**Expert Interview with Charis Eng, MD, PhD, on "Genetic testing, a personalized tool to build a roadmap to manage inherited cancers"**

Featured CPI Researcher
Posted on November 09, 2020

**Dr. Charis Eng is the Director of the Genomic Medicine Institute and its Center for Personalized Genetic Healthcare at the Cleveland Clinic. Her clinical and basic research teams use state-of-the-art technologies to improve on the diagnosis and treatment of patients with inherited conditions. Dr. Eng's laboratory investigates how inherited gene mutations increase cancer risk and determines if existing drugs can reduce that risk. Among many other discoveries, her laboratory has found that mutations in the PTEN gene predispose to many cancers, as well as to autism. In this interview she discusses her career path towards becoming a geneticist. She also discusses genetic testing and the key role of basic research for the diagnosis and management of individuals with a high risk for cancer.** *Dr. Eng is a member of the National Academy of Medicine and a recipient of the 2018 American Cancer Society Medal of Honor for clinical research.*

***What inspired you to become a geneticist?***

I was inspired to become a physician at four years of age by one of my uncles on my mum's side. He was a great clinician and mentor. When I was in 4th grade in Singapore, which is where my family, including my uncle, lived, I started learning about great biomedical discoveries: the microscope, Pasteur and vaccination, bacteria, etc. I knew I wanted to be a physician-scientist. By serendipity, my father was selected to attend the University of Chicago to do a PhD, and my mother and I joined him. I enrolled at the University of Chicago Laboratory Schools, and had several inspiring teachers, especially a biology teacher who taught us genetics. In his spare time, he discussed cancer education. This is the spark that inspired me to merge cancer and genetics. From that time on, I worked my way toward that end.

I did my Bachelors at the University of Chicago and was mentored by the late genetics Professor Ed Garber, and continued on at the University of Chicago for my PhD and MD. I trained in Internal Medicine at the Beth Israel Hospital in Boston and in Medical Oncology at Harvard's Dana-Farber Cancer Institute. At the "Farber," a senior professor, Dr. David Livingston, knew about my interest in Cancer Genetics. He suggested I train in Genetics either in the US or in Cambridge, UK with Professor Bruce Ponder. Without hesitation, I chose to train with Prof. Ponder. Why? Because Prof. Ponder had strengths at the bench and the clinic. The training I would have received elsewhere would have been only at the bench. The key is to bring discoveries from research to people. As I tell my trainees, as physicians, we will touch patient lives one at a time, but if you are a great medical researcher and do it right, you will improve the lives of millions of people around the world. And that is my philosophy.

***What do you consider as your biggest accomplishment?***

I have led my ideal academic life bringing my work at the laboratory bench to the patient's bedside. My team has discovered and mapped the *PTEN* gene, and we found it is critical for suppressing breast, thyroid, and other cancers. Because of our work, we can help people who have inherited mutations in this gene. Our work together with others has informed practice guidelines that include enhanced cancer screening leading to early detection and cure.

When I was recruited to the Cleveland Clinic, Ie founded the Genomic Medicine Institute (GMI). It is a single platform for research, education, and clinical work. The clinical arm is called the Center for Personalized Genetic Healthcare, and it is where discoveries from the lab can be translated. The clinical arm enables the uptake and enrollment of individuals with inherited conditions, not just in cancer. The GMI is a single platform for the whole of genomic medicine, and it includes pharmacogenomics.

***Genetic testing. Why is it important for individuals to get tested and know about their risks of getting cancer?***

When I returned from Cambridge, UK, in 1995, a handful of us started up cancer genetics clinics. Our goal was to translate the discovery of genetic mutations that cause cancer to effective

treatments and prevention. A genetic analysis includes genetic testing and taking family history both of which can provide data to guide patient care.

There are about 400 inherited cancer syndromes with associated genes, and each gene is different. By determining what specific gene is altered, we are able to predict what cancer or cancers that person is at risk for, when the cancers will appear, and, as a result, how to change the clinical care. **Genetic testing is a way to predict what cancer someone is at risk for and improve their care**. It is patient-oriented, it is all about the patient and their family.

***Could you tell us more about the role basic research has to play in improving genetic testing?***

It is not just about discovering a new gene. That is obviously part of it, because if there is no gene, there is no genetic testing. And when there is no genetic testing, there is no personalization of care based on the gene. However, knowing just about the gene could be useless. Knowing about what phenotype is associated with the genetic mutation is what makes it useful. For example, *PTEN* was originally called the breast/thyroid cancer gene. As more work was done, we now know that it also predisposes to uterine, kidney, and colon cancer. We know when the age of risk rises. We know where cancer occurs, and we know how to enhance clinical surveillance. We even know how to advise on prophylactic surgery.

When a gene is translated into a protein, what does it do? It affects other proteins, and that affects processes. When a gene is mutated, molecular processes are changed. With that come targeted therapies. These treatments act against the processes that are changed. Targeted therapies are not new in cancer, but they are newish for people with inherited gene mutations that predispose to cancer. The entire scientific and medical community participates in the discovery and development of targeted and other therapies. Basic scientists discover the deregulated pathways, drug development colleagues select the molecules that are potential drugs, translational scientists conduct preclinical studies and early safety trials and late drug developers design and prosecute late phase clinical trials. Everyone collaborates. Developing a targeted therapy is a long road that of course we should always seek to shorten.

I also want to emphasize that limiting our studies to cancer genetics is not enough. For example, *PTEN* mutations predispose carriers to autism spectrum disorders as well as cancer. By determining that one gene can be part of two different diseases and studying these two different diseases, they can inform each other and accelerate the development of new therapies.

***Where do you see the future of genetic testing going?***

Everyone should get genetic testing. Why are we not doing that now? Because we find things called variants of unknown significance, and we do not know what these variants mean. Once we know exactly what every variation means and what it predisposes to (or to nothing at all), then genetic testing becomes a roadmap to the prevention of disease.

A gene mutation is not crippling. It gives information that guides therapy, decreases mortality and decreases morbidity. We have all the components for everyone to get genetic testing and a roadmap to managing inherited diseases. We have virtual visits and a lot of digital technologies and artificial intelligence to help us, as well. Our genetic counselors can use all of this information to help us be proactive to prevent illness.

*More information on how basic science is brought to the clinic to develop personalized healthcare at the Cleveland Clinic can be found at*
https://www.youtube.com/watch?v=0cLYd_OcXFk&list=PL9CZabk3nD4GageWtKCmRUTOJc_l5YX0L&index=5&t=0s

*Dr. Eng's titles are:*
*Chairwoman, Genomic Medicine Institute*
*Sondra J. and Stephen R. Hardis Endowed Chair in Cancer Genomic Medicine*
*American Cancer Society Clinical Research Professor, Cleveland Clinic Lerner Research Institute*
*Chairwoman and Director, Center for Personalized Genetic Healthcare, Cleveland Clinic Community Care and Population Health*
*Professor and Vice Chair, Department of Genetics and Genome Sciences*
*Leader, Germline High Risk Focus Group, Comprehensive Cancer Center, Case Western Reserve University School of Medicine*