

USC Center for Applied Molecular Medicine and USC Norris Westside Cancer Center

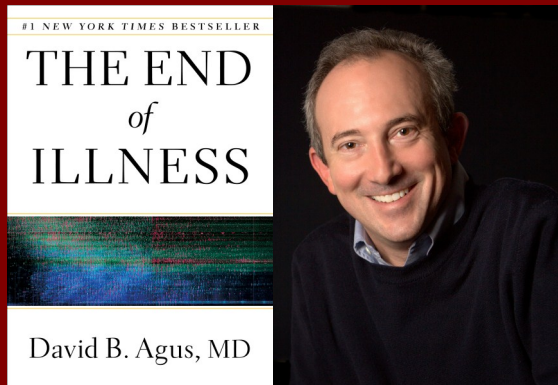


Photo Credit: Phil Channing

Dear Friends,

It's an exciting time at the USC Center for Applied Molecular Medicine and the USC Norris Westside Cancer Center.

I am encouraged by the progress in research to treat cancer. We have new drugs in our arsenal that are bringing real hope to control cancer. Your support has enabled our Centers to be at the head of these developments and develop new ways to approach cancer. It continues to be my honor to work with our team to make a difference.

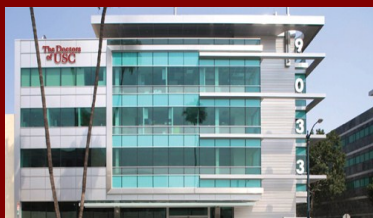
It has been an eventful few months as my book was released and the reception has been positive. I am proud to say that a PBS special on the book will air in September and would love your feedback. You are welcome to go to <http://www.theendofillness.com> to see the press coverage.

Please email or contact us with ideas or comments on the newsletter.

With respect,



David B. Agus, MD



The USC Norris Westside Cancer Center offers the latest in treatments for individuals diagnosed with cancer. The Center is advancing the clinical care of cancer through novel clinical trials and believes in bringing new therapies to patients.

Keck School of
Medicine of USC



CAMM Update

by Jonathan Katz, PhD

The CAMM lab research group focuses on the development of “personal medicine” technologies. In this update, we would like to present two exciting articles we have published since the last update.

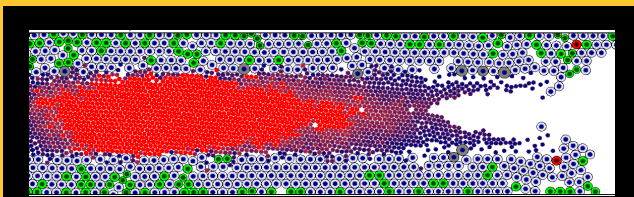
Dr. Macklin (featured in this newsletter’s “Spotlight”) published his research entitled “Patient-calibrated agent-based modeling of ductal carcinoma in situ (DCIS): From microscopic measurements to macroscopic predictions of clinical progression” in the *Journal of Theoretical Biology*. Computational modeling has given great theoretical insights into cancer, but transforming these models into useful clinical tools has been difficult. In this work, Macklin introduced a computer model of individual cancer cells and developed the world’s first method to calibrate it to individual patient pathology data—a key step in developing next-generation clinical planning tools. He tested this approach on DCIS, an important precursor to invasive breast cancer that often requires two or more surgeries for complete removal. The model predicted tumor growth and calcification that agreed with clinical data, gave new insights that may improve our interpretation of mammography, and points to a day when we can use a simulator to combine a patient’s pathology and mammography to improve surgical planning. Macklin plans to apply the same approach to prostate cancer (in coordination with the USC Norris Westside Cancer Center), expand his model to invasive breast cancer, and use simulations to help us more rapidly predict the clinical impact of the novel insights coming out of our lab every day.

Dr. Kani published his work in *Molecular Cancer Therapeutics* titled “Quantitative Proteomic Profiling Identifies Protein Correlates to EGFR Kinase Inhibition.” In this work, Kani is trying to further understand why patients respond differently to cancer drugs. Using tissue culture as an experimental model, Kani grew cells sensitive and resistant to the lung cancer drug gefitinib in different media -- cells grown in the presence of the heavy isotope were easily distinguished from cells grown in the presence of light isotope. In this impressive undertaking, Kani was able to identify almost 6,000 separate proteins! Of these, more than 75% of the proteins produced good quantitative data which he culled down to a list of 400 proteins that showed a significant change in abundance following gefitinib treatment. Efforts are now underway that use these results to both predict and monitor drug effectiveness in patients as well as to study mechanisms of drug resistance that can evolve during treatment.



Spotlight on Paul Macklin, PhD

Dr. Macklin joined CAMM in August 2011 as an Assistant Professor of Research Medicine from the University of Dundee in the UK. As a mathematician, his focus is on building computational models of cancer that can be calibrated to individual patient data, allowing predictions of disease progression and therapy response that he hopes will one day improve clinical planning. See the figure below, <http://www.MathCancer.org>, and the CAMM update for a recent example with ductal carcinoma *in situ* (DCIS)—a precursor to invasive breast cancer. Macklin's models use physical laws to govern cell motion, and simulation rules are written to test and refine (or toss out!) current cancer biology orthodoxy. This work requires close-knit, diverse teams of biologists, clinicians, physical scientists, and modelers—exactly what drew Macklin to CAMM. In Macklin's spare time he likes to take his daughter to organ concerts.



Patient-calibrated simulation of DCIS: Virtual cells in the outer region proliferate (green) or apoptose (red) to match patient pathology. The central necrotic core includes a microcalcification (red region), as is often seen by mammography.



USC Norris Westside Cancer Center

Meet Claire Schloemer the newest member of our team at USC Norris Westside Cancer Center. Claire joined our staff earlier this year part-time as an Administrative Assistant and we are fortunate to have her on board full-time as of May. She graduated this year from University of Southern

California with a degree in *Health Promotion and Disease Prevention*. Impressively, she played NCAA Division I soccer as a lead defender while achieving numerous academic honors. She was awarded Multiple Career Honoree: *PAC-12 All Academic* (2009, 2010, 2011) and Multiple Career Honoree: *Mark's Scholar* (2011, 2012), which is only awarded to two scholarship athletes with the highest GPA on their team. **Way to go Claire!**

How Can You Help?

You can make an impact on this terrible disease. To donate to the USC Center for Applied Molecular Medicine and USC Norris Westside Cancer Center please visit us at http://www.doctorsofusc.com/wcc_donate or use the enclosed envelope to mail in your donation. Thank you in advance, your generosity is greatly appreciated.

Clinical Trials Update

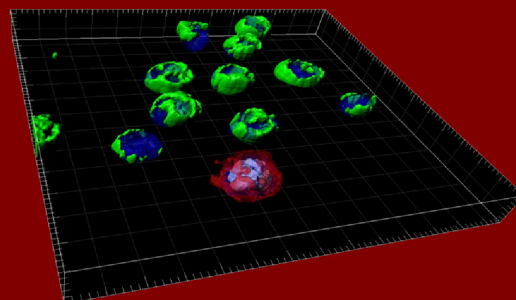
by Mitchell Gross, MD, PhD

These are exciting times in the world of cancer research. Many decades of studies focusing on the basic building-blocks (genes & proteins) involved with the transformation of normal tissue into a cancer are now being “translated” into an ever expanding arsenal of new technologies and therapeutic agents. These agents can be used to alter, and hopefully eventually eliminate, cancer from a healthy person with minimal side-effects. The development of new therapies for prostate cancer has been particularly rapid over the last few years. After a period with no new drugs from 2004 to 2010, we have recently seen the approval of four new agents, and expect the approval of another two in the next year. Our team has been fortunate to be involved in clinical studies involving these and many other agents over this period so as to provide “cutting edge” therapies to our patients. We are committed to continuing this practice as we present a few highlights of our ongoing clinical research efforts below:

- A “GPS”-like ultrasound device that allows for precisely targeting and minimally invasive therapy for prostate and other forms of cancer.
- Developing new ways to find and analyze genes and proteins related to cancer cells based on routine blood tests (See figure below).

We are also continually working with biotechnology and other pharmaceutical partners to develop new drugs which specifically target prostate cancer cells and work on making these treatments available to our patients as part of many clinical trials.

In summary, we dream of a future where customized therapies will be designed for cancer patients based on a deeper understanding of specific gene and protein alterations present in individual patients. On behalf of our entire group of physicians, nurse practitioners, nurses, managers, and coordinators, we are committed to be active participants in the process of making this dream into a reality.



In the above figure: A prostate cancer cell (red) expressing the androgen receptor protein (light blue) is found in the blood of a patient. Normal white blood cells (green and dark blue) are also present.