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MoDiaNo

MOlecular DIAgnostic of brain disease mutations in human embryonic stem cells derived 2D- and 3D- neuronal cultures, using intracellular naNOparticle tracking, synapse naNOscopy, and microcircuit calcium imaging

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Advances in genome sequencing technologies have facilitated the detection of de novo mutations, but the validation of their functional impact remains a challenge. This project aims to (i) develop nanotechnology-based screens of the functional impacts of pre-identified brain disease point mutations and (ii) engineer into human embryonic stem cells from which 2D neuronal cultures and 3D cerebral organoids will be derived. Our screens will rely on (i) quantification of intraneuronal transport in these 2D and 3D cultures by tracking optically active nanoparticles with very high stability, (ii) imaging of key dendritic spine proteins and actins with an automatized 3D nanoscope, and (iii) monitoring neuronal microcircuit activities in order to assess synaptic consequences of the mutations. These complementary readouts are expected to generate a molecular diagnosis of de novo mutations suitable for personalized medicine.