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Blastocyst microglia complementation for in vivo microglia manipulation and validation of gene function

Stanford scientists have developed an accurate, rapid, and efficient tool for in vivo microglial manipulation to validate gene functions after transcriptomic analysis.

Microglia heterogeneity and function in health and disease remains an important and elusive question. RNA Sequencing has revolutionized the transcriptomic analysis of microglia, and the scientific community has churned out large RNA-sequencing microglial datasets. However, follow-up studies manipulating microglia in vivo to validate functions inferred from RNA-sequencing data are needed. Current tools for microglial manipulation include various genetically modified mouse models, all of which are time-intensive and are infeasible for screening multiple candidate genes from transcriptomic datasets if one is financially- and space-constrained. There is a need for an efficient tool that allows accurate microglial manipulation in vivo to validate transcriptomic analysis findings.

Stanford scientists, therefore, developed a non-human animal comprising chimeric microglia and precise methods of performing blastocyst microglia complementation to produce non-human chimeric animals. These methods can be used to create a non-human animal model carrying microglia mutations of interest for gene validation and therapeutic screening.

By injecting pluripotent stem cells (PSCs, e.g., ES cells or iPS cells) into mouse embryos that cannot produce microglia, it is possible to create mice in which all microglia are derived from PSCs during natural development. By injecting PSCs with various genetic modifications, the effects of genetic modifications on microglial development and function can be studied.

Stage of Development
Proof of concept

Applications

- Method for chimeric animal generation.
- Microglial manipulation for research purposes.

Advantages

- Animals can be prepared within four months. Faster than current methods.
- Can proceed with multiple target genes at the same time.
- Efficient gene manipulation
- Accurate
- Specific

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