HEALTH AGE IN SIGHT

Earlier this year, the University of Pittsburgh joined the Leap Health Breakthrough Network. By signing a multiyear partnership with the nonprofit Wellcome Leap, Pitt has committed to partnering to solve the world’s most serious health challenges at record speed.

Pitt’s goals include breakthrough scientific and technological solutions in human physiology and bioengineering within a decade.

“With our deep bench of health sciences innovators and bioengineering pioneers, Pitt can and will help fuel this ambitious global push to realize breakthroughs for society’s gain,” says Pitt Chancellor Patrick Gallagher.

The network’s mission is to spark a “Health Age,” using the organizational model of the DOD’s Defense Advanced Research Projects Agency (DARPA) to fast-track potentially transformational science.

“Science and engineering should move at the pace of breakthroughs, not the pace of contracting,” says Wellcome Leap CEO Regina E. Dugan, who was a leader at DARPA. One of Wellcome Leap’s first funding efforts is its $50 million Program in Human Organs, Physiology and Engineering (HOPE). That program aims to leverage the power of bioengineering to advance work on stem cells, organoids and whole organ systems and to forge connections to answer the “what-ifs” of health care.

“The University is honored to be joining such an incredible initiative,” says Pitt’s Anantha Shekhar, the John and Gertrude Petersen Dean and senior vice chancellor for the health sciences. “The global scale of this effort is intentional—and absolutely essential if we want to solve some of the most daunting health care challenges of our time.”

—Amerigo Allegretto

Tiny Livers

Five years ago, Mo Ebrahimkhani wondered if he could program stem cells to develop into mature lab-grown livers that would increase the lifespan of those with liver disease. The associate professor of pathology and member of the Pittsburgh Liver Research Center found he could combine machine learning, genetic engineering and synthetic biology to generate tissue that formed into almost mature mini-livers. His lab was able to generate the tissue in just 17 days, extending the lives of mice with failing livers.

Through machine learning, Ebrahimkhani’s team identified genes vital to producing the multiple mature cell types a functioning liver requires. They then altered the genes to turn immature liver cells into adult organoids—lab-grown mini-organs—in a fraction of the time mature human livers develop during pregnancy. These several-millimeter-wide organoids, which formed a network of blood vessels, were crucial to developing mature lab-grown livers that might one day help those with liver disease.

“With tissue by design, you can change the design to fit different applications,” he says.

—Samantha Paige Rosen

OF NOTE

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IMAGE REPRINTED WITH ALTERATION FROM "GENE REGULATORY NETWORK ANALYSIS AND ENGINEERING DIRECTS DEVELOPMENT AND VASCULARIZATION OF MULTILINEAGE HUMAN LIVER ORGANOIDS," VELAZQUEZ ET AL. (2020), CELL SYSTEMS. LICENSED BY CREATIVE COMMONS CC-BY-NC-ND.

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Overheard
Catherine Chappell Says Treat Hepatitis C in Pregnancy

Recruiting pregnant women for a drug trial is no small task given the potential risks to the mother and fetus. But Catherine Chappell was convinced pregnancy was an ideal time to treat women with active hepatitis C infections. Chappell, assistant professor of obstetrics, gynecology and reproductive sciences, ran a phase 1 clinical trial with nine pregnant volunteers who were positive for the virus. The women were given the antiviral drug cocktail ledipasvir/sofosbuvir starting in their second trimester. All were cured of the virus and gave birth to healthy, hepatitis-free babies. The results were published in a September 2020 issue of The Lancet Microbe.

What inspired you to do this study?
I had worked in the HIV clinic for four years during my fellowship. We started treating people living with HIV [who were also positive for] hepatitis C with these really fantastic medications. We see about 200 pregnant women a year at UPMC Magee-Womens Hospital who have active hepatitis C infection, and so I thought: “Why aren’t we using this [drug] in pregnancy?” We know if we treat moms for HIV during pregnancy, we can also prevent perinatal transmission of HIV. I thought this might also work for hepatitis C, because you could cure women for hepatitis and prevent perinatal transmission all with a single course of these medications.

Why is pregnancy an ideal time to screen and treat women for hepatitis C?
A lot of women don’t come in for routine [gynecological] care, especially women who may have a history of opioid use disorder or injection drug use. Pregnancy is a time when women are uniquely engaged in care, arguably much more than during any other time in their reproductive life. So it is a perfect window of opportunity for hepatitis C screening and hopefully, in the future, treatment as well.

What’s next?
We are currently doing a phase 1 study of sofosbuvir/velpatasvir (which is effective for all six genotypes of hepatitis C virus, whereas ledipasvir/sofosbuvir only works for four of them). Meanwhile, we are planning a large multicenter study of 100 pregnant women where we are going to further evaluate the safety and efficacy of sofosbuvir/velpatasvir during pregnancy. Pitt will be the primary site, and [we are] coordinating with six others around the country and one in Canada. —Christina Frank

Faculty Snapshots
Earlier this year, several Pitt Med docs were elected into the American Society for Clinical Investigation. The new members include Walid Gellad, an MD and MPH who is associate professor of medicine and health policy, Jacqueline Ho, an MD, MSc associate professor of pediatrics, Philana Ling Lin, an MD, MSc associate professor of pediatrics, Heath D. Skinner, an MD, PhD associate professor of radiation oncology, and Matthew Steinhauser, an MD associate professor of medicine.

—Sarah Stager

Pennell to Chair Neurology
On July 1, Page Pennell, an MD, will step in as chair of the Department of Neurology. Pennell is currently a professor of neurology at Harvard University and vice chair for academic affairs in Brigham and Women’s Hospital’s Department of Neurology. Her research has focused on maternal and fetal outcomes of women with epilepsy, antiseizure medication use during pregnancy and the effects of neuroactive steroids on seizure provocation.

Pennell serves as the principal investigator on the nationwide Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs study, which evaluates the long-term effects of in utero and infant antiepileptic drug exposure.

At Pitt Med, she will work to further the mission of the neurology department, which is to accelerate the understanding of and treatments for many neurological disorders and conditions.
No Average Joe

Joe Murphy's Pitt Med experience has been defined by connection and community. A Pittsburgh native and member of the Class of 2022, Murphy uses his role as a student ambassador to create mentor relationships between upper and lower classmates, as well as current first-year students and med school applicants. Murphy, 27, majored in chemistry at the University of Virginia, but his desire to interact with patients led him to pursue medicine. To that end, he is part of Pitt Med’s Longitudinal Alliance Program (LAP), which matches med students with patients who have chronic health issues. Throughout their four years of study, students learn from the patients and vice versa. Murphy follows a patient with muscular dystrophy, who helped him recognize obstacles patients often face in navigating the health care system. When Murphy’s classmate Sean Dooley, a fellow third-year, asked students to grow mustaches to raise money for charity, Murphy raised $375 for the Little Hercules Foundation for Duchenne Muscular Dystrophy in honor of his LAP partner patient.

Murphy’s research focuses on finding a drug treatment for nonalcoholic fatty liver disease, but he hasn’t ruled out any residency track. “In your third year, you’re really seeing what it’s like to be a physician in whatever field you’re rotating through,” he says. “You have to embrace the attitude that your mind can always be changed, and you can always find something that you’re passionate about.” —CF

What Protects Memory with Age?

When embarking on a 14-year study exploring aging, memory impairment and amyloid plaques, Beth Snitz, associate professor of neurology at Pitt Med, took the opposite approach to most researchers in this area: She asked not what factors predict disease, but what seems to protect older adults from it. Collaborating with Pitt Med colleagues in six different departments, Snitz followed 100 volunteers from their early 80s to their mid-90s—the “oldest-old” as this group is often categorized.

The study, published in Neurology, examined why some of the “oldest-old” never develop amyloid plaques of Alzheimer’s disease when the majority (66%) do, and why some maintain cognitive resilience even with plaques. By pairing thinking and memory tests with PET scans, Snitz discovered that participants who initially performed well on tests were not as likely to develop cognitive problems despite having amyloid plaques. Participants with APOE e2, an uncommon gene variant linked to a decreased risk of Alzheimer’s disease, were six times less likely to develop amyloid plaques. There aren't many studies of this group, but “they're the best examples of resilience around,” Snitz says. Understanding their resilience “may well help identify ways to prevent dementia.” —SPR

FOOTNOTE

They're good. But don't just take it from us! The National Cancer Institute (NCI) has rated the UPMC Hillman Cancer Center “exceptional”—its highest possible rating. The Hillman is one of 51 cancer centers in the country to achieve this designation. The NCI has also provided the Hillman with its largest grant to date—$30 million, which will go toward bettering cancer prevention, diagnosis and treatment.