

Medscape Medical News from:

The Future of Genomic Medicine (FGM) III

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Looking at the Future of Genomic Medicine: An Expert Interview With Eric J. Topol, MD

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March 17, 2010 — *Editor's note: For the past 3 years, Scripps Translational Science Institute has held a conference/course unlike other genomics meetings in its equal appeal to and representation by both clinicians and researchers. This year, the program focused on 4 areas of genomic medicine in which the planners saw the most exciting work going on and sensed changes afoot.*

In an interview with Medscape Pathology, course codirector Eric J. Topol, MD, director of the Scripps Translational Science Institute and chief academic officer for Scripps Health, in La Jolla, California, discusses highlights of the recent conference, The Future of Genomic Medicine III, cosponsored by Scripps and the J. Craig Venter Institute, held March 5 and 6, in San Diego, California.

Medscape: Let's start by discussing the keynote talk by Leroy Hood, MD, PhD, president of the Institute for Systems Biology in Seattle, Washington. What topics did he emphasize?

Dr. Topol: His talk was a standout, unbelievable! They have a paper coming out in *Science* [March 10], which is the first whole-genome sequencing of 4 members of a family — 2 parents and 2 kids. There have only been about a dozen people in the world who have had that done and [who have had it] reported or published.

[Dr. Hood and colleagues] had a whole family and used it to diagnose a rare genetic disorder called Miller's syndrome. He also showed these exquisite maps of the genome — every little piece that came from the mother or the father — so-called recombination maps. So we had a preview of some of the really seminal findings. Of course, when we inherit our genes from our parents, there's also a very tiny rate of mutations that occur de novo. And for the first time, this has actually been quantified because this is the first family that's ever had full sequencing.

Dr. Hood also went on about molecular diagnostics and how, in the future, we'll have hundreds of diagnostics to be able to provide what he calls the 4 *Ps*: personalized, pre-emptive, participatory (because of consumer enablement), and prevention. So when I thanked him for his address, I called him the fifth *P* — "phenom!" That starts with a *P*, right? It was an amazing address, a standing-room-only gathering at 8 a.m. on a Saturday. And people were not disappointed.

Medscape: The program for last year's meeting dealt with technology and holes in our knowledge. This year's program was focused on cancer and infectious disease, more applications. Was this just a choice of theme or does it indicate how the field is shaping up?

Dr. Topol: We were too ambitious last year, because we tried to cover all of medicine. We figured this time we're going to be a little smarter. We only have a day and a half, so let's zoom in on the areas where the most exciting work is going on. We then picked the 4 areas, starting with the keynote on sequencing whole genomes in people because it's come so far in 1 year. With a full day — and only a crazy person could have made up this schedule — every 15 minutes we had another speaker, from 8:00 a.m. to 6:30 p.m. But we had 4 areas that we covered really well, which were the exciting areas of 2010:

- *Aging* — I was able to present a new exciting finding about our "welllderly" program
- *Pharmacogenomics* — there have been some really big breakthroughs in that area
- *Infectious disease* — you can sequence the bacteria, the pathogens, and get tremendous insight
- *Cancer* — which has obviously been the leading edge of this field.

If we had picked 3 areas, it would have probably been more normal, or 2, because then we wouldn't have gone until 6:30 at night. But it was amazing!

Medscape: What did you talk about in your presentation in the session on aging?

Dr. Topol: We have a really exciting finding, which we got via serendipity. I guess that's not so uncommon when you have something exciting. We now have more than 800 "welllderly" individuals, and we also have corresponding elderly people, matched for birth year, who had died in their early 70s. It's extremely difficult to get DNA from people who have died, I can't emphasize how difficult that is. But we were fortunate, through collaborations with our colleagues in Oregon and San Francisco [involved in] other clinical trials, to get DNA from people who had died.

When we did that genome-wide study of the 2 different groups, we found a very impressive spike in what turned out to be a gene that was simultaneously being reported in fruit flies, *Drosophila*, called *4EBP*.

That gene is a critical mediator for all the different things that control lifespan — the 3 pathways — and we just happened onto it.

4EBP is a choke-point in the pathway of insulin-like growth factor (IGF)-1 signaling, TOR (target of rapamycin) signaling, and mitochondrial energy.

Those 3 are the key pathways of cell growth, metabolism, and lifespan, and this gene is right smack in the middle, where all 3 converge. It was certainly gratifying that, for the first time, this gene has been shown to be important in humans. It had been shown to be very important in *Drosophila*, but this is a big step forward.

Medscape: What was your perception of the really hot topics at the conference this year?

Dr. Topol: The hottest topics still go back to the sequencing story. We gave the annual award to Elaine Mardis, from Washington University [St. Louis, Missouri]. We recognized her for her pioneering efforts in cancer genomics.

She was the first person in the world to sequence a tumor in a patient with leukemia, both the tumor DNA and the germ-line DNA. By doing that paired sequencing, which is Herculean, she could then determine what the the driver mutations were in that individual.

She presented data at the meeting — she has now done 50 paired sequencings in patients, and over 10 breast cancer paired sequencings. This is incredible work!

Each person is generating tens of billions of bits of data. And her team, which includes not only the people doing the sequencing, but all the bioinformatics and analytical work, can determine in each individual what went off the track to drive the cancer. This is really a futuristic type effort, so we wanted to recognize her now.

There was also a lot of debate the first day regarding exome sequencing versus whole-genome sequencing. The fact is that exome sequencing is so much cheaper, and produces a lot less data to have to work with. But the whole genome — albeit at higher cost and higher complexity of analysis — does provide a lot more elegant data to work with. So that was a big issue that many people addressed. Many of the exciting findings were presented using either technique, so we got pretty much up to date from that. And where cancer is at the moment, sequencing is really the main thing going on in that field.

In infectious disease and sequencing the pathogen, my colleague Nick Schork presented MRSA [methicillin-resistant *Staphylococcus aureus*] sequencing — being able to distinguish which MRSA, or even methicillin-sensitive SA, is going to be tissue-invasive versus noninvasive. It isn't just being methicillin-resistant, there are signatures in the genome that he and his group have discovered.

Pharmacogenomics is moving forward at a rapid pace, with several very important discoveries. Russ Altman from Stanford [University, California] went over all the different things going on in this space, and actually even used Steve Quake's genome, which has been fully sequenced. (Steve Quake is Russ Altman's colleague at Stanford.) His genome was fully sequenced in 1 week, and it was reported a few months ago. Altman used that to show all the different drugs that Steve should or should not get, and that was pretty amazing, really a glimpse into the future.

Medscape: With all the talk about personalized medicine, do you foresee that in 10 years, 50 years, everyone will have an electronic medical record that will show the medicines they should get and the diseases they're likely to develop? Or will it just be for the rich and famous?

Dr. Topol: No, no, this is not just for the rich and famous. One company, Pacific BioScience, is now saying they can do it soon for \$1000, whole-genome sequencing in 15 minutes! That was in the *Wall Street Journal*.

I think it's going to be doable someday, but it is not going to be next year. We're already down to \$5000 to \$6000 for whole-genome sequencing in 2010, and it's just a matter of time until it does get down to that level.

When you have the whole-genome sequence, there are still missing pieces, like the methylome, the metabolome, and the proteome. You have so much vital information to help individualize that person's health story and preserve their health and prevent diseases, prevent untoward reactions to drugs — it just changes everything. That was a nice example, as I mentioned, with respect to Steve Quake's genome and the pharmacogenetics guys at Stanford.

Medscape: There was a presentation about a new initiative in genomic medicine education. Can you talk about that?

Dr. Topol: Greg Lucier, CEO of Life Technologies, gave a presentation about the future of genomic medicine with a video, and it was captivating! Life Technologies has given us a grant to form an Association of Genomic Medicine, to teach and credential the medical community — physicians in particular — in genomic medicine. We have formed a board that includes physicians and scientists from each of the disciplines, like neurology, diabetes, cardiology, and cancer.

The program would be CME and it would be pretty substantial, a pretty significant commitment. We're going to have to authenticate physicians, because we're going to be giving CME *and* credentialing. It won't be just getting a CME certificate or hours, it's actually credentialing that the individual has taken a test, has gone through the course, and is up to speed on the latest concepts and data in the field. Basically, we're saying that they have demonstrated competency.

We know that 90% of physicians now declare they don't feel any comfort at all in genetics/genomics! That was from a survey done by the [American Medical Association] in October. They said they wouldn't be able to prescribe a drug, even if they were given the data! They just don't feel comfortable with this whole area. So we did a survey at the conference, and we gave out *The Language of Life*, [NIH director] Francis Collins's new book, as a raffle prize for people to do the survey, and we basically drilled down on what the unmet needs are: How much time would people devote? How would they like to get the information? What were they interested in?

We're going to be meeting soon, and developing an incredible curriculum with interactive Web remote-university tools that are going to be used to credential physicians who are interested in getting up to speed. There will be a couple different levels, and it's going to be very interactive and exciting. I hope that we'll get most physicians on *Medscape* to participate!

Dr. Topol has disclosed no relevant financial relationships.

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