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APBDRF

ADULT POLYGLUCOSAN BODY DISEASE RESEARCH FOUNDATION

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Letter from the President

Dear APBDRF Supporters,

On March 14, 2013, APBDRF held its Ninth Annual Scientific Conference in New York City. Dr Kakhlon, Dr Akman, Dr Tropak and Dr Schiffman all spoke about their promising research. Indeed, our researchers are working together on many projects, and a potential treatment to lower the formation of polyglucosans is a real possibility in the foreseeable future.

We know that for laypersons it may be very difficult to understand the research. Therefore, because we want you to feel as excited as we do about the advances being made toward finding treatments for APBD, we have taken the time to develop the "What we are working on" section of the website, which we hope you will find both informative and accessible.

In this and subsequent newsletters, we will highlight a particular project. Below you

Research Projects

Creating a Patient Registry

Genetic Research

Drug Research

The Antisense Project

Developing and Preserving Mouse Models

Human Trials for APBD

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APBDRF-funded research leads to new publication: Polyglucosan neurotoxicity caused by glycogen branching enzyme

will see a short interview with Dr Kakhlon in which he discusses the Antisense project and the potential for human trials in 2014.

An APBD treatment breakthrough will mean that a human trial is necessary. Consequently, the APBDRF is intensely focused on developing an APBD Registry which we hope to start in 2013. The development of a registry will position us to take advantage of any human clinical trials that arise.

We need your help! A small group of our APBD community has given generously of their time and money. We have created a website in order to raise awareness about APBD and bring to you an understanding of the breadth of the research that the APBDRF has been supporting since 2005. Over 98% of our donations go directly to the research. The other 2% has been focused in the last two years on highlighting the extraordinary work in which our researchers are tirelessly engaged.

What can you do?

* Get involved there are many projects that need to be done.

* Tell us your personal APBD story. Whether you are a caregiver, family member or patient, we want to hear from you. The website has received a lot of attention through these stories and you are helping others by telling them your story.

* Donate funds if possible. Drug companies need to be encouraged to take on the basic research necessary to lay the groundwork for the human trials. Fundraising is critical.

* Help us find a dynamic, self motivated, part-time Executive Director to help build our growing non-profit 501(c)3 foundation. We are at a pivotal moment in our

deficiency can be reversed by inhibition of glycogen synthase

Read here

Dr. Kolodny discusses the potential value of establishing an APBD patient registry

Watch Here

Triheptanoin treatment trial for patients with Adult Polyglucosan Body Disease - *Currently the only human trial*

Read here

efforts to find a cure for APBD and need an outgoing person to help coordinate operations. Please send all inquiries to info@apbdrf.org

Sincerely,

Gregory Weiss, APBDRF President

What We're Working On

Our three research centers at Columbia University, Hadassah University Hospital, and Toronto University Sick Kids Hospital are working on several critical projects, which you can learn more about on our new Donation Platform.

This month we will take a closer look at the Antisense Project. Antisense drug therapy is a form of treatment for genetic disorders. When the genetic sequence of a particular gene is known to cause a disease, it is possible to make a strand of nucleic acid (DNA or RNA) that will inactivate it, effectively turning that gene "off". The Antisense project uses an FDA-approved method to safely slow down the accumulation of polyglucosans, an abnormal form of glycogen that cannot be broken down and used for fuel by the body.

Interesting Articles

FDA approves raptor

drug for form of rare genetic disease cystinosis - *a rare disease foundation helps in drug development*

Read here

FDA approves genetic drug to treat rare disease - *Antisense technique used to create FDA approved drug for a rare disease*

Read Here

GMO wheat: A potential cause of liver disease, death?*Gene Silencing and the mention of APBD*

Read here

The Antisense Project

The following is an abridged version of a recent interview with Dr. Or Kakhlon, one of the principal investigators on this project. The full interview is available on our new donation platform, which includes updates on all of our research projects, here.

Is there potential for human trials in 2014?

Antisense oligos (ASOs) are small sequences of DNA that block disease processes by interfering with the production of the particular protein they target. At the moment, we have completed the screening of ASOs against PTG, a protein involved in the formation of polyglucosans, using injections directly into the brain of mice. Some ASO were indeed shown to reduce this protein in specific regions of the brain.

Scientists develop drug that may slow Alzheimer's - *mouse model research and its possible implications for other neurodegenerative diseases*

Read here

Patient Corner

In this section you will find personal accounts of people affected by APBD. The APBDRF as a patient support group does not endorse any health practitioners, therapies, medicines, etc.

Better Branches: Alma Hecht's personal blog about living with APBD

The Story of an APBD

Nevertheless, Isis Pharmaceuticals is still trying to improve this process by increasing the dosage. Therefore, we expect that in about a month, these ASOs will be ready for injection into APBD mice. At least two injections, 3 months apart, are planned and then the effects on different markers of APBD in the mice will be tested. This should be completed within a year and if the results are satisfactory then yes, human trials should begin before the end of 2014 based on these methods.

Isis Pharmaceuticals has also recently begun experiments to reduce the expression of Glycogen Synthase 1 (GSY1), an enzyme involved in glycogen storage diseases such as APBD. This is expected to be more effective than targeting PTG as described above. Therefore, human trials involving GYS1 ASOs are expected to start approximately a year after the PTG ASO trials.

How would an APBD registry facilitate the beginning of trials?
Once the specific ASO is ready for use, it will be a great medical advantage if it could be tested on a variety of patients with APBD who have different underlying genetics and variable natural histories of the disease. This type of variation is a good test of the effectiveness of a drug which would be shown to be more potent if it can correct disease symptoms from a variety of patients.

Why has Isis Pharmaceuticals decided to also do an ASO on glycogen synthase (GS)?
Following a discussion held at Isis Pharmaceuticals headquarters in Carlsbad, CA between Dr. Minassian, myself and Isis Pharmaceuticals representatives it was decided to initiate experiments aimed at GYS1 knockdown, a technique to reduce the conversion of the information encoded in a gene into a protein. Therefore we expect the potentially more effective GYS1 ASO to be ready a year and a half from now at the earliest, once it has gone through all the stages described above for

Allied Organizations

Association for Glycogen Storage Disease

Association for Neuro-Metabolic Disorders (ANMD)

The Dana Foundation

The Doctor's Doctor

Genetic Alliance

Jewish Genetic Disease Consortium (JGDC)

Muscular Dystrophy Association

National Organization for Rare Disorders

National Tay-Sachs & Allied Diseases Association (NTSAD)

Victor Centers for the Prevention of Jewish Genetic Diseases

the PTG ASO.

This research does not rest on one ASO. Isis is also following up on a potentially more effective treatment that could be ready in a year and a half.

What is the significance of Isis' decision to also study glycogenin?
Glycogenin is an enzyme involved in converting glucose to glycogen. Because glycogen leads to the formation of polyglucosan in patients with APBD, reducing glycogenin is expected to reduce polyglucosan levels and is therefore a valid target for knock down.

What will it take for Isis Pharmaceuticals to be convinced to do a human trial on APBD?
I think that once we have convincing results from mice, Isis Pharmaceutical will be ready to take the next step which is clinical trials in patients. All this will, of course, be done in accordance with the FDA guidelines and regulations.

What other antisense-based technologies are being developed for curing APBD?
In collaboration with the Israeli biotechnology company GeneArrest, we have begun a project which will use molecules called Triple Helix Forming Oligos (TFOs) designed to target the enzyme glycogen synthase 1 (GYS1). In contrast to ASOs, TFOs are very stable molecules that bind specifically to the DNA sequence they target. We are only at the beginning of this project. We have shown that TFOs permeate the cell membrane and can accumulate in the nuclei of mouse brain cells. With funding from the APBDRF we plan to move to the next stage which includes designing TFOs that specifically target GYS1 and reduce its levels of expression and activity. As with the ASOs, we will then move on to test its effects on APBD mouse models. By stopping further accumulation of polyglucosans it is hoped that the body will then be able to rid itself of polyglucosans that have already built up (shown in the mouse model of APBD by Akman et al., 2011). Thus,

stopping the disease would not only be a treatment, but ultimately a cure.

Career Opportunity

We are seeking a dynamic, self motivated, part-time Executive DIrector to help build our growing non-profit 501(c)3 foundation. We are at a pivotal moment in our efforts to find a cure for APBD and need an outgoing person to help coordinate operations. Please send all inquiries to info@apbdrf.org

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