A New Task for Artificial Intelligence

Understanding Different Outcomes for Patients with COVID-19

Caring for Patients in a Challenging Time

Join the Fight Against Cancer!

Dear friends,

As always, our researchers have continued to collaborate to secure grants and conduct exciting research, including a new use for artificial intelligence that could help us make great strides in therapy development. They have also used this time to network virtually and streamline their workflows within our new laboratories.

We have continued to assist in the important fight to combat COVID-19. The Ellison Institute is proud to collaborate with Skydance Media on a public service announcement urging citizens to volunteer to be part of the vaccine clinical trials. We worked closely with the COVID-19 Prevention Network to create and circulate the announcement, in the hopes of getting an additional one million volunteers to be part of the study and help get the country back to normal as soon as possible.

The Ellison Institute is pressing on with science and medicine and a commitment to new discoveries. Through the most difficult of times, our mission has remained clear and our drive stronger than ever. We thank you for your continued support, and we look forward to seeing you soon.

Respectfully,

David B. Agus, M.D.
Professor of Medicine and Engineering
Founding Director and CEO
Lawrence J. Ellison Institute for Transformative Medicine of USC

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REBELS REVIEW

From the Desk of David B. Agus, M.D.

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The pandemic has brought new challenges to nearly all aspects of our lives, but especially in healthcare. Patients, understandably, have struggled with decisions about whether to keep or delay doctor appointments. When it comes to oncology, it is critical that patients continue to receive the highest level of care. Here at the Ellison Institute, we moved quickly to implement protocols that would ensure that we can provide continuous care to meet the needs of our patients during this global health crisis.

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-KELLY SANTORO

Collaborating with the VA for More Accurate Study Results

The introduction of immune checkpoint inhibitors (ICIs), more commonly known as immunotherapy drugs, constitutes one of the most important developments in cancer research in the last decade. ICIs work by boosting the body’s immune response against cancer and promisingly, more than 50% of cancer patients with metastatic disease in the U.S. may be eligible for this treatment. Immunotherapy has quickly become a prevalent treatment in clinical settings, and although it has been studied for safety and effectiveness, there have been only a few studies to date that address real-world usage and outcomes of ICIs on a national scale.

During the COVID-19 quarantine, Jerry S.H. Lee, PhD, the Ellison Institute’s Chief Scientific and Innovation Officer, working with clinicians and data scientists from the United States Department of Veterans Affairs (VA), conducted a retrospective analysis to better understand the effectiveness of various immunotherapy regimens for various cancer types. To the authors’ knowledge, this is the largest and most comprehensive real-world cohort of patients treated with ICIs that has been analyzed and reported on in research.

The study, published in JCO Clinical Cancer Informatics in October, tracked outcomes for 11,888 patients treated with ICIs in the national VA healthcare system, which serves over 9 million patients annually that are often older, frailer, and at large.

The VA has a large patient data set, including findings from novel treatments and their outcomes, and the Ellison Institute hopes to continue partnering with them on other projects to help share additional patient outcomes and give non-VA patients hopes to continue partnering with them on other projects to help share additional patient outcomes and give non-VA patients insights into ICIs on a national scale.

Creating an Educational Experience During a Pandemic

This summer marked the tenth anniversary of the Ellison Institute’s tuition-free high school fellowship program. The Junior Fellows program fosters scientific education for rising high school seniors interested in clinical or research oncology by incorporating hands-on experimentation in a collaborative environment. The Institute is passionate about education, particularly for students in our neighboring communities, and this program grew out of a core belief that the “kids are our future.”

For this reason, during the early days of the pandemic, the Ellison team was determined to ensure we could still host the Junior Fellows this year. So, despite the small RNA virus that has lingered the world and amid a cross-town move to our location at 12414 Esplanade Blvd, the Education & Outreach team, led by Director Dr. Kian Kani, designed a new curriculum specifically for a virtual internship. In early July, twelve rising seniors from high schools spanning from Orange County to Santa Barbara converged daily for virtual discussions. “Students have lost so much this year due to the pandemic, so it was important for us to be able to provide them with this program, even virtually,” said Jillian Iuliano, MPH, Education & Outreach Specialist. “Many of our Ellison staff members volunteered to present topics to the Junior Fellows to help make the program as ‘normal’ as possible—this was a team effort!”

Throughout the fellowship, the participants had virtual meetings with Ellison’s diverse team of faculty, scientists, and students. The fellows also met with our clinical team—our doctors, physician assistants, nurses and medical assistant, clinical associates, clinical research team, and our dietitian—which imparted a better understanding of the multitude of career options and educational avenues that are available to them as they narrow down their college choices.

The overarching theme of the internship is cancer. Yet, the focus is not on objective memorization of molecular pathways and various hallmarks of cancer. The goal is to create a real-world environment where each learner, with their experiences and from their own perspective, is encouraged to participate. For example, several of the fellows are competitive video gamers, so the team emphasized artificial intelligence and the importance of mathematical modelling approaches in cancer into group-based discussions. In placing each learner at the hub of the learning environment, we were able to continue to create a framework that encourages collaboration and cooperation. This mirrors our approach to battling cancer—mathematicians, biologists, physicists, data scientists, and clinicians working together can achieve tomorrow’s breakthroughs more effectively than working in silos.

Thus, the main learning objective of the program is to empower the students to think differently, challenge dogma, and utilize various skills to tackle the toughest challenges as a team. And we are encouraged to learn we can accomplish this, even from afar.

We look forward to a more traditional in-person internship and hope to celebrate our eleventh anniversary with our fellows and all the Junior Fellows alumni in 2021. This year’s Junior Fellows are: Nola (Santa Monica), Corryn (Winward), Shua (CA Academy of Math & Science), Ivy (CA Academy of Math & Science), Simon (Wildwood), Sarah (Marlborough), Aidan (Loyola), Abigail (Palos Verdes), Ben (San Marcos), Dylan (Edison), Noemi (Campbell Hall), and Leo (Santa Monica).
treatments safely by limiting capacity in the lobby to one patient at a time, restricting guests, and instituting a one-way flow of patients in the building. As things have progressed, we have continually adapted our policies and procedures to provide the safest environment for patients, family members, and staff. We have implemented telemedicine visits, enabling patients to access care from the comfort of their homes. For those patients coming to our office for an in-person visit, in addition to workflow changes and an updated mask policy, they are directed to self-park, undergo infrared temperature screening, and complete a COVID-19 risk assessment questionnaire. Our staff members are also tested for COVID-19 on a routine basis.

“I am privileged to work with our clinic team—Amber, Beverly, Brian, Caitlin, Erin, Jackie, Mary, Natalie, Olga, Karen, and Kate—as they have been unwavering, and have gone above and beyond to care for our patients during this challenging time,” said Kelly Santoro, MMSc, PA-C, Clinical Physician Assistant and Clinical Director at the Ellinson Clinic. “Under the direction of Dr. David Aguas and Dr. Mitchell Gross, the Ellinson Clinic has not lost sight of our vision. Rather, COVID-19 has pushed us to expand innovation in transforming medicine, and in turn patient lives. I continue to be inspired by this incredible team and the ever-increasing magnitude of the situation, I am confident that we will prevail, and our patients can be confident that COVID-19 will not compromise their care.”

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The study, published in JCO Clinical Cancer Informatics in October, tracked outcomes for 11,888 patients treated with ICIs in the national VA healthcare system, which serves over nine million patients annually that are often older, frailer, and more racially diverse than those in clinical trials. This is crucial for acquiring data that is more representative of the population at large.

The study showed that the results are favorable when compared to historical controls. However, the improvements are not as significant when compared to those found in clinical trials, confirming the assumption that there is a disparity between clinical trial outcomes and real-world clinical practice. This may be a result of the disparity around eligibility and effectiveness of immunotherapy drugs highlighted in the need for supplemental long-term data. This is the focus of Ellison Institute’s Applied Therapeutics Laboratory: we partner with organizations like the VA, whose interoperable national healthcare system allows us to better track the long-term implications of new therapies.

“It is an extraordinary privilege to collaborate with the VA to begin creating a national learning healthcare system that provides evidence and reveals disparities when new therapies are given after clinical trial approval.”

-DR. LEE

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Junior Fellows 2020

Corynn: Plays volleyball; plays piano; sings; likes goofy conventions; has 2 Labrador retrievers

Leo: Yoga; meditation; competitive video games; skiing

Sarah: Reading; drawing; watching movies; golf; collects postcards & bookmarks; plays kalimba (instrument)

Nola: Plays: soccer, beach volleyball, the violin, the piano, in the school orchestra and theater

Simone: Plays beach & beloe volleyball, soccer, music; likes to play poker; can solve a 3x3 Rubik’s cube on Metros (Bunya & Westwood Ranchos)

Noemi: Drawing; digital sketching; hosting; writing creative stories & poetry

Ivy: STEM; medicine; swimming; backpacking; yoga; diving; traveling; is a twin

Abigail: Research; robots; nature; science; art; painting watercolor portraits; swimming; digital design applications; drawing; music

Dylan: Video games; digital design applications; Boy Scouts

Ben: Indoor & beach volleyball; hospital volunteer; VP for SAJ & SJP (local non-profit for students to express voice & art); memorialized over 600 digits of Pi in 3rd grade

Meet the Fellows and learn more about their interests

Aidan: Plays football; ASB President; plays 1 instrument; interested in being a pediatrician

Shua: Research; robots; nature; science; art; painting watercolor portraits; swimming; digital design applications; writing; music

Kelly Santoro: Plays beach & volleyball; enjoys playing with her children; interested in learning more about cancer research
A New Task for Artificial Intelligence

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e celebrate when a new cancer treatment becomes standard of care. Unfortunately, there are always some patients that will not respond to a particular therapy in addition to suffering side effects.

What if there was a better way to determine who will benefit and who would be better suited with an alternate therapy? An important component of that determination are biomarkers, or indicators of the presence or subtype of a disease. Daniel Ruderman, PhD, recognized that an area in which biomarkers could be improved is in the treatment of HER2-positive (HER2+) breast cancer. These tumors are driven by a growth pathway dependent on HER2 signaling. But, only about half the patients given HER2-targeted therapy benefit from it despite their tumor possessing the biomarker suggesting that they would.

Dr. David Agus along with co-investigators Dr. Ruderman; Dr. Michael Press, Ellison Institute Affiliate Member; and Dr. Jerry Lee, Chief Scientific and Innovation Officer, received a grant from the Breast Cancer Research Foundation to pursue research that will determine whether artificial intelligence (AI) can discern who is likely to respond to HER2-targeted therapy using computational interpretation of tumor architecture as a biomarker. Simply put, can they teach AI a better way to "read" microscope slides of HER2+ breast cancer to predict treatment outcomes?

The team has a record of success in this type of research. Last year, they published a paper in Scientific Reports on an AI method for discerning estrogen receptor (ER) status in breast cancers from tissue architecture. ER status is a key factor in choosing treatment, but the current test is based on costly immunohistochemistry, just like the one for HER2. The hope is to make such determinations using AI on the slide already made for diagnosis, thus dramatically reducing cost and time. By leveraging AI to "read" the tissue architecture, the team has a record of success. For example, in a recent study, they showed that AI could predict response to HER2-targeted therapy using computational interpretation of tissue architecture better than pathologists. The team is now looking to further validate this approach in a larger, more diverse patient population.

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s COVID-19 was becoming a major worldwide health crisis, Mitchell E. Groover, M.D., Ph.D., Research Director at the Ellison Institute, was struck by a key scientific question: Why do some patients exhibit little to no symptoms, while others suffer from the most severe form of COVID-19 which can occasionally be fatal?

From the rapidly developing scientific literature, he thought that the major difference between patients with mild or severe COVID-19 would be found in the immune system (known as "host factors"). As a cancer researcher, he also saw that he could apply special expertise, relating to studying blood markers to improve the care of cancer patients, to some of the issues facing patients with COVID-19. Working with Ellison Institute faculty, Drs. Jonathan Katz, Dan Ruderman, and Jerry Lee, and key outside collaborators, Drs. Chambless and Juliet Emmanuelle, Dr. Gross developed a project to take an "immune snapshot" of COVID-19 patients using routinely obtained blood samples. The approach is based on a technology that can simultaneously measure multiple proteins from a single drop of blood. For this study, a dozen proteins were selected to constitute the immune snapshot.

The team hopes to use this information to predict which patients infected with the SARS-CoV-2 virus may go on to have the most severe complications (such as requiring treatment in the intensive care unit and mechanical ventilation). An important aspect of the project will be to include a racially and ethnically diverse group of patients that represents the population of Los Angeles. Much of the existing research in this field involved patients treated outside of the United States or less ethnically diverse patient populations. This study hopes to provide additional insights into host factors that predominate in our local community.

"The analytical and statistical expertise at the Ellison Institute, a key component of the multidisciplinary approach, will be crucial for learning how the 'immune snapshot' can help to predict outcome for COVID-19 patients," said Dr. Gross. "Ultimately, the impact of this work will be to help us understand and design better and more individualized treatment for COVID-19 patients."

Caring for Patients in a Challenging Time

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he pandemic has brought new challenges to nearly all aspects of our lives, but especially in healthcare. Patients, understandably, have struggled with decisions about whether to keep or delay doctor appointments. When it comes to oncology, it is critical that patients continue to receive the highest level of care. Here at the Ellison Institute, we moved quickly to implement protocols that would ensure that we can provide continuous care to meet the needs of our patients during this global health crisis. In the early months, while we were still learning and collecting data about COVID-19, non-urgent appointments were slightly delayed to mitigate exposure risks. For patients who could not delay appointments, we ensured they were able to come in for their visits. As always, our researchers have continued to collaborate to secure grants and conduct exciting research, including a new use for artificial intelligence that could help us make great strides in therapy decisions. They have also used this time to network, publish, and streamline their workflows within our new laboratories.

We have continued to assist in the important fight to combat COVID-19. The Ellison Institute is proud to collaborate with Skydance Media on a public service announcement urging citizens to volunteer to be part of the vaccine clinical trials. We worked closely with the COVID-19 Prevention Network to create and circulate the announcement, in the hopes of getting an additional one million volunteers to be part of the study.

As a research center with the strongest Preclinical Medicine of USC, we are in a unique position to leverage our abilities to contribute to the vaccine effort. This year, we are working to increase our recruitment efforts to establish the additional one million volunteers necessary for growing the number of volunteers. We are committed to doing our part in the fight against COVID-19 and we are working tirelessly to ensure that we can provide the highest level of care to our patients.

As always, we are grateful to our donors who have supported our mission and continue to support our efforts. We want to thank all of our donors for their continued support and we look forward to working with you in the future.

Respectfully,

David B. Agus, M.D.
Professor of Medicine and Engineering
Founding Director and CEO
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