

MADGIC

Generation of Improved Cellular and Animal Models for Identification of Disease Phenotype and New Therapeutic Targets of Alzheimer's Disease

The mechanisms of Alzheimer's disease (AD) have remained poorly understood while common animal models have not helped in finding efficient therapies for the disease. This project aims to generate new human cellular models allowing for the purification of specific neural cell types involved in AD. We generate patient neural cells through reprogramming patients' skin cells, grow them alone or in mixed 3-dimensional cultures, and use them to address disease relevant mechanisms both in a dish and in animals after transplantation.

Such approaches will allow for the characterization of cellular dysfunction and death processes in neurons and their supporting glia cells and will help establish whether neuroinflammation by glial cells truly determines the disease progression. We will substantiate our approaches through the implementation of relevant stressors known to contribute to AD pathogenesis, considering the relationships between risk (such as aging, ischemic insults, inflammation, oxidative stress), protective factors and genetic determinants. The usefulness of our approach will be confirmed by monitoring disease progression using innovative imaging techniques. As our AD models are based on human cells, they are clinically relevant and are expected help lead to the development of early diagnosis and the design of drugs and the application of personalized treatments for people suffering from AD.

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