

Familial Alzheimer's disease transferred via bone marrow transplant in mice

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A painting representing Alzheimer's transmissibility as reported in this *Stem Cell*

Reports study. Credit: Chaahat Singh

Familial Alzheimer's disease can be transferred via bone marrow transplant, [researchers show](#) in the journal *Stem Cell Reports*. When the team transplanted bone marrow stem cells from mice carrying a hereditary version of Alzheimer's disease into normal lab mice, the recipients developed Alzheimer's disease—and at an accelerated rate.

The study highlights the role of amyloid that originates outside of the brain in the development of Alzheimer's disease, which changes the paradigm of Alzheimer's from being a disease that is exclusively produced in the brain to a more systemic disease.

Based on their findings, the researchers say that donors of blood, tissue, organ, and stem cells should be screened for Alzheimer's disease to prevent its inadvertent transfer during blood product transfusions and cellular therapies.

"This supports the idea that Alzheimer's is a systemic disease where amyloids that are expressed outside of the brain contribute to central nervous system pathology," says senior author and immunologist Wilfred Jefferies, of the University of British Columbia.

"As we continue to explore this mechanism, Alzheimer's disease may be the tip of the iceberg and we need to have far better controls and screening of the donors used in blood, organ and [tissue transplants](#) as well as in the transfers of human derived stem cells or blood products."

To test whether a peripheral source of amyloid could contribute to the

development of Alzheimer's in the brain, the researchers transplanted bone marrow containing stem cells from mice carrying a familial version of the disease—a variant of the human amyloid precursor protein (APP) gene, which, when cleaved, misfolded and aggregated, forms the [amyloid plaques](#) that are a hallmark of Alzheimer's disease. They performed transplants into two different strains of recipient mice: APP-knockout mice that lacked an APP gene altogether, and mice that carried a normal APP gene.

In this model of heritable Alzheimer's disease, mice usually begin developing plaques at nine to 10 months of age, and behavioral signs of [cognitive decline](#) begin to appear at 11 to 12 months of age. Surprisingly, the transplant recipients began showing symptoms of cognitive decline much earlier—at six months post-transplant for the APP-knockout mice and at nine months for the "normal" mice.

"The fact that we could see significant behavioral differences and cognitive decline in the APP-knockouts at six months was surprising but also intriguing because it just showed the appearance of the disease that was being accelerated after being transferred," says first author Chaahat Singh of the University of British Columbia.

In mice, signs of cognitive decline present as an absence of normal fear and a loss of short and long-term memory. Both groups of recipient mice also showed clear molecular and cellular hallmarks of Alzheimer's disease, including leaky blood-brain barriers and buildup of amyloid in the brain.

Observing the transfer of disease in APP-knockout mice that lacked an APP gene altogether, the team concluded that the [mutated gene](#) in the donor cells can cause the disease and observing that recipient animals that carried a normal APP gene are susceptible to the disease suggests that the disease can be transferred to health individuals.

Because the transplanted stem cells were hematopoietic cells, meaning that they could develop into blood and immune cells but not neurons, the researchers' demonstration of amyloid in the brains of APP knockout mice shows definitively that Alzheimer's disease can result from amyloid that is produced outside of the central nervous system.

Finally the source of the disease in mice is a human APP gene demonstrating the mutated human gene can transfer the disease in a different species.

In future studies, the researchers plan to test whether transplanting tissues from normal mice to [mice](#) with familial Alzheimer's could mitigate the disease and to test whether the disease is also transferable via other types of transplants or transfusions and to expand the investigation of the transfer of disease between species.

"In this study, we examined bone marrow and [stem cells](#) transplantation. However, next it will be important to examine if inadvertent transmission of disease takes place during the application of other forms of cellular therapies, as well as to directly examine the transfer of disease from contaminated sources, independent from cellular mechanisms," says Jefferies.

More information: Conclusive Demonstration of Iatrogenic Alzheimer's Disease Transmission in a Model of Stem Cell Transplantation, *Stem Cell Reports* (2024). [DOI: 10.1016/j.stemcr.2024.02.012](#). [www.cell.com/stem-cell-reports ... 2213-6711\(24\)00049-3](#)

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