is critical to study the effects of the mutated RARB protein in all cellular contexts and paradigms. One such paradigm is to use MCOPS12 patient blood cells that we reprogram to a stem cell state, and to differentiate these in culture to defined cell-types of the body**. This reprogramming technology enables us to study the functional consequences of RARB mutations in difficult to obtain cells including neurons of the brain.** As MCOPS12 is a rare disorder, obtaining patient cells was a major challenge. However, we have been lucky enough and succeeded in generating iPSCs from Simon who is carrying the p.R387C mutation in the RARB protein.

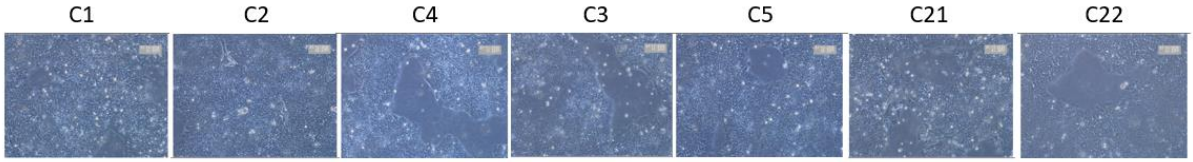

Figure 1: Seven clones of Simon`s induced pluripotent stem cells (iPSCs).

With these iPSCs in hand, we are now differentiating them into different types of neuron and glial cells of the brain to understand how this mutation affects the functions of brain cells. To achieve this, we are examining how the p.R387C mutation in the RARB protein affects gene expression, metabolic status and neuron signaling in an attempt to understand the processes that cause the symptoms associated with MCOPS12. We believe that these experiments will give us new insights into MCOPS12 and potential avenues for treatment.

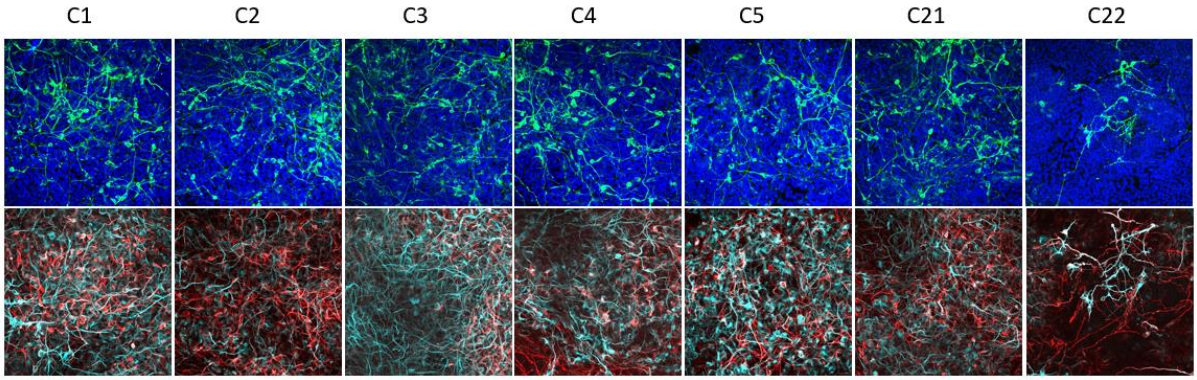

Figure 2: Seven clones of Simon`s neuron cells using different immunostaining techniques for visualization.

In addition, we hope that these iPSCs and the functional changes associated with the RARB mutations will form a platform for screening drugs to alleviate the cellular effects of the mutation. As a team of four research groups spread across Europe and Canada, we are combining clinical data and fundamental research data in a unique consortium to study RARB functions in MCOPS12.