

# REBELS

# REVIEW

Winter 2016

## Doctor's Notes

From the Desk of David B. Agus, MD

Lawrence J. Ellison Institute for Transformative Medicine of USC  
USC Center for Applied Molecular Medicine  
USC Norris Westside Cancer Center



When I reflect on 2016, I cannot help but feel gratitude.

I am grateful for the patients who have touched my life and have entrusted me to help shape the course of their care. I am grateful for my compassionate clinical team and for my scientific collaborators and colleagues – some of the best and brightest minds in the world – who have joined with me in the quest to change the face of cancer research and treatment and improve the lives of cancer patients. I am grateful for the visionary gifts of people like Larry Ellison, who have deeply invested in this research and believe that we can change the world.

I also have a new transformative gift to be grateful for: Marc and Lynne Benioff have pledged \$20 million to the Lawrence J. Ellison Institute for Transformative Medicine. We will name the lobby of the Ellison Institute in honor of Marc's father, Russell Benioff, who passed away in 2012 from prostate cancer. Marc attributes his astonishing work ethic and entrepreneurialism to Russell, a retail executive who began at his parents' department store, working his way up to president of a chain of apparel stores in the Bay Area.

Like his father, Marc worked his way up to the top in business. In fact, after graduating college, Marc joined Larry Ellison's company Oracle in a customer service role. Three years later, he was promoted to vice president and

*"We truly believe that by empowering and funding institutions doing important cancer research we will be able to change the course of this disease."*

-MARC BENIOFF, CEO OF SALESFORCE

became the youngest person to ever hold that position at Oracle. Larry has been a longtime mentor to Marc, and today they join forces again – this time to battle cancer.

The last six months at the Ellison Institute have brought new scientific developments in the fight against cancer that I am excited to share with you, including some brand new collaborations that could lead to truly world-changing discoveries. We are making great strides forward, and this is possible because of your support.

I am deeply thankful for the gift Marc and Lynne have so generously pledged. I am also humbled. Like far too many of us, they have a personal understanding of what it means to lose someone to cancer. In remembering Russell, and so many other friends and patients, I am reminded that we still have a long road ahead of us.

As we end another year, I want to renew my commitment to all of you to continue to combat this deadly disease. I will continue to champion this fight along with the brilliant and visionary colleagues, researchers and benefactors who stand with me. I am honored – and grateful – that you've chosen to join us on this journey.



Marc & Lynne Benioff

# Great Minds “Think Different”

## *The Ellison Institute for Transformative Medicine of USC and Emulate, Inc. begin a collaboration for patient-driven advances in cancer treatment*

Shannon Mumenthaler, PhD, Director of the Stephenson Family Personalized Medicine Center at the Ellison Institute, is excited. She enthusiastically gestures to the images on her computer screen while describing one of the biggest challenges she faces as a cancer researcher: tumor models. She explains the benefits and limitations of each model—animal models are very complex, but she has limited control over, or insight into, what happens within the animal. Cell cultures and tumor spheroids are easier to manipulate environmentally, but they are fairly simple models which cannot replicate the complex internal functions within a patient.

“What we need is a way to peek into the inner-workings of the human body while maintaining strict control over the cellular environment,” she says. “That’s why I’m especially eager to begin this new collaboration with Emulate.”

Emulate has joined forces with the Ellison Institute in a new strategic collaboration. Emulate has offered their groundbreaking technology to our cancer researchers for investigation into how tumors develop, metastasize and respond to treatment. In their efforts to recreate a near “in vivo” (inside the body) environment, Emulate’s visionary team of biologists, designers and engineers has successfully developed a clinically relevant model of multiple human organs. Their pioneering “Organs-on-Chips” technology provides a high-fidelity window into human biology and disease. Organ-Chips – such as the lung, kidney, brain or liver – are micro-engineered environments lined with living human cells and tissues that recreate the natural physiology and mechanical forces cells experience within the human body. Ultimately, they are designed to predict human responses to

***“What we need is a way to peek into the inner-workings of the human body while maintaining strict control over the cellular environment.”***

–SHANNON M. MUMENTHALER, PHD

diseases, medicines, chemicals and foods with greater precision than conventional cell culture dishes or animal models.

Shannon and her fellow researchers at the Ellison Institute will also gain early access to Emulate’s lab-ready product platform, the Human Emulation System™. This plug-and-play system, integrating the Organs-Chips with automated instrumentation and software apps, will readily allow for the technology’s easy use within laboratories across the world without the need for specialized expertise. A widely available Human Emulation System could mean moving new therapies from the laboratory to the bedside faster and with more accuracy than ever before.

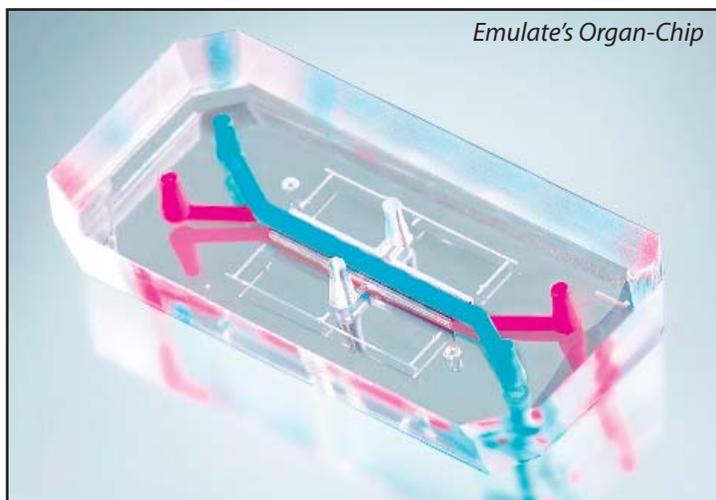
Geraldine A. Hamilton, PhD, President and Chief Scientific Officer of Emulate, is eager to begin this R&D collaboration

as well. “The human-relevant insight offered by Organs-on-Chips technology opens up new ways to understand diseases and medicines so that we can bring new solutions and treatments to patients. We are delighted to collaborate with the world-leading researchers at the Ellison Institute and USC, who have the expertise to advance new understanding of challenging diseases, such as cancer, and are dedicated

to translating their research to patients quickly and effectively.”

You may have heard Dr. Agus say, “If you change the soil, the seed won’t grow.” Emulate’s technology allows us to change the ‘soil’ (the tumor’s environment) in subtle ways, whether with oxygen levels, nutrients, or drug treatments. The Ellison Institute is then able to capture the effects of those changes in real-time through the power of their microscopy image-based methods of tracking cells.

“This opportunity to observe and control the tumor microenvironments is unprecedented,” Shannon explains. “Up until now, we have been limited in how well we can truly recreate the environment supporting a tumor. With the use of



## Great Minds “Think Different” (continued from page 2)

the Organs-on-Chips technology and the Human Emulation System™, we hope to begin to understand and uncover long-hidden mysteries of cancer, and how to successfully fight it.”

And that is exactly why Shannon is so excited. She isn't just enthusiastic about cool science. She has one thing in common with her multi-disciplinary coworkers and the patients who are treated here: she is passionate about finding treatment options for cancer - and finding them as soon as possible. These tiny living Organ-Chips represent new hope for researchers and patients alike.

Shannon smiles. “It’s a good day to be a part of the Ellison Institute.”



Shannon M. Mumenthaler, PhD, is an Assistant Professor of Research Medicine at Keck School of Medicine of USC. She serves as the Director of the Stephenson Family Personalized Medicine Center and Lab Director of the Ellison Institute. Shannon is the mother of three (including fraternal twins), and enjoys spending time with both her family at home and her research family at the Ellison Institute.

## What do NASA, Mountain Climbing, and Cancer Research Have in Common?

Colin Flinders, PhD, is an avid mountain climber, but he never imagined that hobby would intersect with his passion for cancer research. A postdoctoral scholar at the Ellison



Colin Flinders, PhD, a Postdoctoral Scholar at the Ellison Institute, is pictured scouting for bacterial collection sites at El Tatio (a geyser field in the Andes Mountains of Chile).

Institute, Colin has departed on a NASA Astrobiology Institute expedition with colleagues from NASA and SETI. Their destination? The Altiplano, a mountain standing 12,300 feet above sea level in the Andean Mountains of South America. At the southern end of the Altiplano lies the Atacama Desert, a dry, desolate environment that experiences little rainfall, below freezing temperatures, and has the highest recorded levels of ultraviolet radiation in the world.

“UV is what causes our skin to burn. It can also cause cell damage, premature aging and skin cancer. To give you some context, a hot July day in Los Angeles may have a UV index of 11. The Atacama Desert commonly has an index of 26 and has levels on record as high as 29.”

Colin is traveling to this extreme environment to collect and study diverse microbial communities found in the lakes of its volcanic craters. Prior research has identified novel ways in which these microbes tolerate the intense UV radiation they encounter. Colin and the Ellison Institute are hopeful that the analysis of these specially adapted organisms may identify novel genes or metabolic substances that could have therapeutic applications for treating or preventing cancer.

“This is an amazing opportunity. I’m very excited about the prospect of what we could learn from these microbes, and how we might be able to apply this to cancer therapy.”

*Watch for updates on Colin’s expedition in our summer issue of Rebels Review!*

## Flu Shots offered at WCC!

“Did you know the flu creates an inflammatory storm that can potentially increase your lifetime risk for obesity, heart attack, strokes, or cancer? We are offering flu vaccinations to our patients at the USC Norris Westside Cancer Center. Contact us today and keep yourself and your family safe and healthy!”

-KELLY SANTORO, PA FOR THE USC WESTSIDE CANCER CENTER



Kelly Santoro, PA

# A Self-Driving Microscope?

## Machine learning to save lives around the world

Between self-driving cars, talking smart phones and Facebook's ability to recognize friends in photos, we seem to be surrounded by ever-smarter technology. Technology that can *learn*. In fact, the method for programming cars to drive themselves and computers to recognize faces is called "deep learning," a type of "machine learning." Here at the Ellison Institute, we are using that same technology to help patients battle cancer around the world.

Rishi Rawat, a 26-year old MD/PhD student with a background in computer science and machine learning, was completing a student rotation at the Ellison Institute when the experience of a close friend changed the course of his work. His friend's father was diagnosed with late-stage pancreatic cancer, one of the most lethal of all cancers.

Rishi explains, "It really affected me. I started to ask myself, 'how can I use

my thesis to do something good for the world?'"

Rishi met with Dr. Agus for advice. After a few discussions, he realized that his background in machine learning might be put to use in the war on cancer. He began focusing on one of the biggest challenges facing global medicine today: access to quality pathology. For the best outcome, patients must receive the correct diagnosis. This is a foundational need, yet a global shortage of pathologists means that obtaining results from a biopsy can be difficult, time-consuming, or even impossible in some parts of the world.

Rishi decided that instead of using his skills to make a smarter phone or a better self-driving car, he would create a software program that can accurately diagnose cancer. In essence, he wants to create a digital pathologist. With this goal in mind, Rishi and the Ellison Institute are collaborating with leaders in pathology, cancer biology and artificial intelligence to build a computerized platform that diagnoses cancer from tissue specimens.

This coming year, due in part to a generous grant from the Breast Cancer Research Foundation (BCRF), the Ellison Institute will work in partnership with collaborators at Memorial Sloan Kettering and Yale University to move this project forward. Our core technology is based on state-of-the-art deep learning algorithms,

*A shortage of pathologists makes receiving the correct cancer diagnosis impossible in some parts of the world.*

which are very similar to the algorithms that power Google's image search and Facebook's facial-identification. Instead of training our systems to recognize faces or everyday objects like Google and Facebook, we train them to identify patterns on microscope slides that distinguish cancer from normal tissue or identify which drugs are best suited for the patient.

"Although scientists have tried in the past to accomplish similar goals, the needed technology was not available until very recently," says Rishi. "One of our biggest challenges so far has been obtaining data sets large enough to adequately train the computer. With these new collaborations and the support of BCRF, we believe we will have enough data to overcome that obstacle. Things could move very quickly," he pauses, "but we have a long road ahead of us."

It may be a long road, but it is one that will pave the way for other "self-driving" diagnostic services. Because of everyday heroes- like Rishi and Dr. Agus- it is a road bright with hope for the future.



Originally from Colorado, Rishi Rawat received his undergraduate degree at UC Berkeley and then came to USC for its MD/PhD Program in Cancer Biology. When he's not trying to solve cancer, Rishi enjoys cooking, judo and hiking.

### Join the fight against cancer!

Every gift matters in the fight against cancer. By supporting our disruptive, multi-disciplinary research you will help change the face of cancer treatment and significantly benefit the lives of those battling cancer today. Simply fill out the enclosed envelope to donate to the Lawrence J. Ellison Institute for Transformative Medicine of USC or visit our website now!

[ellison.usc.edu/donate](http://ellison.usc.edu/donate) or text **REBELS** to 9-1999

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