

# Noninvasive intranasal stem cells bypass the blood-brain barrier to target the brain to treat Parkinson's disease, stroke, MS, brain tumors, cerebral ischemia, Alzheimer's and other CNS disorders

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Together with my collaborators in Germany, especially Lusine Danielyan M.D., we discovered and patented (1) that therapeutic cells, including adult stem cells and genetically-engineered cells, can be non-invasively delivered to the CNS using the noninvasive intranasal delivery method that I developed (2). The first of our scientific papers on this new discovery describes this successful method of delivery and proprietary formulations that enhance delivery (3). The second of our papers describes the successful treatment of Parkinson's disease in an animal model with intranasal adult bone marrow derived mesenchymal stem cells (4).

Intranasal stem cells bypass the blood-brain barrier to target the brain by traveling extracellularly along the olfactory neural pathway with minimal delivery to other organs. Once in the brain, adult stem cells target the damaged areas of the brain specifically to treat the underlying disease (4). Researchers at University Medical Center Utrecht in the Netherlands have demonstrated the effectiveness of intranasal stem cell treatment technology in an animal model of neonatal cerebral ischemia (5) and also in animals with neonatal brain damage (6) and subarachnoid hemorrhage (6a).

Researchers at Emory University have used our intranasal stem cell treatment successfully in an animal model of stroke (7), and researchers at Uppsala University in Sweden have demonstrated that intranasal T regulatory cell therapy delivered and targeted the cells to the brain and efficiently suppressed ongoing inflammation in an EAE model of multiple sclerosis leading to reduced disease symptoms (8). Intranasal adult neural stem cells have also been shown to improve the EAE model of MS (9) as have intranasal mesenchymal stromal cells (10).

Other researchers have reported that intranasal stem cells target and treat brain tumors (11, 12). This intranasal delivery, targeting and treatment technology can make stem cell treatments practical for CNS disorders by eliminating the need for invasive neurosurgical implantation of cells and by eliminating the need for intravenous delivery that disperses cells throughout the body resulting in unwanted systemic exposure. This delivery and treatment method can facilitate the development of stem cell and genetically-engineered cell therapies for Parkinson's, PSP, Huntington's, Alzheimer's, MS, epilepsy, stroke, neonatal ischemia, brain tumors, traumatic brain injury (TBI), spinal cord (SCI) injury, etc.

In humans, GnRH neurons or Gonadotropin-releasing hormone expressing neurons are known to reach the brain by using this same olfactory neural pathway during development. In addition, pathologic cells, such as the amoeba *Naegleria fowleri*, are known to enter the brains of humans by this same pathway and cause amoebic infection of the brain. We have discovered how to use this pathway to deliver therapeutic cells, including stem cells, to the brain to treat disorders of the central nervous system. This intranasal therapeutic cell delivery, targeting and treatment technology is available for licensing.

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