

Mesenchymal stem cells for the treatment of neurodegenerative disease.

Journal:	Regen Med
Publication Year:	2010
Authors:	N Joyce, G Annett, L Wirthlin, S Olson, G Bauer, J A Nolte
PubMed link:	21082892
Funding Grants:	Sustained siRNA production from human MSC to treat Huntingtons Disease and other neurodegenerative disorders, UC Davis Stem Cell Training Program

Public Summary:

Mesenchymal stem cells/marrow stromal cells (MSCs) are currently being tested in US FDA-approved human clinical trials for many diseases. They have been extensively tested and proven effective in preclinical studies that were done in small and large animal models. There is currently a great deal of interest in the use of MSCs to treat neurodegenerative diseases, in particular for those that are fatal and difficult to treat, such as Huntington's disease and amyotrophic lateral sclerosis. For these applications, MSCs would be best delivered directly into the brain or spinal cord, since they cannot cross the intact blood brain barrier effectively. Upon transplantation into the brain, MSCs promote endogenous neuronal growth, decrease apoptosis, reduce levels of free radicals, encourage connections between damaged neurons and regulate inflammation, primarily through factors that they secrete. MSCs transplanted into the brain have been demonstrated to promote functional recovery by producing factors that induce survival and regeneration of host neurons. Clinical trials for MSC injection into the CNS to treat traumatic brain injury and stroke are currently ongoing. The current data in support of applying MSC-based cellular therapies to the treatment of neurodegenerative disorders are discussed.

Scientific Abstract:

Mesenchymal stem cells/marrow stromal cells (MSCs) present a promising tool for cell therapy, and are currently being tested in US FDA-approved clinical trials for myocardial infarction, stroke, meniscus injury, limb ischemia, graft-versus-host disease and autoimmune disorders. They have been extensively tested and proven effective in preclinical studies for these and many other disorders. There is currently a great deal of interest in the use of MSCs to treat neurodegenerative diseases, in particular for those that are fatal and difficult to treat, such as Huntington's disease and amyotrophic lateral sclerosis. Proposed regenerative approaches to neurological diseases using MSCs include cell therapies in which cells are delivered via intracerebral or intrathecal injection. Upon transplantation into the brain, MSCs promote endogenous neuronal growth, decrease apoptosis, reduce levels of free radicals, encourage synaptic connection from damaged neurons and regulate inflammation, primarily through paracrine actions. MSCs transplanted into the brain have been demonstrated to promote functional recovery by producing trophic factors that induce survival and regeneration of host neurons. Therapies will capitalize on the innate trophic support from MSCs or on augmented growth factor support, such as delivering brain-derived neurotrophic factor or glial-derived neurotrophic factor into the brain to support injured neurons, using genetically engineered MSCs as the delivery vehicles. Clinical trials for MSC injection into the CNS to treat traumatic brain injury and stroke are currently ongoing. The current data in support of applying MSC-based cellular therapies to the treatment of neurodegenerative disorders are discussed.

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