

Cell Therapy for Myotonic Dystrophy

(Internship Project)

Myotonic Dystrophy (DM1) is a multisystemic neuromuscular disorder and the most common inheritable form of muscular dystrophy in adults. The genetic basis of DM1 is a CTG repeat expansion in the 3' untranslated region of the *DMPK* gene. The unstable trinucleotide repeat expansions cause the formation of abnormal transcripts which sequester proteins that function in transcription, splicing or RNA export. This in turn leads to disturbances in cell metabolism causing myotonia and progressive muscle weakness. At present, no treatment is available for the neuromuscular phenotype seen in DM1.

Pericytes (PCs), also known as adult mesoangioblasts (aMABs), are newly identified progenitor cells with regenerative capacity. The cells can be isolated from muscle fragments and have many characteristics that make them excellent candidates for stem cell therapy.

Research –

We started with isolation and characterization of PCs from DMSXL mice. These transgenic mice express an expanded human *DMPK* transgene and replicate several muscle symptoms of the disease. We are now in the exciting process of isolating and genetically correcting PCs from biopsy material of DM1 patients and healthy controls. These cells need to be characterized and we aim to unravel their myogenic potential.

Your project –

The human PCs need to be characterized with specific markers via immunocytochemistry and RT-qPCR. Moreover, the DM1 phenotype of muscle isolated cells should be visualized via fluorescent *in situ* hybridization (FISH), since the expanded transcripts accumulate in nuclear foci, an important disease hallmark. Finally, we should investigate myogenic fusion characteristics via differentiation cultures, microscopy and ImageJ analysis, to see whether DM1 and control PCs efficiently differentiate into multinucleated myotubes.

What we offer and expect –

We are looking for a highly motivated, persistent and communicative student. Our working culture is important to us and we appreciate that you will want to join a lab where you feel both excited by what you do and energized by the people and research around you. You will be working in a stimulating multidisciplinary setting at the departments of Human Genetics, Cell Biology and Neurology. We value people who, after being introduced to new techniques, can work independently.

Is this the internship position for you?

Convince us by sending a motivation letter and resume to Rosanne Ausems
MSc (daily supervisor), Depts of Human Genetics/Cell Biology
(Rosanne.Ausems@radboudumc.nl)

This is a joint project supervised by Dr. Rick Wansink (Dept. of Cell Biology), Prof. dr. Hans van Bokhoven (Dept. of Human Genetics) and Prof. dr. Baziel van Engelen (Dept. of Neurology)