Tay-Sachs Sheep HOPE for a Cure

Doug Martin, PhD, Auburn University, received Research Initiative Grants from NTSAD to characterize natural disease progression in the Tay-Sachs sheep model and therapeutic benefits of gene therapy in Tay-Sachs sheep.

For two years, sheep with Tay-Sachs were studied in a controlled research environment to clearly chart the disease course in this newly identified animal model. This study is important because it provides a baseline to measure therapeutic interventions such as gene therapy. Here is a summary of the results:

1. The lifespan of an untreated Tay-Sachs sheep is approximately 9 months with disease onset around 2.5 months.

2. Most disease signs in Tay-Sachs sheep relate to gait abnormalities, such as hind limb weakness or ataxia, that worsen with age.

3. All Tay-Sachs sheep have clouding of the eye's cornea but none have the 'cherry-red spot' found in children which is likely due to differences in eye structure.

4. No startle or hearing abnormalities were observed.

5. Residual enzyme Hex-A activity along with slow onset and progression suggest the sheep have a later onset form of Tay-Sachs (Juvenile or Late Onset).

Gene therapy studies in Tay-Sachs sheep had two main goals: (1) identify the best way to restore HexA activity in sheep brains, which is about 20% the size of a child's brain, and (2) study the effect of gene therapy on disease progression and lifespan. Here is a summary of the results:

1. HexA activity is optimized when treatment consists of both alpha and beta subunits, even though Tay-Sachs sheep have a defect solely in the alpha subunit.

2. Lifespan increased to an average 14.4 months (~60% increase over untreated sheep) in two-thirds of treated sheep.

3. Treatment improved quality of life by delaying onset of symptoms such as muscle weakness.

4. Important to note that all Tay-Sachs sheep were treated after onset of symptoms, as will be true of most clinical trial candidates.

Click here to download final report. NTSAD has awarded a year 3 grant to continue these studies.

Clinical Trial Update

The Tay-Sachs Gene Therapy Consortium is gathering data from follow up animal studies attempting to understand the adverse neurological response in primates. We hope to have a full report and new timeline to a cure by mid-April.