DEMENTIA
**RESEARCH**

SYNAPSIS FOUNDATION SWITZERLAND

# Principal Investigator Grant

## Project

Janine Reichenbach:
"Development of gene therapy for granulin-related neurodegeneration"

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| **Granted amount** | CHF 200'000 |
| **Starting date** | 1.3.2024 |
| **Duration** | 24 months |


**Main applicant**

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**Development of gene therapy for granulin-related neurodegeneration**

Mutations of the granulin (GRN) gene cause reduction or complete absence of progranulin (PGRN) protein. This in turn leads to two fatal neurodegenerative diseases – frontotemporal dementia (FTD) and neuronal ceroid lipofuscinosis-11 (CLN11), respectively. Brain microglia cells are the main producers of PGRN and thus play a major role in both diseases.

We aim at developing gene therapy for these neurodegenerative diseases, based on correction of patient's hematopoietic stem cells (HSC) that are isolated from the blood. These HSC are treated in the laboratory with a gene therapy vector to introduce a normal GRN gene. After reinfusion into the patients' blood, gene-corrected HSC engraft the bone marrow and provide a continuous source of blood and immune cells derived from them, including microglia(-like) cells that can migrate to the brain and normalise PGRN production. Previously, we tested the vector in disease models including microglia and HSCs, proving its efficacy in reconstituting PGRN expression.

To prepare a clinical gene therapy trial in FTD and CLN11 patients, in this project we will evaluate its efficacy against neurodegeneration in vivo in a mouse model of PGRN deficiency. These results will lay the essential grounds for further clinical development of gene therapy for GRN-related neurodegeneration.