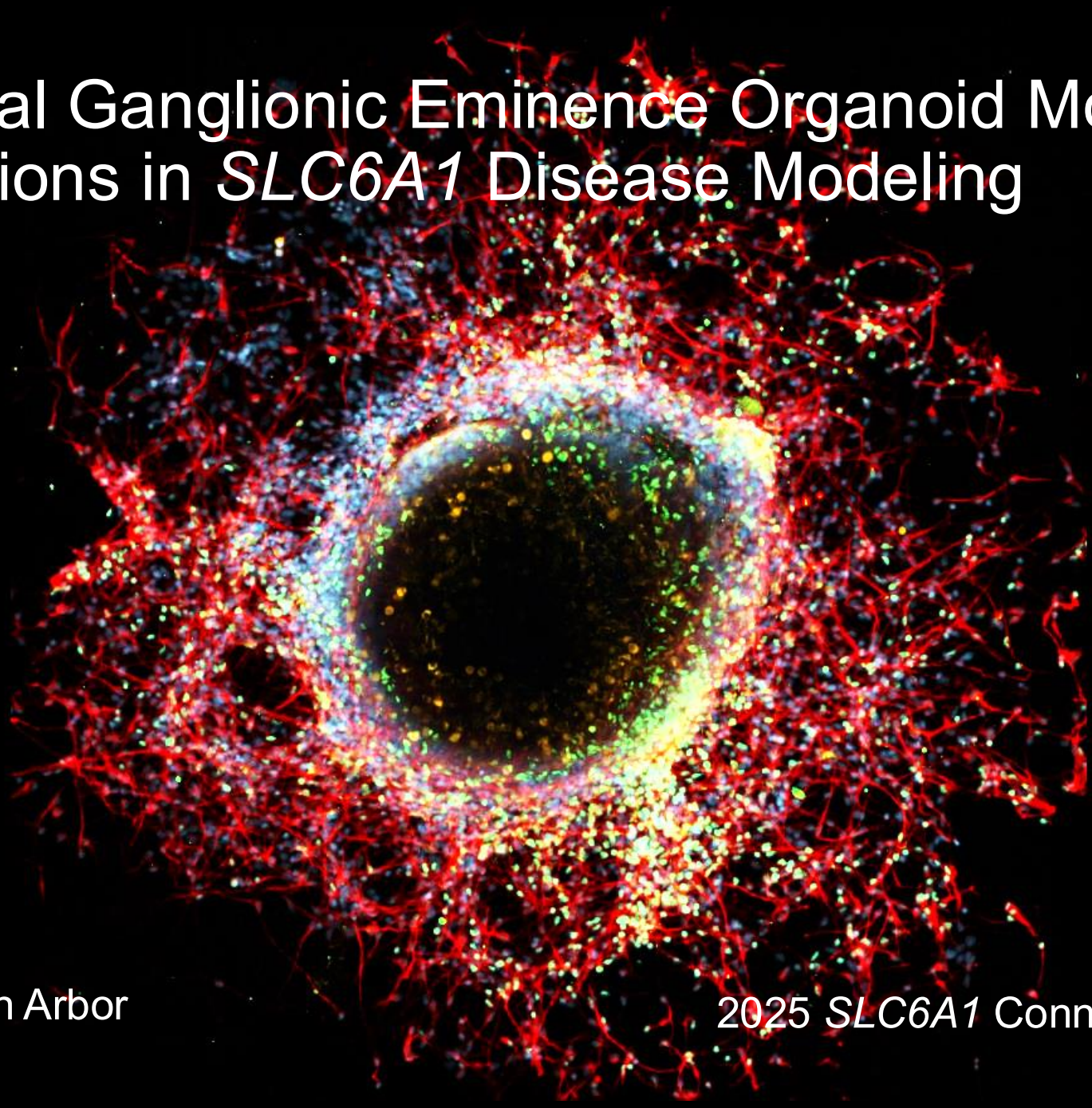
# A Human Medial Ganglionic Eminence Organoid Model: Applications in *SLC6A1* Disease Modeling



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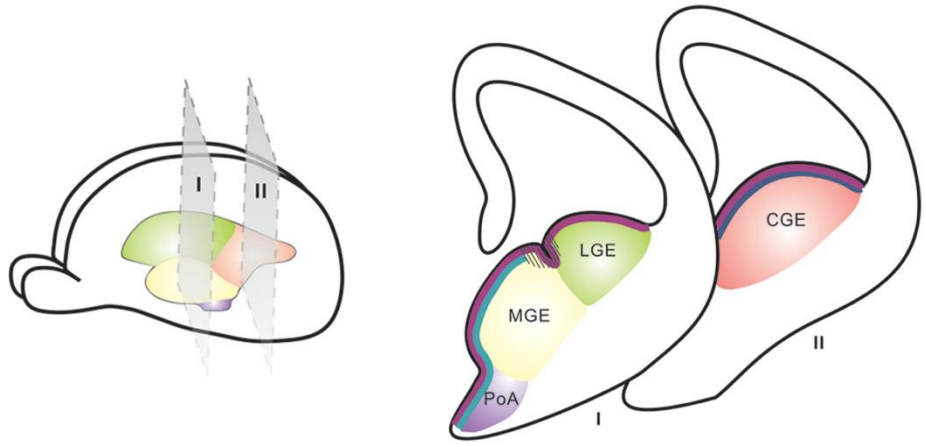
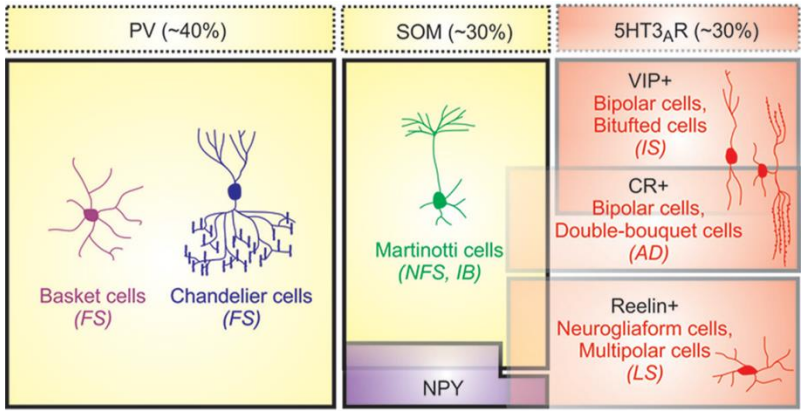
# Outline

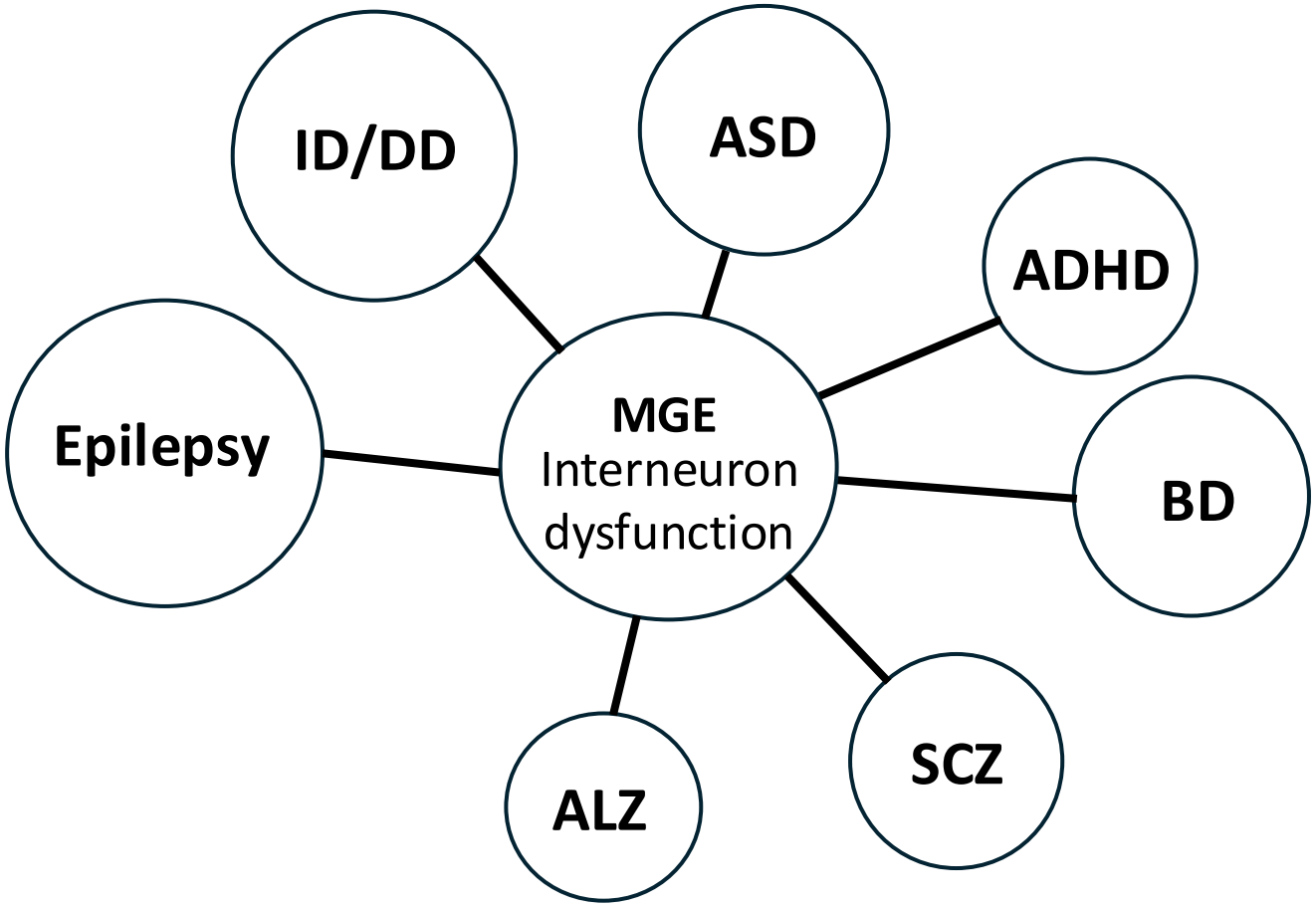
- Importance of the medial ganglionic eminence (MGE)in development
- Introduction to single rosette organoids
- Generating an MGE-like organoid
- Modelling *SLC6A1*
- Migration deficits in *SLC6A1* interneurons
- Future applications in DEE disease modelling

# Medial Ganglionic Eminence in Development

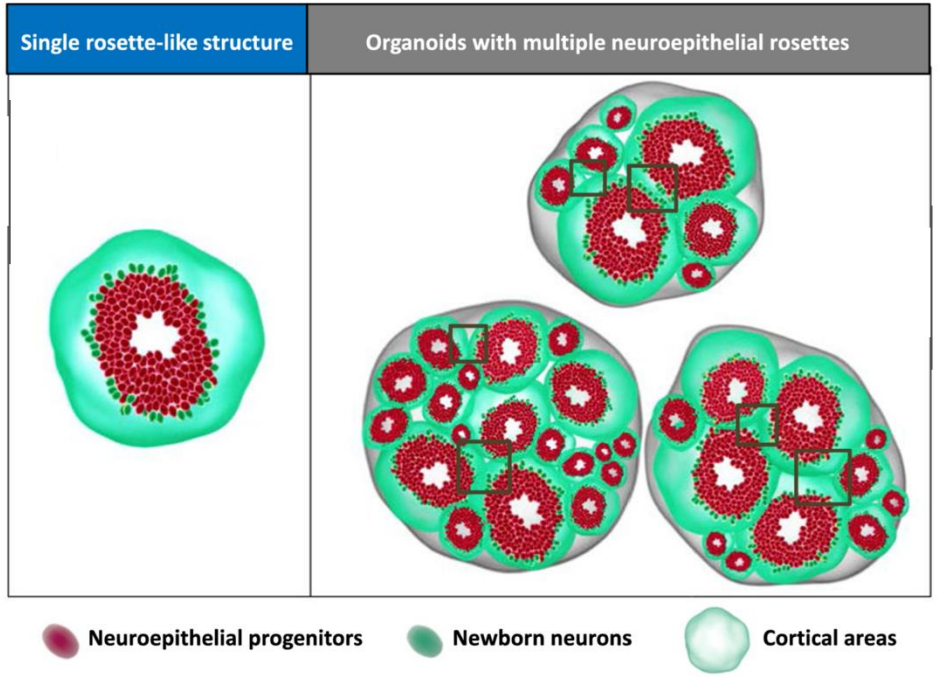


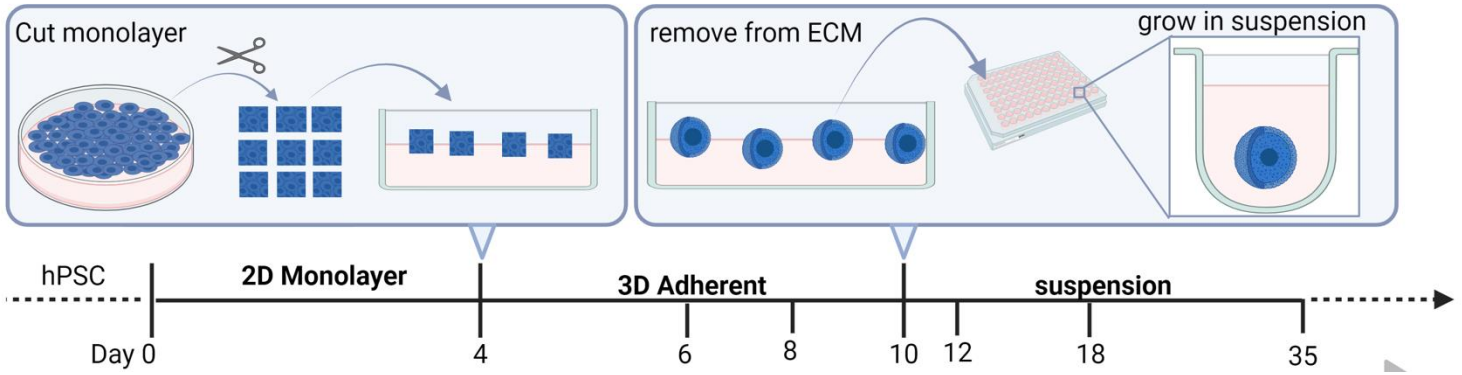

Adapted from Sultan et al., 2013

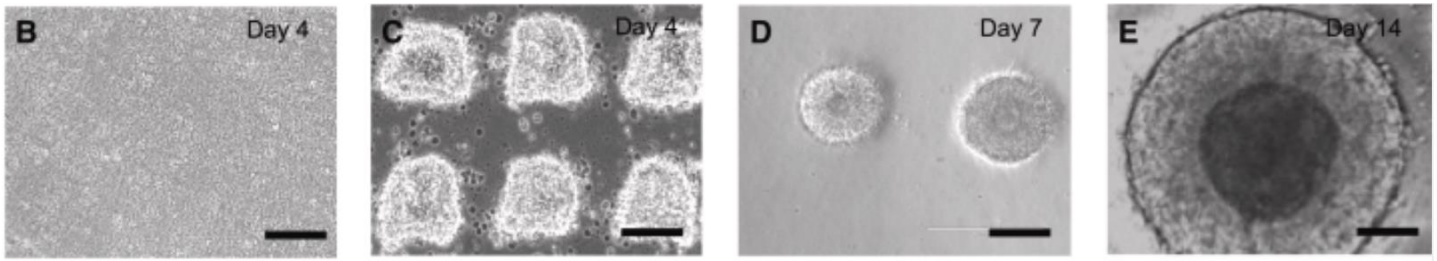


# Single rosette organoid as a platform for medial ganglionic eminence organoid (MGEO) development

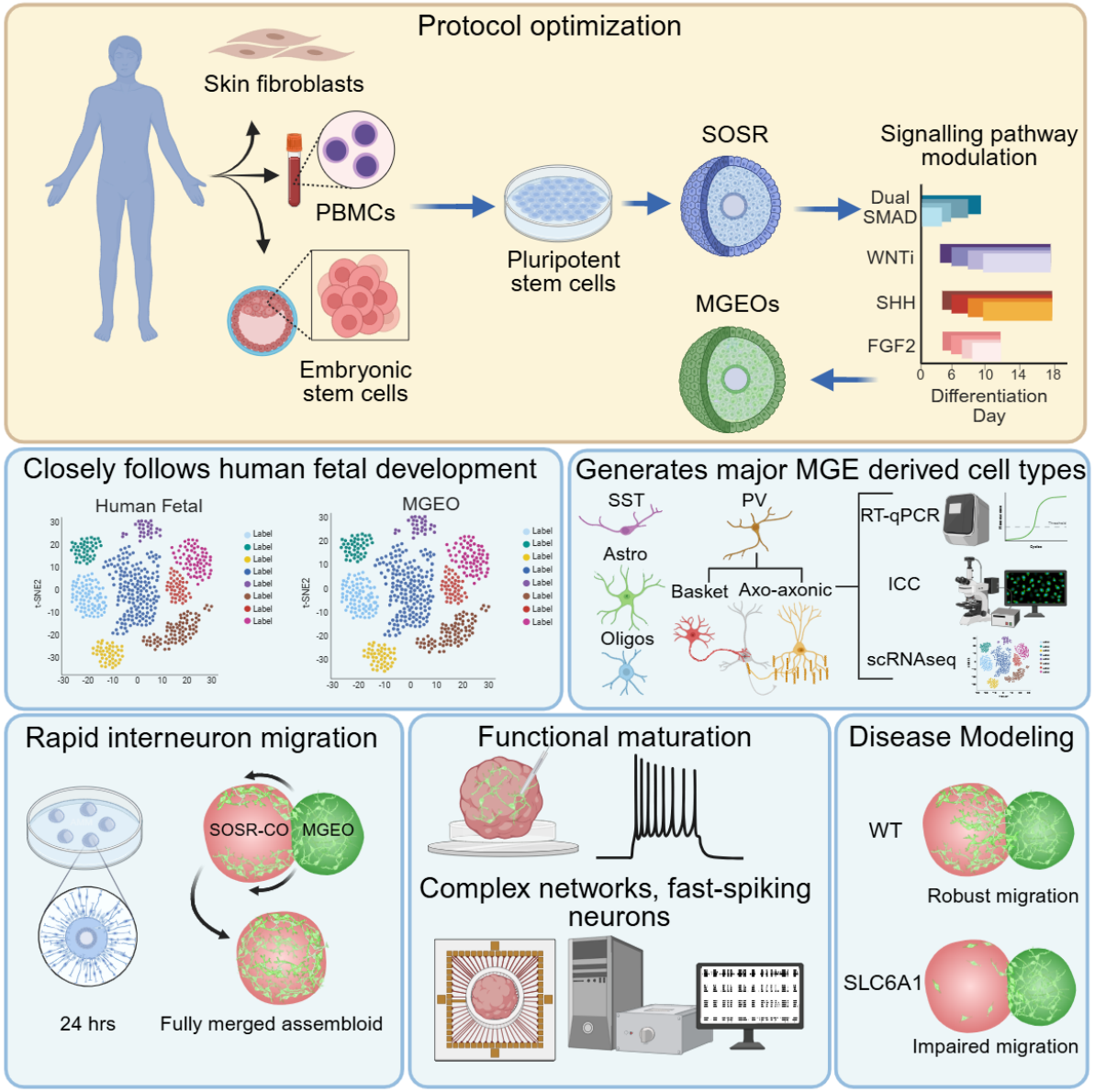



Adapted from Lee et al., 2017

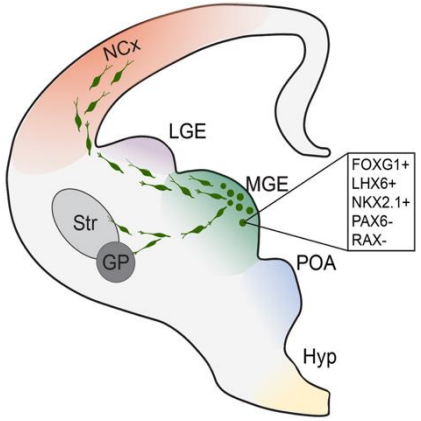


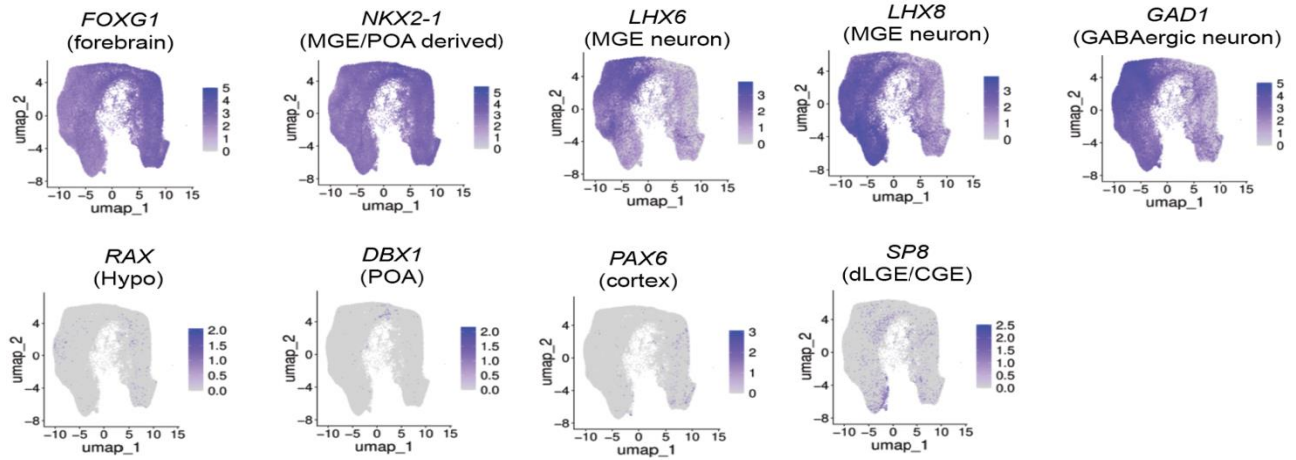



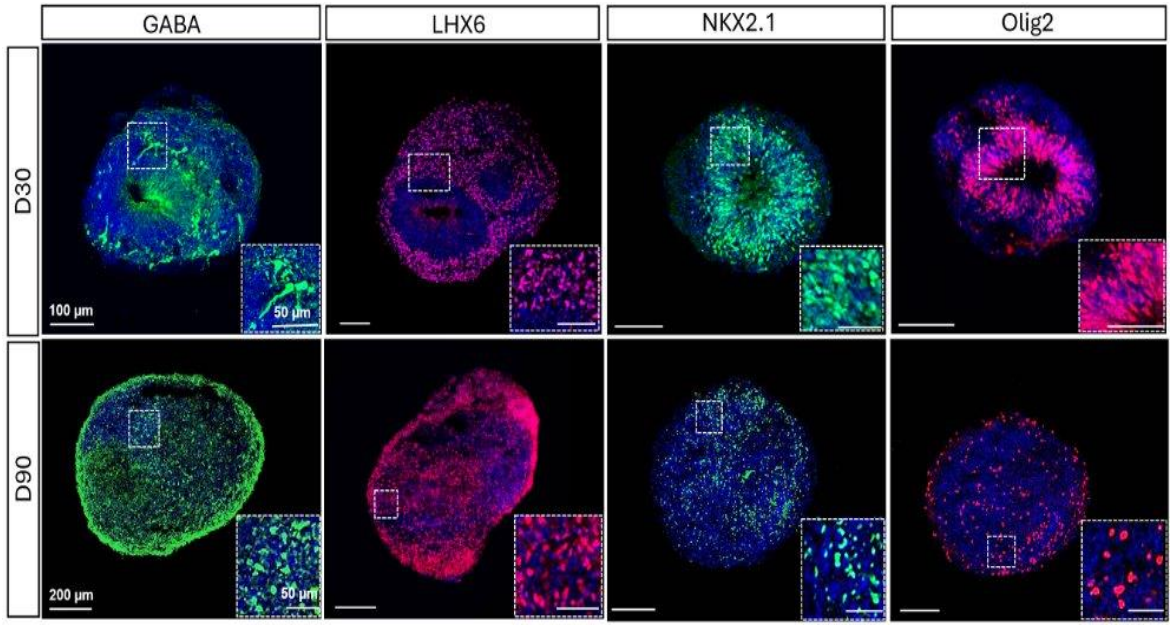
# Development of a medial ganglionic eminence organoid

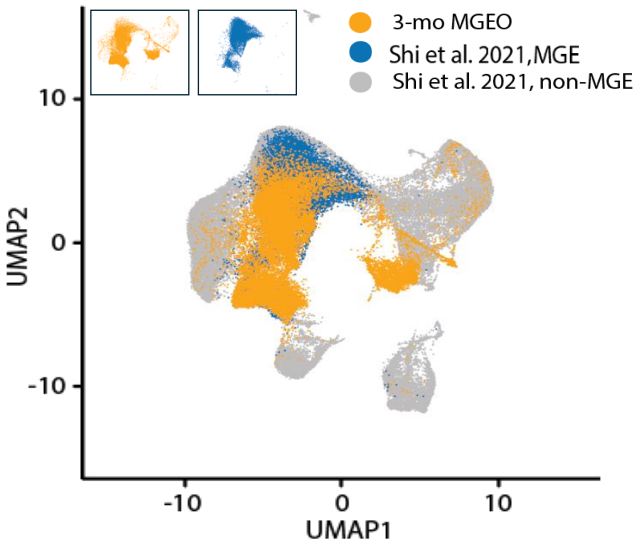


# MGEOs display MGE regional Identity



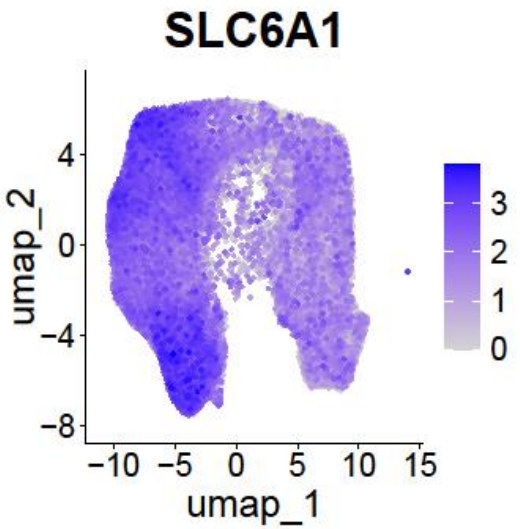



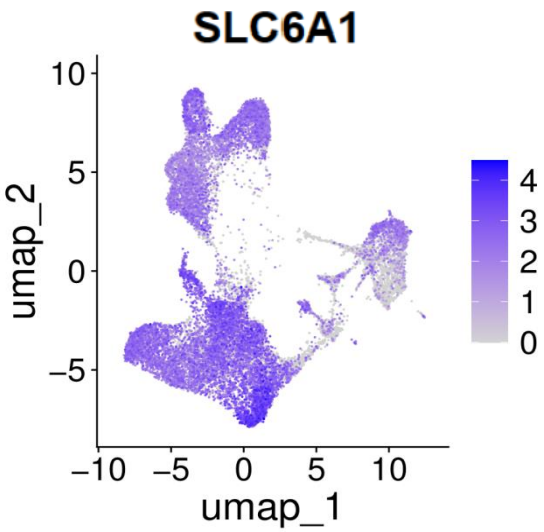



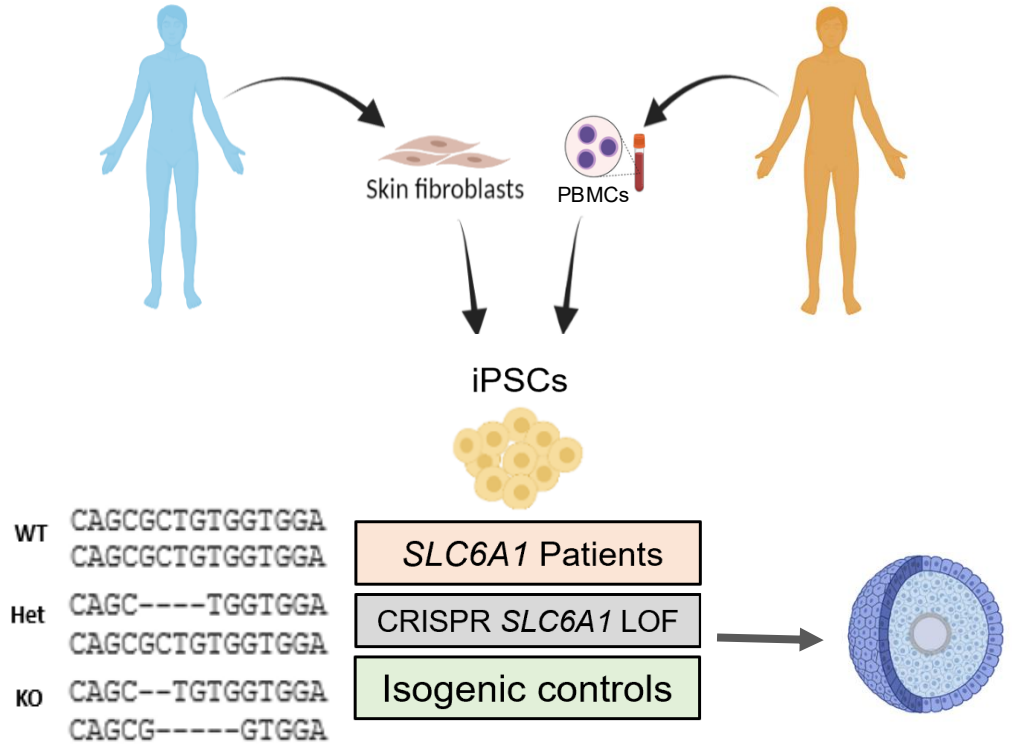
# MGEOs as a disease model for *SLC6A1*

**1 Month MGEOs**

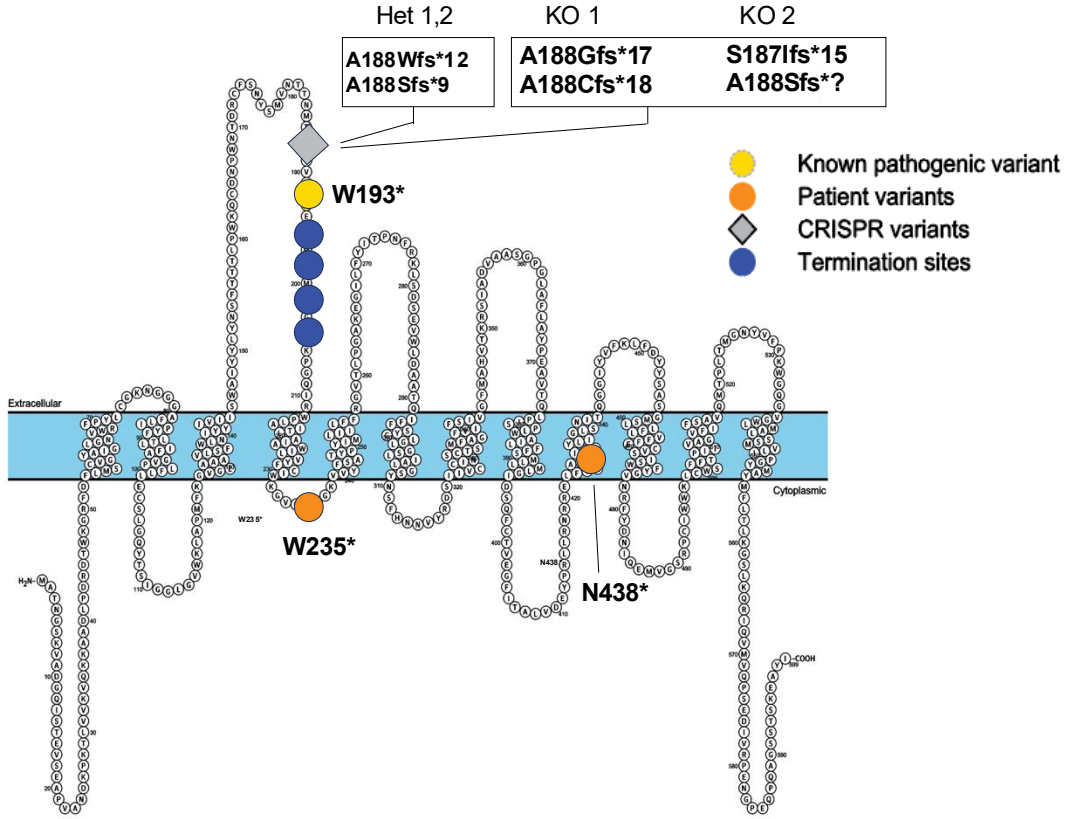


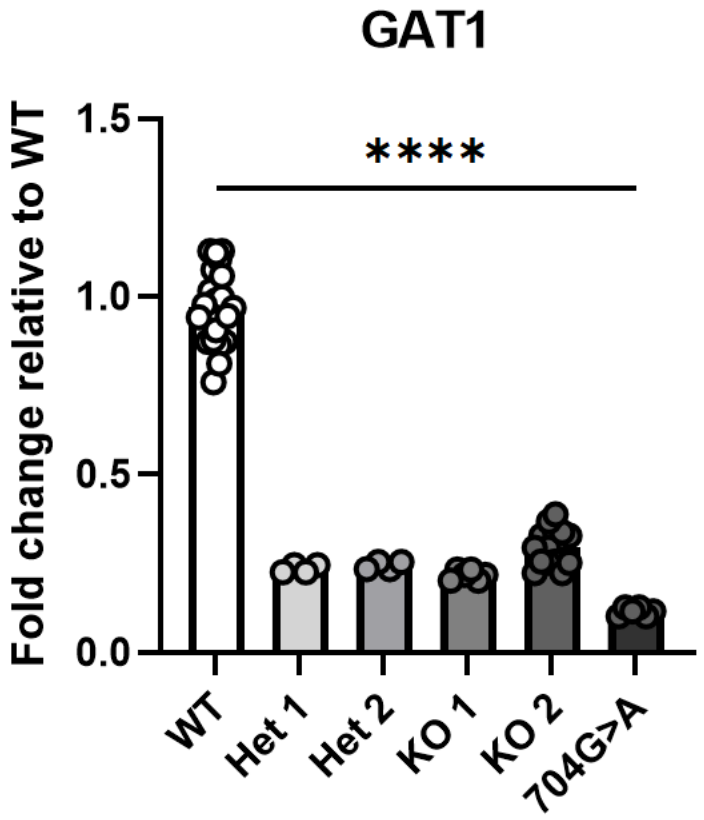

**3 Month MGEOs**



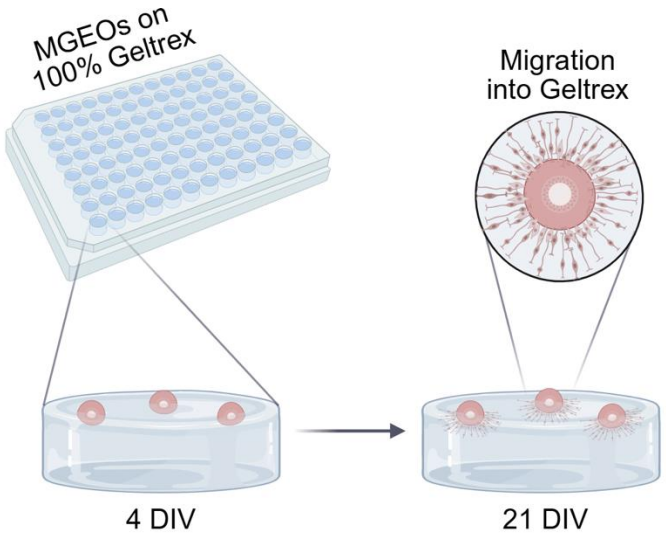



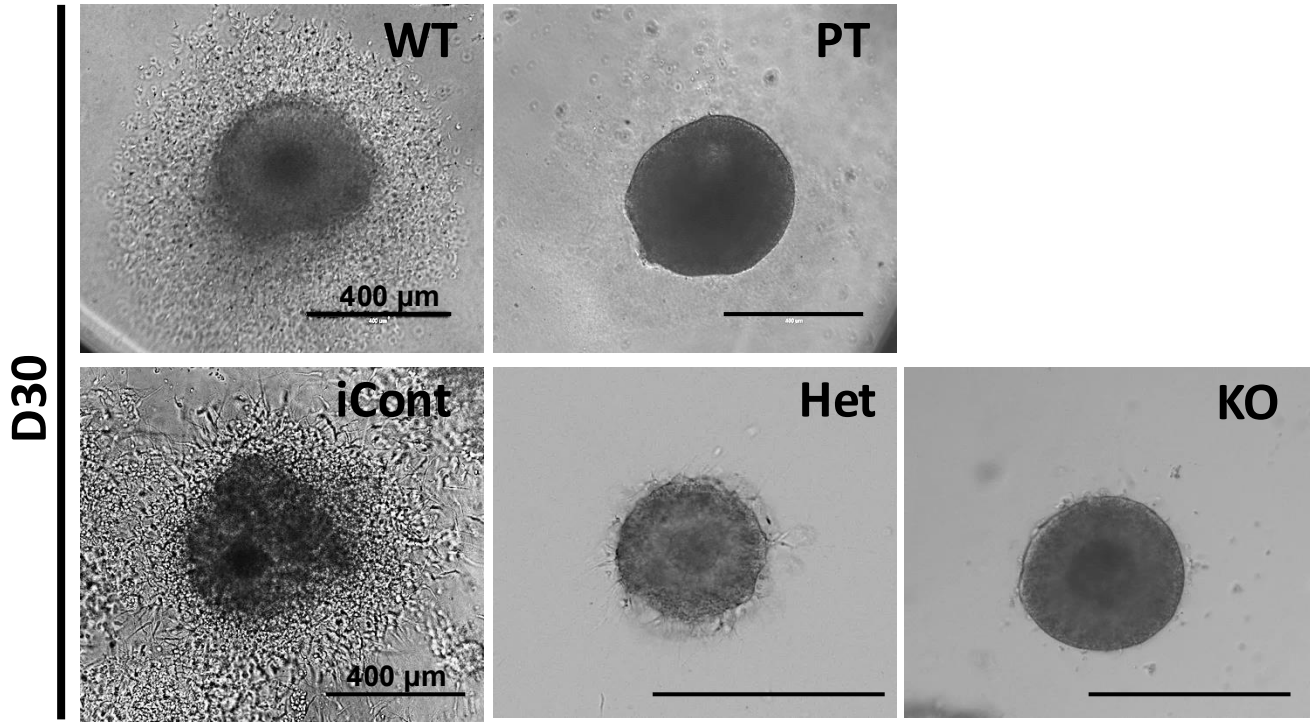
# SLC6A1 patient and CRISPR iPSC lines

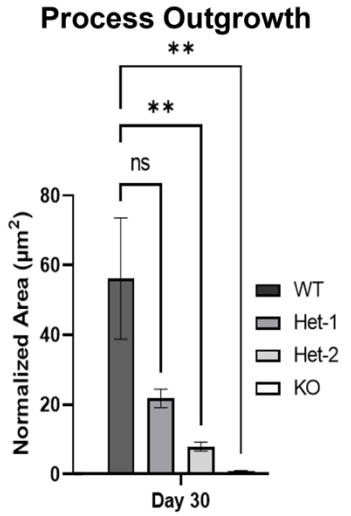


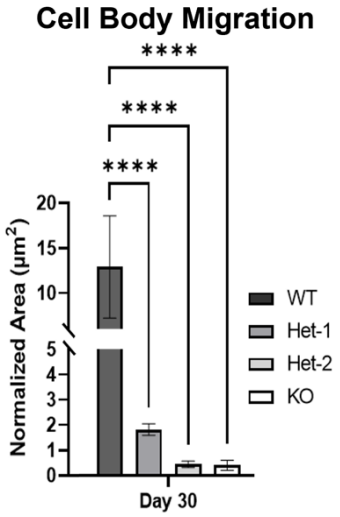



# Unexpected migratory deficits in *SLC6A1* MGEOs

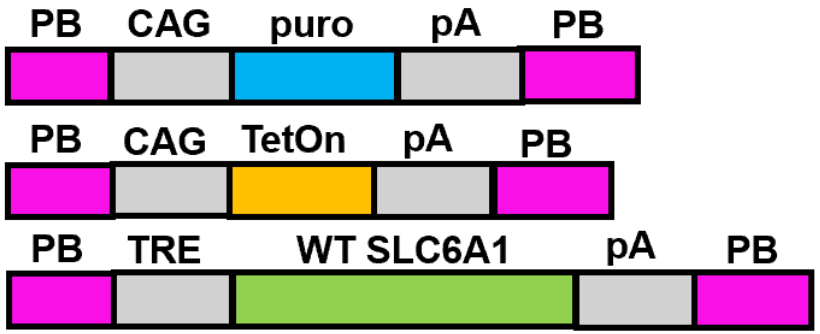


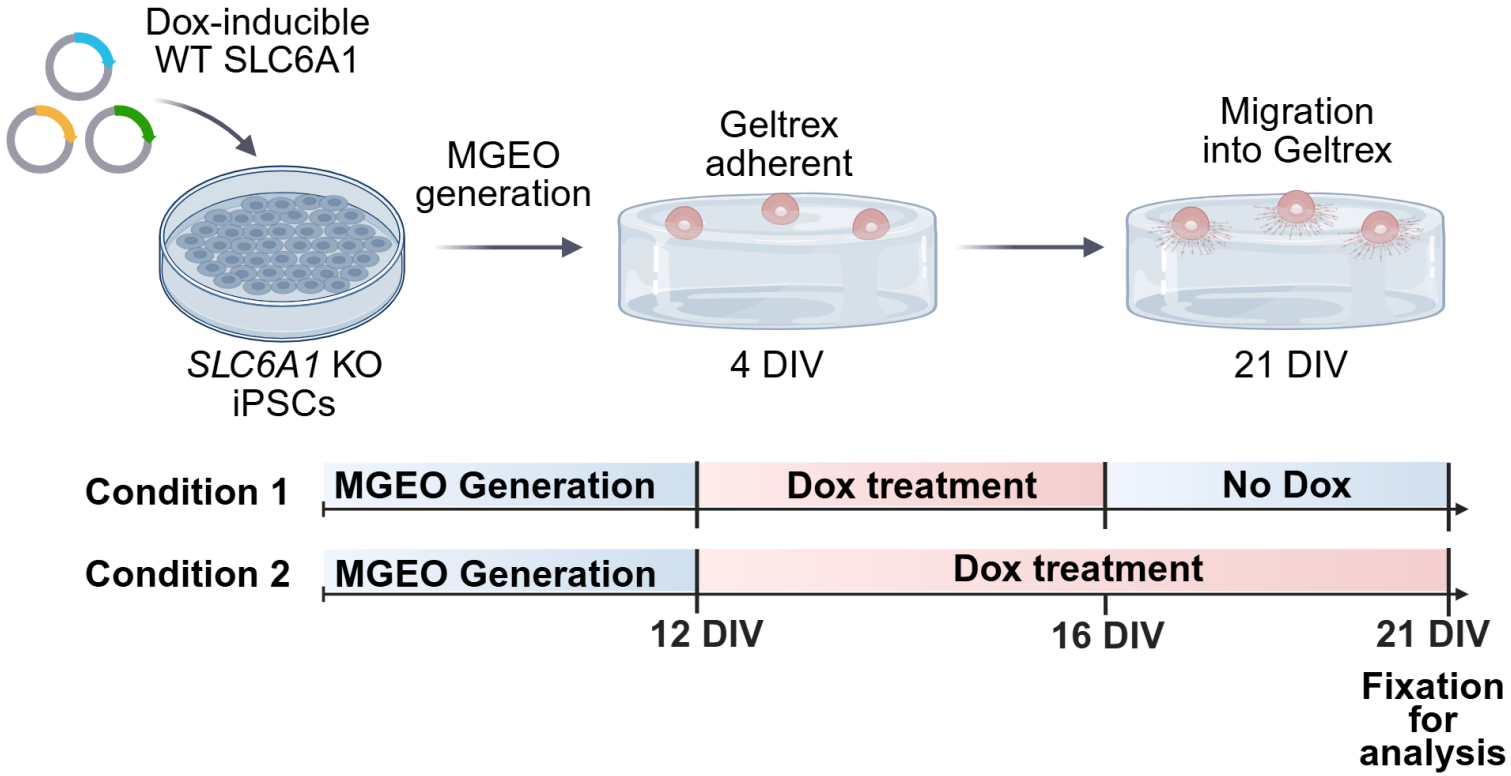



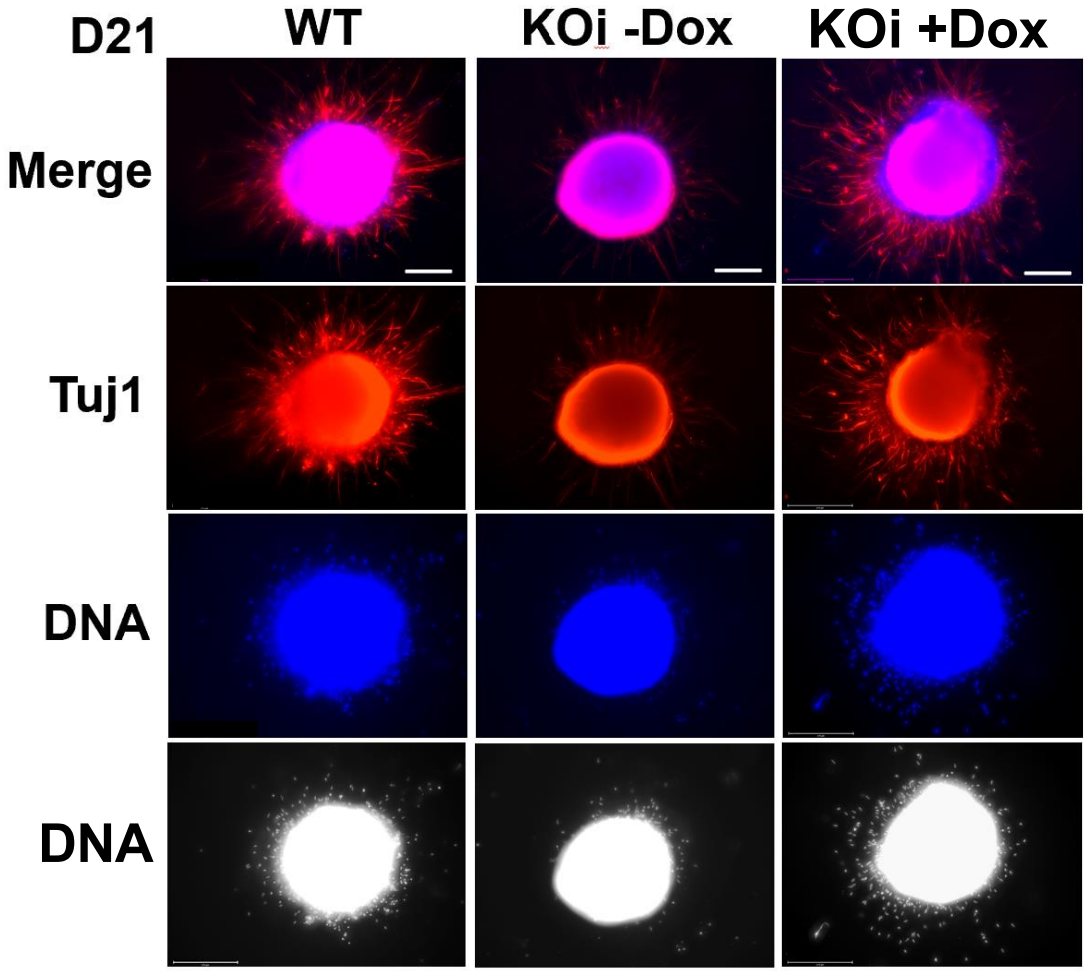



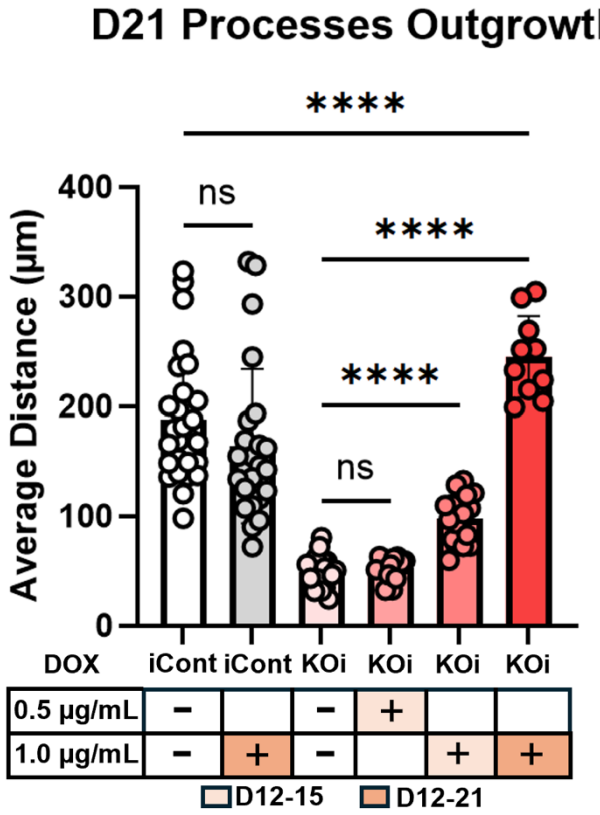
# Wildtype GAT1 rescues migratory deficits

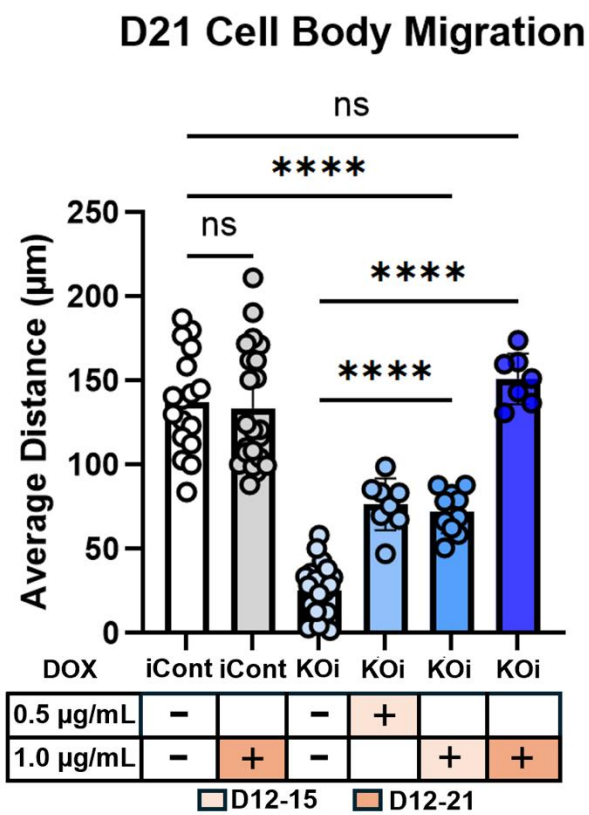


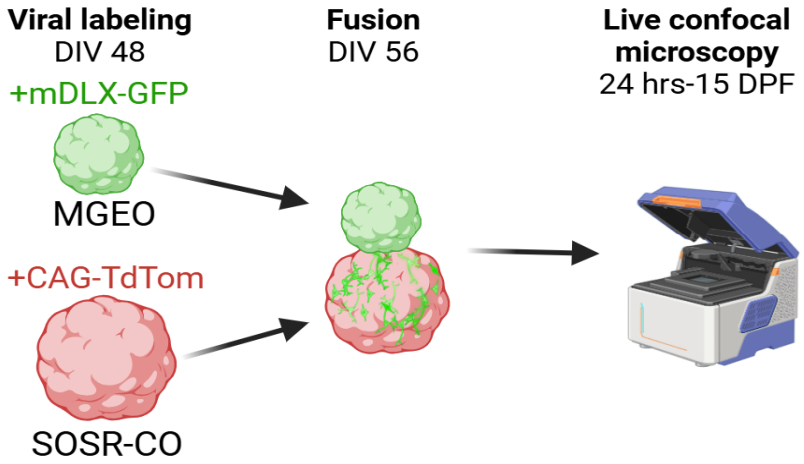
# GAT1 rescue is dose- and duration-dependent

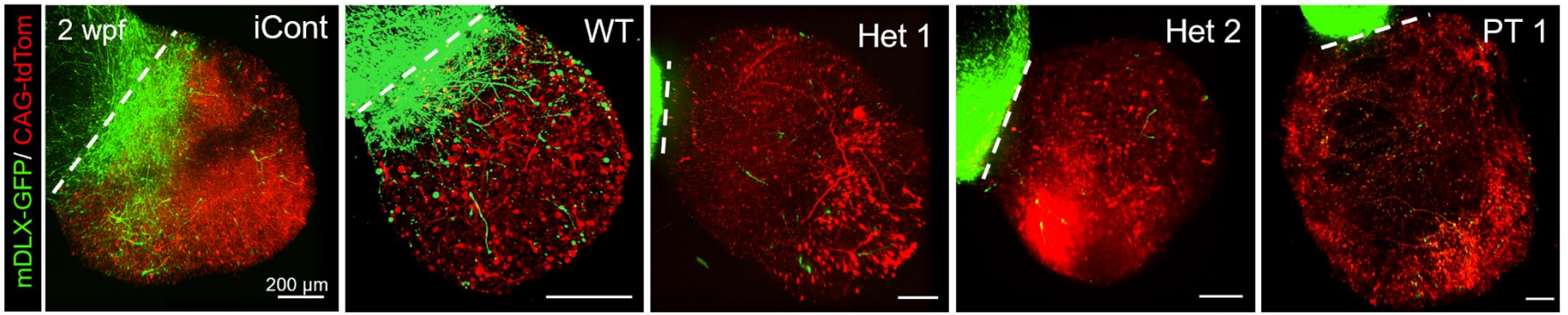


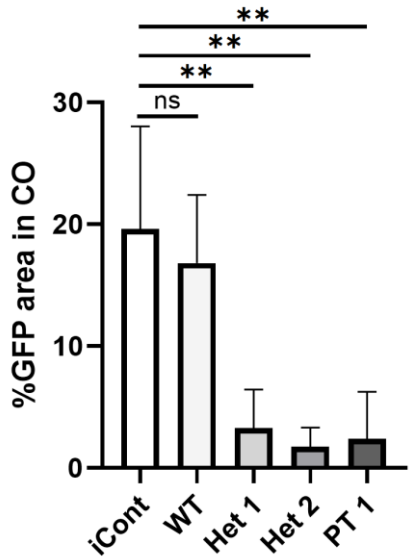



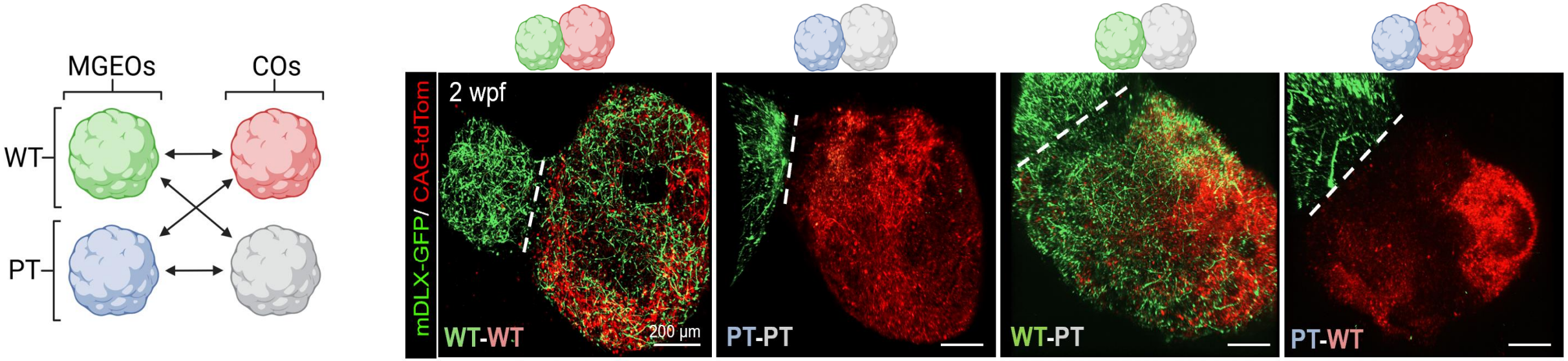
# Migration deficits in Cortical-MGEO assembloids



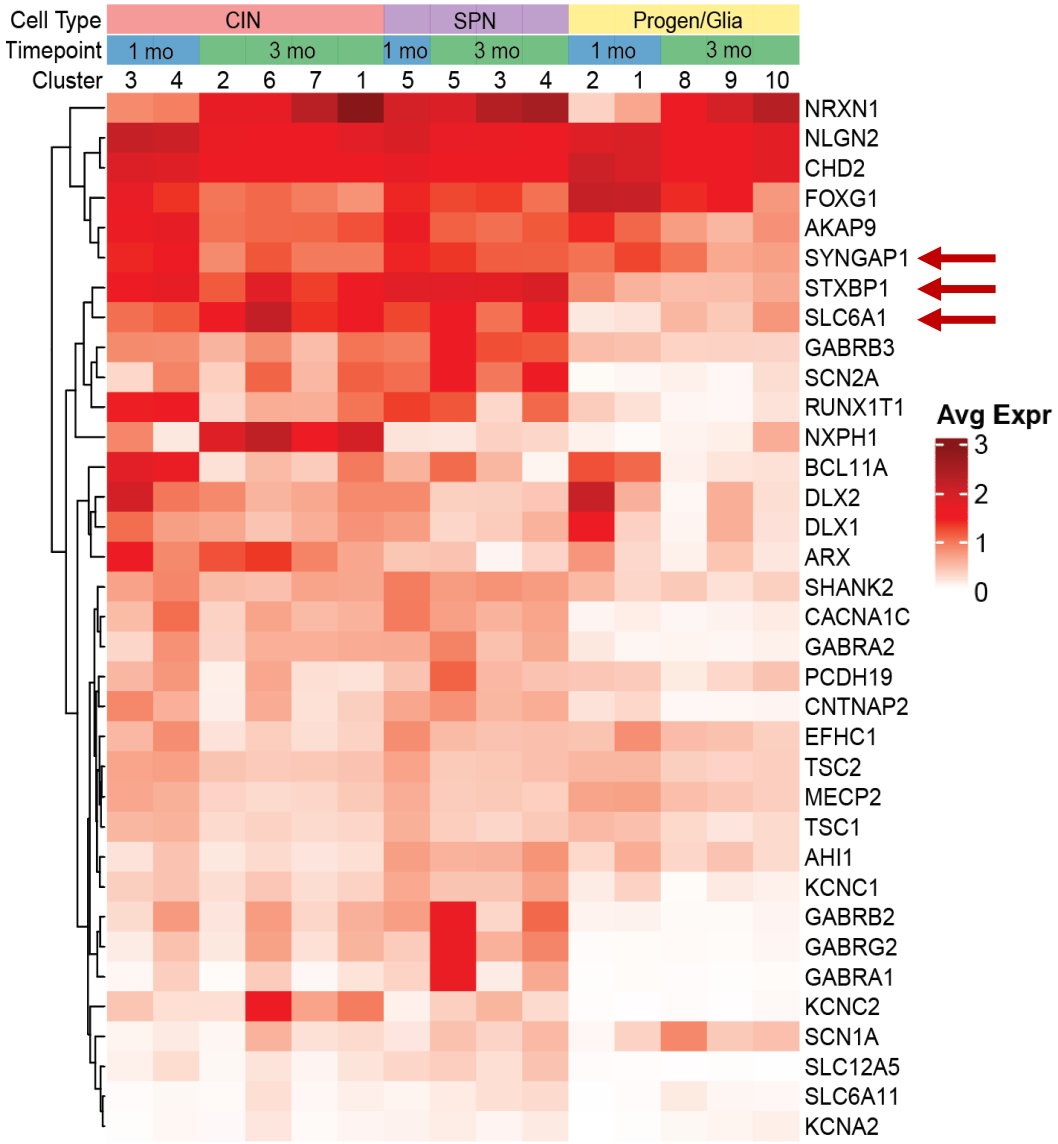



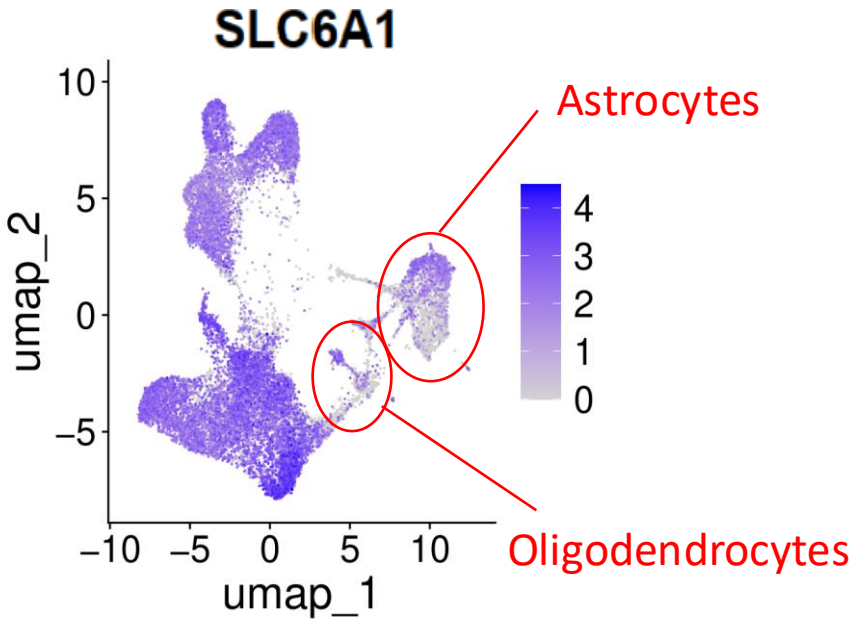



# *SLC6A1* Migratory deficits are cell autonomous



# Applications of MGEOs in DEE disease modelling



# Summary

- MGEOs closely resemble the human MGE during development
- MGEOs produce interneurons with high *SLC6A1* expression which is also expressed in MGEO astrocyte and oligodendrocyte populations.
- MGEO models of *SLC6A1* reveal an interneuron migration deficit which is fully rescued by the expression of WT GAT1 in KO MGEOs.
- Observed migration deficits are cell autonomous.
- Impaired migration on interneurons could lead to dysregulation of cortical network which contribute to the pathogenesis of *SLC6A1* DEE.
- MGEOs provide a useful tool for modelling *SLC6A1 as well as other* DEE genes in interneurons, astrocytes, and oligodendrocytes.
- Platform for drug screening, gene therapy, or cell-based therapies

# Acknowledgements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-Sami Barmada


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The Parent Lab


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* Select schematics made with BioRender