# Utilization of TALEN technology to investigate the microRNA dependence of PD-associated defects in neural stem cell activity.

https://neurodegenerationresearch.eu/survey/utilization-of-talen-technology-to-investigate-the-microrna-dependence-of-pd-associated-defects-in-neural-stem-cell-activity/

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**Country**

Luxembourg

**Title of project or programme**

Utilization of TALEN technology to investigate the microRNA dependence of PD-associated defects in neural stem cell activity.

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FNR

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€ 174,744

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4

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**Research Abstract**

Parkinson’s disease (PD) is not only characterized by the classically known degeneration of dopaminergic neurons. Instead other characteristics like hyposmia, depression and anxiety are frequently observed in PD patients. Interestingly, these non-motor symptoms are likely to be caused by a deregulated activity of adult neural stem cells. Differentiation of neural stem cells is controlled by the activity of microRNAs. Additionally, accumulating evidences suggest that

microRNAs are deregulated at the onset of PD. Generation of mature microRNAs largely depends on the activity of the proteins Drosha and Dicer. In the here described project we aim on investing the global importance of microRNAs for the development of PD. Therefore, we will make use of transcription activator-like effector nuclease (TALENs) in combination with homologous recombination to introduce two kinds of mutations in human induced pluripotent stem cells (hiPSCs):I) Introduction of a Stop-Codon early in the genomic sequence of the genes Drosha or Dicer ? This will lead to a deficiency for mature microRNAs.II) Introduction of PD-associated point mutations in the gene LRRK2 in the background of the Dicer or Drosha deficient hiPSCs. My working hypothesis is that neural stem cells carrying mutations in LRRK2 (G2019S or R1441G/H) that are additionally deficient for Drosha or Dicer should develop early onset and/or very severe PD associated cellular phenotypes. Thereby, these cells would represent an ideal tool to address whether the exogenous addition of one or several microRNAs would be sufficient to rescue these cellular phenotypes. Consequently, these effective microRNAs might become therapeutically relevant.

**Further information available at:**

https://www.fnr.lu/projects/utilization-of-talen-technology-to-investigate-the-microrna-dependence-of-pd-associated-defects-in-neural-stem-cell-activity-2/

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