Factor Nine News

The Coalition for Hemophilia B Fall 2010

Topics in Hemophilia

Save the Date!

Saturday, March 5, 2011

The Coalition for Hemophilia B
5th Annual Symposium
The Millennium Broadway Hotel
New York, New York

Friday, March 4, 2011

The Coalition for Hemophilia B
4th Annual Fundraising Dinner
The Millennium Broadway Hotel
New York, New York

Please visit our website for more information: **www.coalitionforhemophiliab.org**

Gene Therapy Update

By Dr. David Clark

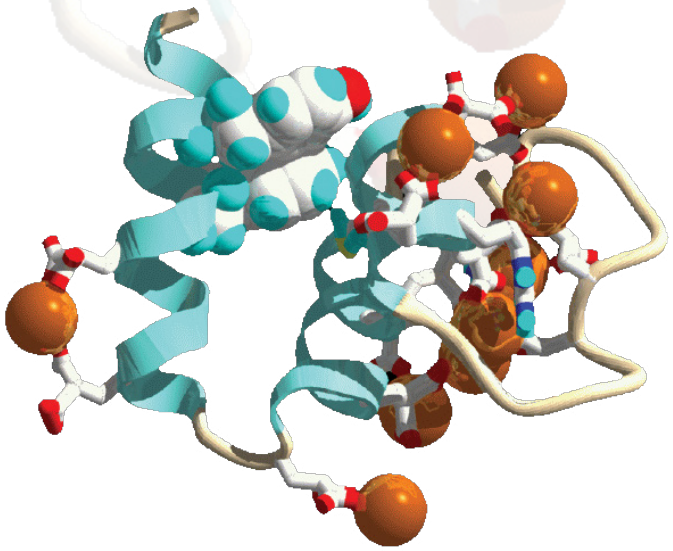
After a long break to try to figure out why previous attempts had failed, a new clinical trial of gene therapy for hemophilia B was started early in 2010. In results from the Phase I/II study, which were presented at the recent American Society of Hematology (ASH) meeting, investigators from St. Jude Children's Research Hospital in Memphis and University College London reported on four patients who have been treated with a factor IX gene therapy vector. Three of the patients now have low but sustained production of factor IX with no significant side effects.

The vector used in the study is an Adeno-Associated Virus-Type 8 (AAV8) in which the viral genes have been replaced by a normal factor IX gene. A gene therapy vector is the means of introducing the desired gene into the body. Viruses are popular vectors because a virus's entire purpose in life is getting its DNA (genes) into a cell. In gene therapy, viruses are used to "infect" cells with the desired gene, instead of with a disease.

AAV vectors are popular because they can infect cells, but do not reproduce on their own, so they're easier to control. The St. Jude study used the AAV8 vector to introduce normal factor IX genes into cells in the patient's livers, where factor IX is normally produced. The idea is that the "infected" liver cells will produce factor IX and secrete it into the bloodstream.

Another benefit of AAV is that it does not insert its genes into a cell's genome. The genome is the person's complete collection of genes, a copy of which is contained in the nucleus of almost every cell in the body. One earlier non-hemophilia study in Europe that used a retrovirus vector had two patients who developed leukemia. That result brought all gene therapy clinical trials to a halt for awhile. Retroviruses do insert their genes into the genome, and what probably happened in the European study is that the new gene inserted itself in the middle of an oncogene, possibly in the regulatory section that turns the gene on or off. Oncogenes are cancer genes that are present in all human cells, for unknown reasons. The new gene could have inadvertently turned on the cancer gene, causing leukemia in the patients. This is called insertional mutagenesis. By inserting itself in the wrong place, the new gene caused a mutation in the genome.

Some previous gene therapy studies have used AAV-Type 2 (AAV2), a virus that causes upper respiratory infections in humans. However, although AAV2 vectors worked fine in animals, in humans the production of factor IX died out over time. This is thought to probably have happened because most humans already have antibodies from previous AAV2 infections. About 80 - 90 % of humans have been infected with AAV2. The antibodies probably attacked the transformed cells thinking that the cells were infected with AAV2.



The current study uses AAV8 vectors because AAV8 infection is rarer in humans. AAV8 is a virus that generally infects non-human primates, such as chimpanzees and gorillas. Humans can be infected with AAV8, but they do

not become sick. They can apparently produce anti-AAV8 antibodies, though. The gene therapy treatment failed in one of the four study patients, who was then found to have anti-AAV8 antibodies. Now all potential patients are screened for anti-AAV8 antibodies, prior to being enrolled in the study.

At this point, the study is mainly looking at safety and side effects. The first patient, however, even though he received the lowest dose of virus, had an unexpectedly high level of factor IX expression. His factor level rose from less than one percent to almost two percent of normal, and has persisted for ten months now. Since the treatment, the patient has had no bleeds and has not needed any additional factor infusions. The other lowest-dose patient now has a factor level of about one percent, but is still on prophylaxis because of bleeding issues.

Two more patients received the next-higher level of vector. One was the one who rejected the treatment because he already had anti-AAV8 antibodies in his system. The other is expressing factor IX and has not needed additional infusions for 1.5 months, but that's too short a time for any meaningful conclusions. The study will continue with increased levels of vector as long as no adverse side effects are encountered. The goal is to eventually bring patients up to a factor IX level of greater than 5 %, at which they would only have mild hemophilia.

This is some of the best news for hemophilia treatment in a long time. There is still a long way to go with the study, but if the results continue to be positive, this could finally represent a true cure for hemophilia B.

94 Year Old Man with Hemophilia B

In our Summer 2010 Newsletter, we told our readers about Leeroy Carter from Highland Park, Michigan turning 90 years old. The articles stated he was the second oldest person with hemophilia in the country – by two months (information obtained from Joshua Jamerson, Free Presss Special writer, Freep.com).

We have updated information for you. Mark Cleary (hemophilia B) of North Carolina informed us that his Uncle (his mother's oldest brother,) Harvey L. Smith was born in May of 1915 in Pittsylvania County, Virginia. He is 94 years old and currently living in North Carolina.

The photo above was taken at the Cleary's Family Reunion on October 2, 2010.
Pictured are three of the four surviving siblings (left to right) Marion Smith Hart, Harvley L. Smith and Margaret Smith Wade.

Thank you to Mark Cleary for sending us the information. Well, there you have it folks! As far as we know, Harvey L. Smith is the oldest person with hemophilia B!

Advocacy in the Age of Healthcare Reform

By Glenn Mones

It has often been asked whether healthcare is regulated primarily at the Federal or State level, and in turn, what is the correct address for advocacy efforts.. The easy answer is – both. Many programs such as Medicare are regulated at the Federal level. Others, like Medicaid, are a Federal-State partnership. Private insurance has generally been, and to a large extent still is, regulated at the state level.

In the years leading up to the latest Federal healthcare reform measures, the conventional wisdom said that most of the important activity was taking place at the state level. By establishing broad programs like Medicaid and CHIP (Children's Health Insurance Program), the Feds already had their say. Now it was up to the states to work out the details, such as where a family's income had to fall compared to the Federal Poverty Level (FPL) to qualify for a particular program. States could also decide which conditions were covered by these programs, which treatments and providers were eligible for reimbursement and much more.

Then the new administration arrived and with it, healthcare reforms as we now are coming to know it. Suddenly it seemed that the game had changed substantially and all eyes were back on the Feds. Sweeping change were introduced that, if left intact, will eliminate pre-existing condition clauses, eliminate lifetime benefit caps, create additional coverage options and more.

So what happens now? Well, attempts are being made by those who oppose healthcare reform to retract some of the changes that have either already been instituted or will be in the coming years. For that reason, it will remain critical to monitor activities at the Federal level and speak out about these potential retractions.

At the same time, the statehouse remains a critical target for advocacy efforts, and it will remain so in the foreseeable future. This is true for several reasons. Firstly, many provisions of Federal healthcare reform - including elimination of annual caps, the creation of insurance exchanges and others – will be implemented over several years. Therefore, stop-gap efforts at the state level will still be necessary in

order to ensure broad access to care. For example, in New York State, programs designed to provide coverage for the "working poor," including CHIP and others, do not currently cover outpatient clotting factor. A coalition of local bleeding disorders chapters and associations is working with legislators to change that.

In addition, although Federal healthcare reform will create many changes to the system, it will not replace the system with a new one. Most of the currently existing state programs, as well as private insurance providers, will remain in place. Yes, improvements to coverage will be mandated by the Federal government, but much of the actual implementation will happen at the state level. We will therefore need to advocate for methods of implementation that provide the best possible coverage and care, especially in instances where considerable discretion will be left to the states.

Finally, the states often have the ability to go above and beyond what has been mandated on the Federal level. For example, in Florida, Illinois, New York, and Pennsylvania, many dependent children can remain on their parents' insurance. The new Federal laws only require coverage of dependents up to age 26, although with less restrictions than are usually in place in the state laws. Therefore, there is ample room to improve coverage, for example, by asking more states to increase the maximum age for dependent children to be covered under their parent's policies.

In summary, there are some important lessons to be learned about advocacy in the age of healthcare reform. One, while most of the legislation at the Federal level is complete, it is not necessarily permanent and therefore must be monitored and safeguarded. Two, healthcare reform will be phased in, and even then must be implemented at the state level. Therefore, the statehouse is the correct address for stop-gap measures and for implementation. Three, however helpful the Federal measures may be, the individual states always have the ability to go above and beyond – so let's not forget to ask!

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On Saturday, November 13, 2010, The Coalition for Hemophilia B held its Factor Nine Family Breakfast meeting in conjunction with the National Hemophilia Foundation's 62nd Annual Meeting in New Orleans, Louisiana.

Over 50 members of The Coaltion for Hemophilia B were in attendance at the Breakfast Meeting.

Factor Nine Santa would like to give a heartfelt "Thank you" to all of the wonderful people and companies that so generously gave to the Santa Fund this holiday Season. The Coalition for Hemophilia B was very happy and proud to be able to make the holidays a little bit brighter for 48 children!

"Thank you very much for the Christmas gifts. It helped make this Christmas special for Dylan. He was so happy to receive the toys!
~ Michelle B.
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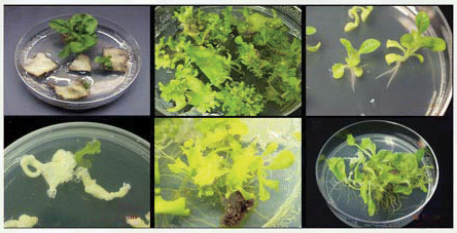
GRIFOLS

PLANTS HELP PREVENT INHIBITORS AND ALLERGIC REACTIONS

(NHF eNotes, November 2010)

Using genetically modified plants, researchers from two Florida universities are developing a technique that could help prevent treatment-related complications such as inhibitors, an immune reaction that neutralizes infused factor, and anaphylaxis, severe allergic reactions, in people with hemophilia B. The lead authors of the study were Dheeraj Verma, PhD, Department of Molecular Biology and Microbiology, College of Medicine, at the University of Central Florida (UCF) in Orlando and Babak Moghimi, MD, Department of Pediatrics, College of Medicine, at the University of Florida (UF) in Gainesville.



Inhibitors result in approximately 25% of patients with hemophilia A and up to 4% of patients with hemophilia B. Clinicians often use immune tolerance (IT) induction to eliminate an inhibitor. By administering daily doses of factor over time, the body begins to tolerate the therapy. The process is similar to desensitization therapy used to treat food and environmental allergies. The technique is less effective in individuals with hemophilia B than in those with hemophilia A. In addition, because of the large amounts of factor used, IT becomes very expensive. The approach being developed by Verma, Moghimi and colleagues could be more cost effective.

The researchers used a so-called "gene gun" to insert the genetic material that manufactures factor IX (FIX) into chloroplasts, the energy production centers of plants. They then fed the modified plants to mice with hemophilia B for a prolonged time period. Insulated from digestive acids and enzymes by durable plant cell walls, the FIX protein traveled through the stomach and into the small intestines. Once inside the small intestines, bacteria then broke down the cell walls and released the protein, which induced tolerance by the immune system.

"We have made them develop tolerance, and removed the allergic part of this treatment," said coauthor Henry Daniell, PhD, a Pegasus professor and University Board of Trustees Chair in the College of Medicine at the UCF.

Later the mice were infused with factor product, which triggered little to no inhibitor responses and no anaphylactic events. "I think this is a milestone — nobody has previously achieved such levels of robust immune tolerance by any means using a noninvasive procedure," explained Thierry Vandendriessche, PhD, an associate professor of medicine at the University of Leuven in Belgium, who was not involved in the study. He is president of the European Society of Gene Cell Therapy.

Investigators will conduct follow-up studies to test the approach in mice with hemophilia A and then carry out trials in humans using lettuce to produce the therapeutic proteins.

"We're hoping that our research will, in the future, result in better and more cost-effective therapies," said study co-author Roland Herzog, PhD, an associate professor of pediatrics, molecular genetics and microbiology in the UF College of Medicine and a member of the UF Genetics Institute.

The study, "Oral Delivery of Bioencapsulated Coagulation Factor IX Prevents Inhibitor Formation and Fatal Anaphylaxis in Hemophilia B Mice," was published in the April 2010 issue of the Proceedings of the National Academy of Sciences.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Community News

Law Signed to Improve Access to Clinical Trials (www.hemophilia.org)

On October 5th, 2010, the Improving Access to Clinical Trials Act (P.L. 111-255) was signed into law. This legislation helps reduce barriers for certain people wanting to participate in clinical trials. Often, clinical trials sponsors compensate participants financially for their time. The money is regarded as personal income for tax purposes. This payment may threaten the eligibility of some people to collect Supplemental Security Income.

With a small number of potential trial participants, and the possible loss of Supplemental Security Income and Medicaid benefits for many who wish to participate, clinical trial research for rare diseases and condition becomes exceptionally difficult and may hinder research on new treatments and potential cures. The new law will allow compensation up to $2,000 to be excluded from taxable income, thereby making it easier for people to participate in clinical trials.

Hemophilia Association of New York

The Hemophilia Association of New York (HANY) welcomes Linda E. Mugford as their new Executive Director. Linda has twenty-five years experience in a not-for-profit and health-related careers. Linda is the former Manager of Comprehensive Hemophilia services of the New York Blood Services. She not only brings knowledge of the issues facing those with bleeding disorders, but has a track record of action, working with both consumers and health care providers, and as an advocate for affordable access to medical treatment. We wish her the best of luck in her new position!

Scholarships

The William N. Drohan Scholarship application form for 2011 is now available on our website under scholarships: www.coalitionforhemophiliab.org. The deadline is February 15, 2011.

HANY Scholarship Program is available for persons with inherited genetic bleeding disorders The deadline is June 3, 2011. Call for an application 212-682-5510.

Pfizer Pharmaceutical is offering the Soozie Courter Hemophilia Scholarship to undergraduate, graduate, and vocations school students. For more information, visit:
www.hemophiliavillage.com

For a full list of available scholarships please visit LA Kelley Communication:
(www.kelleycom.com)

The Coalition for Hemophilia B Welcomes Jean Ryan as part of our Coalition B-Team!

I am sure many of you in the community have probably had the pleasure of meeting Jean Ryan at our exhibit booth, Factor Nine Family meetings, New York Fundraising Dinner/Symposium, and at Washington Days the past year. We would like to share some information about Jean so you could get to know her as she is relatively new to the community and our team.

Jean is a retired NYPD Detective with a Masters Degree in Human Resources. She has training and experience in Critical Incident Stress Management (CISM). "Helping the Helper" she has peer counseled many emergency workers such as police, firefighters, EMS workers, and war veterans over the past 15 years.

She is the eldest of six children and has twelve nieces and nephews that help keep her quite busy! Jean has also travelled with her brother, Edward, who is a Quad Rugby player for over 20 years. Quad Rugby is a sport for people who are quadriplegic. Last year, Edward's team won the gold in an international competition played in Vancouver, Canada. His team also won the gold in the Olympics in China.

Another of Jean's brothers, Daniel Suhr, was the first firefighter killed on September 11 at the World Trade Center.

Jean has done a lot of volunteer work with children and adults with autism, mental retardation, brain damage, and the deaf.

She is truly a people-person with a hearty laugh and a great smile! Please join us in making her feel welcome - we are proud to have Jean on our B-Team!

Scholarship Notice!

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Wishing you all a most wonderful 2011 filled with love, good health and happiness!

Reminder

The Factor Nine Group moderated by Jill Lathrop is located on Yahoo.com Search "Factor 9" on Yahoo Groups

For back issues of **Factor Nine Newsletter** or for more information on research, please call or write to:
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