

## **Mesenchymal Stem Cells are Helpful with Behavioral Deficits in the YAC128 HD Mouse**

Mesenchymal stem cells (MSCs) are emerging both as a potential treatment and as a possible vector for other treatments in Huntington's Disease. MSCs travel towards damaged or dying cells. They 'query' each cell and if a chemical signal is received indicating that the cell is in trouble, they merge with the cell and heal and protect it through neurotrophic factors which are found naturally within the stem cells. They also can be used as a vector for other treatments.

In 2009, we interviewed Dr. Jan Nolte about her plans to use MSCs in a Phase I trial for Huntington's Disease patients. Before filing for trial approval with the FDA she was required to provide primate safety data. That study has now been completed successfully and she is working on the application. If all goes well in the Phase I trial, future plans include adding BDNF and using MSCs as a vector for RNA interference.

A new study conducted by Dr. Gary Dunbar and colleagues supports the idea that MSCs have promise for the treatment of Huntington's Disease. Working with four month old mice, the researchers compared six groups. The four experimental groups of YAC128 mice were those treated with mesenchymal stem cells alone, with MSCs that were genetically engineered to overexpress BDNF (brain derived neurotrophic factor), with MSCs that were genetically engineered to overexpress NGF (nerve growth factor), or with both. The two control groups were YAC128 and normal mice both of which were treated with a placebo (the vehicle solution without the MSCs).

They found that mice in all of the treatment groups had fewer incidents of clasping, an abnormal behavior found in HD mice but not normal ones. This appears to be a result of improvement in early cellular dysfunction since only the BDNF groups were associated with reduced neuronal loss.

Only the mice treated with BDNF improved their performance on the rotarod compared to untreated HD mice. The rotarod is a standard measure of movement. In addition, only the BDNF groups had increased neuronal survival. Since decline in rotarod performance is correlated with neuronal loss this suggests that this improvement is a result of increased neuronal survival. The mice were sacrificed at thirteen months so animal survival data is not available.

The study provides additional support that MSCs may be useful both as therapy and as vectors for other therapeutic agents.

### **Reference:**

Nicholas D. Dey, Matthew C. Bombard, Bartholomew P. Roland, Stacy Davidson, Ming Lu, Julien Rossignol, Michael I. Sandstrom, Reid L. Skeel, Laurent Lescaudron, and Gary L. Dunbar. "Genetically-Engineered Mesenchymal Stem Cells Reduce Behavioral Deficits in the YAC 128 Mouse Model of Huntington's Disease." Behavioural Brain Research 2010 May 19. [Epub ahead of print]

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