

It takes two to tango_ a decryption of Marfan cardiomyopathy using human iPSC- derived cardiac cells and engineered heart tissues

Stem cell modeling of genetic diseases is one of the greatest achievements of the last decade. Thanks to the appropriate conditions created in the laboratory, **scientists can obtain heart or brain cells from stem cells that show symptoms similar to those observed patients.**

The aim of the project is to obtain **heart cells** (muscle and stromal cells) and **engineered heart tissue (EHT)** construct that would show the **characteristics of the heart of patients diagnosed with Marfan Syndrome (MFS)**. For this purpose, we plan to obtain induced pluripotent cells (hiPSCs) derived in the laboratory from patients suffering from this disease.

Thanks to the cooperation between the University of Ghent, where intensive research on MFS is being conducted, and the Institute of Human Genetics in Poznan whose expertise is based on the ability to produce heart tissue from hiPSC cells, it will be possible to **create a platform for an in-depth analysis of the mechanism of heart function damage in patients with MFS**. This analysis will be based on the study of two types of cells present in the heart (muscle cells and stromal cells) but also on the extracellular matrix, which, as recent studies show, seems to be much more important in the proper functioning of the heart than we initially assumed, Research will be conducted using the cutting-edge technologies such as confocal microscopy, atomic force microscopy and molecular analysis including high-throughput next-generation sequencing. We will verify how DNA variants in the fibrillin-1 gene (*FBN1*), which are the cause of Marfan syndrome, affect the functions of heart cells and its microenvironment.

Knowledge of the effects of *FBN1* gene variants and the signaling pathways involved in the development of the disease will allow us to propose **new therapeutic approaches** as well as to **explain the mechanisms** of action of drugs that are used to alleviate the symptoms associated with the malfunctioning of the cardiovascular system in patients with Marfan syndrome

