SOAR-NPC
Interim Progress Report
September 2011

SOAR
Support Of Accelerated Research for Niemann-Pick Type C

Dear Friends of SOAR:

The SOAR-NPC Collaborative was established in 2008 with a central goal of accelerating the development of new therapies for NPC disease. Over the past three years, we have tested in NPC animal models 18 compounds, of which one has already been studied in an NIH trial, and another, hydroxypropyl-b-cyclodextrin (CD) is the subject of developing clinical trial. Our efforts have also led to designation of NPC as only one of five pilot projects for the Therapies for Rare and Neglected Diseases (TRND) at the NIH.

Since April 2011, a major focus of SOAR investigators has been working with NIH TRND team to accelerate CD through pre-clinical testing and regulatory approvals to achieve a clinical trial, possibly as early as 2012. This has involved performing pre-clinical testing of CD in the NPC cat and mouse models to determine route of administration, dosing and how to monitor the effects of CD in patients. The TRND-SOAR team also included scientists from Johnson & Johnson, who are working closely with the SOAR investigators to help develop the analytical tools required to measure CD levels in humans. These intensive efforts have led to a pre-Investigational New Drug (IND) meeting with the FDA, which is scheduled for early November 2011, to seek approval for a Phase I clinical trial for direct brain delivery of CD.

Concurrent with these efforts, SOAR-NPC investigators have vigorously pursued discovery of NPC disease biomarkers, in collaboration with the NIH. Such biomarkers are critical to serve as outcome measures in clinical trials, and will be required to gain FDA approval for clinical trials. NPC-SOAR scientists recently published identification of cholesterol metabolites, known as oxysterols, as sensitive and specific markers for NPC disease. The biomarkers are now being evaluated to assess their utility for monitoring therapeutic effects of the CD. This has involved measurement of these biomarkers in NPC animal models following brain delivery of the drug, as well as development of clinical laboratory assays to measure the levels of the biomarkers in human plasma and cerebrospinal fluid.

The oxysterol biomarkers also have tremendous potential as diagnostic markers for NPC disease. In contrast to the current diagnostic methods – which are invasive, of limited sensitivity, and require up to two months – oxysterols provide a simple, rapid test and can be performed on a drop of blood. NPC-SOAR scientists met in early September 2011 with the heads of the major reference labs that diagnose NPC disease in six countries (Brazil, France, Germany, Italy, Switzerland, UK) to develop a program for dissemination of our biomarker technology. It is anticipated that the oxysterol assay will be implemented in these countries by early 2012, which is expected to reduce the diagnostic delay, lead to earlier initiation of therapy and provide a tool to clinicians to monitor therapies in NPC patients.

SOAR-NPC labs are also investigating the potential that this technology can be applied to newborn screening, which would open up for the first time the possibility of early initiation of therapy in pre-symptomatic patients.

SOAR-NPC has continued to serve a vital role in the NPC research community by developing a compound pipeline for future clinical trials. In past several months, SOAR-NPC labs have received approval to test in NPC animal models novel anti-inflammatory and anti-neurodegenerative compounds. New compounds have also emerged from high throughput screens of libraries containing up a half-million compounds, and will undergo extensive chemical modifications to yield candidates for testing in cell-based and animal models. Together, these compound discovery and testing efforts will provide a robust pipeline of candidate compounds for future clinical trials.

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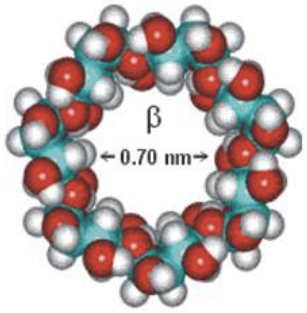

Cyclodextrins are a family of compounds made up of sugar molecules bound together in a ring. They are produced from starch by means of enzymatic conversion. They are used in food, pharmaceutical, and chemical industries, as well as agriculture and environmental engineering. (Source: Wikipedia and "Water Structure and Science," London South Bank University)
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