Breakthrough in Niemann-Pick Type C research reported

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A paper announcing a breakthrough discovery in the fight against Niemann-Pick Type C, coauthored by Olaf Wiest and Paul Helquist of the University of Notre Dame's Department Chemistry & Biochemistry and Frederick Maxfield, Chair of Biochemistry at Cornell University Weill College of Medicine, appears in the *Proceedings of the National Academy of Sciences* this week. The paper shows how use of a histone deacetylase inhibitor correct the damage done by the genetic disorder and allowed once-diseased cells to function normally.

Niemann-PickType C (NPC) involves a genetic flaw that keeps cells from using lipids appropriately and leaves the lipids trapped in the cell. Brain cells are especially impacted, and destruction of brain cells typically kills victims by their teen years and there is currently no treatment available in the U.S. NPC is an inherited cholesterol metabolism disorder that strikes one in every 150,000 children. It has been referred to by the National Institutes of Health as "childhood Alzheimer's" because of similarities in the brains of NPC and Alzheimer's disease patients.

Three of the four grandchildren of former Notre Dame head football coach Ara Parseghian died of NPC, and the University has been involved in research on the disorder for years. Last year, it formally united with the Parseghian Foundation, which sponsored this work.

Last summer, Notre Dame College of Science Dean Gregory Crawford and his wife Renate bicycled 2,300 miles from Tucson to Notre Dame to

raise awareness of the newly strengthened partnership with the Parseghian Foundation. Notre Dame's Center for Rare and Neglected Diseases works to develop therapies and outreach efforts for people suffering from conditions, like NPC, that have bee3n largely ignored by pharmaceutical companies.

A team of led by Wiest and Helquist at Notre Dame and Maxfield at Cornell, uncovered evidence that histone deacetylase inhibitors correct NPC's genetic flaw. Detailed images obtained at Cornell by Maxfield's group gave vivid evidence of the drug's effectiveness, showing how NPC cells became indistinguishable from normal human cells after treatment with the drug. The histine deacetylase inhibitors have a wide range of potential uses, from rare diseases, the focus at Notre Dame, to several forms of cancer, including leukemia, where they can increase the number of bone marrow cells.

Several of the compounds studied are shown to be safe in advanced clinical studies of cancer and one compound is currently approved by the FDA.

"Our biggest single emphasis the last few years has been Niemann-Pick among these rare diseases," Helquist said. "We developed several processes for the efficient preparation of these types of drugs. There's a stream of publications and also a stream of patents starting in June 2007 and continuing this year."

"If the results in human cells can be confirmed in clinical trials, the fact that the histone deacetylase inhibitors are already in advanced clinical trials or even approved drugs could greatly accelerate the development of a treatment for this devastating disease."

Provided by University of Notre Dame