Cellular materials for organ on chip research

Giacinto Scoles (Nanotec-CNR, Lecce, Italy); Daniela Cesselli (UniUD, Udine, Italy); Denis Scaini (SISSA, Trieste, Italy)

Micro- and nano-composite materials will be considered from the point of view of the realization of organoids for applications to in-vitro diagnostics for neuro-degenerative diseases. Unfortunately, right where the realization of these devices would be more beneficial, there the difficulties are larger because the connection with

An application will be described to the diagnostics of neuro-degenerative diseases choosing the area where the methods would be more beneficial (i.e. the area innovation showing that this area is still in the Proof Of Concept (POC) stage.
We will consider a class of TAUopathies, known as Progressive Supranuclear Palsy (PSP), both in their main phenotype and in the rare PAGF phenotype i.e. Pure Akinesia with Gait Freezing that has an "abundance" of about 1 in a million individuals. Our approach involves the production of pluri-potent stem cells from the adipose tissue of a well, clinically, diagnosed individual and their subsequent differentiation to neurons. If the latter result to be diseased then the road to the cure is possible and well planned. The main difficulty is in the complexity of the brain that sees, for example, the localization of the disease in the brain stem. The method has been, however, already proven to be effective in genetic diseases but our interest involves now the more difficult case of sporadic diseases.

First, of course, we will need to measure the diseased portion of the neurons in AVERAGE which will determine the precision of the proteomics measurements that are meant to establish the diseased level of the neurons. Our goal is to-establish the level of production of protein TAU and compare it to the cells of a healthy individual

from the adipose tissue of which the neurons will be produced following a similar protocol. Two complementary approaches will be followed: (i) if the cellular dilution factor (diseased neurons over the total number of neurons obtained) will not prove to be too limiting, we will be able to proceed directly to search for the molecules that may "wash" out the extra amount of TAU. Otherwise (ii), we will need to go to the second level looking to establish the presence of disease molecular fingerprint at the single cell level establishing, in such way, the heterogeneity of the disease. At this second level of investigation we plan to use a nanopipette to be inserted into the cell and used to suck some of the fluid contained into the cell. By coating the interior of the nanopipette with nanobodies that recognize the PROTEIN of interest the latter will become trapped inside the channel of the pipette changing its value of the ionic conductivity. Next to the nanopipette there will be a reference (uncoated) pipette to provide a reference level for the ionic conductivity.