DEMENTIA
RESEARCH

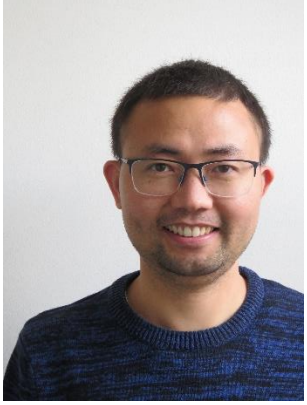
SYNAPSIS FOUNDATION SWITZERLAND

Career Development Award

Project

«Dissecting phagocytosis-deficient microglia in Alzheimer's and Prion diseases via genome-wide CRISPR screens»

Granted amount	CHF 200'000
Starting date	1.2.2022
Duration	24 months



Main applicant

Dr. Jiang-An Yin
Institute of Neuropathology
University of Zurich/University Hospital
Schmelzbergstrasse 12
8091 Zurich

Gaining new insights in the role of microglia in neurodegenerative diseases

Microglia are immune cells in the brain and major players for the clearance of protein aggregates, which are considered major drivers of neurodegenerative diseases (NDs). Loss of microglia phagocytotic capability has been described in patients with NDs, however, the factors resulting in this impairment, as well as the role of phagocytosis-deficient microglia in neurodegeneration are poorly understood.

Here we propose to utilize our newly generated human genome-wide CRISPR libraries to perform genome-wide screenings to address the above questions. We will first recapitulate the impaired phagocytotic activity of human microglia via Aβ treatment, and subsequently perform both genome-wide pooled CRISPR activation and knockout screenings to identify modifiers that restore the phagocytotic activity of the cells.

To assess the functional role of phagocytosis-deficit microglia in neurodegeneration, we will genetically impair the phagocytotic capability of microglia and microglial genes with our newly generated CRISPR libraries and investigate their further consequences on neurodegeneration.