fellow SPOTLIGHT:

KATHERINE A. HIGH, M.D., FCPP

Fellow since 2012

By Jon Goff, Associate Director of Fellowship Relations

What initially interested you about joining the College?

Dr. Howard Snyder and Dr. Lucy Rorke Adams, two of my faculty colleagues at CHOP, first introduced me to the existence of the College. As everyone knows they are great supporters and proponents of the CPP, and their level of enthusiasm was infectious. I remember very clearly Dr. Snyder asking me to give a lecture for a campus event, obtaining my CV ahead of time in order to introduce me, and then calling me to say that he was very surprised that I was not a member of the College, and that he would work on that right away!

A recent article on Philly.com highlighted the groundbreaking work you are doing with Spark Therapeutics in the field of gene therapy for patients with hemophilia. Tell us about that work.

For much of my career, I have been focused on establishing a clear basis for the use of gene transfer to treat genetic disease. Because I am a hematologist, I have focused on hemophilia. The genes for Factor VIII and Factor IX were cloned in the early 1980's, and provided the means to generate recombinant clotting factors, rather than the earlier plasma-derived factors

that had initially carried the risk of blood borne viruses. But therapy with clotting factor proteins still carries the need for repetitive intravenous infusions, sometimes 2-3 times/week, and results in peaks and troughs of factor levels, depending on the half-life of the clotting factor in the patient. At the trough, the person is at risk for bleeding episodes. Our goal in gene therapy had been to infuse a gene delivery particle containing the FVIII or FIX gene into the liver (via an intravenous infusion), which would then allow the subject to make his own clotting factor protein from the transferred gene. We published successful studies carrying this out in the canine model of hemophilia in 2002, but it has proven challenging to achieve similar results in humans. More recently however, in a trial for hemophilia B, we have been able to achieve consistent levels of FIX, in the range of ~30% of normal. At this level, for the ten men who participated in the Phase 1/2 trial, use of clotting factor was reduced by 99%, and 9 of the 10 subjects experienced no bleeds after vector infusion. These results were presented at the plenary session of the 2016 American Society of Hematology annual meeting in December. We are now engaged in moving this work forward (it is partnered with Pfizer, who will direct the Phase 3 studies). Moreover we have recently begun a Phase 1/2 study of a similar vector for hemophilia A, and we are excited about this study as well.

Spark is also working on gene therapy for patients with a number of other inherited conditions. Can you talk a bit about other therapies that are in the pipeline?

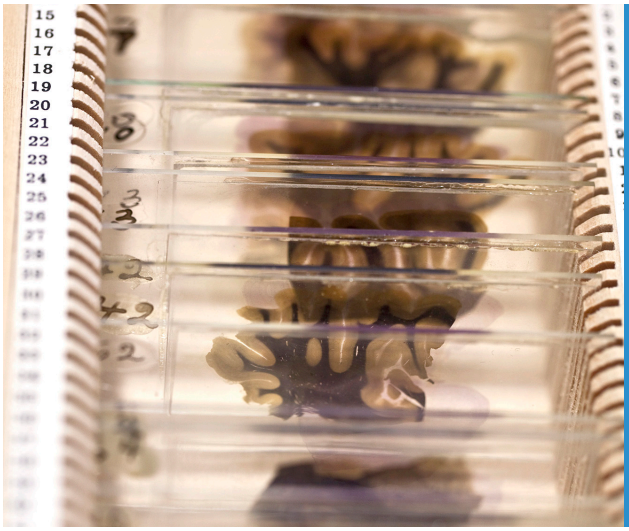
Yes, we recently announced that we have filed the licensing application with the FDA for a vector that was developed to address a rare form of congenital blindness. This disease is due to mutations in a gene called RPE65; the clinical disease has many different names but the most common one is Leber's congenital amaurosis. If this product goes to licensing, it would be the first gene therapy product for a genetic disease in the US.

One of the controversies surrounding gene therapy is the sometimes extremely high cost of these interventions. How do you envision delivering gene therapy to the people who need it most, regardless of the cost?

The clinical development program for the investigational agent for blindness spanned a decade. Those of us who have worked on this program for so long have as a high priority insuring that anyone who can benefit from the vector will be able to receive it. Access to approved therapies is an important goal for what we do.

Tell us about one of your favorite items in the Library or the Museum?

My very first exposure to the Mütter Museum was about twenty years ago. When Bill Kelly was the dean of the medical school at Penn, he used to hold periodic dinners for the members of the faculty holding endowed chairs. One of these dinners was at the Mütter Museum. It was certainly sobering to sit at dinner in the midst of the collection. I suppose one of my favorite items is the ***section of Einstein's brain***. ■



The Mütter Museum is one of only two places in the world where you can see pieces of Albert Einstein's brain.

Scientists who have examined his brain have concluded that it is not normal. While Einstein's brain weighs less than the brain of an average adult male, 2.7lbs versus 3 lbs, the inferior parietal region of the brain is 15% larger than in an average brain. Neuroscientists speculate that these features could account for Einstein's increased mathematical and spatial reasoning skills. Despite these observations, the source of Einstein's genius remains a mystery.