oo570 Generation of Isogenic Human G2019S Parkinson's Disease Model

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Aims: To dissect the molecular functions of LRRK₂ G₂₀₁₉S mutations in Parkinson's disease.

Methodology: An isogenic stem cell line of G2019S based on H9 human ES cell line was created using CRISPR technology. The stem cell lines were systematic characterized and directed differentiated into dopaminergic neurons. The mitophagy and autophagy functions were studied and compared to control lines.

Result: Two homogeneous stem cell line with G2019S mutation were created. They displayed stem cell markers expression and gene expression profile. Mature dopaminergic neurons were induced from these isogenic lines. The G2019S neurons showed inhibition of LRRK2 kinase activity and defects in mitophagy and autophagy functions. These isogenic lines can be served as an in vitro Parkinson's disease model and used for drug screening.

Conclusion: The G2019S isogenic lines showed the typical features of Parkinson's disease, and can be served as an in vitro Parkinson's disease model and used for mechanism study and drug screening.