# Microglia Replacement Therapy for CNS Diseases

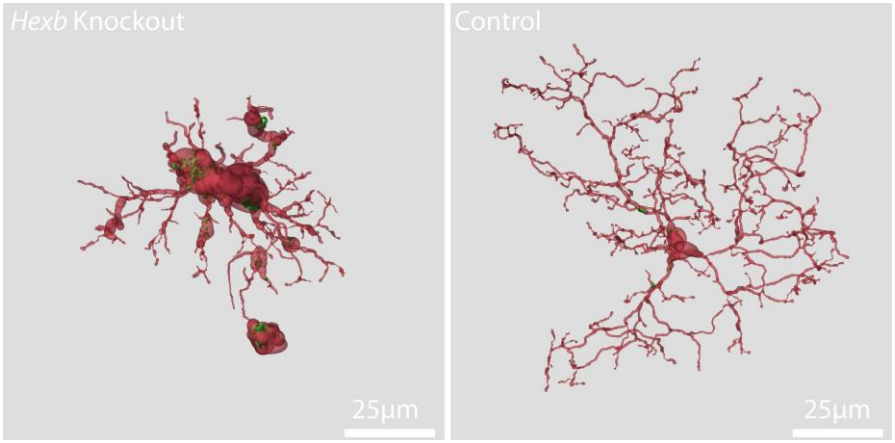
## Innovative CSF1R-based method replaces dysfunctional microglia with healthy bone marrow cells in lysosomal storage disorders exemplified by Sandhoff disease

# Technology

The invention develops a therapeutic method for CNS disorders, demonstrated using a Sandhoff disease mouse model. HEXB-mutated microglia are replaced throughout the entire central nervous system with healthy microglia.

Sandhoff disease is a rare hereditary lysosomal storage disorder (LSD) caused by HEXB gene defects, leading to β-hexosaminidase enzyme deficiency and GM2 ganglioside accumulation in neurons. Autosomal recessive inheritance gives affected children (25% risk if both parents are carriers) a rapidly progressive, fatal course, primarily in infancy (death by age 2-3), juvenile, or late-onset forms with motor/cognitive decline, seizures, and spasticity. Currently untreatable.

Microglia replacement therapy, tested in Sandhoff model, uses CSF1R inhibitor BLZ945 to deplete mutant microglia followed by i.v. healthy bone marrow cell injection. Achieved 80-100% CNS-wide replacement, full survival, and prevention of severe motor symptoms (vs. controls). Applicable to LSDs, Alzheimer's, Parkinson's, MS, schizophrenia, autism, depression; adapts established bone marrow transplant protocols.

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## Innovation

- **CNS-wide Microglia Replacement Therapy:** First complete exchange of dysfunctional microglia with healthy bone marrow cells throughout brain and spinal cord.
- **Selective CSF1R Depletion:** BLZ945 specifically eliminates mutated microglia (80-100% efficiency) without blood-brain barrier damage – preparing for transplantation.
- **Causal Cure Validated:** Complete survival and symptom-free outcome in lethal Sandhoff mouse model; extendable to Alzheimer's, MS, LSDs

## Application

- **Primary Application:** Treatment of Sandhoff disease through CNS-wide replacement of mutated HexB microglia with healthy donor cells.
- **Extended Indications:** Therapy for neurodegenerative diseases like Alzheimer's, Parkinson's, MS, and neuropsychiatric disorders (autism, schizophrenia).

## Development Status

- Early stage

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