

REBELS

REVIEW

Winter 2015

USC CENTER *for* APPLIED MOLECULAR MEDICINE
USC NORRIS WESTSIDE CANCER CENTER

Doctor's Notes

From the Desk of David B. Agus, MD



Photo Credit: Bryce Duffly

I am excited to update you on the changes and progress at the USC Center for Applied Molecular Medicine (CAMM) and the USC Westside Cancer Center (WCC). These have been an especially busy few months both in the lab and clinic. Our team is expanding and you will meet some of our fantastic new members in this newsletter.

I also want to introduce our 'Big Data' effort (page 4). The power of Big Data cannot be overstated. In an era where we still treat cancers by their body part of origin, we need to find ways to improve. Consider how search engines work. Every time you run a Google search, Google learns from it, continuously creating results which are better today than yesterday. They look at the data and actually improve the hierarchy of search results; we should be doing the same with medicine. Unlike Google,

I am not able to quantify and extrapolate from every physician's experience. Current medical treatments are the equivalent of giving everyone an umbrella every day to just cover the handful of people who need the umbrella for the rain in their cities. Big Data will help us figure out exactly who needs the umbrella. Given our current lack of data, we just don't know which aspects of disease need different and better treatments. Big Data can give us this information and so much more. I think you will be excited as we describe the team and a few of our current projects. We will have even more to share in the coming year.

Lastly, I am honored to share the news of the publication of my new book, *The Lucky Years: How to Thrive in the Brave New World of Health*. The book will be released January 5, 2016 and I hope to hear your thoughts on the content. Please find an excerpt from it below.

"Given our current lack of data, we just don't know which aspects of disease need different and better treatments. Big Data can give us this information and so much more."

The Lucky Years A Snapshot

“We are indeed living in a brave new world, but this one won't be dystopian as the one Aldous Huxley portrayed in his famous book.

Chances are you stand to live a much longer, more enjoyable life than you ever thought possible—thanks not only to such age-reversing remedies as plasma transfusions, but also to a staggering volume of other new knowledge and technologies in medicine. Scientists are developing drugs to reverse once-fatal ailments such as heart disease and figuring out how to harness a person's immune system to melt away cancer. They are designing computer applications

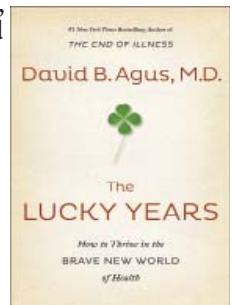
to help us regularly and effortlessly track key features of our biological functions including blood sugar, sleep quality, heart rate, blood pressure, stress levels, moods, and even risk for problems ranging from depression to cancer.

For the first time, we have at our disposal all the information we need to design our own health—and, in turn, the health of the planet. Put simply, people living in the twenty-first century are the most fortunate of all previous generations. That's why these are the Lucky Years.

If you are fifteen years old or younger and living in a high-income country, your chances of developing and dying from breast cancer, heart disease, lung cancer, or leukemia before your sixtieth birthday are declining dramatically. Despite much higher rates of obesity and physical inactivity, premature death and disability from

noncommunicable diseases (e.g. heart attacks, chronic respiratory diseases, and diabetes) have declined significantly in the United States and other high-income countries, thanks to inexpensive and effective prevention, early detection, management, and treatment tools and policies. But more needs to be done, and it will come from us if we can do three things: believe that aging is optional, think about our future, and act on it today.”

Check out my new book! Available January 5, 2016.



Tumor DNA Offers Real-time Results, Longer Lives

In cancer therapy, time is of the essence. In spite of this urgency, doctors often have to administer a single treatment for several months before they can evaluate how successfully it is working. We don't want to waste those precious months on the wrong therapy, leaving patients vulnerable to the spread of cancer. Nevertheless, we currently have no choice but to wait for results.

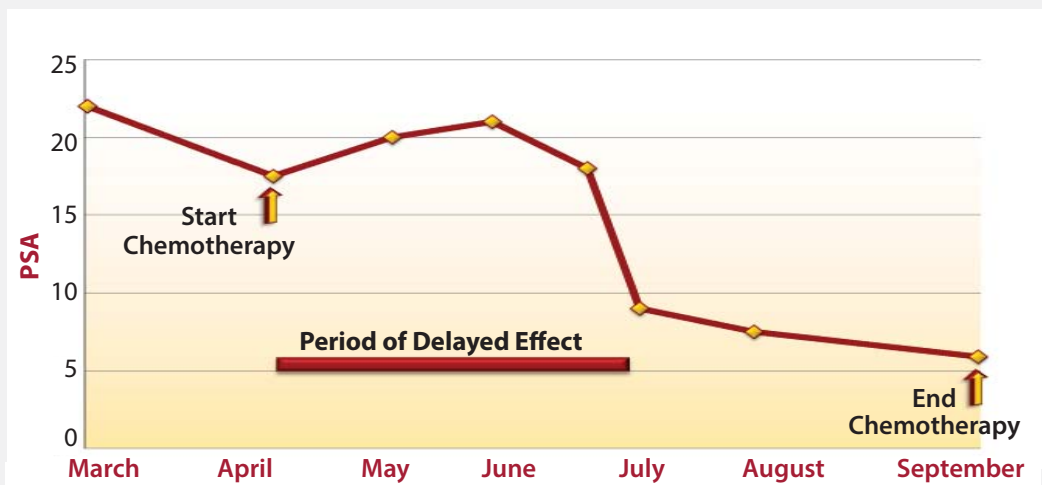
Within CAMM's Stephenson Family Personalized Medicine Center, our scientists are reassessing this problem. What if there was a way to find out how a patient is responding rapidly—perhaps even the same day of his treatment? We are piloting a project which one day may be able to do just that. Recent evidence suggests that as cancer cells die, they release their DNA into the bloodstream. Our scientists believe that immediately following an effective treatment, tumor DNA levels in the blood will climb swiftly, reflecting the death of many cancerous cells and indicating success. In order to confirm this, our scientists are comparing DNA in a patient's blood just before and then again shortly after therapy to obtain a real-time understanding of how the tumor is

responding. Our team of doctors, physicists and biologists are developing ways to identify and monitor tumor-derived DNA present in the blood to gauge how effective a therapy is.

Drs. Mitchell Gross and Dan Ruderman are collaborating to find out how we can use circulating tumor DNA measurements to predict patient outcomes. Their team, consisting of Dr. Katherin Patsch, Dr. Naim Matasci, Patricia Diaz, and Anjana Soundararajan, has successfully developed methods to accurately measure the amount of tumor DNA present in blood from advanced prostate cancer patients. This DNA often

contains mutations which can provide further biological insight to doctors and directly influence treatment decisions.

The project's first milestone is to demonstrate that changes in the amount of tumor DNA just after therapy can predict the patient's long-term response to that therapy. If we can develop a rapid test for therapeutic success, it may allow us to try multiple treatments in sequence in order to choose the most effective option. We hope to provide a way for doctors to quickly choose the best therapy for each individual and ultimately offer patients longer, cancer-free lives.



We are measuring early changes in tumor-derived DNA in blood as an indication of therapeutic response. In this case, the prostate cancer patient was treated with chemotherapy for almost 3 months before PSA decreased, an indication that the treatment was working. Blood-borne DNA levels will help us find this out much sooner, perhaps even the day of treatment.

Spotlight on: The Nurses of WCC



Kelly La Mont, RN, OCN

Q: Where are you from originally?

A: I am from Minnesota. I came out here to sunny California to pursue a career in nursing. While working in Minnesota on a cold winter night, a fellow nurse mentioned to me she was considering becoming a traveling nurse. I contacted an agency and before I knew it, I was on the road to California for my first assignment.

Q: What are your hobbies?

A: I enjoy spending time with my

husband, Eric, my stepdaughter, Daryan, and our furry child, Lola! As a family, we enjoy the beach, hiking, a nice meal and our family parties. We have a big family and host a lot of parties with good Mexican food, mariachi, dancing and singing.

Q: What keeps you motivated?

A: Over the years, I have kept letters, gifts, and memories of those changing moments that have shaped my life and the lives of others. Moments of fear, letting go, grief, loss, great news and

survivorship have kept me in this career to fight on and to respect the struggle.

Q: Why did you join WCC?

A: I believe the Westside Cancer Center's multi-disciplinary approach to patient care, outstanding team, and great leadership can truly make a difference against this devastating disease. I am so proud to be part of a team that takes the time to focus on the individual patient and provide excellent care.

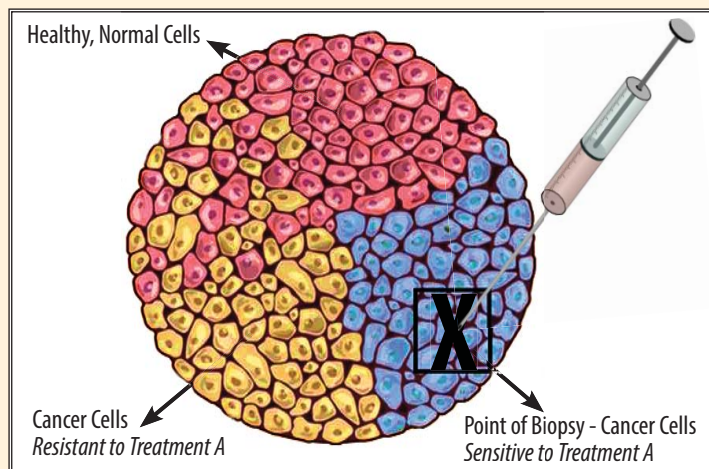
(continued on pg. 3)

Genetic Mapping & Cancer Recurrence: HOPE ON THE HORIZON

For the 13.7 million cancer survivors in the US today, the threat of cancer recurrence looms like a storm cloud in the distance. Although doctors have no way of predicting which patients will recur, scientists at CAMM's Stephenson Family Center for Personalized Medicine are trying to better understand both why cancer recurrence happens and how to prevent it.

Recent findings may provide new insight about why cancer recurs. Researchers have learned that cells within a single tumor can vary widely in their genetic makeup. They can also mutate and change over time throughout the course of treatment. These diverse cell populations may include a few cells which are resistant to therapy. While one treatment successfully destroys the majority of a tumor, a few resistant cells may survive, multiply, and lead to cancer recurrence. Until recently, there has been no way to monitor or map out the genetic differences in tumor cell populations. However, with the evolution of tumor genetic sequencing, our researchers have begun to develop these genetic "geographical maps."

Together with Drs. Ruderman, Gross and Matasci, Dr. Katherin Patsch applies DNA sequencing to create a "geographical map" of genetic changes throughout tumors. In collaboration with industry partner Thermo Fisher Scientific, Dr. Patsch draws her maps by comparing mutations across many biopsies from a single tumor. She aims to use this critical information to design optimized patient biopsy methods in order to guide personalized treatment strategies. There is no current standardization for how many tissue samples should be collected during tumor biopsies. However, our team hopes to standardize this process using the information gathered through genetic mapping,



ultimately providing all physicians the most complete and informative view of a tumor.

Through the standardization of the biopsy process and genetic evaluation, doctors may soon be able to identify and target resistant cells from the time of diagnosis. With this revolutionary insight, Dr. Patsch believes we could be one step closer to eliminating the looming threat of cancer recurrence.



Dr. Patsch's commitment to taking a multi-disciplinary approach in fighting cancer may not be surprising considering her multi-cultural background. Born in Houston, Texas, she spent her childhood growing up in the Austrian Alps. This diversity led to her deep passion for traveling to different countries whenever possible. Since joining CAMM in 2012, she lives in Silver Lake with her husband, Thomas, and cat, Bo.

Nursing (continued from pg. 2)



Cindy Richards, RN, OCN

Q: Where are you from originally?

A: I am a native of Southern

California. I was born in Northridge and moved to Simi Valley when I was 6 months old.

Q: Why did you become a nurse?

A: I was drawn to nursing at a young age. I told my mother I wanted to be a nurse in kindergarten!

Q: Tell us about yourself!

A: My husband Ken and I have one daughter, Mady. She is a sophomore pre-med student at USC and is a long jumper on the USC Track and Field Team. In

my spare time, I enjoy spending time with my family and friends. I also volunteer as a youth long jump coach and serve on the board of directors of a Ventura County nonprofit cancer foundation.

Q: Why did you join WCC?

A: I was immediately drawn to the Westside Cancer Center during my interview, particularly to the team atmosphere and the fact that every person I met that day had been a part of the practice for a long time. I share the philosophies of the Center which includes treating

patients as individuals, promoting wellness and offering the best possible therapies. I was also very impressed with the CAMM lab and the difference their research has made and will continue to make in the lives of patients. I feel very blessed to have the opportunity to bring my oncology nursing experience to WCC and look forward to working with this fantastic group.

Join us in welcoming our new nurses!

Unifying Data to Fight Disease



To understand the origin of diseases and develop therapies, physicians have always relied on the clinic and the laboratory. Now they have another powerful tool: computers. Data that have been collected over the years are now accessible to researchers, and it is already making a difference. For example, Vioxx, an anti-inflammatory drug used for arthritis, was pulled because data from electronic medical records linked it to heart attacks, saving thousands of lives per year. But to make these discoveries, we need data collected by different groups to have the same format and meaning so they can be combined. We rarely find data in equivalent formats, however. Simply combining medical data for comparison across the city of Los Angeles is vastly complex, and the problem is exponentially multiplied across the globe.

This year, the Leona M. and Harry B. Helmsley Charitable Trust has funded Drs. David Agus and Dan Ruderman at CAMM to address this problem for Type 1 Diabetes (T1D) research. This devastating disease's incidence has risen sharply in recent years, with studies suggesting a 21% increase of T1D in the pediatric population of the U.S.¹ Our goal is to develop new theories to explain this increase and then test them in a clinical trial. One powerful way to generate new theories

“Data standards will mean that we can promote efficient sharing of information between doctors and scientists around the world.”

is to assemble data from existing studies around the world and explore them using modern tools for big data analytics.

Unfortunately, it is hard to find commonalities among studies that started decades ago. Back then, data

standards that provided definitions of various measurements were not widely used in clinical trials. Consequently, two studies may represent blood sugar in different units or they may measure it using different methods. This makes unifying the data both error-prone and painstaking. To avoid this sort of problem in the future, we need to develop standards that ensure the same format and meaning from the start.

Data standards will mean that we can promote efficient and accurate sharing of information between doctors and scientists around the world. We aim to develop agreed upon guidelines for representation, format, definition, structuring and collection in order to truly revolutionize data sharing and pave the way for future breakthroughs. This will not only be invaluable in T1D, but also across many disorders, from heart disease to cancer.

CAMM's Dr. Naim Matasci and Mark Engeln have been leading the charge for T1D, by both proposing data standards, and also creating software tools to ease the adoption of these standards worldwide. Using them will soon enable us to design a multi-center T1D prevention trial: one whose data can be meaningfully combined with other studies by researchers globally. Championing the cause of data standards in clinical trials will place us at the forefront of the promising new field of computational medicine.

¹Dabelea D, Mayer-Davis EJ, Saydah S, et al. Prevalence of Type 1 and Type 2 Diabetes Among Children and Adolescents From 2001 to 2009. *JAMA*. 2014;311(17):1778-1786. doi:10.1001/jama.2014.3201.

Let's Defeat Cancer Together!

Our cross-disciplinary approach enables us to integrate principals from physics, biology, math and engineering into new ways of managing and treating cancer. While some may call it visionary, for us, there is simply no better way to help us succeed in our fight.

Your support will dramatically advance our research to the next level, allowing the most effective treatments to benefit patients who are in urgent need of new therapies—today. Simply fill out the enclosed envelope to donate to the USC Center for Applied Molecular Medicine and USC Westside Cancer Center or visit our website now!

<http://keck.usc.edu/donateWCC>

Thank you in advance for your generosity!

Keck School of
Medicine of USC

USC Norris Westside Cancer Center & USC Center for Applied Molecular Medicine
9033 Wilshire Blvd., Suite 300, Beverly Hills, CA 90211
Tel: (310) 272-7640 Fax: (310) 272-7656
www.keckmedicine.org/usc-wcc & www.camm.usc.edu