

## AU researchers work with consortium to find a cure for Tay-Sachs disease

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By Heather Finch  
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Auburn University researchers in the College of Veterinary Medicine and Scott-Ritchey Research Center have joined researchers from Boston College, the University of Cambridge (UK) and Massachusetts General Hospital/Harvard Medical School to find a cure for Tay-Sachs disease.

Drs. Douglas Martin, Nancy Cox and Henry Baker are among the eight researchers who have formed the Tay-Sachs Gene Therapy Consortium and are working diligently to begin human clinical trials within the next four years with the hope of providing a gene therapy that will prolong the lives of children in which this inherited neurological disorder proves to be fatal.

Tay-Sachs disease can occur in three phases: infantile, juvenile, and late onset. The infantile form of this rare genetic disorder, also known as GM2-gangliosidosis (GM2), is the most common, and in its classic form begins to slow the infected child's development during the third to sixth months of life. By the age of two, the child begins to suffer from many complications ranging from frequent seizures to the loss of



From left to right: Drs. Nancy Cox, Henry Baker, and Douglas Martin

all motor controls. Death usually occurs before the child's fifth birthday. In addition, gangliosidosis is common among certain cat breeds, such as Siamese, Korat and European Burmese, where extremely high carrier frequency rates (up to 25%) are capable of decimating a breed. As in humans, feline gangliosidosis is neurodegenerative and fatal.

While in the general population, one in every 250 people carries the mutated gene that causes Tay-Sachs, one in every 27 Ashkenazi Jews, Cajuns or French Canadians and one in every 50 Irish-Americans are carriers.

Each of the AU researchers on the team brings expertise and previous research to the Tay-Sachs Gene Therapy Consortium.

Baker, Professor Emeritus of Pathobiology, discovered and has studied feline gangliosidosis for 35 years. Cox, Interim Director of the Scott-Ritchey Research Center and Associate Professor of Pathobiology, is a veterinary neuropathologist with 25 years of experience evaluating disease progression in the feline gangliosidosis models, while Martin, Assistant Research Professor, has 15 years' experience with the feline gangliosidosis models, having characterized the genetic mutations responsible for the disease.

In order to reach the goal of finding a way to treat Tay-Sachs disease, Baker, Cox, and Martin are comparing experimental therapies in the feline model of GM2 gangliosidosis to those tested in mice by researchers at the University of Cambridge, Boston College and Massachusetts. “[The consortium] has to demonstrate measurable therapeutic benefit in mice, which has been done, but also in what we call a large animal model of the disease which is the cat,” Martin explains. “We feel that it is important to have therapeutic efficacy in cats before beginning human clinical trials.” The size and complexity of a cat's brain, which is only about 15 times smaller than a child's brain, make cats better models for humans than mice.

The Auburn researchers have put enormous effort into maintaining cat colonies, but, as Martin says, “It's worth the effort, time, and expense.”

The gene therapy that Baker, Cox, and Martin are performing on the cats is done with adeno-associated virus (AAV) vectors. These vectors have shown efficiency in complete correction of lysosomal storage

throughout the brain. “The good thing about these [AAV] vectors is that they are so advanced and highly engineered that a little bit of vector goes a long way,” Martin explains.

Tay-Sachs, though commonly considered a rare disease, is one of over 40 lysosomal storage diseases, which are inherited genetic diseases that cause a physical and/or mental deterioration and eventually death. Of these diseases, 75 percent, like Tay-Sachs, have a neurological component, thus the consortium's findings could apply to many other human diseases. Also, information that the researchers are learning about cats as human disease models and about AAV-based therapies can be applied directly to feline diseases

The consortium first met in March 2007 and is highly committed to this project. “This is a great group of people coalescing around a promising therapy – gene therapy,” Martin says, “We've all seen this disease devastate so many families for so long and there was really nothing we could offer. But now we think we have a real chance at offering something that could help. These are committed, hard-working people who want to make a contribution – a difference.”

More information about the Tay-Sachs Gene Therapy Consortium can be found on their web site: [www.tsgtconsortium.com](http://www.tsgtconsortium.com). Donations to support the consortium can be made through the Auburn University Foundation (317 South College Street, Auburn University, AL 36849; specify Tay-Sachs Gene Therapy Consortium at the Scott-Ritchey Research Center), through the Cure Tay-Sachs Foundation ([www.curetay-sachs.org](http://www.curetay-sachs.org)), or through the consortium's site.