

GBA D409V KI Mouse Model

GBA D409V KI mice have a knock in of the D409V mutation in the murine GBA gene at exon 10, which corresponds to the D409V mutation in the mature human GBA protein. The gene is driven by the murine GBA promoter. Mice additionally contain loxP sites flanking exons 6 to 8 of the GBA gene, so it is possible to knockout this gene segment.

Pathological characteristics of GBA D409V KI mice:

GBA D409V KI mice

- Severely decreased GCase levels in the brain and liver at 4 months
- Severely increased glucosylsphingosine levels in the brain and liver at 4 months
- Severely increased α -Synuclein levels at 12 months



GBA D409V/+ mice (12 months of age)

- Highly reduced GCase levels in the hippocampus and cortex
- Increased activated microglia and astrogliosis levels in the hippocampus
- Decreased synaptophysin and vAChT levels in the hippocampus
- Increased CHAT levels in the hippocampus
- Neither α -Synuclein aggregates nor pSer129 α -Synuclein in the hippocampus
- Cognitive impairments in the Morris Water Maze and Y-Maze
- No motor deficits

Due to the association of the GBA1 gene to Parkinson's disease, the model is also valuable for crossbreeding studies with Parkinson's disease mice to model GBA-associated Parkinson's disease.

References:

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Burballa et al., 2019 Oct 16;11(514):eaau6870. doi: 10.1126/scitranslmed.aau6870.