

Oncologists as clinical trials investigators



Dr. Han Koh

Receiving a cancer diagnosis can be a terrifying moment for a patient. But when patients at Kaiser Permanente Southern California see a physician for cancer, they can take comfort knowing they are also seeing a clinician researcher who can help them access the latest tools being studied for fighting the disease.

“We are an integrated health care system, and our clinical trials are integrated into that system,” said William J. Towner, MD, FACP, FIDSA, regional physician director for the Department of Research & Evaluation’s Division of Clinical Trials Research. “So, in other words, if you are diagnosed with a malignancy and you go in and see your oncologist, that same oncologist has access to many clinical trial options should you qualify for them.”

There are typically about 50 active clinical trials available through the Cancer Clinical Trials Access Program.

“Participation in clinical trials can give our patients access to medications that they wouldn’t otherwise have been able to get,” Dr. Towner said. “They also have the opportunity to be part of the medical discovery process while receiving first-rate Kaiser Permanente health care.”

As a result of Kaiser Permanente’s integrated model, all the 80 KPSC medical oncologists are also co-investigators on clinical trials research. Four of the principal investigators have overall responsibility for the cancer clinical trials: Gary L. Buchschacher Jr., MD, PhD; Lara Durna, MD, MS; Han A. Koh, MD; and Helen Moon, MD.

Dr. Koh explained that cancer treatment is evolving from treating all cancers with basically the same tools of chemotherapy and radiation into targeting specific cancers. Parts of that evolution are the clinical trials that show whether a treatment is safe and effective.

KPSC has clinical trials in both targeted therapy and immunotherapy. Immunotherapy helps a patient's immune system fight cancer. Targeted therapy is a type of precision medicine that attempts to target the cancer's specific genes, proteins, or the tissue environment that contributes to cancer growth and survival.

These are the stories of who the principal investigators are, what inspires them, and why they were drawn to medicine and cancer research.

Gary L. Buchschacher Jr., MD, PhD

Los Angeles Medical Center

Cancer specialty: Gastrointestinal cancer



Dr. Buchschacher grew up in northern Wisconsin and developed an interest in science as a child exploring the outdoors.

"I was always checking things out: animals, plants, insects—all of the things we would come across

in the outdoors—exploring was a big part of our playing," he said. "I was particularly interested in how a caterpillar could grow and transform into a monarch butterfly."

When he was in junior high and high school, he became interested in chemistry and molecular biology.

His fascination with science continued into college, where he became interested in the molecular biology behind cell functions. While he was working toward his undergraduate and graduate degrees at the University of Wisconsin-Madison, he also worked at the McArdle Laboratory for Cancer Research

"When I was studying molecular biology during undergrad and graduate school, my main interest was in the study of viral replication and the development of viral vectors (which are tools used to deliver genetic material into cells)," Dr. Buchschacher explained. "Basically, I was interested in determining how viruses might



Dr. Helen Moon, Dr. Jonathan Polikoff, Dr. Han Koh

be used as vectors to introduce genes, and the potential for gene transfer therapy applications."

That research translated directly into the precision medicine trials he works on today.

His typical workweek includes direct patient care as well as seeking out new potential trials that might be opened as part of the cancer clinical trials program.

"I'm always looking for opportunities for clinical trials in which we might be interested in participating," he said, "or discussing and participating in the development of trials."

Dr. Buchschacher, who specializes in gastrointestinal malignancies, said that he looks for trials targeted at specific cancer characteristics that some of his patients may share.

"In the past, before the science was able to identify potential treatment targets as readily, clinical trials were a bit more broadly designed," he said. "Now, with the advancements in molecular biology and molecular genetics, when it is possible to identify certain genetic defects or other specific characteristics of cancer cells, sometimes it can open up possibilities for treatments that can be targeted to those particular defects."

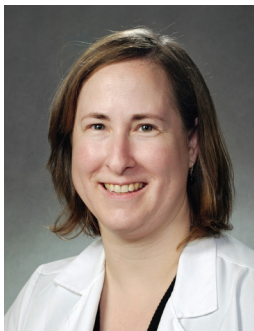
In the last few years there has been significant progress and there is the potential for the development of new targeted therapies, Dr. Buchschacher said. Much progress has been made regarding treatments for melanoma, lung cancer, breast cancer, and some cancers of the blood.

"While there are now a variety of new treatments that have helped many people, precision cancer therapy isn't quite the panacea that people sometimes make it out to be," he said. "There are still many limitations, as well. We still have a lot of research and work to do, which is why it is important to have a robust cancer clinical trials program."

Lara Durna, MD, MS

South Bay Medical Center (Harbor City)

Cancer specialties: Hematology and breast cancer



In college, Dr. Durna focused on plant biochemistry. While studying plants, she met an HIV researcher whose work inspired her to learn about medical biochemistry. She began a school internship at a drug company working on cancer pathways, and

she thought she had found her field. She was pursuing her PhD when a statistician introduced her to the world of clinical trials.

"I changed my mind after that and decided that I really wanted to get an MD, because I was interested in trying to help people with these cancers through cancer drug development," Dr. Durna said.

So, despite being a natural introvert who thought she would always be working in a lab, she changed her career trajectory.

"Once I started getting exposed to people as patients, I learned I really loved working with patients, and cancer patients, specifically," she said. "I felt like all of my background came together to have more meaning when I was looking across the



Dr. Gary Buchschacher, Dr. Lara Durna, Dr. Helen Moon

room at a human being that I could really help."

Dr. Durna said she has great hope for the advancement of cancer treatment through clinical trials.

"Because of my biochemistry background, it's always been clear to me that there's much more science to know than we currently do," she said. "There are far too many people who still die of this disease far too young."

She said she is driven to utilize science advancements to improve cancer therapies, "so people can go on living their lives, as fully as possible."

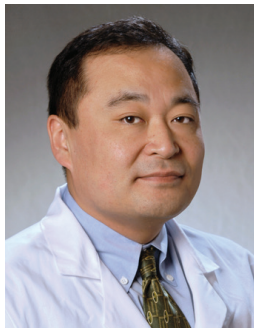
When available, targeted precision cancer treatments can have a lot of advantages, she said. Often, they can decrease the side effects that people are having while they're undergoing cancer treatment.

"Ultimately, these therapies have led to more people being cured of some diseases," Dr. Durna said, "and we hope in the future, to cure even more."

Han A. Koh, MD

Downey Medical Center

Cancer specialty: Lung cancer



Dr. Koh was introduced to medicine at an early age: His grandfather and father were both physicians. What drew him to medicine, though, was an intense fascination with science that began in elementary school, he said.

"I wanted to be a scientist, and particularly a practical scientist, where the scientific knowledge could actually be used to help other people," Dr. Koh said. "So, that's how I ended up in medicine."

About 10 years ago, he was working as an oncologist at the Downey Medical Center doing chemotherapy clinical trials and research—when he was introduced to precision medicine.

"As I witnessed the development of precision medicine in the oncology area, I came to see that this was the future," he said. "I knew that this is where we would have to concentrate our research efforts, and that's exactly what's happening now."

Initially, he thought that precision medicine might be the "magic bullet" for curing cancer, "but as you do more research in the area, it's not that simple. There are a lot more barriers we have to overcome."

So, Dr. Koh and the other oncologists continue to do research to better understand how the different cancer-causing genes work. He's seen cases where they target one cancer-causing gene only to have the target mutate and another target pop up.

"I always say cancer cells are smarter than doctors," he said.

He said lung cancer, which he specializes in, is a good example of a cancer for which precision medicine can be helpful.

"Precision medicine can contribute a lot because lung cancer is not a single cancer," Dr. Koh said.

"There are probably at least 50 or 60 different subtypes, so it's an ideal area for developing the targeted therapy."

He said one of the main trials is the STRATA trial, in which researchers are conducting "next-generation gene sequencing on the tumor cells," that allows them to identify the genetic aberration causing a cancer and to try to target that specific cancer.

Helen Moon, MD

Riverside Medical Center

Cancer specialties: Genito-urinary cancer, melanoma, and immuno-oncology



As a young person, Dr. Moon wanted to become an international diplomat. But instead she followed a boyfriend to medical school. While it didn't work out with the boyfriend, it did turn out to be one of the best decisions of her life.

She realized helping to make people healthy was her calling, and one of her strongest motivators was the desire to not let people down. It was the perfect combination for a physician researcher, who could continually work to find new possible treatments.

"After I joined Kaiser Permanente, that's when I became really excited by the possibilities to do research," she said.

In the last 5 years or so, precision medicine has been making a big difference in her area of cancer, which are cancers of the urinary and male genital tract.

"So, in some ways, I was in the right place at the right time for the right specialty," she said.

Overall, she said the oncologist's job hasn't changed all that much. Most of it is about reassuring patients and helping them through difficult and uncertain times using the best treatments available.



(From left) Joseph Rosales, assistant manager ambulatory care nurse; Dr. David Wu, sub-investigator; Dr. Sunil Patel, sub-investigator; Dr. Han Koh, principal investigator; Maria Arriola, clinical research nurse; Susan Nottmeier, clinical trials nurse manager; Derek Bucheli, clinical research associate; Deborah Shipley, clinical research nurse; Nikki Williams, regulatory specialist; Dr. William Towner, regional physician director of clinical trials; Denise Martinez, clinical trials nurse manager; Dr. Wanping Hu, sub-investigator; Lorena Bacon, clinical research associate; and Dr. Fengyu Shu, sub-investigator

"For Gary, Lara, Han, and I, we have roles, not only in research, but also as physicians and regional cancer leadership," she said. "And so, you think about how to move the whole field forward, but also, what can we do for each of our patients?"

Dr. Moon said the role that Kaiser Permanente plays is critical to learning about new therapies and helping cancer patients get their best treatments. She called it the "concept of the last mile."

Often drugs and therapies can be developed that have incredible potential. But if the side effects are too unpleasant, patients won't continue with them and won't see the benefits. Kaiser Permanente's clinical trials are done typically in the stage where the treatment already has been shown to be safe for patients, but before it is available to the public. The Kaiser Permanente data show how

the treatment works for large, diverse groups of people.

"Are patients able to afford the medications that we're giving them? Are they understanding that, even if it's a pill, it has side effects? Can we effectively manage nausea, so they don't throw away the pill?" she said. "We are able to optimize those pieces of the puzzle so all of that research into new medications can be relevant."

The cancer clinical trials space that she, Dr. Buchschacher, Dr. Durna, and Dr. Koh are involved in is exciting because it is constantly growing as they search out new opportunities and treatments for patients, she said.

"Oncology clinical trials will lead Kaiser Permanente into the next frontier," she said. "And we're all just hungry for more."