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# Researchers discover origin of immune cells in the brain

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Mount Sinai researchers have discovered that microglia, the immune cells that reside in the brain, have a unique origin and are formed shortly after conception. It was previously thought that microglia originated at the same time as macrophages, which are other immune cells that are thought to develop at birth. This groundbreaking discovery has the potential to lead to future treatments of degenerative brain diseases such as Alzheimer's and autoimmune diseases such as multiple sclerosis. The study is published online October 21 in *Science Express*.

Microglia are thought to play an important role in the development of many brain diseases, and that defective microglia could lead to the release of inflammatory molecules, which could participate in the development of degenerative brain diseases.

"This really is a startling discovery," said Miriam Merad, MD, PhD, Associate Professor of Gene and Cell Medicine at Mount Sinai School of Medicine and Principal Investigator of the study. "We've shown that the precursor cells develop into microglia only during a short period after conception. Now that we know that microglia originate in early embryos, theoretically we should be able to generate microglia from embryonic stem cells to treat brain diseases caused by defective microglia. This is a very good example of why scientists need to be able to conduct research with embryonic stem cells."

For the first part of the study, researchers transplanted blood cell precursors, which are precursors for all macrophages, from one newborn

mouse to another. The transplanted cells could not be differentiated in the recipient animal. These results suggest that microglia originated prior to birth during embryonic life.

Next, researchers used a mouse model that expresses fluorescent biosensors in blood precursors to determine when, during embryonic age, precursors develop into microglia. Once activated the fluorescence does not go away and all cells that develop from the fluorescent precursors should remain fluorescent. The researchers activated the fluorescence as early as seven days after conception. When they examined adult mice they found fluorescent microglia but no fluorescent macrophages. These results established that microglia are unique in that they originate from precursors that arise around seven days after conception.

"Moving forward we need to further study the normal development of precursor blood cells into microglia, which should help identify the role of microglia in various brain diseases and ultimately lead to advances in treatments," said Dr. Merad.

Provided by The Mount Sinai Hospital