



## Principal Investigator Grant

### Project

«Augmentation of basal forebrain gamma oscillations in a rat model of Down syndrome (DS) as novel therapeutic approach for DS and Alzheimer disease»

**Granted amount** CHF 300'000

**Starting date** 1.5.2023

**Duration** 36 months



### Main applicant

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### Lay summary of the project

Individuals with Down syndrome (DS) have a high likelihood of developing Alzheimer disease (AD) with age, but the underlying mechanisms are at present unknown.

We hypothesize that impaired brain gamma oscillations, triggered by the basal forebrain and transmitted to the cortical mantle, underlie cognitive deficits in DS and vulnerability to AD. We further posit that cortical structures belonging to the default mode network are crucially affected by impaired gamma oscillations.

We propose to use a recently developed DS rat model to delineate functional relationships between basal forebrain and cortical projection targets, as well as identify specific functions of identified neural circuits. We then use continuous chronic, wireless, cell-type specific optogenetic activation to trigger gamma oscillations in target circuits. We hypothesize that this manipulation should slow or halt DS disease progression and AD development in terms of behaviour, brain circuit activity and marker aggregation.