STEM CELLS

A good nose for stem cells

Cells can be delivered to the rodent brain noninvasively, via the nasal cavity.

Stem cell–based therapy is predicated on delivering cells to the afflicted part of the body. Researchers now show that there may be an alternative to direct surgical transplant for delivery of cells to the brain.

Almost two decades ago, William Frey, director of the Alzheimer's Research Center at what is now Regions Hospital, in St. Paul, Minnesota, showed that it is possible to use an intranasal route to deliver therapeutic proteins directly to the brain. More recently, he and Lusine Danielyan tested whether this route could be used for cells. In experiments done in Danielyan's lab at the University Hospital of Tuebingen, the researchers administered fluorescently labeled mesenchymal stem cells or human glioma cells to the upper nasal cavity of adult mice or young rats, respectively. They observed a measurable number (hundreds to thousands) of labeled cells in the olfactory bulb, the hippocampus, the thalamus and the cerebral cortex within an hour after administration of 3×10^5 cells.

Proteins delivered by the intranasal route bypass the blood-brain barrier and access the brain by passing through the cribriform plate, a perforated bone that separates the nasal mucosa from the olfactory bulb. It is likely, say Frey and Danielyan, that cells delivered intranasally also follow this route. "The stem cell field," says Frey, "is plagued by the problem of delivery." In addition to being noninvasive, and therefore potentially safer and less costly, intranasal delivery can be used for repeat dosing and avoids the inflammation associated with invasive methods.

A potential disadvantage could be that the cells are not targeted to specific areas of the brain. However, as stem cells are known to migrate to sites of neuroinflammation, specific targeting mechanisms may not be necessary to achieve functional effects in disease models.

Is this route of cell delivery likely to work in humans? Frey thinks there is little doubt. Proteins pass from the nasal cavity to the brain in humans as well. Moreover, Danielyan explains, there is reason to believe that such cell movements happen in nature: gonadotrophin-secreting neurons migrate from the nasal mucosa to the brain during human embryonic development, and there are reports of direct infection of the human brain with amoeba and bacteria via the nasal route. It remains to be seen whether intranasally delivered cells can have functional effects, but if they do, the approach may prove useful for studying animal models of disease as well as eventually for cell-based therapy.

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RESEARCH PAPERS

Danielyan, L. *et al.* Intranasal delivery of cells to the brain. *Eur. J. Cell Biol.* **88**, 315–324 (2009).