

Progress Report
January 11, 2010
Tay-Sachs Gene Therapy Consortium

1. The NIH funded studies are well under way and showing very good results. Detailed analysis of the behavior of GM2 mice treated by our gene therapy approach is showing exceptionally positive results that meet or exceed our pre-defined success criteria.

2. We have cloned the genes for alpha- and beta-subunits of cat hexosaminidase (not available until now) into AAV vectors and demonstrated their ability to generate large amounts of HexA activity in cultured cells. These are critical for our efficacy studies in GM2 cats.

3. The support that the TSGT Consortium received over the last few years allowed the expansion of the GM2 cat colony, which is highly productive at the moment with 13 new kittens born in the last month alone. Eight new litters are anticipated in the next few weeks. This increased productivity is crucial to our project to generate the necessary GM2 kittens for the efficacy studies, and testing of additional delivery routes.

4. Tay-Sachs Natural History study. We have received 145 questionnaires of which our target group, infantile GM2, comprise 90 (62.1%). We continue to work with the NTSAD to increase the number of responses to our questionnaires. We have a preliminary report on milestones gained/lost and aberrant behavior (seizures, etc.) in 60 infants, but are awaiting complete data entry. In addition we are also surveying the literature to pick up all reported cases. We anticipate submitting a report of our findings for publication in the first half of 2010.

5. We have started an imaging study in late onset GM2 patients to assess structural and metabolic changes in the CNS. First results have been accepted for presentation at the International Society for Magnetic Resonance in Medicine (Stockholm, Presentation May 2010).

6. Also we are analyzing existing MR imaging data in infantile Tay-Sachs patients with the goal of developing an MRI scoring system. For this initial phase we will need at least 12 MRIs, and thus far we have collected 5 through the NTSAD. We are working with several physicians in different centers in the United States and England to collect data from additional patients. In a second stage, we will use a second set of MRIs to validate the scoring system.

Finally we are in the planning stages of a prospective study to assess disease progression in infantile patients using the new imaging and clinical scoring systems, validate MR spectroscopy findings from our studies in LOTS patients and their applicability to infantile patients, and also validate biochemical markers of disease progression. These studies will give us the tools to assess accurately the effect of gene therapy on disease progression in the clinical trial.