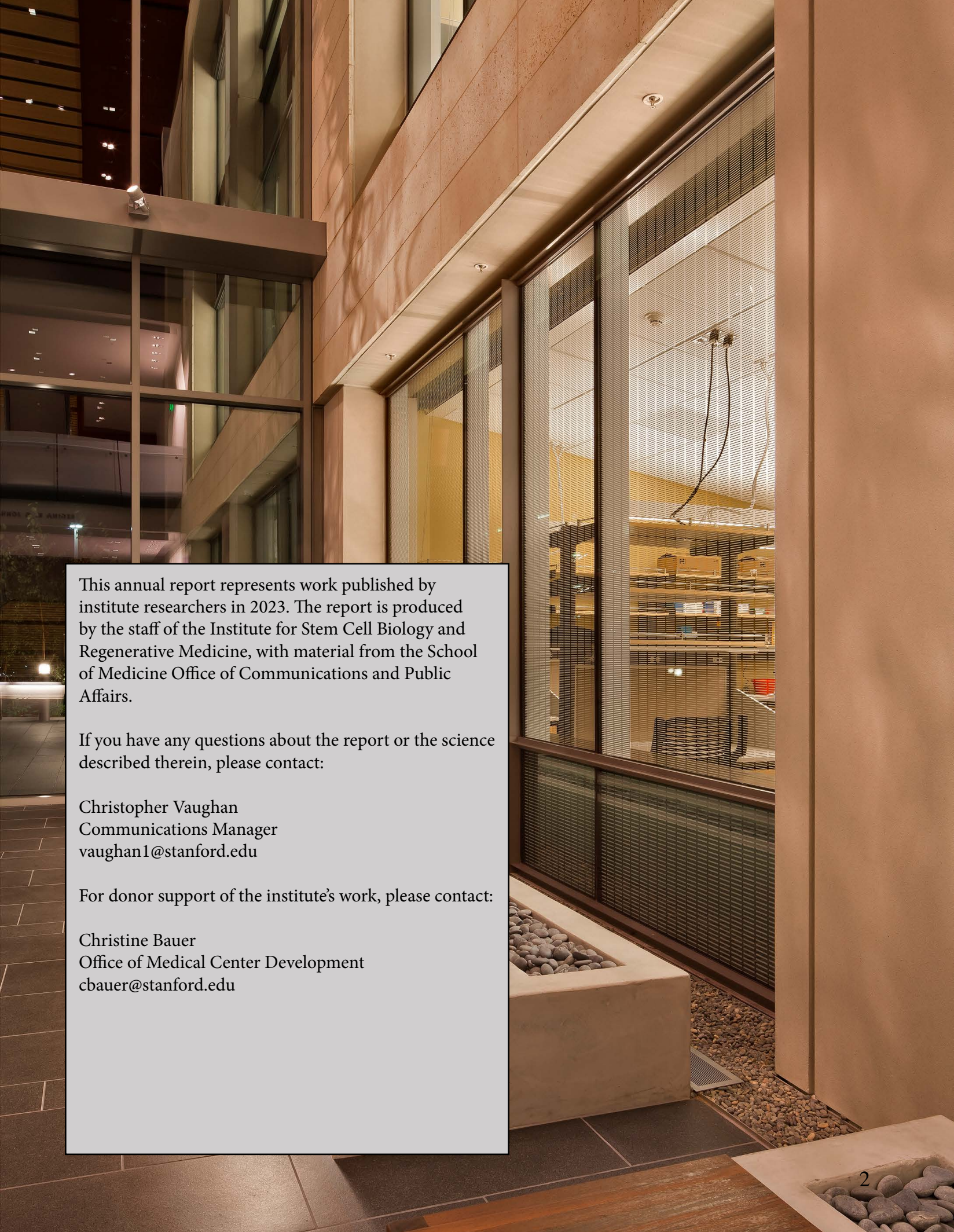




2023 ANNUAL REPORT

STANFORD INSTITUTE FOR STEM CELL BIOLOGY AND
REGENERATIVE MEDICINE



This annual report represents work published by institute researchers in 2023. The report is produced by the staff of the Institute for Stem Cell Biology and Regenerative Medicine, with material from the School of Medicine Office of Communications and Public Affairs.

If you have any questions about the report or the science described therein, please contact:

Christopher Vaughan
Communications Manager
vaughan1@stanford.edu

For donor support of the institute's work, please contact:

Christine Bauer
Office of Medical Center Development
cbauer@stanford.edu

2023 ANNUAL REPORT

Message from the Director	4
Stem Cell Research	
Tissue Stem Cells in Health and Disease	5
Pluripotent Stem Cells and Development	17
Regenerative Biology and Medicine	22
Stem Cell Technology	29
Publications	32

Message from the Director

Dear Friends of the Institute,

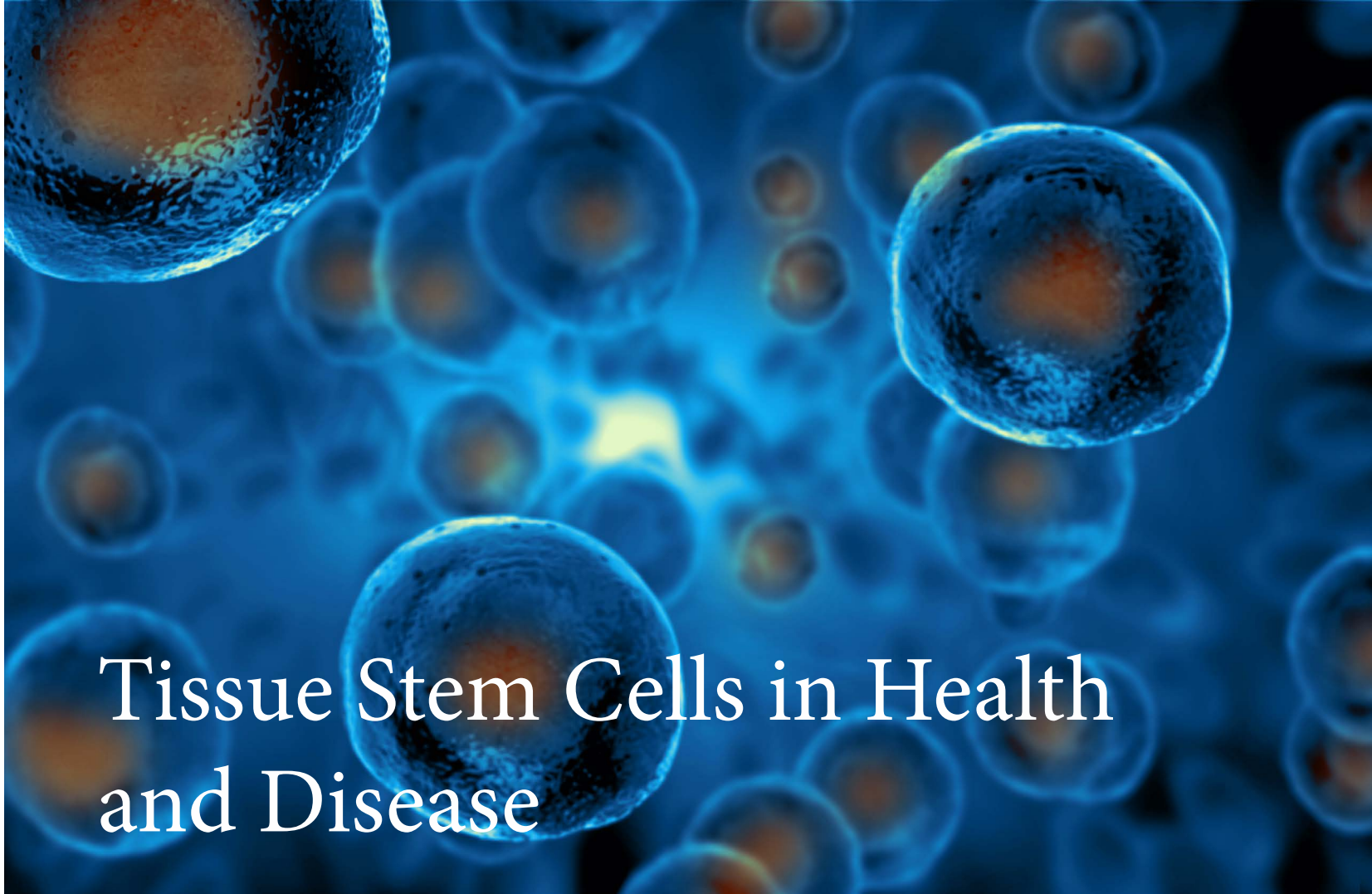
I hope this last year has been good to you and your family. The ISCBRM continues to advance across many fronts of our research and educational missions. I'm excited to share that the faculty and I have undertaken a strategic planning process to develop our goals for the next five years including expanding our membership through new internal and external recruitments, developing multi-investigator research projects and grant applications, organizing into several research focus areas, building our community, and engaging broadly with the many departments, institutes, centers, and initiatives across the Stanford School of Medicine.

We hope that the ISCBRM will complement the amazing research and translational activities of our current faculty with new activities in domains including single cell studies and technology, manipulation of cell fate directly in living organisms, and modulation of immunological interactions with stem cell biology. We think these are key areas to advance our research and translational goals to have broad impact for science and patients.

To ensure success in achieving our goals, I am delighted to have recruited Heather Gentner as our new Director of Finance and Administration. Heather brings a wealth of experience at Stanford, in academic research management, and leadership. We hope to share more details in the coming year. As always, we thank you for your support and look forward to your continued partnership with the ISCBRM.

Best Regards,

Ravi Majeti MD, PhD
Virginia and D.K. Ludwig Professor
Professor of Medicine, Hematology
Director, Institute for Stem Cell Biology and Regenerative Medicine
Stanford University School of Medicine

A microscopic image showing numerous spherical stem cells with a blue glow and a darker, textured center. The cells are set against a dark blue background. The text 'Tissue Stem Cells in Health and Disease' is overlaid in white serif font.

Tissue Stem Cells in Health and Disease

Stem cell science and technology has massive potential applications for maintaining healthy tissue function and treating a wide range of diseases such as cancer, Alzheimer's and COVID. Stem cell applications also offer hope of curing diseases that are currently incurable. One of the institute's primary goals is to translate research findings in our labs into therapies that can be used in clinics.

Researchers find success using stem cell therapy in mouse model of Alzheimer’s disease

Researchers at the institute have shown that cell transplantation can be used to treat Alzheimer’s disease in a mouse model, raising the hope that cell therapy might be a viable treatment for human Alzheimer’s patients in the future.

“This is a great proof-of-concept demonstration that we can replace defective brain cells with transplanted blood cells,” says Professor of Pathology Marius Wernig, MD, PhD. “This cell therapy approach is unique in the field because most researchers are working to find pills or injectables to treat Alzheimer’s disease.” Despite extensive research on Alzheimer’s disease, the cause and development of the neurodegenerative disorder is not well understood. Most therapies focus on clearing the buildup of amyloid plaques found in familial Alzheimer’s disease (AD), even though there is not a clear connection between clinical signs of AD and the presence of these plaques.

There is, however, a clear association between non-familial, late onset AD and various mutations in microglia—brain cells that protect other brain cells against invaders and function as a cleanup crew, taking out the metabolic trash that can accumulate in the working brain

Scientists looking at Alzheimer’s disease in humans have observed that certain genetic variations in brain cells called microglia show a strong correlation with their risk of getting AD. One of the strongest associations is between AD and a microglia associated gene called TREM2. “In fact, genetic variants of TREM2 are among the strongest genetic risk factors for Alzheimer’s disease,” Wernig says.

“The data are convincing that microglial dysfunction can cause neurodegeneration in the brain, so it makes sense that restoring defective microglial function might be a way to fight neurodegeneration in Alzheimer’s disease,” Wernig said.

Wernig and his colleagues worked with a mouse model of Alzheimer’s disease in which the mice were bred to have a defective TREM2 gene. They then transplanted blood stem and progenitor cells from mice that had normal TREM2 function into the mice with a defective TREM2 gene. By using a fluorescent tag that would mark only cells that developed from the transplanted, normal cells, the researchers were

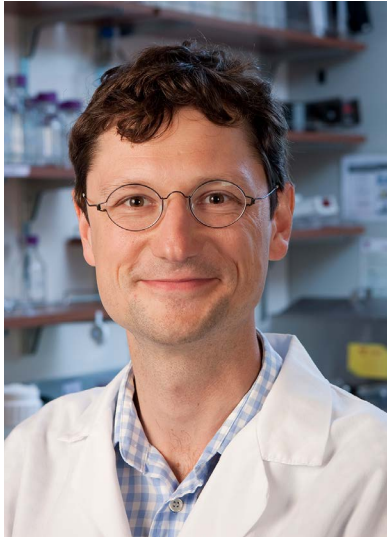
able to show that some of the transplanted cells were able to migrate into mouse brain and become cells that looked and behaved like microglia.

“We showed that most of the brain’s original microglia were replaced by healthy cells which led to a restoration of normal TREM2 activity,” Wernig said.

Next, they asked if the restored TREM2 activity was enough to positively affect the pathologies that the TREM2 deficient mice exhibited. “Indeed, in the transplanted mice we saw a clear reduction in the deposits of amyloid plaques that normally afflict TREM2-deficient mice,” Wernig said. They were also able to show improvement in a number of other disease-associated signatures that indicate that restoring the function of this one gene has widespread positive effects.

Wernig and colleagues point out that they could potentially even transplant cells that had been engineered to have supercharged TREM2 activity for even greater effect. They caution, however, that the microglia derived from the transplanted cells are slightly different than the natural microglia in the brain. “These differences might in some way have their own detrimental effect on neurodegeneration,” Wernig said. “We have to look at that.”

The other caution is that transplantation of the blood stem cells require a highly toxic preconditioning to kill off native blood stem cells. This would make the current procedure highly risky if it were eventually developed into a human therapy. However, many researchers, including some at the Institute for Stem Cell Biology and Regenerative Medicine, are developing less toxic methods of preconditioning for stem cell transplants.



Institute scientists transform cancer cells into weapons against cancer

Researchers found that when they turned cancer cells into immune cells, the transformed cells were able to teach other immune cells how to attack cancer.

Some cities fight gangs with ex-members who educate kids and starve gangs of new recruits. Stanford Medicine researchers have done something similar with cancer — altering cancer cells so that they teach the body’s immune system to fight the very cancer the cells came from.

“This approach could open up an entirely new therapeutic approach to treating cancer,” said Ravi Majeti, MD, PhD, a professor of hematology and the study’s senior author. The research was published March 1 in Cancer Discovery. The lead author is Miles Linde,



Ravi Majeti, MD, PhD

PhD, a former PhD student in immunology who is now at the Fred Hutchinson Cancer Institute in Seattle.

Some of the most promising cancer treatments use the patient’s own immune system to attack the cancer, often by taking the brakes off immune responses to cancer or by teaching the immune system to recognize and attack the cancer more vigorously. T cells, part of the immune system that learns to identify and attack new pathogens such as viruses, can be trained to recognize specific cancer antigens, which are proteins that generate an immune response.

For instance, in CAR T-cell therapy, T cells are taken from a patient, programmed to recognize a specific cancer antigen, then returned to the patient. But there are many cancer antigens, and physicians sometimes need to guess which ones will be most potent.

A better approach would be to train T cells to recognize cancer via processes that more closely mimic the way things naturally occur in the body — like the way a vaccine teaches the immune system to recognize pathogens. T cells learn to recognize pathogens because special antigen presenting cells (APCs) gather pieces of the pathogen and show them to the T cells in a way that tells the T cells, “Here is what the pathogen looks like — go get it.”

Something similar in cancer would be for APCs to gather up the many antigens that characterize a cancer cell. That way, instead of T cells being programmed to attack one or a few antigens, they are trained to recognize many cancer antigens and are more likely to wage a multipronged attack on the cancer.

Now that researchers have become adept at transforming one kind of cell into another, Majeti and his colleagues had a hunch that if they turned cancer cells into a type of APC called macrophages, they would be naturally adept at teaching T cells what to attack.

“We hypothesized that maybe cancer cells reprogrammed into macrophage cells could stimulate T cells because those APCs carry all the antigens of the cancer cells they came from,” said Majeti, who is also the RZ Cao Professor, assistant director of the Insti-

tute for Stem Cell Biology and Regenerative Medicine and director of the Ludwig Center for Cancer Stem Cell Research and Medicine.

Cell conversion

The study builds on prior research from the Majeti lab showing that cells taken from patients with a type of acute leukemia could be converted into non-leukemic macrophages with many of the properties of APCs.

In the current study, the researchers programmed mouse leukemia cells so that some of them could be induced to transform themselves into APCs. When they tested their cancer vaccine strategy on the mouse immune system, the mice successfully cleared the cancer.

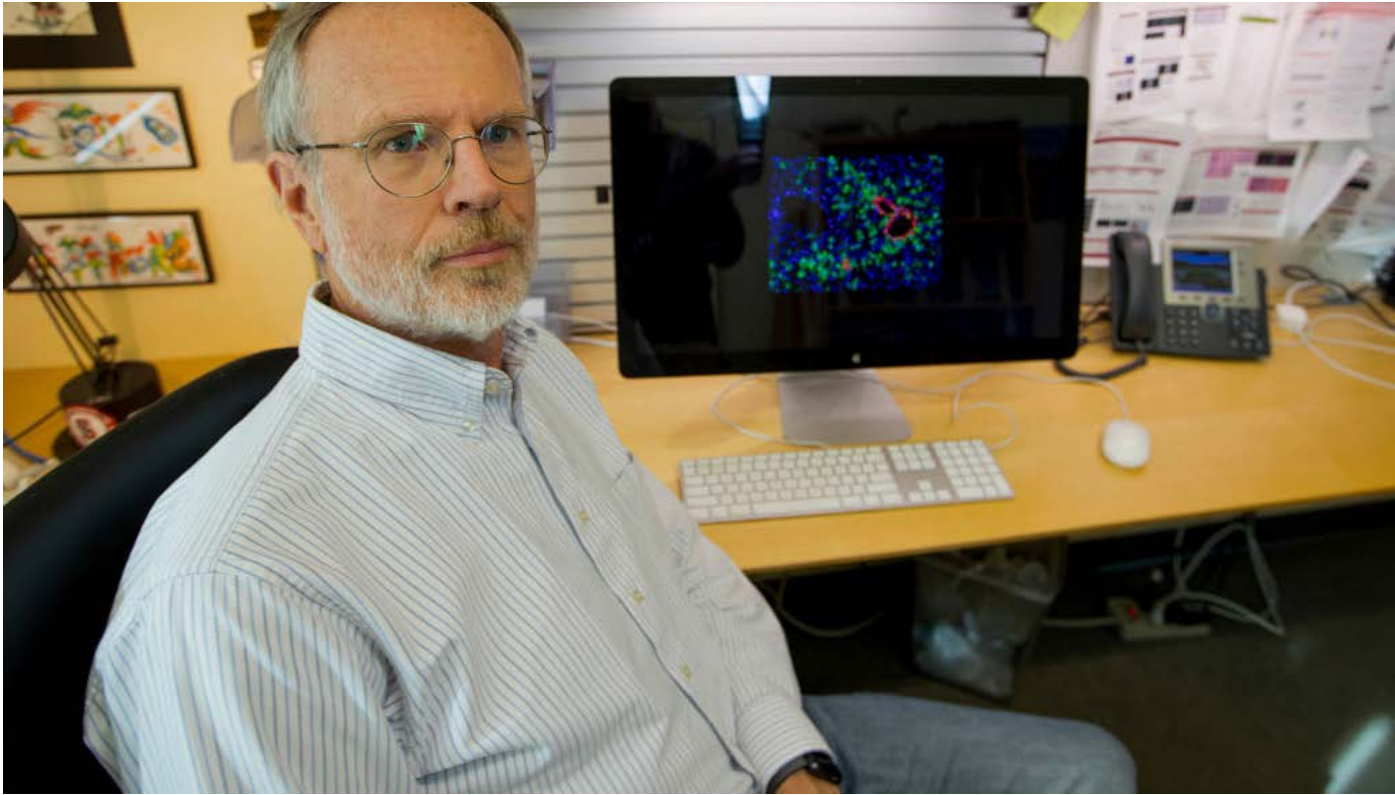
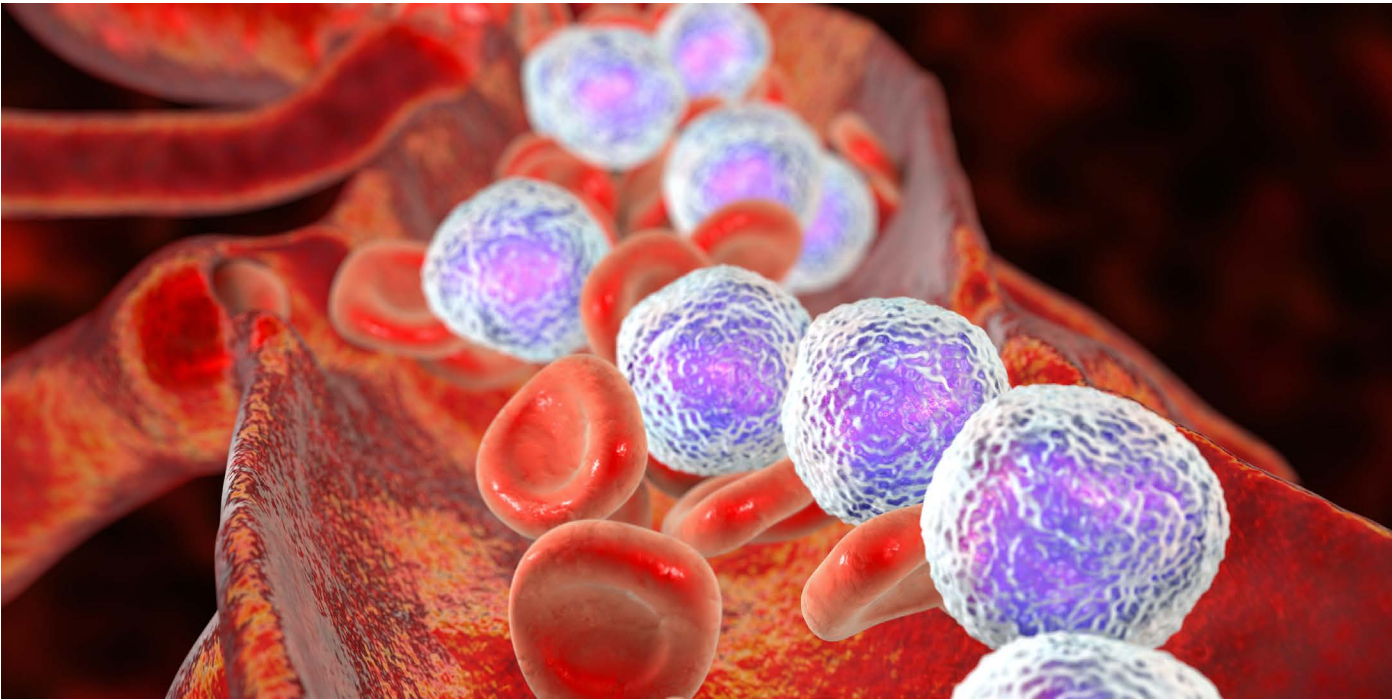
“When we first saw the data showing clearance of the leukemia in the mice with working immune systems, we were blown away,” Majeti said. “We couldn’t believe it worked as well as it did.”

Other experiments showed that the cells created from cancer cells were indeed acting as antigen-presenting cells that sensitized T cells to the cancer. “What’s more, we showed that the immune system remembered what these cells taught them,” Majeti said. “When we reintroduced cancer to these mice over 100 days after the initial tumor inoculation, they still had a strong immunological response that protected them.”

“We wondered, If this works with leukemias, will it also work with solid tumors?” Majeti said. The team tested the same approach using mouse fibrosarcoma,

breast cancer, and bone cancer. “The transformation of cancer cells from solid tumors was not as efficient, but we still observed positive results,” Majeti said. With all three cancers, the creation of tumor-derived APCs led to significantly improved survival. Lastly, the researchers returned to the original type of acute leukemia. When the human leukemia cell-derived APCs were exposed to human T cells from the same patient, they observed all the signs that would be expected if the APCs were indeed teaching the T cells how to attack the leukemia. “We showed that reprogrammed tumor cells could lead to a durable and systemic attack on the cancer in mice and a similar response with human patient immune cells,” Majeti said. “In the future we might be able to take out tumor cells, transform them into APCs and give them back to patients as a therapeutic cancer vaccine.”

“Ultimately, we might be able to inject RNA into patients and transform enough cells to activate the immune system against cancer without having to take cells out first,” Majeti said. “That’s science fiction at this point, but that’s the direction we are interested in going.”



Roel Nusse, PhD

Intermittent fasting spurs proliferation of liver cells in lab mice, institute researchers find

Intermittent fasting — abstaining from eating for lengthy periods of time — spurs liver cells in laboratory mice to divide rapidly, according to a study led by researchers at Stanford Medicine. The finding challenges the long-standing belief that cells in the adult liver divide rarely and, when they do, primarily to repair damage to the organ. It is also the first to show an immediate effect of diet on liver cell biology.

“One of the most defining characteristics of the adult liver has been that it is fairly stable in terms of cell turnover,” said Roeland Nusse, PhD, professor of developmental biology. “But we found the turnover of cells in the liver goes up dramatically after several periods of 24-hour fasting followed by refeeding. Interestingly, this type of diet mirrors the natural diet of wild animals and of early humans, before the development of agriculture, when there were periods with scarce or absent food.”

It’s not known what, if any, effect the increased cell replication has on the health of the animals. But the

finding implies that liver biology is more dynamic and responsive to dietary changes than previously believed, and it raises the question as to how other diets might affect its biology.

Nusse, who is the Reed-Hodgson Professor in Human Biology and the Virginia and Daniel K. Ludwig Professor in Cancer Research, is the senior author of the study, which was published online Jan. 31 in eLife. Former postdoctoral scholar Abby Sarkar, PhD, is the first author of the research.

The liver’s job

The liver is one of the largest organs in the body, weighing about 3 pounds in an adult human, or roughly 2% of one’s body weight. In mice, it accounts for nearly 5% of body weight. The liver removes toxins from the blood for excretion, and it converts the food we eat into nutrients the body can absorb. “Abby Sarkar wondered if an organ like the liver that is so involved in digestion would exhibit altered patterns of cell divisions, or turnover, when an animal’s

diet changed,” Nusse said.

Laboratory mice typically have unlimited access to food at all times. But for these experiments, Sarkar withheld food from the animals for 24 hours, then allowed them to feed freely for 24 hours before another fast of 24 hours. She then analyzed cell division in the animals’ livers after one week and three weeks of the intermittent fasting diet and compared it with that of animals that had been fed normally.

“We saw that the turnover of cells in the liver went up fairly dramatically shortly after refeeding began,” Nusse said. “There were many more new cells than in animals that had been fed on a standard diet. This was very exciting.”

The liver’s role in metabolism means that the ratio between the weight of the liver and that of the body must remain constant to allow the organ to function efficiently. This is the reason the liver will regenerate to its normal size if a portion of it is removed due to injury or surgery.

Sarkar found that the cell division she observed was sparked by a decrease in the ratio of liver to body weight in the study animals after a week of intermittent fasting. She also learned that most of the cell division was localized to liver cells near the central vein of the organ.

Further investigation identified two molecular pathways responsible for maintaining appropriate liver size in the fasted animals. One is a growth factor called fibroblast growth factor, or FGF, that is produced by the intestines and travels throughout the body; another, a family of proteins called Wnts, is crucial to embryonic development and the growth and maintenance of many tissues.

Wnt proteins are secreted by endothelial cells in the central vein, but, unlike FGF, they travel only a short distance. The two signals overlap on liver cells near the central vein, called pericentral hepatocytes, to stimulate their division after fasting.

“Interestingly, the Wnt pathway is not affected by intermittent fasting,” said Nusse, who identified the first Wnt protein in 1982, “but the production of



FGF is. Intermittent fasting or other changes in the food supply stimulate the production of FGF, which circulates to the liver. It wakens the liver cells from resting, then Wnt proteins give those near the central vein the signal to divide.”

Sarkar next tested the effect of intermittent fasting in mice that had been genetically engineered to be unable to respond to either the FGF signal or the Wnt

signal. In that phase of the research, “The effect of intermittent fasting was attenuated,” Nusse said. “The cells more or less lost their ability to divide. This is a very strong indication that you need both these signaling pathways to see this effect of fasting on cell replication.”

The researchers don’t know whether the increased cell proliferation in the liver due to fasting has health benefits. But it’s an intriguing look

into how dietary changes can affect one of the largest organs in the body. They are now planning to extend their studies to include other types of diets, including ketogenic or high-fat.

“I wouldn’t recommend that people start intermittently fasting to improve their liver health,” Nusse said. “But it’s an exciting observation — it shows that the idea that the liver is a tissue that turns over slowly should be taken with a grain of salt.”

Cells in the adult liver were thought to divide rarely.

But a study led by institute researchers found that intermittent fasting causes rapid cell division

Scar tissue holds hints about pancreatic cancer outcome, patient longevity

Scar tissue that forms around a growing pancreatic tumor called a pancreatic ductal adenocarcinoma harbors valuable clues as to how long people with these cancers are likely to live, according to a new study led by researchers at Stanford Medicine.

The architecture and organization of cells in the scar tissue can be used to categorize patients into two groups. Members of one group lived a median of nearly two years longer than members of the other group — a substantial difference for a cancer with a five-year survival rate after surgery of only 20% to 25%.

In fact, the researchers found that the patterns of a patient’s scar tissue are among the most predictive prognostic elements for this type of cancer — second only to the stage of the tumor at diagnosis.

The finding suggests that cells in the scar tissue, as well as its overall structure, interact with the cancer cells to either egg on or tamp down their growth. Drugs that intercept pro-growth messages, or mimic cellular conversations that discourage growth, may lead to new avenues of therapy.

“Our study puts new therapeutic approaches on the table,” said professor of surgery Michael Longaker, MD. “Should we be treating not just the tumor but also the scar tissue? I would say yes. Both obviously play a role in patient outcome.”

Longaker, the Deane P. and Louise Mitchell Professor in the School of Medicine, is the senior author of the study. Post-doctoral scholar Jason Guo, PhD, and former graduate student Shamik Mascharak, MD, PhD, are the lead authors of the research.

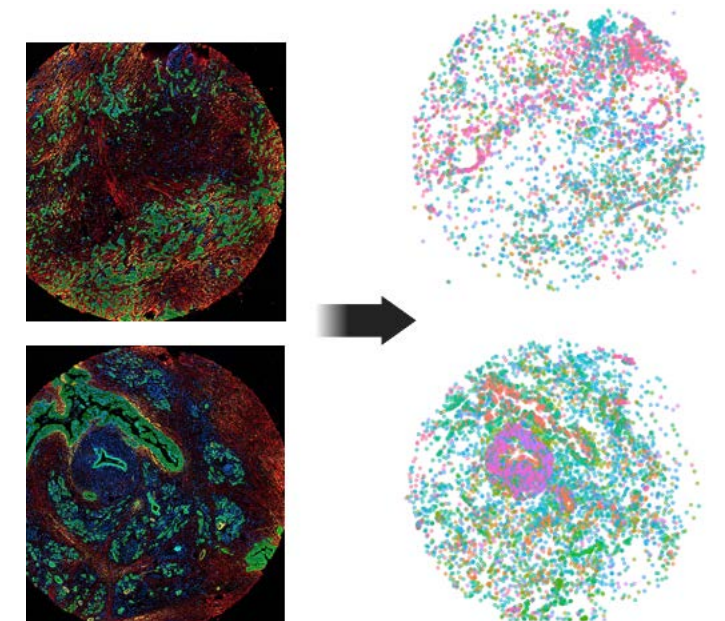
Deaths from pancreatic ductal adenocarcinoma, the most common type of pancreatic cancer, are rising, and it is projected to be the second leading cause of cancer deaths in the next 10 years. Because the disease metastasizes, or invades other parts of the body, early and quickly, it often recurs within two years of initial treatment.

Pancreatic ductal adenocarcinoma sparks a particularly strong response by cells called fibroblasts found in the connective tissue surrounding the pancreas. The fibroblasts secrete collagen and other components of what’s known as the extracellular matrix to bind the tumor in a web of cancer-associated scar

tissue called desmoplasia. Earlier research has hinted that this scar tissue affects patient prognosis, but the analyses were confined primarily to simple quantitative measurements.

“Previous studies have focused on the cancer cells themselves, or how much fibrosis, or scarring, surrounds the tumor,” Guo said. “But our findings reveal that maybe the critical information comes not from the quantity or mass of the scar tissue, but from its internal components and organization.”

Guo and his colleagues studied hundreds of samples of pancreatic ductal adenocarcinoma tissue collected during surgery to remove the cancerous portion of the pancreas — a standard treatment for the condition. They used a computer algorithm to identify and analyze nearly 300 distinct attributes of the desmoplasia, including the length, width, alignment and



Scar patterning hints at lifespan after a pancreatic cancer diagnosis. Top, disrupted pancreatic glands (green) are nested within thickened, cable-like scar fibers (red, yellow) — a pattern associated with shorter survival. Bottom, intact glands are embedded in spindle-like fibers, suggesting a longer lifespan.



Michael Longaker, MD

density of their fibers, and another technique called CODEX to assess the prevalence and location of immune and other types of cells in the desmoplasia.

Survival patterns

The researchers then used a machine-learning approach to combine the data about multiple cellular interactions and fiber architecture with clinical information about each patient to uncover specific patterns associated with overall survival in the months and years after the initial diagnosis. They found that the presence of a specific type of T cell called a cytotoxic T cell was strongly associated with longer overall survival, while an abundance of tumor cells that modulate the immune system, as well as activated B cells, were associated with poorer survival. “Pro-inflammatory fibroblasts also popped up in our analyses, which we were happy to see,” Guo said. “Knocking out these fibroblasts or inhibiting their activity is a potential target for new therapies. We also saw close relationships between B cells and these fibroblasts, which is interesting. What are they talking about? We’d love to follow up and see what cellular signals are being exchanged.”

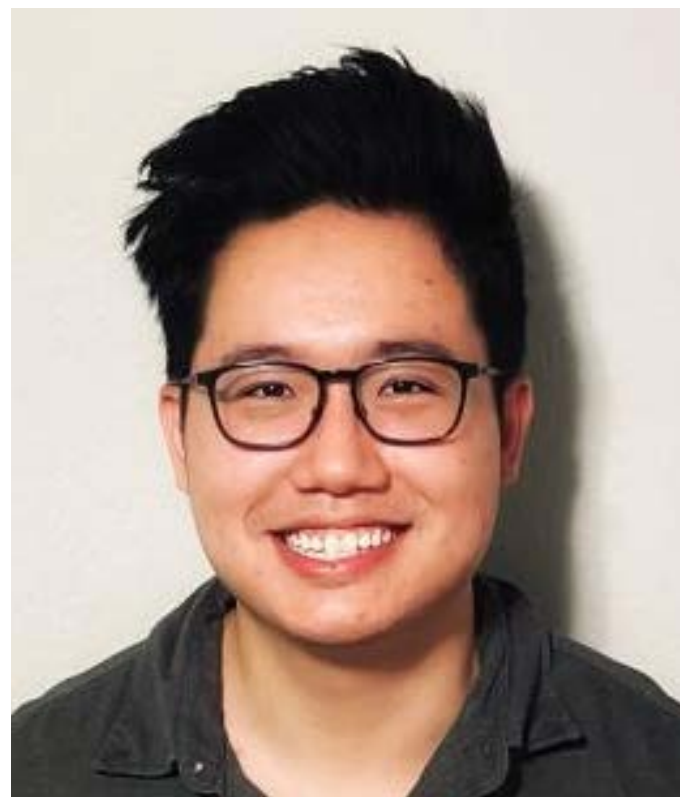
They also found that thinner fibers predicted better survival than the beefy, densely packed fibers found in samples from patients who died soon after diagnosis.

When all the data were incorporated, the computers were able to categorize patients with pancreatic ductal carcinoma into two main groups. Patients in one group lived a median of 655 days longer than the other.

Longaker, Guo and their colleagues hope that new information about the contributions of the desmoplasia to pancreatic cancer growth will not just open doors for new therapies but that it will also be used to guide clinical decisions.

“In the future, I envision that a patient gets a biopsy before treatment has started, and doctors will look not just at the cancer but also at the patterns and types of cells in the desmoplasia,” Longaker said. “This could also help doctors decide which patients are likely to need more aggressive therapy early in the course of their disease, and who could be spared invasive or harsh chemotherapy or radiation. I hope we can develop a chemotherapeutic approach that doesn’t just focus on the cancer but that also impacts fibroblasts and their role in promoting tumor growth.”

Researchers from the University of Virginia School of Medicine contributed to the work.



Jason Guo, PhD

Runaway immune reactions cause long COVID breathing problems

Institute researchers have found a mechanism behind one of the most common symptoms of long COVID -- shortness of breath. Post COVID-19 breathing problems are caused by a condition known as lung fibrosis, when damaged lungs form scar tissue, which makes it difficult for lungs to expand and contract. Long COVID cases can be severely debilitating and resistant to treatment, said Gerlinde Wernig, MD, PhD, assistant professor of pathology, who led the study. What’s worse, lung function can continue to decline, even without a new COVID-19 infection. The team’s new research pinpoints what’s happening in the lungs to cause fibrosis: overactivity of genes that regulate inflammation and immune responses. The finding, which was published in the Proceedings of the National Academy of Sciences in February, offers hope that, one day, targeted drugs could intervene to quell the genes behind the damage, something they’re already testing out in mouse studies, Wernig said.

“This was an extension of our work with chronic pulmonary fibrosis,” said Wernig. Previously, Wernig and her colleagues conducted research showing that the dysregulation of particular immune processes caused fibrosis in the lungs. Wernig wondered if something similar was happening in the lungs of people with long COVID.

The team started by looking at lung tissue samples from five COVID-19 patients who had had symptoms of the disease -- such as shortness of breath -- for one or more months. The lungs of people who had symptoms after infection with SARS-CoV-2 (the virus that causes COVID-19) looked like the lungs of people with end-stage pulmonary fibrosis, said Wernig.

By analyzing single cells from the patients’ tissue samples, the scientists also saw similarities in the pattern of RNA production -- which can hint a cell’s overall function -- between samples of tissue from long COVID patients and samples from patients with pulmonary fibrosis.

“We saw this same pattern across all human COVID lung samples,” Wernig said. As with other lung infections, the initial COVID-19 infection in the lungs kicked off an inflammatory process. In the



case of long-COVID patients, however, the immune dysfunction keeps going long after the virus is gone -- similar to what happens in chronic pulmonary fibrosis.

In her previous research, Wernig showed that pulmonary fibrosis was characterized by a spike in the production of an inflammatory marker called interleukin-6 in the lungs, which is associated with chronic inflammation and scar formation. Furthermore, in pulmonary fibrosis, scar-forming cells called fibroblasts increase production of a protein called CD47, which stops the immune system from keeping fibroblasts under control, meaning scar tissue forms unchecked. The researchers also saw increases in a protein called pJUN, which is a key promoter of scar formation.

To test whether lung fibrosis could be firmly connected to COVID-19 infections, they looked at lung fibrosis in mice infected with a SARS-CoV-2-like virus and found significant increases in fibrosis and immune dysfunction. “Innate immune cells go crazy after that infection,” Wernig said, referring to the part of the immune system that forms the first line of defense against pathogens.

In a mouse model engineered to more closely represent human biology, researchers showed that, when the mice contracted SARS-CoV-2, scarring in the lung tissues shot up, as did levels of interleukin-6, CD47 and pJUN. There was also a bright side to these experiments. “When we did the same experiments but blocked CD47 and Il-6, we saw very little fibrosis,” Wernig said. “This hints at possible treatments for long COVID involving drugs that carry out targeted immune blockades.”

Blood condition called CHIP linked to protection against Alzheimer's

Stanford Medicine researchers have found that a common blood condition associated with several diseases may have a protective effect against Alzheimer's disease.

In the condition, clonal hematopoiesis of indeterminate potential, or CHIP, certain blood stem cells acquire mutations that strengthen their ability to survive and multiply. As a result, the mutant cells dominate, and just a few cells can give rise to much or even all of the body's blood and immune cells. In most cases of CHIP, a dominant blood stem cell gives rise to between 4% and 30% of blood and immune cells.

Studies by Stanford Medicine assistant professor of pathology Siddhartha Jaiswal, MD, PhD, and others have shown that people with CHIP are at much higher risk of developing various diseases. By analyzing medical databases and stored blood samples, Siddhartha and his colleagues have shown that people with CHIP are about twice as likely to develop coronary heart disease, twice as likely to develop chronic liver disease and 10 times as likely to develop blood cancers such as myeloid leukemias. Researchers don't yet fully understand why CHIP is linked to diseases other than blood cancer, though some studies have suggested that CHIP mutations cause increased activation of the immune system. Jaiswal and his colleagues investigated an association between CHIP and Alzheimer's disease, expecting to see either no association or a positive association with Alzheimer's disease.

He and colleagues analyzed a cohort of participants who had been followed over a period of 10 to 15 years, comparing medical records and blood samples. "We were surprised to find that CHIP was actually associated with a substantially lower risk of Alzheimer's disease," Jaiswal said. People with CHIP were found to have a 30% to 50% lower risk of developing the neurodegenerative disorder, compared with those who did not have the CHIP mutation, he said.

"The degree of protection from Alzheimer's dementia seen in CHIP carriers is similar to carrying an APOE ε2 allele," said Jaiswal, referring to a genetic variant that's known to decrease the risk of Alzheimer's.



Siddhartha Jaiswal, PhD

The team saw the negative association with Alzheimer's and CHIP even when they accounted for other risk factors. "We thought there might be some kind of survivor bias -- that people with CHIP were more likely to die before developing Alzheimer's disease -- but the decrease in risk still held after adjusting for that," Jaiswal said. They also analyzed the association in another way, to see if people who had Alzheimer's disease were less likely to have CHIP. The researchers confirmed that they were. A paper published on June 15 in Nature Medicine detailed the findings.

Digging deeper

Of course, an association doesn't mean that there is a cause-and-effect relationship. So, Jaiswal and his colleagues conducted different forms of genetic analyses, finding evidence that CHIP could causally inhibit the development of Alzheimer's. The connection between CHIP and Alzheimer's implied a somewhat unexpected link between brain cells and the cells that give rise to blood and the immune system, Jaiswal said.

The brain has its own immune cells, called microglia, and there is some evidence that microglia combat the inflammation and buildup of toxins that are

associated with Alzheimer's disease. But over the last 10 years, scientists have come to believe that all microglia become established in the brain very early in human development, during the embryo stage. Since the blood-brain barrier normally prevents blood cells from crossing into the brain, there has been no known way for blood stem cells to become brain cells like microglia.

Yet, when Jaiswal and his colleagues looked at brain samples of people with CHIP for the CHIP-associated blood cell mutations, they saw them. And these mutations seem to exist in microglia cells. The investigators found that between 30% and 90% of the microglia in brain samples of those with CHIP harbored the CHIP mutations. The proportion of mutant microglia in any individual brain tended to match the proportion of mutant blood cells in the rest of the body.

"This suggests that cells are migrating from the blood into the brain," said Jaiswal, adding that the finding is in contradiction to the accepted dogma. "It's a remarkable finding."

How this affects the development of Alzheimer's disease is not yet clear, but researchers know that microglia help fight microbial invaders and clean up

waste products in the brain. "One hypothesis is that the mutations that promote a growth advantage in blood stem cells also promote microglial expansion and activity, boosting microglia's ability to fight the conditions that lead to brain disease," Jaiswal said.

The scientists also saw that, in the brain samples of people with CHIP, levels of neurofibrillary tangles and amyloid plaques, both associated with Alzheimer's disease and thought to be causative, were lower.

Jaiswal and his colleagues are planning follow-up studies to learn more about how the mutated microglia might be protecting against Alzheimer's disease. Jaiswal plans to work with professor of pathology Marius Wernig, MD, PhD, to transform CHIP blood stem cells into microglia so they can understand how these cells behave differently than normal microglia.

Although there's much work to be done, the researchers hope that if they are able to understand these mechanisms, it could help guide the development of new therapeutics that could one day protect against Alzheimer's disease, they said.



Why does CHIP lead to cardiovascular disease?

The answers are becoming clearer

Some people, as they age, get a condition in which mutant blood stem cells gain a competitive advantage over other blood stem cells and begin to take over. People with this condition, called CHIP (clonal hematopoiesis of indeterminate potential), will harbor a clone of blood and immune cells derived from a single mutant stem cell. Previous research has shown that people with CHIP may seem perfectly healthy, and yet are at higher risk for atherosclerosis, blood cancers, and other diseases.

Institute researchers have now shown why people with CHIP may be at higher risk for some cardiovascular diseases. Assistant Professor of Pathology Siddhartha Jaiswal, MD, PhD and his colleagues have discovered that the two most common mutations in CHIP, in the genes TET2 and DNMT3A, can both induce similar inflammatory programs in mice.

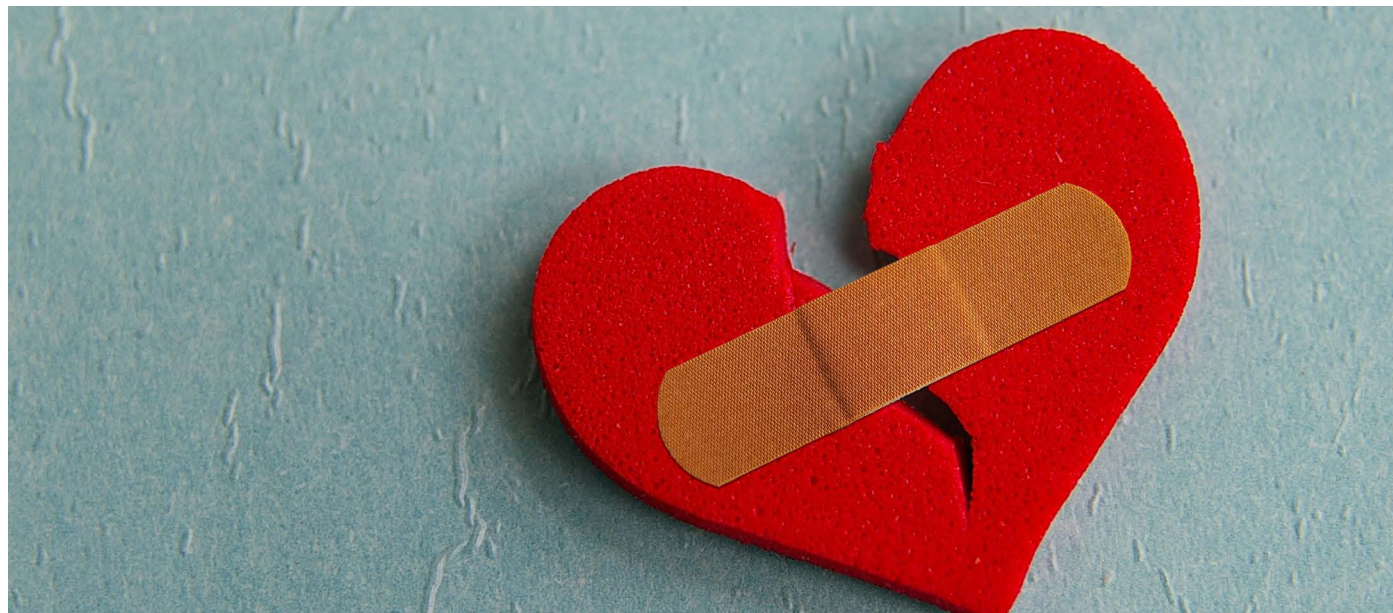
Inflammation has long been associated with the atherosclerosis disease process, providing an explanation for a likely mechanism connecting mutations in these two genes and cardiovascular disease.

“This was surprising, because these two genes have opposite effects biochemically,” Jaiswal said. “DNMT3A encodes an enzyme that promotes the methylation of methylcytosine, while TET2 encodes an enzyme that initiates the demethylation of methylcytosine.”

The research was published in the journal *Nature Cardiovascular Research*. Jaiswal is senior author. Philipp J. Rauch, MD, an instructor in Medicine at Harvard Medical School, and Stanford medical student Jayakrishnan Gopakumar are first authors. The researchers tested a few possible ways that the loss of a functional DNMT3 might promote atherosclerosis. They had previously shown that stem cells with TET2 mutations gave rise to macrophages that promoted inflammation when exposed to high levels of LDL cholesterol (the “bad” cholesterol). In the end, they were able to show that macrophages derived from blood stem cells with mutant DNMT3A also promoted inflammatory processes.

“So even though these two genes have opposite effects on a basic biochemical level, the effects of the loss of function in either gene converge at the cellular level to produce a common, pro-inflammatory effect on cardiovascular tissues,” Rauch said.

Such pro-inflammatory effects might be part of the reason CHIP is associated with other diseases, the researchers note. Patients with heart failure who have mutations in TET2 or DNMT3A face a far worse prognosis than those who don’t. CHIP associated with DNMT3A mutations also raises the risk for osteoporosis. The researchers hope that by understanding some of the underlying mechanisms by which CHIP acts to raise disease risk, they might be able to come up with interventions to reduce those risks.



Pluripotent Stem Cells and Development

Much of the future of stem cell science and regenerative medicine depends on understanding exactly how stem cells differentiate and become more specialized cells. Institute researchers strive to understand how this happens in the natural world, and how to precisely replicate and control that process in the lab.



Researchers discover how to purify human neural stem and progenitor cells and map their further development in the brain

How can you study king salmon if you can't tell them apart from any other fish? How can you study a particular kind of cell if you can't distinguish it out from other cells? Scientists are praising recent research by Irv Weissman and his colleagues at the institute as a "tour de force" that gives researchers the ability to identify and trace the development of all important neural stem and progenitor cells that give rise to the human brain. The technique promises to open a door to fully understanding human brain development, and may offer new avenues for studying brain disorders.

The research, published in the journal *Cell*, has already resulted in the characterization of a functionally distinct cell type that was previously unknown. Irv Weissman, MD, is the senior author on the paper. MD/PhD student Daniel Liu is first author on the paper.

"Being able to separate cell types is central to biology," Liu said. "In the mouse, we can use techniques like genetic lineage tracing to map cell development, but this requires genetic modification of cells in a growing brain, and of course in humans we can't do that."

"While most human neural cell types were known, there weren't good ways of purifying those cells," Liu said. "Without such purification methods, we will always be studying mixtures of different cell types."

The researchers started with mid-gestational brain cells and looked for the presence or absence of a number of cell surface markers. They also analyzed the cells' RNA activity. The investigators then took these characterized cells, transplanted them into mouse brain, and watched how they developed. By matching surface markers and RNA activity with developmental outcomes of the various cells, they were able to tell which markers were truly important in identifying various neural stem and progenitor cells, as well as map their respective developmental lineages.

"This method is powerful because we were able to identify purification schemes for all cell types in one go," Liu said. "For every single cell type, we were able to show their lineage hierarchy as well as their transplant potential in a systematic way."

One particular surprise that came out of the research concerned neural progenitor cells with high levels of the protein Thy1. Previously, such cells were thought to develop into neurons, but Weissman and colleagues found a subset of these cells that would develop into oligodendrocytes but not into neurons. The work is proof-in-principle that this method could ultimately be applied to create a complete scheme for the development of all brain cells from the very first neural stem cells to the most mature and differentiated neural cells. Such a well-defined

developmental tree has been mapped out over decades for human blood and immune cells, and has proven immensely valuable for studying blood and immune disorders. A well-defined map of human brain cell development would also be hugely beneficial, the researchers say.

"There are several surprises that come from this study" said Weissman. "First, we could study the properties of these cells by transplantation into newborn immune deficient mouse brain lateral ventricles; the human stem cells migrated to the mouse 'home' for brain stem cells, then accurately produced all brain lineages by site appropriate events." This implies that despite over 85 million years of evolution between mice and humans, the signals for neurodevelopment in the brain were conserved, Weissman said.

"Now the transition to postnatal and adult neurogenesis by stem cells needs to be worked out so that we and others can begin to trace their activities in the human adult brain to find out how such cells change in human brain diseases," Weissman said. This study presents a method of achieving that well-defined map of human brain development, but there is still a lot of work to be done, the researchers say. "We have identified several more candidate markers that may further resolve heterogeneity in the hierarchy of human neural development," Liu said. "That is something that will be the focus of future studies."



Irv Weissman, MD

Liu says. "Being able to characterize and isolate all the various kinds of cells in the developing human brain will be a huge boon for studying brain function and dysfunction, as well as help us develop clinically feasible brain stem cell transplants."

Other Stanford scientists involved in the research were Joy He, Rahul Sinha, Anna Eastman, Angus Toland, Maurizio Morri, Norma Neff, Hannes Vogel and Nobuku Uchida.



A new stem cell technique leads to new understanding of germ cell development

In mathematics, physics, and engineering, it's common to take a difficult, complex problem in three dimensions and simplify it by modelling it in two dimensions. Institute researchers have done something similar in order to study stem cell development and differentiation by creating a two-dimensional, monolayer model of cell development to precisely study what is normally a hard-to-study, three-dimensional process.

"Our system has a lot of advantages," said institute member and associate professor of obstetrics and gynecology Vittorio Sebastiano, PhD. "We are able to answer a lot of longstanding questions about human cell development."

A common way to study cell development and differentiation is to study embryoid bodies: a cluster of pluripotent cells that specialize, or differentiate, as the cells grow and divide. Researchers can study the direct interactions between cells in the embryoid body as it grows, but they have trouble studying how the cells are affected by molecular signals that diffuse through the embryoid body, Sebastiano said.

"There are molecular signals that diffuse out from individual cells and it's hard to know other cells in the embryoid body experience the concentration and



Kyle Loh, PhD



Vittorio Sebastiano, PhD

timing of those signals," Sebastiano said. "The way cells react to various local concentrations of signal can be very different."

Sebastiano and his colleagues therefore went about creating an embryoid body in two dimensions, laying the cells out flat on media so that they knew precisely the concentrations and timing of various molecular signals that each cell was exposed to.

"All the cells growing on the monolayer are homogenously exposed to whatever is in the culture media (e.g., signaling factors) and we can systematically interrogate their impact on cell differentiation and development," Sebastiano said. The system is a boon for discovering important new cell signaling pathways, Sebastiano says. "With a three-dimensional embryoid body, you have to already know what pathways are important," he said. "With the monolayer approach, you can guess what signals you think will be important and then test that hypothesis."

Sebastiano teamed up with assistant professor of developmental biology Kyle Loh, PhD and Siebel Investigator Lay Teng Ang, PhD to apply to system to a specific scientific problem.

Primordial germ cells (PGCs) exist early in

embryonic development and are later transformed into eggs and sperm. Being able to generate PGCs from human pluripotent stem cells would help our understanding of human development and might provide future treatments for infertility. But scientist have been stuck trying to understand how to generate PGCs because the 3-dimensional environment in which they develop is complex. Sebastiano, Loh and Ang used the simplified monolayer approach to study the exact steps that were required to transition cells from pluripotent stem cells to PGCs.

"We discovered that at a specific time in the development of the early embryo, the WNT signal needs to be active for 12 hours and then inactivated in order for PGCs to develop," Loh said. If the WNT signal stays active for more than 12 hours, the cells go on to form the primitive streak."

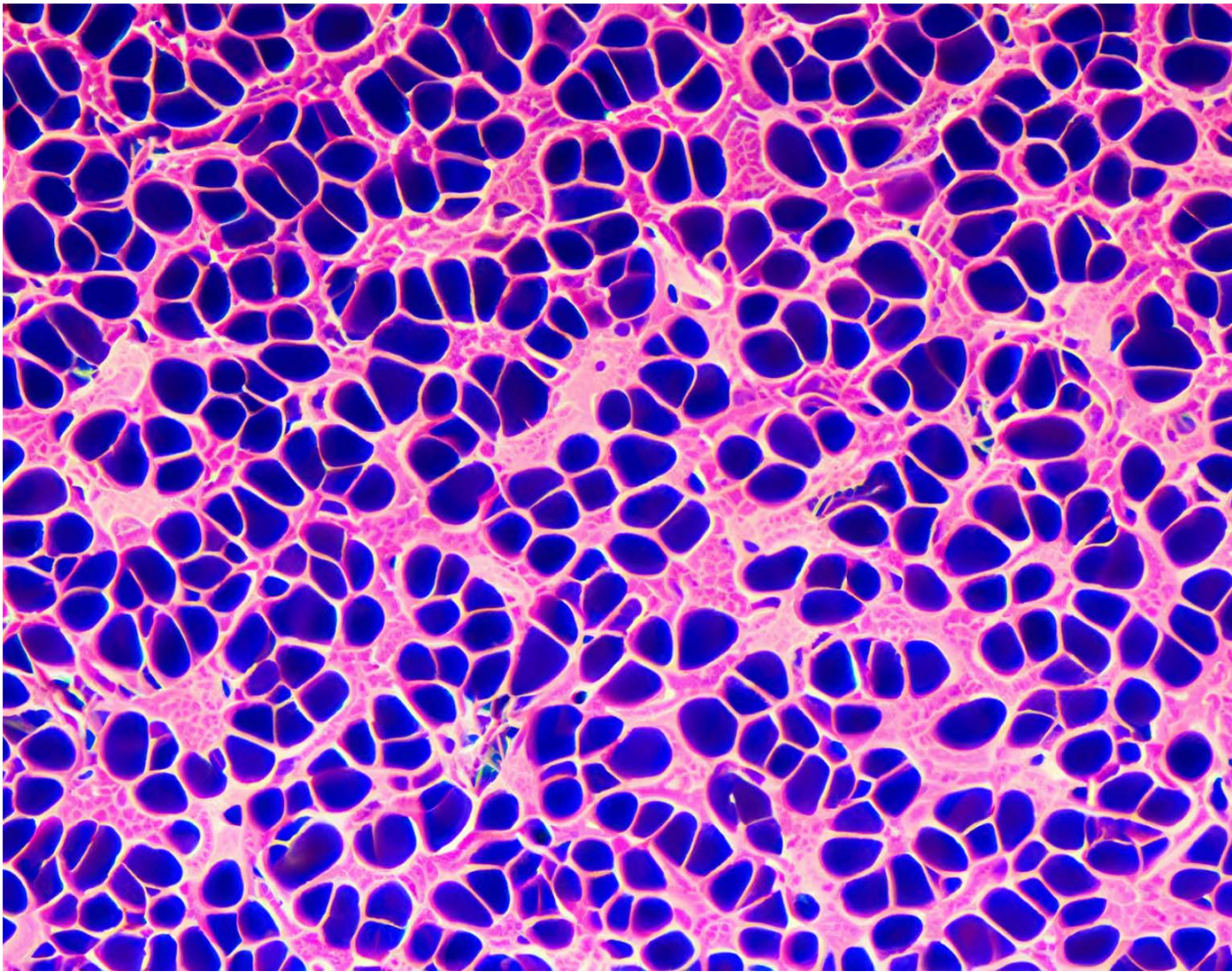
Scientists also knew that embryonic stem cells and PGCs had a very similar profile of pluripotency gene expression but were uncertain if, in the process of

becoming PGCs, those pluripotency genes needed to be turned off and then turned back on. "By studying the process using the monolayer system, we now know that these gene stay on and don't shut down temporarily," Loh and Sebastiano said.

Knowing exactly what genes are active and when they are during the developmental process will be important for regenerative medicine, Loh said. "If you want to grow organs, you need to have a precise protocol for reproducing these conditions in the lab."

Ultimately, Sebastiano says, the work is a first step that could lead to a new understanding of how to generate youthful patient-specific ovarian tissues, which could impact women's health and longevity, a critical goal and focus of the Sebastiano Lab.

The work was published in the journal Nature Communications.



Regenerative Biology and Medicine

Aging and disease are accompanied by the degeneration or destruction of various organs or tissues. The dream of regenerative medicine is to use our understanding of stem cell science to grow new cell therapies in the lab or to help the body regenerate those organs and tissues.



Growing new blood vessels when arteries are blocked

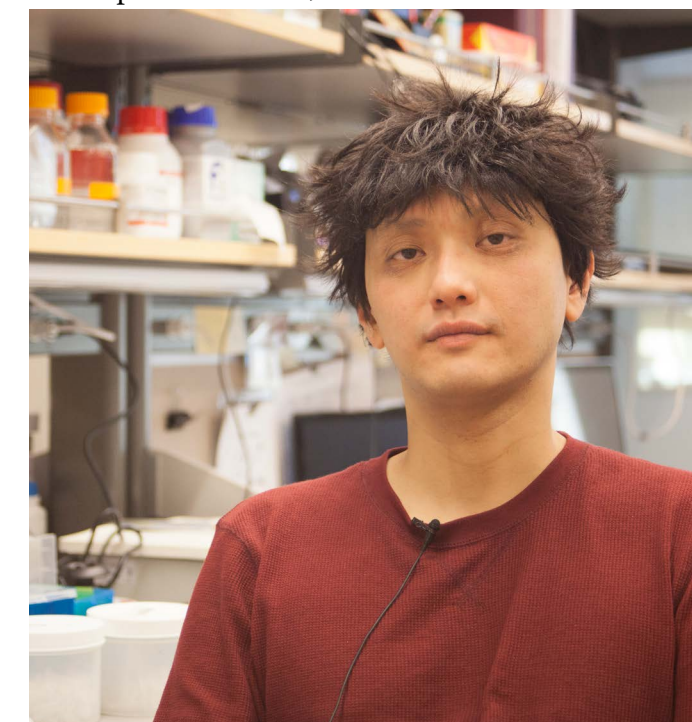
Institute researchers have discovered that certain purified stem cell components of normal body fat, when combined in the right proportions and transplanted into the body, will grow into new blood vessels. The researchers showed that when the technique was used in mice it restored blood flow to areas where areas where arteries were blocked. The discovery may lead to effective new therapies that use people's own fat to treat heart attacks and promote organ transplantation.

"Vascular disease is still a major cause of illness and death throughout the world, and currently we can only restore blood flow to existing arteries," say institute member Charles Chan, PhD. "Our work shows promise that we might help the body generate large blood vessels, bypassing blocked or diseased arteries." Chan, an assistant professor of Surgery, Patricia Nguyen, MD, an associate professor of Medicine, and Michael Longaker, MD, the Deane P. and Louise Mitchel Professor in the Stanford School of Medicine, are co-senior authors on the paper, which was published in the Journal of Arteriosclerosis, Thrombosis and Vascular Biology (ATVB). Institute member Irving Weissman, MD, was also involved in the research. Postdoctoral fellow Liming Zhao, MD, former Stanford PhD & MD student, Andrew Lee, and former Stanford bioinformatician, Koki Sasagawa, are co-first authors on the paper.

Scientists have known that the body can create small "collateral" arteries or capillaries in response ischemia (when the supply of blood and oxygen to tissue is cut off). However, the blood vessels that grow are too small and sparse to supply an ischemic organ. As a result, researchers have been unsuccessfully trying to identify the cells that give rise to these collateral arteries, in hopes of creating a more robust arterial growth. The collateral vessels seem to arise from

so-called "mesenchymal" stem cells (MSC), which include a mix of different kinds of stem and progenitor cells for bone, fat, blood vessels and various other tissues.

The researchers used an array of advanced analytical techniques to narrow down exactly which cells in the mixed MSC population were actually responsible for growing the new arteries. They focused in on two populations that they call VSPC1 and VSPC2, but were confounded to find that neither of these pure populations gave rise to functional vessels. VSPC1 cells, when transplanted into animals, gave rise to stunted, incomplete blood vessels. VSPC2 cells gave rise to stunted vessels and fat. However, when the two populations were transplanted into mice together in a particular ratio, functional new blood vessels



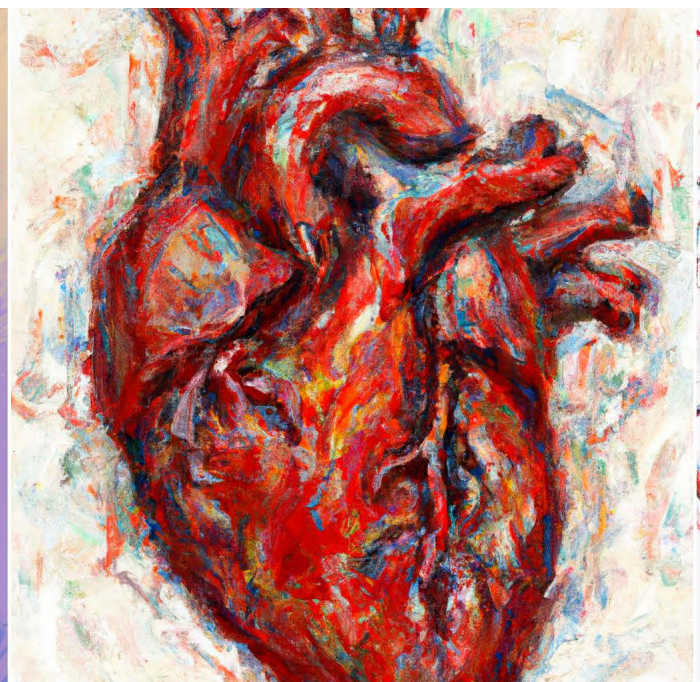
Charles Chan, PhD



Michael Longaker, MD

would arise. “We found these two distinct cell populations have to be transplanted together to work because one kind of cell serves as the developmental niche that is required for the other cell to become a functional blood vessel,” Chan said. “Vessels start forming as soon as you transplant them.” The discovery is clinically important because the treatment for a heart attack or other ischemic event

might be found in the patient’s own fat, Chan says. “If someone has a heart attack, you first want to deal with the blockages, but then you want to encourage new artery growth,” Chan said. “In principle, doctors could potentially use liposuction to collect a patient’s fat, separate out these two cell populations, and transplant them back into heart tissue that has been deprived of oxygen,” Chan said. “Fat is a readily available, abundant and renewable resource in America,” Longaker said. “It is promising to be able to use it to induce new blood vessels” The technique could also be used for tissue transplants, Chan said. Currently, doctors performing tissue or organ transplants surgically connect only the major vessels, meaning that the tissue is not getting as much blood as it was before transplantation. “Surgeons could apply these two cell populations in a gel to the transplant area, and those cells would do the job of connecting the small vessels,” Chan said. In addition, there is the possibility of using banked cells, collected from the fat of anyone who cared to donate. “Because these cells wouldn’t be immunologically matched to the patient, you would have to use anti-rejection drugs at first, but then you would gradually wean patients off the drugs as they regenerated their own vessels,” Chan said. “It’s like if a bridge is knocked out, these VSPC cells act like a pontoon bridge that you put up temporarily to keep supplies moving until you are able to repair the permanent bridge.”



Hiro Nakauchi, MD, PhD

Institute researcher discovers “Holy Grail” of human blood stem cell expansion in culture

Institute researcher Hiro Nakauchi, MD, PhD and his colleagues have found what has been called the “holy grail” of blood stem cell research: a way to expand the number of human blood stem cells in the lab. The discovery opens the door to new research and new therapies for diseases that are currently untreatable.

Their work is published in the journal Nature. Nakauchi shares co-authorship with Satoshi Yamazaki, PhD, an associate professor of stem cell biology at the University of Tokyo. Former Stanford postdoctoral scholar Adam Wilkinson, PhD, is one of the lead authors.

Blood stem cells (called hematopoietic stem cells or HSC) give rise to all the various blood and immune cells in the body. But HSCs are incredibly rare, and hard to isolate in large numbers. Only about 1 out of 30,000 cells in the bone marrow is a blood stem cell. This makes it difficult to obtain sufficient number of cells to do research.

Bone marrow transplantation, in which HSCs and other blood products are transplanted from one patient to another, is a well-established treatment for advanced leukemia, but opportunities to treat these cancers, as well as many other disorders, are limited by the difficulty of isolating HSCs in large volumes. Historically, HSCs can only be isolated from living organisms. Once they are out of the body, research-

ers have not been able to get HSCs to multiply in culture to create more HSCs.

“Clinically, the rarity of HSCs and the difficulty of isolating many of them has been an issue for over 50 years,” Nakauchi said.

Nakauchi is well aware of this issue, having been personally involved in trying to expand samples of HSCs ever since he first isolated purified mouse HSCs in the 1980s. “I thought it would be very easy to expand HSCs,” Nakauchi says. “I tried many different ways of going about it, but it never worked.”

Nakauchi and his colleagues had a breakthrough in recent years when they discovered how to expand mouse HSCs in culture, a result that they published in 2019. “Over the years I tried adding many different cytokines” -- molecules that prompt various cell activities—“but none of them worked.”

The trick turned out to be not adding things to the culture medium, but taking things away. “The difficulty was that even very slight impurities in the culture medium, even very small amounts of inflammatory cytokines in the culture medium, would push the stem cells to differentiate into other kinds of cells,” Nakauchi said. As they had when culturing mouse HSCs, the researchers decided not to use common culture media that may be contaminated with various compounds. Instead, they used polyvinyl alcohol, a synthetic chemical that can be obtained

in pure, uncontaminated form.

But the protocol that the researchers had successfully used to expand mouse HSCs didn't work well with human blood stem cells. To understand why, they analyzed the molecular pathways connected to the signal that prompts the stem cells to divide. They found that a certain molecular mechanism called PI3K phosphorylation was not as active in human cells as in mouse cells. Artificially boosting the activity of that pathway turned out to be the key to getting better replication of the human HSCs.

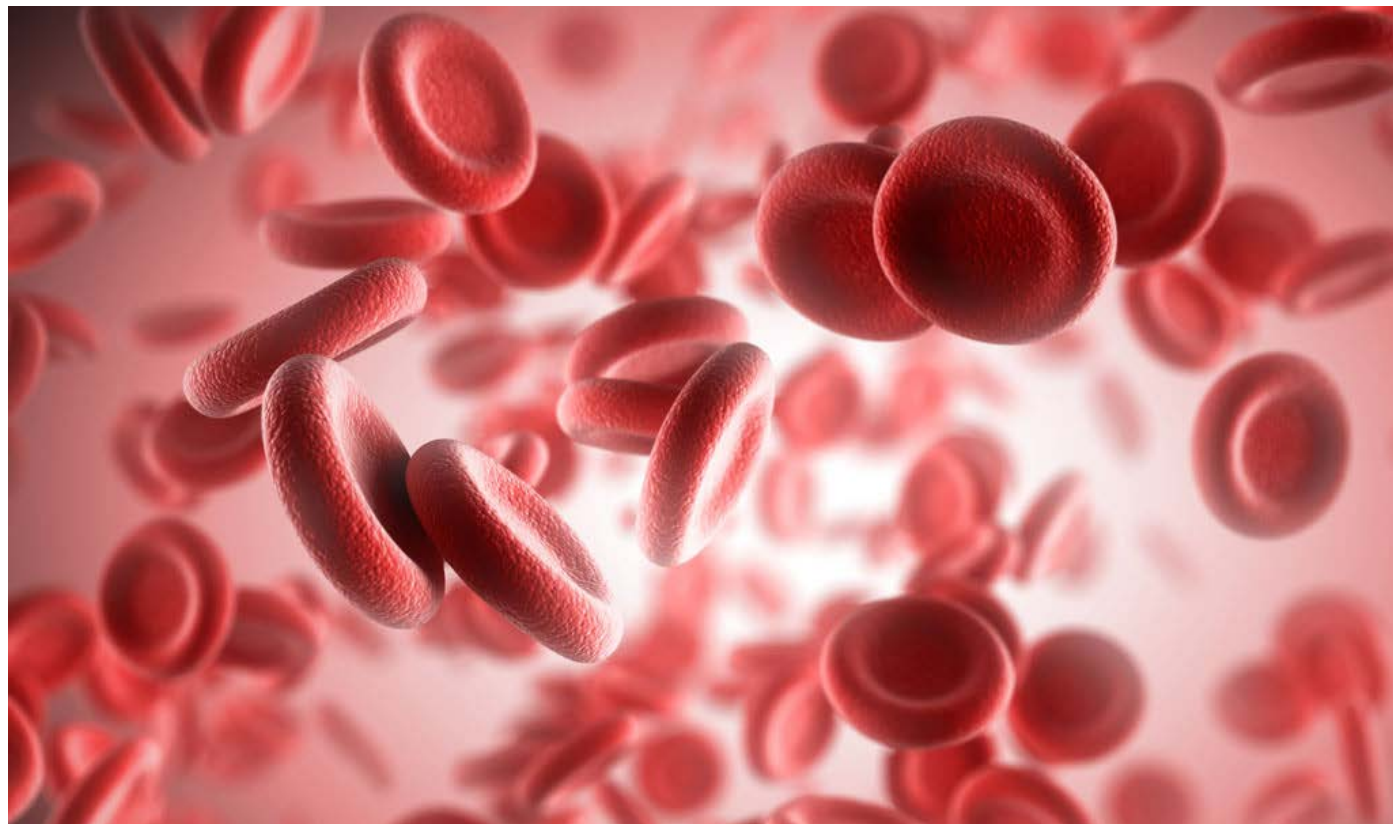
Now that Nakauchi and his colleagues have found out how to grow a few human blood stem cells into many, there are new possibilities for medical therapies. Currently, people with acute leukemia can only undergo stem cell transplantation if they can find a donor who has a matching immunological profile. While Caucasian patients have an 80 percent chance of finding a donor among bone marrow registries, many minorities have a much lower chance. African Americans have only about a 20 percent chance of finding a match, for instance.

Cord blood registries are much more representative of the population at large, but leukemia patients have not been able to make use of them because the samples are small and contain so few blood stem cells. "If we can grow those few cells into many, cord blood samples could be the source for blood stem

cell transplantation, including for those patients who are immunologically hard to match," Nakauchi says. In addition, because the HSCs from cord blood are so young and immature, the immunological match does not have to be as exact as it does for the stem cells taken from adult donors.

Currently, blood stem cell transplantation most often requires a dangerous, pre-transplant preparation procedure involving high doses of chemotherapy or radiation. This wipes out the existing blood stem cells, making room for the transplanted stem cells to engraft. Researchers have discovered, however, that if very large quantities of HSC are transplanted, they can take up residence in the patient's body without the need for removing the patient's own HSCs first. Institute researcher Matthew Porteus, MD, PhD, for instance, is interested in potentially making use of this effect to more safely transplant a blood stem cell that has been genetically modified to provide a cure for young patients with sickle cell disease.

The ability to create large numbers of HSC in the lab should also be a boon for basic researchers, who will now be able to obtain the materials they need for larger, more in depth studies of blood stem function. With such wide applicability in medicine, the interest in this research has been strong. "We are getting inquiries from around the world about our results," Nakauchi said.



Institute researchers identify three key roadblocks to stem cell therapies

As the stem cell sciences progresses rapidly, we are drawing ever closer to a world in which once incurable diseases and conditions will find treatments. But a recent review by researchers at the Institute for Stem Cell Biology and Regenerative Medicine, New York University and Harvard have identified three key roadblocks to developing discoveries into therapies: fibrosis, immune activity, and cell over-proliferation.

"What was once considered the future of medicine is now becoming a reality," said Michael Longaker, MD. "But to get to that new reality we have to be able to overcome these significant hurdles."

Longaker and his colleagues observe that nearly every human malady, be it injury, chronic disease, or degenerative disease, damages tissues in the body. The body has the capacity to heal itself, to regenerate the tissues that have been damaged, but often inflammation and fibrosis (the development of scar tissue) interferes with that regenerative process. In fact, 45% of all deaths can be traced to regenerative failures caused by inflammation and fibrosis.

"I was shocked by that statistic," Longaker said. "Following heart attack, inflammatory bowel disease, liv-

er disease, you name it---most organs in the human body fall short of complete repair after injury."

Longaker began his career decades ago studying how scarring did not occur in the fetus, and has since continued to study why scar tissues develop or do not. "Scars are a kind of spot-weld in the skin—a quick repair that lets the person continue to survive and procreate, even though the tissue might not function quite as well as before." But in many cases, reduction in function caused by scar tissue can lead to major problems over time. The stiffening of heart tissue caused by scarring after a heart attack make the heart muscles work harder to pump the same amount of blood, setting off a reinforcing cycle that can eventually lead to heart failure.

By studying the underlying biology of scar formation, however, Longaker and his colleagues have discovered how to interfere with the signals that put cells on a path to become fibroblasts (scar tissues). With that pathway blocked, normal skin will regenerate where a scar would otherwise form.

"Regeneration turns out to be the default pathway if you block other options, like fibrosis," Longaker said. Inflammation brings its own challenges, the re-

searchers found. Inflammation is a complex response to injury by the immune system. Inflammation is largely a beneficial process that is needed to fight off invading organisms. Many of the inflammatory signals are also necessary to start and maintain the regenerative process.

But inflammation can also promote fibrosis on its own, the researchers said. “Precisely targeting inflammation may ameliorate fibrosis and unlock latent regenerative capacity,” Longaker said.

The immune system is also a roadblock to promise that stem cell transplants might help injured tissues repair themselves. Unless the implanted stem cells come from the patient’s own body, the immune system is designed to recognize them as foreign invaders and attack. Currently, this attack is controlled by strong immunosuppressive medications, but these therapies have their own problems.

“The good news is that many scientists, including some in the institute such as Agnieszka Czechowicz, are currently studying ways to carefully recreate the immune system so that it doesn’t attack transplanted tissues and cells.

Lastly, there is the roadblock of cell over-proliferation. “When you transplant stem cells, there is always the worry that those cells may proliferate more than

you want and in a disorganized fashion,” Longaker said. Such uncontrolled growth can result in a non-cancerous mass of tissue that can interfere with bodily functions. If that were to happen to neural stem cells transplanted into the spinal cord, for

“I’m optimistic because now we are understanding these roadblocks and have potential strategies to address all of them”

instance, the resulting teratoma could squeeze the spinal column and cause paralysis.

“We can think of stem cells as seeds that we plant in the ‘soil’ of the body,” Longaker said. “We need to think not only about the nature of the cell we are implanting, but also about the environment that the cell is going into, the ‘soil’ that will support and nurture that seed and help it grow.”

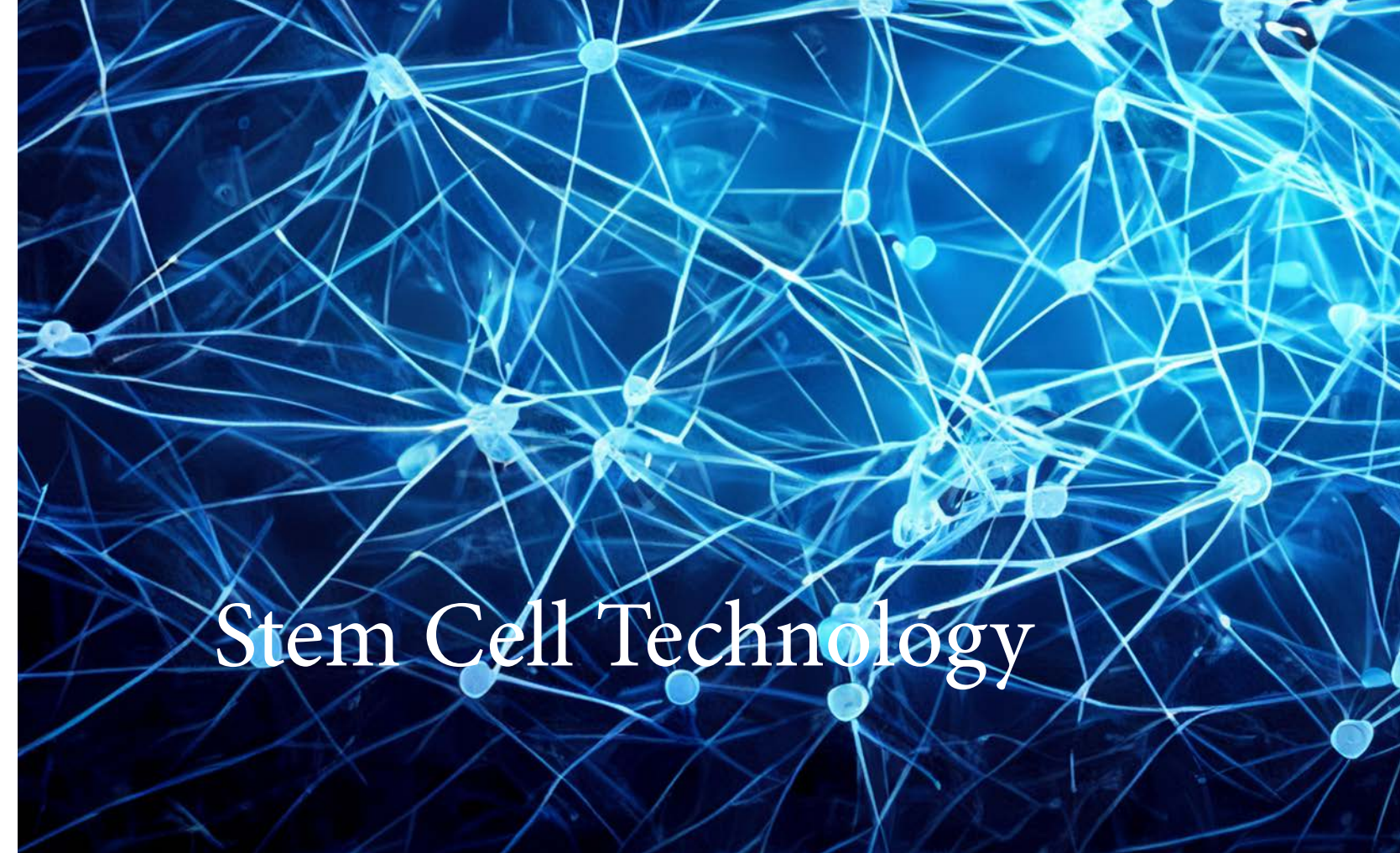
Stem cells often operate in a complex “niche,” a cradle of non-stem cells that provide key signals and support. “If you put stem cells in a hostile ‘soil,’ you don’t get what you want. Understanding the supportive environment and the key signals that each kind of stem cell needs will be essential to overcoming this roadblock, the researchers say.

“The more we understand the better,” Longaker said. “I’m optimistic because we are now understanding these roadblocks and have potential strategies to address all of them.”

“Further understanding will require an interdisciplinary effort that brings together biologists, biomedical engineers and clinicians,” Longaker said. “What we can see in the distance is a transformed medical landscape that is able to seamlessly rejuvenate organs, ultimately extending human lifespan and health span.”



Michael Longaker, MD



Stem Cell Technology

The advancement of science and medicine depends on the development of creative new tools for investigation. Institute researchers are leaders in the development of biostatistical tools which give unprecedented insights into stem cell activity in health and disease.



Aaron Newman, PhD

Researchers invent a tool to create high-resolution maps of gene activity, opening a path to improved diagnostics and therapies

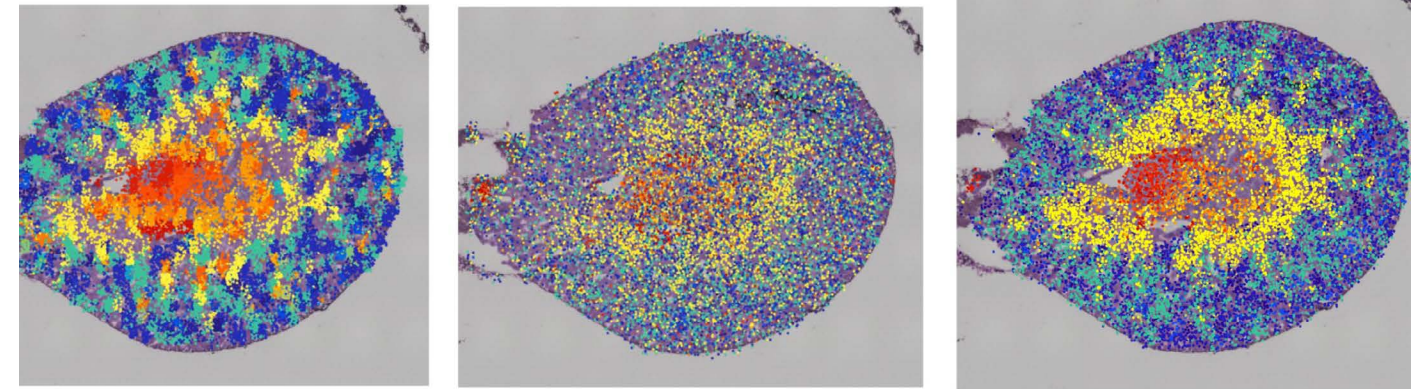
Most people aren't exactly the same everywhere they go. People act in ways that are appropriate for their environment, for the people they interact with. At work they have certain sorts of conversations, while at home, they talk about other things. On vacation, they may ride a zipline or lie on the beach, activities they do neither at home nor at work.

Cells in the human body are much the same. How a particular kind of cell behaves, the proteins it produces, the signals it sends out or receives, are highly dependent on the kind of environment that cell finds itself in. Which makes all the difference for understanding biology and treating disease.

"Cells don't exist in isolation," said Aaron Newman, PhD, an Assistant Professor of Biomedical Data Science, a member of the Stanford Institute for Stem Cell Biology and Regenerative Medicine, and the senior author of the study. "They exist in communities that are communicating with them and shaping those cells in terms of what they do. Cells have to be understood based on their context and surroundings."

Newman and his colleagues have now developed a new method for profiling activity of single cells while also identifying exactly where those cells are geographically in a sample. The method, published March 6, 2023, in the journal *Nature Biotechnology*, is in many ways more powerful than other methods and will provide researchers with a significant new tool for drug discovery and the development of improved diagnostics, Newman said.

Newman and his colleagues are not alone in realizing the importance of spatial information in biology. "In the last few years there have been really rapid advances in the development of spatial assays," Newman said. But each method has its own limitations. 10x Visium is a tool that allows researchers to do an analysis of all the genes being expressed by cells, but the location of each gene's activity can only be narrowed down to within a spot 55 microns wide, an area that might hold dozens of individual cells. The result resembles a crime "heat map" of a city—useful for knowing generally in which areas crimes will occur, but not much use in identifying individuals who



Outputs of various methods of analyzing gene expression of cells in a tissue. 10X visium (left) can survey the activity of all genes in cells but can only say what general area each cell is in. MERSCOPE (middle) reveals the exact location of each cell, but can only survey the activity of about 500 genes. CytoSpace (right) can survey the activity of 20,000 genes in each cell and provide a high resolution spatial map of the location of each cell.

will commit crimes.

Another method, called Vizgen MERSCOPE, very accurately pinpoints the exact location of every cell, but researchers can only look at the activity of 500 genes within each cell. Since there are over 20,000 genes that might be activate in any given cell, MERSCOPE is unable to gather information about differences in cell activity that might be very important. "It's like coming to a foreign city and trying to get to know someone using only a phrase book," Newman says. "You can gather enough basic information to get a general idea of the person, but you can't ask the questions that might reveal, for instance, that this person you are meeting was also born on a farm and shares an interest in modern agricultural technology."

What Newman set out to do was combine these features and generate accurate, high-resolution spatial information while also being able to look at the activity of all 20,000 genes in each cell. He and his team accomplished this by creating a new method called CytoSPACE, which uses mathematical techniques to combine spatial assays like Visium and MERSCOPE along with an existing technology for measuring gene activity in individual cells.

As mentioned before, cells will change their behavior depending on how near or far they are from other specific kinds of cells. Some of these differences are well documented. For instance, immune cells that are cheek by jowl with cancer cells experience "immune exhaustion" and put the brakes on their immune activities in defined ways. (This discovery, and the discovery of how to take the brakes off these exhaust-

ed cells and revitalize their cancer-fighting abilities, garnered a Nobel Prize in 2018.) By measuring such changes in cell state, the researchers were able to tell how far certain cells were from certain other cells.

CytoSPACE starts with a low resolution map of a sample that provides information on the few dozen cells a 55 micron-wide cluster, and then adds information about how near of far some of those cells are from each other. When the researchers gave that information to a computer program that sorts through all possible configurations, the correct configuration pops out. "It's like puzzling out a map of a foreign country if you only know the distances between the major cities," Newman says. "Once you get those pieces put in place, the remaining pieces can only fit in certain ways."

Being able to piece together the exact organization of cells in a sample, and being able to look at the activity level of all the genes in each cell, will open avenues to basic biological discoveries and possible new therapies for disease, Newman said. "For instance, if we didn't know anything about cell exhaustion and how to reverse that to treat cancer, that information would pop out of this sort of high-resolution, spatial analysis of cancer and immune cells," he said. "I'm sure there are many other cell behavioral changes, of which we know nothing about now, just waiting to be discovered once investigators start creating these information-rich, high-resolution maps."

Publications

Ash Alizadeh

A clinical trial of therapeutic vaccination in lymphoma with serial tumor sampling and single cell analysis.

Shree T, Haebe SE, Czerwinski DK, Eckhert E, Day G, Sathe A, Grimes SM, Frank MJ, Maeda L, Alizadeh AA, Advani RH, Hoppe RT, Long SR, Martin BA, Ozawa MG, Khodadoust MS, Ji HP, Levy R.Blood Adv. 2023 Nov 8:bloodadvances.2023011589. doi: 10.1182/bloodadvances.2023011589. Online ahead of print.PMID: 37939259

Improved early outcome prediction by MRI-based 3D tumor volume assessment in patients with CNS lymphomas.
Lauer EM, Riegler E, Mutter JA, Alig SK, Bleul S, Kuehn J, Ranganathan L, Klingler C, Demerath T, Würtemberger U, Rau A, Weiß J, Eisenblaetter M, Bamberg F, Prinz M, Finke J, Duyster J, Illerhaus G, Diehn M, Alizadeh AA, Schorb E, Reinacher PC, Scherer F.Neuro Oncol. 2023 Sep 15:oad177. doi: 10.1093/neuonc/oad177. Online ahead of print. PMID: 37713267

Diversity of intratumoral regulatory T cells in B-cell non-Hodgkin lymphoma.
Spasevska I, Sharma A, Steen CB, Josefsson SE, Blaker YN, Kolstad A, Rustad EH, Meyer S, Isaksen KT, Chellappa S, Kushekhar K, Beiske K, Førsum MS, Spetalen S, Holte H, Ostenstad B, Brodt-korb M, Kimby EK, Olweus J, Taskén K, Newman AM, Lorenz S, Smeland EB, Alizadeh AA, Huse K, Myklebust JH.Blood Adv. 2023 Sep 11:bloodadvances.2023010158. doi: 10.1182/bloodadvances.2023010158. Online ahead of print.PMID: 37695745

Cell-of-Origin Subtypes and Therapeutic Benefit from Polatuzumab Vedotin.
Palmer AC, Kurtz DM, Alizadeh AA.N Engl J Med. 2023 Aug 24;389(8):764-766. doi: 10.1056/NEJMc2306105.PMID: 37611128 No abstract available.

Outcome prediction by interim positron emission tomography and IgM monoclonal gammopathy in

diffuse large B-cell lymphoma.
Johansson P, Alig S, Richter J, Hanoun C, Rekowski J, Dürig J, Ylstra B, de Jong D, Klapper W, Alizadeh AA, Dührsen U, Hüttmann A.Ann Hematol. 2023 Dec;102(12):3445-3455. doi: 10.1007/s00277-023-05393-1. Epub 2023 Aug 11.PMID: 37566280

Tracing Founder Mutations in Circulating and Tissue-Resident Follicular Lymphoma Precursors.
Schroers-Martin JG, Soo J, Brisou G, Scherer F, Kurtz DM, Swarder BJ, Khodadoust MS, Jin MC, Bru A, Liu CL, Stehr H, Vineis P; EPIC Consortium; Natkunam Y, Teras LR, Song JY, Nadel B, Diehn M, Roulland S, Alizadeh AA.Cancer Discov. 2023 Jun 2;13(6):1310-1323. doi: 10.1158/2159-8290.CD-23-0111.PMID: 36939219

Profiling Cellular Ecosystems at Single-Cell Resolution and at Scale with EcoTyper.
Steen CB, Luca BA, Alizadeh AA, Gentles AJ, Newman AM.Methods Mol Biol. 2023;2629:43-71. doi: 10.1007/978-1-0716-2986-4_4.PMID: 36929073
Concurrent pembrolizumab with AVD for untreated classic Hodgkin lymphoma.
Lynch RC, Ujjani CS, Poh C, Warren EH, Smith SD, Shadman M, Till B, Raghunathan VM, Alig S, Alizadeh AA, Gulhane A, Chen DL, Tseng Y, Coye H, Shelby M, Ottemiller S, Keo S, Verni K, Du H, Vandermeer J, Gaston A, Rasmussen H, Martin P, Marzbani E, Voutsinas J, Gopal AK.Blood. 2023 May 25;141(21):2576-2586. doi: 10.1182/blood.2022019254.PMID: 36913694 Clinical Trial.

From patterns to patients: Advances in clinical machine learning for cancer diagnosis, prognosis, and treatment.
Swanson K, Wu E, Zhang A, Alizadeh AA, Zou J.Cell. 2023 Apr 13;186(8):1772-1791. doi: 10.1016/j.cell.2023.01.035. Epub 2023 Mar 10.PMID: 36905928 Review.

Investigating and modeling positron emission tomography factors associated with large cell transformation from low-grade lymphomas.
Obeid JP, Hiniker SM, Schroers-Martin J, Guo HH, No HJ, Moding EJ, Advani RH, Alizadeh AA, Hoppe RT, Binkley MS.EJHaem. 2022 Nov 25;4(1):90-99. doi: 10.1002/jha2.615. eCollection 2023 Feb.PMID: 36819184

Determinants of resistance to engineered T cell therapies targeting CD19 in large B cell lymphomas.
Sworder BJ, Kurtz DM, Alig SK, Frank MJ, Shukla N, Garofalo A, Macaulay CW, Shahrokh Esfahani M, Olsen MN, Hamilton J, Hosoya H, Hamilton M, Spiegel JY, Baird JH, Sugio T, Carleton M, Craig AFM, Younes SF, Sahaf B, Sheybani ND, Schroers-Martin JG, Liu CL, Oak JS, Jin MC, Beygi S, Hüttmann A, Hanoun C, Dührsen U, Westin JR, Khodadoust MS, Natkunam Y, Majzner RG, Mackall CL, Diehn M, Miklos DB, Alizadeh AA.Cancer Cell. 2023 Jan 9;41(1):210-225.e5. doi: 10.1016/j.ccell.2022.12.005. Epub 2022 Dec 29.PMID: 36584673

Circulating Tumor DNA Profiling for Detection, Risk Stratification, and Classification of Brain Lymphomas.
Mutter JA, Alig SK, Esfahani MS, Lauer EM, Mitschke J, Kurtz DM, Kühn J, Bleul S, Olsen M, Liu CL, Jin MC, Macaulay CW, Neidert N, Volk T, Eisenblaetter M, Rauer S, Heiland DH, Finke J, Duyster J, Wehrle J, Prinz M, Illerhaus G, Reinacher PC, Schorb E, Diehn M, Alizadeh AA, Scherer F.J Clin Oncol. 2023 Mar 20;41(9):1684-1694. doi: 10.1200/JCO.22.00826. Epub 2022 Dec 21.PMID: 36542815

Polatuzumab vedotin with infusional chemotherapy for untreated aggressive B-cell non-Hodgkin lymphomas.
Lynch RC, Poh C, Ujjani CS, Warren EH, Smith SD, Shadman M, Morris K, Lee S, Rasmussen H, Ottemiller S, Shelby M, Keo S, Verni K, Kurtz DM, Alizadeh AA, Chabon JJ, Hogan GJ, Schulz A, Gooley T, Voutsinas JM, Gopal AK.Blood Adv. 2023 Jun 13;7(11):2449-2458. doi: 10.1182/bloodadvances.2022009145.PMID: 36521030 Clinical Trial.

A phase 1/2 study of lenalidomide and obinutuzumab with CHOP for newly diagnosed DLBCL.
Cherng HJ, Alig SK, Oki Y, Nastoupil LJ, Fayad L, Neelapu SS, Turturro F, Hagemeister F, Craig AFM, Macaulay CW, Rodriguez MA, Lee HJ, McDonnell TJ, Flowers CR, Vega F, Green MR, Feng L, Kurtz DM, Alizadeh AA, Davis RE, Westin JR.Blood Adv. 2023 Apr 11;7(7):1137-1145. doi: 10.1182/bloodadvances.2022008174.PMID: 36375046 Clinical Trial.

Molecular Monitoring of Lymphomas.
Schroers-Martin JG, Alig S, Garofalo A, Tesoulin B, Sugio T, Alizadeh AA.Annu Rev Pathol. 2023 Jan 24;18:149-180. doi: 10.1146/annurev-pathol-050520-044652. Epub 2022 Sep 21.PMID: 36130071

Phil Beachy

Cellular and molecular mechanisms of Hedgehog signalling.
Zhang Y, Beachy PA.Nat Rev Mol Cell Biol. 2023 Sep;24(9):668-687. doi: 10.1038/s41580-023-00591-1. Epub 2023 Mar 17.PMID: 36932157

Charles Chan
Brain-Derived CCN3 Is An Osteoanabolic Hormone That Sustains Bone in Lactating Females.
Babey ME, Krause WC, Herber CB, Chen K, Nikkanen J, Rodriquez R, Zhang X, Castro-Navarro F, Wang Y, Villeda S, Lane NE, Scheller EL, Chan CKF, Ambrosi TH, Ingraham HA.bioRxiv. 2023 Aug 29:2023.08.28.554707. doi: 10.1101/2023.08.28.554707. Preprint.PMID: 37693376

Efficient and multiplexed tracking of single cells using whole-body PET/CT.
Nguyen HTM, Das N, Wang Y, Ruvalcaba C, Mehadji B, Roncali E, Chan CKF, Pratz G.bioRxiv. 2023 Sep 1:2023.08.23.554536. doi: 10.1101/2023.08.23.554536. Preprint.PMID: 37662335

Del1 Is a Growth Factor for Skeletal Progenitor Cells in the Fracture Callus.
Sun Y, Boyko T, Marecic O, Struck D, Mann RK, Andrew TW, Lopez M, Tong X, Goodman SB, Yang F, Longaker MT, Chan CKF, Yang GP.Biomolecules. 2023 Aug 3;13(8):1214. doi: 10.3390/biom13081214. PMID: 37627279

Gla-domain mediated targeting of externalized phosphatidylserine for intracellular delivery.
Hardy J, Bauzon M, Chan CKF, Makela AV, Kanada M, Schneider D, Blankenberg F, Contag CH, Hermiston T.FASEB J. 2023 Aug;37(8):e23113. doi: 10.1096/fj.202201250RRR.PMID: 37486772

Purification and functional characterization of novel

human skeletal stem cell lineages.
Hoover MY, Ambrosi TH, Steininger HM, Koepke LS, Wang Y, Zhao L, Murphy MP, Alam AA, Arouge EJ, Butler MGK, Takematsu E, Stavitsky SP, Hu S, Sa-hoo D, Sinha R, Morri M, Neff N, Bishop J, Gardner M, Goodman S, Longaker M, Chan CKF.Nat Protoc. 2023 Jul;18(7):2256-2282. doi: 10.1038/s41596-023-00836-5. Epub 2023 Jun 14.PMID: 37316563 Re-view.

Optimizing Delivery of Therapeutic Growth Factors for Bone and Cartilage Regeneration.
Takematsu E, Murphy M, Hou S, Steininger H, Alam A, Ambrosi TH, Chan CKF.Gels. 2023 May 3;9(5):377. doi: 10.3390/gels9050377.PMID: 37232969 Review.

A Combination of Distinct Vascular Stem/Progenitor Cells for Neovascularization and Ischemic Rescue.
Zhao L, Lee AS, Sasagawa K, Sokol J, Wang Y, Ransom RC, Zhao X, Ma C, Steininger HM, Koepke LS, Borrelli MR, Brewer RE, Lee LLY, Huang X, Ambrosi TH, Sinha R, Hoover MY, Seita J, Weissman IL, Wu JC, Wan DC, Xiao J, Longaker MT, Nguyen PK, Chan CKF.Arterioscler Thromb Vasc Biol. 2023 Jul;43(7):1262-1277. doi: 10.1161/ATVBA-HA.122.317943. Epub 2023 Apr 13.PMID: 37051932

Denervation during mandibular distraction osteogenesis results in impaired bone formation.
Tevlin R, Griffin M, Chen K, Januszyk M, Guardino N, Spielman A, Walters S, Gold GE, Chan CKF, Gurtner GC, Wan DC, Longaker MT.Sci Rep. 2023 Feb 6;13(1):2097. doi: 10.1038/s41598-023-27921-9. PMID: 36747028

A seed-and-soil theory for blood ageing.
Ambrosi TH, Chan CKF.Nat Cell Biol. 2023 Jan;25(1):9-11. doi: 10.1038/s41556-022-01062-z. PMID: 36650380

Agnieszka Czechowicz
Physioxia improves the selectivity of hematopoietic stem cell expansion cultures.
Igarashi KJ, Kucinski I, Chan YY, Tan TK, Khoo HM, Kealy D, Bhadury J, Hsu I, Ho PY, Niizuma K, Hickey JW, Nolan GP, Bridge KS, Czechowicz A, Gottgens B, Nakauchi H, Wilkinson AC.Blood Adv. 2023 Jul 25;7(14):3366-3377. doi: 10.1182/bloodad-

vances.2023009668.PMID: 36809781
Non-genotoxic Restoration of the Hematolymphoid System in Fanconi Anemia.
Chan YY, Ho PY, Swartzrock L, Rayburn M, Nofal R, Thongthip S, Weinberg KI, Czechowicz A.Transplant Cell Ther. 2023 Mar;29(3):164.e1-164.e9. doi: 10.1016/j.jtct.2022.08.015. Epub 2022 Aug 19.PMID: 35995393

Max Diehn
Improved early outcome prediction by MRI-based 3D tumor volume assessment in patients with CNS lymphomas.
Lauer EM, Riegler E, Mutter JA, Alig SK, Bleul S, Kuehn J, Ranganathan L, Klingler C, Demerath T, Würtemberger U, Rau A, Weiß J, Eisenblaetter M, Bamberg F, Prinz M, Finke J, Duyster J, Illerhaus G, Diehn M, Alizadeh AA, Schorb E, Reinacher PC, Scherer F.Neuro Oncol. 2023 Sep 15:noad177. doi: 10.1093/neuonc/noad177. Online ahead of print. PMID: 37713267

Individualized Stereotactic Ablative Radiotherapy for Lung Tumors: The iSABR Phase 2 Nonrandomized Controlled Trial.
Gensheimer MF, Gee H, Shirato H, Taguchi H, Snyder JM, Chin AL, Vitzthum LK, Maxim PG, Wakelee HA, Neal J, Das M, Chang DT, Kidd E, Hancock SL, Shultz DB, Horst KC, Le QT, Wong S, Brown E, Nguyen N, Liang R, Loo BW Jr, Diehn M.JAMA Oncol. 2023 Sep 14:e233495. doi: 10.1001/jamaoncol.2023.3495. Online ahead of print.PMID: 37707820

Early-Stage Lung Cancer: Using Circulating Tumor DNA to Get Personal.
Bestvina CM, Garassino MC, Neal JW, Wakelee HA, Diehn M, Vokes EE.J Clin Oncol. 2023 Sep 1;41(25):4093-4096. doi: 10.1200/JCO.23.00258. Epub 2023 Jun 23.PMID: 37352477 No abstract available.

Unilateral Diaphragmatic Paralysis After Stereotactic Ablative Radiation Therapy to a Lung Tumor Abutting the Course of the Phrenic Nerve.
Eke I, Guo HH, Loo BW Jr, Sung AW, Diehn M, Vitzthum L, Chin AL, Gensheimer MF.Pract Radiat Oncol. 2023 Sep-Oct;13(5):e383-e388. doi: 10.1016/j.

prro.2023.04.010. Epub 2023 May 6.PMID: 37150318
Pulmonary Hemorrhage in Patients Treated With Thoracic Stereotactic Ablative Radiotherapy and Antiangiogenic Agents.
Lau BC, Wu YF, No HJ, Ko RB, Devine MD, Das MS, Neal JW, Wakelee HA, Ramchandran K, Gensheimer MF, Diehn M, Chin AL, Loo BW Jr, Vitzthum LK.J Thorac Oncol. 2023 Jul;18(7):922-930. doi: 10.1016/j.jtho.2023.04.007. Epub 2023 Apr 20.PMID: 37085030

Real-world risk of brain metastases in stage III non-small cell lung cancer in the era of PET and MRI staging.
Alhusaini S, Lanman TA, Ko RB, Therkelsen KE, Eyben RV, Diehn M, Soltys SG, Pollom EL, Chin A, Vitzthum L, Wakelee HA, Padda SK, Ramchandran K, Loo BW Jr, Neal JW, Nagpal S.Front Oncol. 2023 Mar 24;13:1139940. doi: 10.3389/fonc.2023.1139940. eCollection 2023.PMID: 37035171

Tracing Founder Mutations in Circulating and Tissue-Resident Follicular Lymphoma Precursors.
Schroers-Martin JG, Soo J, Brisou G, Scherer F, Kurtz DM, Swarder BJ, Khodadoust MS, Jin MC, Bru A, Liu CL, Stehr H, Vineis P; EPIC Consortium; Natkunam Y, Teras LR, Song JY, Nadel B, Diehn M, Roulland S, Alizadeh AA.Cancer Discov. 2023 Jun 2;13(6):1310-1323. doi: 10.1158/2159-8290.CD-23-0111.PMID: 36939219

NFE2L2 Mutations Enhance Radioresistance in Head and Neck Cancer by Modulating Intratumoral Myeloid Cells.
Guan L, Nambiar DK, Cao H, Viswanathan V, Kwok S, Hui AB, Hou Y, Hildebrand R, von Eyben R, Holmes BJ, Zhao J, Kong CS, Wamsley N, Zhang W, Major MB, Seol SW, Sunwoo JB, Hayes DN, Diehn M, Le QT.Cancer Res. 2023 Mar 15;83(6):861-874. doi: 10.1158/0008-5472.CAN-22-1903.PMID: 36652552

STK11 Inactivation Predicts Rapid Recurrence in Inoperable Early-Stage Non-Small-Cell Lung Cancer.
Katipally RR, Spurr LF, Gutiontov SI, Turchan WT, Connell P, Juloori A, Malik R, Binkley MS, Jiang AL, Rouhani SJ, Chervin CS, Wanjari P, Segal JP, Ng V, Loo BW, Gomez DR, Bestvina CM, Vokes EE, Ferguson MK, Donington JS, Diehn M, Pitroda SP.JCO

Precis Oncol. 2023 Jan;7:e2200273. doi: 10.1200/PO.22.00273.PMID: 36603171
Determinants of resistance to engineered T cell therapies targeting CD19 in large B cell lymphomas.
Sworder BJ, Kurtz DM, Alig SK, Frank MJ, Shukla N, Garofalo A, Macaulay CW, Shahrokh Esfahani M, Olsen MN, Hamilton J, Hosoya H, Hamilton M, Spiegel JY, Baird JH, Sugio T, Carleton M, Craig AFM, Younes SF, Sahaf B, Sheybani ND, Schroers-Martin JG, Liu CL, Oak JS, Jin MC, Beygi S, Hüttmann A, Hanoun C, Dührsen U, Westin JR, Khodadoust MS, Natkunam Y, Majzner RG, Mackall CL, Diehn M, Miklos DB, Alizadeh AA.Cancer Cell. 2023 Jan 9;41(1):210-225.e5. doi: 10.1016/j.ccell.2022.12.005. Epub 2022 Dec 29.PMID: 36584673

Circulating Tumor DNA Profiling for Detection, Risk Stratification, and Classification of Brain Lymphomas.
Mutter JA, Alig SK, Esfahani MS, Lauer EM, Mitschke J, Kurtz DM, Kühn J, Bleul S, Olsen M, Liu CL, Jin MC, Macaulay CW, Neidert N, Volk T, Eisenblaetter M, Rauer S, Heiland DH, Finke J, Duyster J, Wehrle J, Prinz M, Illerhaus G, Reinacher PC, Schorb E, Diehn M, Alizadeh AA, Scherer F.J Clin Oncol. 2023 Mar 20;41(9):1684-1694. doi: 10.1200/JCO.22.00826. Epub 2022 Dec 21.PMID: 36542815

Tushar Desai
Evidence for lung barrier regeneration by differentiation prior to binucleated and stem cell division.
Guild J, Juul NH, Andalon A, Taenaka H, Coffey RJ, Matthay MA, Desai TJ.J Cell Biol. 2023 Dec 4;222(12):e202212088. doi: 10.1083/jcb.202212088. Epub 2023 Oct 16.PMID: 37843535

A single-cell atlas of in vitro multiculture systems uncovers the in vivo lineage trajectory and cell state in the human lung.
Lee W, Lee S, Yoon JK, Lee D, Kim Y, Han YB, Kim R, Moon S, Park YJ, Park K, Cha B, Choi J, Kim J, Ha NY, Kim K, Cho S, Cho NH, Desai TJ, Chung JH, Lee JH, Kim JI.Exp Mol Med. 2023 Aug;55(8):1831-1842. doi: 10.1038/s12276-023-01076-z. Epub 2023 Aug 15.PMID: 37582976

KRAS(G12D) drives lepidic adenocarcinoma through stem-cell reprogramming. Juul NH, Yoon JK, Martinez MC, Rishi N, Kazadaeva YI, Morri M, Neff NF, Trope WL, Shrager JB, Sinha R, Desai TJ.Nature. 2023 Jul;619(7971):860-867. doi: 10.1038/s41586-023-06324-w. Epub 2023 Jul 19.PMID: 37468622
Changes and debates in male stress urinary incontinence surgery practice patterns: a contemporary review. Desai TJ, Rozanski AT.Transl Androl Urol. 2023 May 31;12(5):918-925. doi: 10.21037/tau-22-646. Epub 2023 Jan 11.PMID: 37305630 Review.

An integrated cell atlas of the lung in health and disease. Sikkema L, Ramírez-Suástegui C, Strobl DC, Gillett TE, Zappia L, Madissoon E, Markov NS, Zaragosi LE, Ji Y, Ansari M, Arguel MJ, Apperloo L, Ban- chero M, Bécavin C, Berg M, Chichelnitskiy E, Chung MI, Collin A, Gay ACA, Gote-Schniering J, Hooshiar Kashani B, Inecik K, Jain M, Kapellos TS, Kole TM, Leroy S, Mayr CH, Oliver AJ, von Papen M, Peter L, Taylor CJ, Walzthoeni T, Xu C, Bui LT, De Donno C, Dony L, Faiz A, Guo M, Gutierrez AJ, Heumos L, Huang N, Ibarra IL, Jackson ND, Kadur Lakshminarasimha Murthy P, Lotfollahi M, Tabib T, Talavera-López C, Travaglini KJ, Wilbrey-Clark A, Worlock KB, Yoshida M; Lung Biological Network Consortium; van den Berge M, Bossé Y, Desai TJ, Eickelberg O, Kaminski N, Krasnow MA, Lafyatis R, Nikolic MZ, Powell JE, Rajagopal J, Rojas M, Rozenblatt-Rosen O, Seibold MA, Sheppard D, Shepherd DP, Sin DD, Timens W, Tsankov AM, Whitsett J, Xu Y, Banovich NE, Barbry P, Duong TE, Falk CS, Meyer KB, Kropski JA, Péer D, Schiller HB, Tata PR, Schultze JL, Teichmann SA, Misharin AV, Nawijn MC, Luecken MD, Theis FJ.Nat Med. 2023 Jun;29(6):1563-1577. doi: 10.1038/s41591-023-02327-2. Epub 2023 Jun 8.PMID: 37291214

Casey Gifford
Genetic analysis and multimodal imaging identify novel mtDNA 12148T>C leading to multisystem dysfunction with tissue-specific heteroplasmy. Belle K, Kreymerman A, Vadgama N, Ji MH, Randhawa S, Caicedo J, Wong M, Muscat SP, Gifford CA, Lee RT, Nasir J, Young JL, Enns G, Karakikes I, Mercola M, Wood EH.medRx-

iv. 2023 Nov 5:2023.11.03.23297854. doi: 10.1101/2023.11.03.23297854. Preprint.PMID: 37961166

The multi-lineage transcription factor ISL1 controls cardiomyocyte cell fate through interaction with NKX2.5. Maven BEJ, Gifford CA, Weilert M, Gonzalez-Teran B, Hüttenhain R, Pelonero A, Ivey KN, Samse-Knapp K, Kwong W, Gordon D, McGregor M, Nishino T, Okorie E, Rossman S, Costa MW, Krogan NJ, Zeitlinger J, Srivastava D.Stem Cell Reports. 2023 Oct 11:S2213-6711(23)00373-9. doi: 10.1016/j.stemcr.2023.09.014. Online ahead of print.PMID: 37863045

Low-dose lipopolysaccharide exposure during oocyte maturation disrupts early bovine embryonic development. Castro B, Candelaria JI, Austin MM, Shuster CB, Gifford CA, Denicol AC, Hernandez Gifford JA.Theriogenology. 2023 Oct 12;214:57-65. doi: 10.1016/j.theriogenology.2023.10.010. Online ahead of print. PMID: 37857151

Calves severely affected by bovine respiratory disease have reduced protection against histone toxicity and exhibit lower complement activity. Flores VV, Hernandez Gifford JA, Soto-Navarro SA, Matera J, Wilson BK, Hartson S, Byrum SD, Gifford CA.J Anim Sci. 2023 Jan 3;101:skad221. doi: 10.1093/jas/skad221.PMID: 37410397

Natalia Gomez Ospina
CNS Repopulation by Hematopoietic-Derived Microglia-Like Cells Corrects Progranulin deficiency. Colella P, Sayana R, Suarez-Nieto MV, Sarno J, Nyame K, Xiong J, Vera LNP, Basurto JA, Corbo M, Limaye A, Davis KL, Abu-Remaileh M, Gomez-Ospina N.Res Sq. 2023 Sep 12:rs.3.rs-3263412. doi: 10.21203/rs.3.rs-3263412/v1. Preprint.PMID: 37790525

High-efficiency transgene integration by homology-directed repair in human primary cells using DNA-PKcs inhibition. Selvaraj S, Feist WN, Viel S, Vaidyanathan S, Dudek AM, Gastou M, Rockwood SJ, Ekman FK, Oseghale AR, Xu L, Pavel-Dinu M, Luna SE, Cromer MK, Say-

ana R, Gomez-Ospina N, Porteus MH.Nat Biotechnol. 2023 Aug 3. doi: 10.1038/s41587-023-01888-4. Online ahead of print.PMID: 37537500

Editorial: Ex-vivo and in-vivo genome engineering for metabolic and neurometabolic diseases. Colella P, Meneghini V, Baldo G, Gomez-Ospina N.Front Genome Ed. 2023 Jul 6;5:1248904. doi: 10.3389/fgeed.2023.1248904. eCollection 2023. PMID: 37484653 No abstract available.

The clinical and genetic spectrum of autosomal-recessive TOR1A-related disorders. Saffari A, Lau T, Tajsharghi H, Karimiani EG, Kariminejad A, Efthymiou S, Zifarelli G, Sultan T, Toosi MB, Sedighzadeh S, Siu VM, Ortigoza-Escobar JD, AlShamsi AM, Ibrahim S, Al-Sannaa NA, Al-Hertani W, Sandra W, Tarnopolsky M, Alavi S, Li C, Day-Salvatore DL, Martínez-González MJ, Levandoski KM, Bedoukian E, Madan-Khetarpal S, Idleburg MJ, Menezes MJ, Siddharth A, Platzer K, Oppermann H, Smitka M, Collins F, Lek M, Shahrooei M, Ghavidelarestani M, Herman I, Rendu J, Faure J, Baker J, Bhambhani V, Calderwood L, Akhondian J, Imannezhad S, Mirzadeh HS, Hashemi N, Doosti M, Safi M, Ahangari N, Torbati PN, Abedini S, Salpietro V, Gulec EY, Eshaghian S, Ghazavi M, Pascher MT, Vogel M, Abicht A, Moutton S, Bruel AL, Rieubland C, Gallati S, Strom TM, Lochmüller H, Mohammadi MH, Alvi JR, Zackai EH, Keena BA, Skraban CM, Berger SI, Andrew EH, Rahimian E, Morrow MM, Wentzensen IM, Millan F, Henderson LB, Dafsari HS, Jungbluth H, Gomez-Ospina N, McRae A, Peter M, Veltra D, Marinakis NM, Sofocleous C, Ashrafzadeh F, Pehlivan D, Lemke JR, Melki J, Benezit A, Bauer P, Weis D, Lupski JR, Senderek J, Christodoulou J, Chung WK, Goodchild R, Offiah AC, Moreno-De-Luca A, Suri M, Ebrahimi-Fak...See abstract for full author list Brain. 2023 Aug 1;146(8):3273-3288. doi: 10.1093/brain/awad039.PMID: 36757831

Siddhartha Jaiswal
Clonal haematopoiesis of indeterminate potential predicts incident cardiac arrhythmias. Schuermans A, Vlasschaert C, Nauffal V, Cho SMJ, Uddin MM, Nakao T, Niroula A, Klarqvist MDR, Weeks LD, Lin AE, Saadatagah S, Lannery K, Wong M, Hornsby W, Lubitz SA, Ballantyne C, Jaiswal S, Libby P, Ebert BL, Bick AG, Ellinor PT, Natarajan P,

Honigberg MC.Eur Heart J. 2023 Nov 11:ehad670. doi: 10.1093/eurheartj/ehad670. Online ahead of print.PMID: 37952204

Determinants of mosaic chromosomal alteration fitness. Pershad Y, Mack T, Poisner H, Jakubek YA, Stilp AM, Mitchell BD, Lewis JP, Boerwinkle E, Loos RJ, Chami N, Wang Z, Barnes K, Pankratz N, Fornage M, Redline S, Psaty BM, Bis JC, Shojaiie A, Silverman EK, Cho MH, Yun J, DeMeo D, Levy D, Johnson A, Mathias R, Taub M, Arnett D, North K, Raffield LM, Carson A, Doyle MF, Rich SS, Rotter JI, Guo X, Cox N, Roden DM, Franceschini N, Desai P, Reiner A, Auer PL, Scheet P, Jaiswal S, Weinstock JS, Bick AG.medRxiv. 2023 Oct 21:2023.10.20.23297280. doi: 10.1101/2023.10.20.23297280. Preprint.PMID: 37905118

Genetic modification of inflammation- and clonal hematopoiesis-associated cardiovascular risk. Yu Z, Fidler TP, Ruan Y, Vlasschaert C, Nakao T, Uddin MM, Mack T, Niroula A, Heimlich JB, Zekavat SM, Gibson CJ, Griffin GK, Wang Y, Peloso GM, Heard-Costa N, Levy D, Vasan RS, Aguet F, Ardlie KG, Taylor KD, Rich SS, Rotter JI, Libby P, Jaiswal S, Ebert BL, Bick AG, Tall AR, Natarajan PJ Clin Invest. 2023 Sep 15;133(18):e168597. doi: 10.1172/JCI168597.PMID: 37498674

Prediction of risk for myeloid malignancy in clonal hematopoiesis. Weeks LD, Niroula A, Neuberg D, Wong W, Lindsley RC, Luskin M, Berliner N, Stone RM, DeAngelo DJ, Soiffer R, Uddin MM, Griffin G, Vlasschaert C, Gibson CJ, Jaiswal S, Bick AG, Malcovati L, Natarajan P, Ebert BL.NEJM Evid. 2023 May;2(5):10.1056/evidoa2200310. doi: 10.1056/evidoa2200310. Epub 2023 Apr 25.PMID: 37483562

Author Correction: Clonal haematopoiesis and risk of chronic liver disease. Wong WJ, Emdin C, Bick AG, Zekavat SM, Niroula A, Pirruccello JP, Dichtel L, Griffin G, Uddin MM, Gibson CJ, Kovalcik V, Lin AE, McConkey ME, Vromman A, Sellar RS, Kim PG, Agrawal M, Weinstock J, Long MT, Yu B, Banerjee R, Nicholls RC, Dennis A, Kelly M, Loh PR, McCarroll S, Boerwinkle E, Vasan RS, Jaiswal S, Johnson AD, Chung RT,

Corey K, Levy D, Ballantyne C; NHLBI TOPMed Hematology Working Group; Ebert BL, Natarajan P. *Nature*. 2023 Jul;619(7970):E47. doi: 10.1038/s41586-023-06375-z.PMID: 37400552 No abstract available.

Birth Weight Is Associated With Clonal Hematopoiesis of Indeterminate Potential and Cardiovascular Outcomes in Adulthood. Schuermans A, Nakao T, Ruan Y, Koyama S, Yu Z, Uddin MM, Haidermota S, Hornsby W, Lewandowski AJ, Bick AG, Niroula A, Jaiswal S, Ebert BL, Natarajan P, Honigberg MC. *J Am Heart Assoc*. 2023 Jul 4;12(13):e030220. doi: 10.1161/JAHA.123.030220. Epub 2023 Jun 22.PMID: 37345823

Clonal hematopoiesis is associated with protection from Alzheimer’s disease. Bouzid H, Belk JA, Jan M, Qi Y, Sarnowski C, Wirth S, Ma L, Chrostek MR, Ahmad H, Nachun D, Yao W; NHLBI Trans-Omics for Precision Medicine (TOPMed) Consortium; Beiser A, Bick AG, Bis JC, Fornage M, Longstreth WT Jr, Lopez OL, Natarajan P, Psaty BM, Satizabal CL, Weinstock J, Larson EB, Crane PK, Keene CD, Seshadri S, Satpathy AT, Montine TJ, Jaiswal S. *Nat Med*. 2023 Jul;29(7):1662-1670. doi: 10.1038/s41591-023-02397-2. Epub 2023 Jun 15.PMID: 37322115

Clonal Hematopoiesis of Indeterminate Potential Predicts Adverse Outcomes in Patients With Atherosclerotic Cardiovascular Disease. Gumuser ED, Schuermans A, Cho SMJ, Sporn ZA, Uddin MM, Paruchuri K, Nakao T, Yu Z, Haidermota S, Hornsby W, Weeks LD, Niroula A, Jaiswal S, Libby P, Ebert BL, Bick AG, Natarajan P, Honigberg MC. *J Am Coll Cardiol*. 2023 May 23;81(20):1996-2009. doi: 10.1016/j.jacc.2023.03.401.PMID: 37197843

Clonal haematopoiesis and atherosclerotic cardiovascular disease. Ahmad H, Jaiswal S. *Nat Rev Cardiol*. 2023 Jul;20(7):437-438. doi: 10.1038/s41569-023-00882-2. PMID: 37169832 No abstract available.

The genetic determinants of recurrent somatic mutations in 43,693 blood genomes. Weinstock JS, Laurie CA, Broome JG, Taylor KD, Guo X, Shuldiner AR, O’Connell JR, Lewis JP, Boer-

winkle E, Barnes KC, Chami N, Kenny EE, Loos RJF, Fornage M, Redline S, Cade BE, Gilliland FD, Chen Z, Gauderman WJ, Kumar R, Grammer L, Schleimer RP, Psaty BM, Bis JC, Brody JA, Silverman EK, Yun JH, Qiao D, Weiss ST, Lasky-Su J, DeMeo DL, Palmer ND, Freedman BI, Bowden DW, Cho MH, Vasana RS, Johnson AD, Yanek LR, Becker LC, Kardia S, He J, Kaplan R, Heckbert SR, Smith NL, Wiggins KL, Arnett DK, Irvin MR, Tiwari H, Correa A, Raffield LM, Gao Y, de Andrade M, Rotter JI, Rich SS, Manichaikul AW, Konkle BA, Johnsen JM, Wheeler MM, Custer BS, Duggirala R, Curran JE, Blangero J, Gu H, Xiao S, Williams LK, Meyers DA, Li X, Ortega V, McGarvey S, Gu CC, Chen YI, Lee WJ, Shoemaker MB, Darbar D, Roden D, Albert C, Kooperberg C, Desai P, Blackwell TW, Abecasis GR, Smith AV, Kang HM, Mathias R, Natarajan P, Jaiswal S, Reinher AP, Bick AG; NHLBI Trans-Omics for Precision Medicine (TOPMed) Consortium. *Sci Adv*. 2023 Apr 28;9(17):eabm4945. doi: 10.1126/sciadv.abm4945. Epub 2023 Apr 26.PMID: 37126548

Clonal haematopoiesis and risk of chronic liver disease. Wong WJ, Emdin C, Bick AG, Zekavat SM, Niroula A, Pirruccello JP, Dichtel L, Griffin G, Uddin MM, Gibson CJ, Kovalcik V, Lin AE, McConkey ME, Vromman A, Sellar RS, Kim PG, Agrawal M, Weinstock J, Long MT, Yu B, Banerjee R, Nicholls RC, Dennis A, Kelly M, Loh PR, McCarroll S, Boerwinkle E, Vasana RS, Jaiswal S, Johnson AD, Chung RT, Corey K, Levy D, Ballantyne C; NHLBI TOPMed Hematology Working Group; Ebert BL, Natarajan P. *Nature*. 2023 Apr;616(7958):747-754. doi: 10.1038/s41586-023-05857-4. Epub 2023 Apr 12.PMID: 37046084

Aberrant activation of TCL1A promotes stem cell expansion in clonal haematopoiesis. Weinstock JS, Gopakumar J, Burugula BB, Uddin MM, Jahn N, Belk JA, Bouzid H, Daniel B, Miao Z, Ly N, Mack TM, Luna SE, Prothro KP, Mitchell SR, Laurie CA, Broome JG, Taylor KD, Guo X, Sinner MF, von Falkenhausen AS, Käab S, Shuldiner AR, O’Connell JR, Lewis JP, Boerwinkle E, Barnes KC, Chami N, Kenny EE, Loos RJF, Fornage M, Hou L, Lloyd-Jones DM, Redline S, Cade BE, Psaty BM, Bis JC, Brody JA, Silverman EK, Yun JH, Qiao D, Palmer ND, Freedman BI, Bowden DW, Cho MH, DeMeo

DL, Vasana RS, Yanek LR, Becker LC, Kardia SLR, Peyser PA, He J, Rienstra M, Van der Harst P, Kaplan R, Heckbert SR, Smith NL, Wiggins KL, Arnett DK, Irvin MR, Tiwari H, Cutler MJ, Knight S, Muhlestein JB, Correa A, Raffield LM, Gao Y, de Andrade M, Rotter JI, Rich SS, Tracy RP, Konkle BA, Johnsen JM, Wheeler MM, Smith JG, Melander O, Nilsson PM, Custer BS, Duggirala R, Curran JE, Blangero J, McGarvey S, Williams LK, Xiao S, Yang M, Gu CC, Chen YI, Lee WJ, Marcus GM, Kane JP, Pullinger CR, Shoemaker MB, Darbar D, Roden DM, Albert C, Kooperberg C, Zhou Y, Manson JE, Desai P, Johnson AD, Mathias RA; NHLBI Trans-Omics for Precision Medicine (TOPMed) Consortium; Blackwell TW, Abecasis GR, Smith AV, Kang HM, Satpathy A...See abstract for full author list *Nature*. 2023 Apr;616(7958):755-763. doi: 10.1038/s41586-023-05806-1. Epub 2023 Apr 12.PMID: 37046083

A practical approach to curate clonal hematopoiesis of indeterminate potential in human genetic data sets. Vlasschaert C, Mack T, Heimlich JB, Niroula A, Uddin MM, Weinstock J, Sharber B, Silver AJ, Xu Y, Savona M, Gibson C, Lanktree MB, Rauh MJ, Ebert BL, Natarajan P, Jaiswal S, Bick AG. *Blood*. 2023 May 4;141(18):2214-2223. doi: 10.1182/blood.2022018825.PMID: 36652671

Clonal Hematopoiesis and Its Impact on Human Health. Ahmad H, Jahn N, Jaiswal S. *Annu Rev Med*. 2023 Jan 27;74:249-260. doi: 10.1146/annurev-med-042921-112347. Epub 2022 Nov 30.PMID: 36450282

Kyle Loh
Monolayer platform to generate and purify primordial germ-like cells in vitro provides insights into human germline specification. Vijayakumar S, Sala R, Kang G, Chen A, Pablo MA, Adebayo AI, Cipriano A, Fowler JL, Gomes DL, Ang LT, Loh KM, Sebastiano V. *Nat Commun*. 2023 Sep 14;14(1):5690. doi: 10.1038/s41467-023-41302-w. PMID: 37709760

Building human artery and vein endothelial cells from pluripotent stem cells, and enduring mysteries surrounding arteriovenous development.

Loh KM, Ang LT. *Semin Cell Dev Biol*. 2024 Mar 1;155(Pt C):62-75. doi: 10.1016/j.semcdb.2023.06.004. Epub 2023 Jun 29.PMID: 37393122 Review.

An atlas of lamina-associated chromatin across twelve human cell types reveals an intermediate chromatin subtype. Shah PP, Keough KC, Gjoni K, Santini GT, Abdill RJ, Wickramasinghe NM, Dundes CE, Karnay A, Chen A, Salomon REA, Walsh PJ, Nguyen SC, Whalen S, Joyce EF, Loh KM, Dubois N, Pollard KS, Jain R. *Genome Biol*. 2023 Jan 23;24(1):16. doi: 10.1186/s13059-023-02849-5.PMID: 36691074

Creating artificial signaling gradients to spatially pattern engineered tissues. Zheng SL, Loh KM. *Curr Opin Biotechnol*. 2022 Dec;78:102810. doi: 10.1016/j.copbio.2022.102810. Epub 2022 Sep 29.PMID: 36182872

Michael Longaker
A Review of Radiation-Induced Vascular Injury and Clinical Impact. Kameni LE, Januszyk M, Berry CE, Downer MA Jr, Parker JB, Morgan AG, Valencia C, Griffin M, Li DJ, Liang NE, Momeni A, Longaker MT, Wan DC. *Ann Plast Surg*. 2023 Oct 23. doi: 10.1097/SAP.0000000000003723. Online ahead of print. PMID: 37962260

Optimized Nuclei Isolation from Fresh and Frozen Solid Tumor Specimens for Multiome Sequencing. Foster DS, Griffin M, Januszyk M, Delitto D, Norton JA, Longaker MT. *J Vis Exp*. 2023 Oct 13;(200). doi: 10.3791/65831.PMID: 37902368

Desmoplastic stromal signatures predict patient outcomes in pancreatic ductal adenocarcinoma. Mascharak S, Guo JL, Foster DS, Khan A, Davitt MF, Nguyen AT, Burcham AR, Chinta MS, Guardino NJ, Griffin M, Lopez DM, Miller E, Januszyk M, Raghavan SS, Longacre TA, Delitto DJ, Norton JA, Longaker MT. *Cell Rep Med*. 2023 Oct 11:101248. doi: 10.1016/j.xcrm.2023.101248. Online ahead of print. PMID: 37865092

Allele-specific expression reveals genetic drivers of tissue regeneration in mice.

Mack KL, Talbott HE, Griffin MF, Parker JBL, Guardino NJ, Spielman AF, Davitt MF, Mascharak S, Downer M, Morgan A, Valencia C, Akas D, Berger MJ, Wan DC, Fraser HB, Longaker MT. *Cell Stem Cell*. 2023 Oct 5;30(10):1368-1381.e6. doi: 10.1016/j.stem.2023.08.010. Epub 2023 Sep 14. PMID: 37714154

Del1 Is a Growth Factor for Skeletal Progenitor Cells in the Fracture Callus.
Sun Y, Boyko T, Marecic O, Struck D, Mann RK, Andrew TW, Lopez M, Tong X, Goodman SB, Yang F, Longaker MT, Chan CKF, Yang GP. *Biomolecules*. 2023 Aug 3;13(8):1214. doi: 10.3390/biom13081214. PMID: 37627279

Medical Biology of Cancer-Associated Fibroblasts in Pancreatic Cancer.
Morgan A, Griffin M, Kamen L, Wan DC, Longaker MT, Norton JA. *Biology (Basel)*. 2023 Jul 25;12(8):1044. doi: 10.3390/biology12081044. PMID: 37626931 Review.

Understanding Fibroblast Heterogeneity in Form and Function.
Parker JB, Valencia C, Akas D, DiIorio SE, Griffin MF, Longaker MT, Wan DC. *Biomedicines*. 2023 Aug 14;11(8):2264. doi: 10.3390/biomedicines11082264. PMID: 37626760 Review.

Commentary on: Postoperative Mechanomodulation Decreases T-Junction Dehiscence After Reduction Mammoplasty: Early Scar Analysis From a Randomized Controlled Trial.
Berry CE, Longaker MT, Wan DC. *Aesthet Surg J*. 2023 Aug 25:sjad281. doi: 10.1093/asj/sjad281. Online ahead of print. PMID: 37625787 No abstract available.

Understanding the Role of Adipocytes and Fibroblasts in Cancer.
Downer MA, Griffin MF, Morgan AG, Parker JB, Li DJ, Berry CE, Liang NE, Kamen L, Cotterell AC, Akas D, Valencia C, Longaker MT, Wan DC. *Ann Plast Surg*. 2023 Aug 9. doi: 10.1097/SAP.0000000000003658. Online ahead of print. PMID: 37553786

Cas9-mediated knockout of NdrG2 enhances the

regenerative potential of dendritic cells for wound healing.
Henn D, Zhao D, Sivaraj D, Trotsyuk A, Bonham CA, Fischer KS, Kehl T, Fehlmann T, Greco AH, Kussie HC, Moortgat Illouz SE, Padmanabhan J, Barrera JA, Kneser U, Lenhof HP, Januszyk M, Levi B, Keller A, Longaker MT, Chen K, Qi LS, Gurtner GC. *Nat Commun*. 2023 Aug 7;14(1):4729. doi: 10.1038/s41467-023-40519-z. PMID: 37550295

Call for Special Issue Papers: Artificial Intelligence in Tissue Engineering and Biology.
Guo JL, Januszyk M, Longaker MT. *Tissue Eng Part A*. 2023 Aug;29(15-16):411-412. doi: 10.1089/ten.tea.2023.29049.cfp. Epub 2023 Jul 19. PMID: 37466469 No abstract available.

Call for Special Issue Papers: Artificial Intelligence in Tissue Engineering and Biology.
Guo JL, Januszyk M, Longaker MT. *Tissue Eng Part C Methods*. 2023 Aug;29(8):347-348. doi: 10.1089/ten.tec.2023.29040.cfp. Epub 2023 Jul 19. PMID: 37466465 No abstract available.

Call for Special Issue Papers: Artificial Intelligence in Tissue Engineering and Biology.
Guo JL, Januszyk M, Longaker MT. *Tissue Eng Part B Rev*. 2023 Aug;29(4):332-333. doi: 10.1089/ten.teb.2023.29019.cfp. Epub 2023 Jul 19. PMID: 37466464 No abstract available.

Reduction of Tendon Fibrosis Using Galectin-3 Inhibitors.
Spielman AF, Griffin MF, Titan AL, Guardino N, Cotterell AC, Akas D, Wan DC, Longaker MT. *Plast Reconstr Surg*. 2023 Jun 22. doi: 10.1097/PRS.00000000000010880. Online ahead of print. PMID: 37344932

Purification and functional characterization of novel human skeletal stem cell lineages.
Hoover MY, Ambrosi TH, Steininger HM, Koepke LS, Wang Y, Zhao L, Murphy MP, Alam AA, Arouge EJ, Butler MGK, Takematsu E, Stavitsky SP, Hu S, Sahoo D, Sinha R, Morri M, Neff N, Bishop J, Gardner M, Goodman S, Longaker M, Chan CKF. *Nat Protoc*. 2023 Jul;18(7):2256-2282. doi: 10.1038/s41596-023-00836-5. Epub 2023 Jun 14. PMID: 37316563 Review.

Circulating and extracellular vesicle-derived microRNAs as biomarkers in bone-related diseases.
Huber J, Longaker MT, Quarto N. *Front Endocrinol (Lausanne)*. 2023 May 24;14:1168898. doi: 10.3389/fendo.2023.1168898. eCollection 2023. PMID: 37293498 Review.
Emerging frontiers in regenerative medicine.
McKinley KL, Longaker MT, Naik S. *Science*. 2023 May 26;380(6647):796-798. doi: 10.1126/science.add6492. Epub 2023 May 25. PMID: 37228215

Attenuating Chronic Fibrosis: Decreasing Foreign Body Response with Acellular Dermal Matrix.
Liang NE, Griffin MF, Berry CE, Parker JB, Downer MA, Wan DC, Longaker MT. *Tissue Eng Part B Rev*. 2023 Jun 7. doi: 10.1089/ten.TEB.2023.0060. Online ahead of print. PMID: 37212342

The effects of mechanical force on fibroblast behavior in cutaneous injury.
Berry CE, Downer M Jr, Morgan AG, Griffin M, Liang NE, Kamen L, Laufey Parker JB, Guo J, Longaker MT, Wan DC. *Front Surg*. 2023 Apr 18;10:1167067. doi: 10.3389/fsurg.2023.1167067. eCollection 2023. PMID: 37143767 Review.

Piezo inhibition prevents and rescues scarring by targeting the adipocyte to fibroblast transition.
Griffin MF, Talbott HE, Guardino NJ, Guo JL, Spielman AF, Chen K, Parker JBL, Mascharak S, Henn D, Liang N, King M, Cotterell AC, Bauer-Rowe KE, Abbas DB, Diaz DeLeon NM, Sivaraj D, Fahy EJ, Downer M, Akas D, Berry C, Cook J, Quarto N, Klein OD, Lorenz HP, Gurtner GC, Januszyk M, Wan DC, Longaker MT. *bioRxiv*. 2023 Apr 4:2023.04.03.535302. doi: 10.1101/2023.04.03.535302. Preprint. PMID: 37066136

A Combination of Distinct Vascular Stem/Progenitor Cells for Neovascularization and Ischemic Rescue.
Zhao L, Lee AS, Sasagawa K, Sokol J, Wang Y, Ransom RC, Zhao X, Ma C, Steininger HM, Koepke LS, Borrelli MR, Brewer RE, Lee LLY, Huang X, Ambrosi TH, Sinha R, Hoover MY, Seita J, Weissman IL, Wu JC, Wan DC, Xiao J, Longaker MT, Nguyen PK, Chan CKF. *Arterioscler Thromb Vasc Biol*. 2023 Jul;43(7):1262-1277. doi: 10.1161/ATVBAHA.122.317943. Epub 2023 Apr 13. PMID: 37051932

Establishing a xenograft model with CD-1 nude mice to study human skin wound repair.
Abbas DB, Griffin M, Fahy EJ, Spielman AF, Guardino NJ, Pu A, Lintel H, Lorenz HP, Longaker MT, Wan DC. *Plast Reconstr Surg*. 2023 Mar 27. doi: 10.1097/PRS.00000000000010465. Online ahead of print. PMID: 36988644

Chelating the valley of death: Deferoxamine's path from bench to wound clinic.
Parker JB, Griffin MF, Downer MA, Akas D, Berry CE, Cotterell AC, Gurtner GC, Longaker MT, Wan DC. *Front Med (Lausanne)*. 2023 Feb 15;10:1015711. doi: 10.3389/fmed.2023.1015711. eCollection 2023. PMID: 36873870

An Inexpensive 3D Printed Mouse Model of Successful, Complication-free Long Bone Distraction Osteogenesis.
Tevlin R, Shah HN, Salhotra A, Di Iorio SE, Griffin M, Januszyk M, Wan DC, Longaker MT. *Plast Reconstr Surg Glob Open*. 2023 Feb 13;11(2):e4674. doi: 10.1097/GOX.00000000000004674. eCollection 2023 Feb. PMID: 36798717

Denervation during mandibular distraction osteogenesis results in impaired bone formation.
Tevlin R, Griffin M, Chen K, Januszyk M, Guardino N, Spielman A, Walters S, Gold GE, Chan CKF, Gurtner GC, Wan DC, Longaker MT. *Sci Rep*. 2023 Feb 6;13(1):2097. doi: 10.1038/s41598-023-27921-9. PMID: 36747028

Bioprinted Hydrogels for Fibrosis and Wound Healing: Treatment and Modeling.
Guo JL, Longaker MT. *Gels*. 2022 Dec 27;9(1):19. doi: 10.3390/gels9010019. PMID: 36661787 Review.

Multiplexed evaluation of mouse wound tissue using oligonucleotide barcoding with single-cell RNA sequencing.
Januszyk M, Griffin M, Mascharak S, Talbott HE, Chen K, Henn D, Spielman AF, Parker JBL, Liang NE, Cotterell A, Guardino N, Foster DS, Wagh D, Coller J, Gurtner GC, Wan DC, Longaker MT. *STAR Protoc*. 2023 Mar 17;4(1):101946. doi: 10.1016/j.xpro.2022.101946. Epub 2022 Dec 15. PMID: 36525348

<p>Macrophage inflammatory and regenerative response periodicity is programmed by cell cycle and chromatin state. Daniel B, Belk JA, Meier SL, Chen AY, Sandor K, Czimmerer Z, Varga Z, Bene K, Buquicchio FA, Qi Y, Kitano H, Wheeler JR, Foster DS, Januszyk M, Longaker MT, Chang HY, Satpathy AT.Mol Cell. 2023 Jan 5;83(1):121-138.e7. doi: 10.1016/j.molcel.2022.11.017. Epub 2022 Dec 14.PMID: 36521490</p>	<p>Progenitor Cells. Nelde A, Schuster H, Heitmann JS, Bauer J, Maringer Y, Zwick M, Volkmer JP, Chen JY, Stanger AMP, Lehmann A, Appiah B, Märklin M, Rücker-Braun E, Salih HR, Roerden M, Schroeder SM, Häring MF, Schlosser A, Schetelig J, Schmitz M, Boerries M, Köhler N, Lengerke C, Majeti R, Weissman IL, Rammensee HG, Walz JS.Blood Cancer Discov. 2023 Nov 1;4(6):468-489. doi: 10.1158/2643-3230.BCD-23-0020.PMID: 37847741</p>	<p>Patient-Derived iPSCs Faithfully Represent the Genetic Diversity and Cellular Architecture of Human Acute Myeloid Leukemia. Kotini AG, Carcamo S, Cruz-Rodriguez N, Olszewska M, Wang T, Demircioglu D, Chang CJ, Bernard E, Chao MP, Majeti R, Luo H, Kharas MG, Hasson D, Papapetrou EP.Blood Cancer Discov. 2023 Jul 5;4(4):318-335. doi: 10.1158/2643-3230.BCD-22-0167.PMID: 37067914</p>	<p>Cells as a Novel Immunotherapy. Linde MH, Fan AC, Köhnke T, Trotman-Grant AC, Gurev SF, Phan P, Zhao F, Haddock NL, Nuno KA, Gars EJ, Stafford M, Marshall PL, Dove CG, Linde IL, Landberg N, Miller LP, Majzner RG, Zhang TY, Majeti R.Cancer Discov. 2023 May 4;13(5):1164-1185. doi: 10.1158/2159-8290.CD-21-0502.PMID: 36856575</p>
<p>Topical vanadate improves tensile strength and alters collagen organisation of excisional wounds in a mouse model. Lintel H, Abbas DB, Mackay DJ, Griffin M, Lavin CV, Berry CE, Guardino NJ, Guo JL, Momeni A, Mackay DR, Longaker MT, Wan DC.Wound Repair Regen. 2023 Jan;31(1):77-86. doi: 10.1111/wrr.13062. Epub 2022 Dec 14.PMID: 36484112</p>	<p>AML/T cell interactomics uncover correlates of patient outcomes and the key role of ICAM1 in T cell killing of AML. Sayitoglu EC, Luca BA, Boss AP, Thomas BC, Freeborn RA, Uyeda MJ, Chen PP, Nakau-chi Y, Waichler C, Lacayo N, Bacchetta R, Majeti R, Gentles AJ, Cepika AM, Roncarolo MG.bioRxiv. 2023 Sep 23:2023.09.21.558911. doi: 10.1101/2023.09.21.558911. Preprint.PMID: 37790561</p>	<p>Engineering Oncogenic Heterozygous Gain-of-Function Mutations in Human Hematopoietic Stem and Progenitor Cells. Sconocchia T, Foßelteder J, Köhnke T, Majeti R, Reinisch A.J Vis Exp. 2023 Mar 10;(193). doi: 10.3791/64558.PMID: 36971438</p>	<p>Dysregulated Lipid Synthesis by Oncogenic IDH1 Mutation Is a Targetable Synthetic Lethal Vulnerability. Thomas D, Wu M, Nakauchi Y, Zheng M, Thompson-Peach CAL, Lim K, Landberg N, Köhnke T, Robinson N, Kaur S, Kutyna M, Stafford M, Hiwase D, Reinisch A, Peltz G, Majeti R.Cancer Discov. 2023 Feb 6;13(2):496-515. doi: 10.1158/2159-8290.CD-21-0218.PMID: 36355448</p>
<p>Standardized Quantitative Sensory Testing to Assess Insufficient Recovery of Touch Discrimination in Free Flap Surgery. Huber J, Scharberth A, Maier C, Wallner C, Wagner JM, Dadras M, Longaker MT, Lehnhardt M, Behr B.Plast Reconstr Surg. 2023 Feb 1;151(2):429-438. doi: 10.1097/PRS.0000000000009860. Epub 2022 Nov 15.PMID: 36374559</p>	<p>Classification, risk stratification and response assessment in myelodysplastic syndromes/neoplasms (MDS): A state-of-the-art report on behalf of the International Consortium for MDS (icMDS). Stahl M, Bewersdorf JP, Xie Z, Porta MGD, Komrokji R, Xu ML, Abdel-Wahab O, Taylor J, Steensma DP, Starczynowski DT, Sekeres MA, Sanz G, Sallman DA, Roboz GJ, Platzbecker U, Patnaik MM, Padron E, Odenike O, Nimer SD, Nazha A, Majeti R, Loghavi S, Little RF, List AF, Kim TK, Hourigan CS, Hasserjian RP, Halene S, Griffiths EA, Gore SD, Greenberg P, Figueroa ME, Fenaux P, Efficace F, DeZern AE, Daver NG, Churpek JE, Carraway HE, Buckstein R, Brunner AM, Boultonwood J, Borate U, Bejar R, Bennett JM, Wei AH, Santini V, Savona MR, Zeidan AM.Blood Rev. 2023 Aug 19:101128. doi: 10.1016/j.blre.2023.101128. Online ahead of print.PMID: 37704469 Review.</p>	<p>Current landscape of translational and clinical research in myelodysplastic syndromes/neoplasms (MDS): Proceedings from the 1st International Workshop on MDS (iwMDS) Of the International Consortium for MDS (icMDS). Bewersdorf JP, Xie Z, Bejar R, Borate U, Boultonwood J, Brunner AM, Buckstein R, Carraway HE, Churpek JE, Daver NG, Porta MGD, DeZern AE, Fenaux P, Figueroa ME, Gore SD, Griffiths EA, Halene S, Hasserjian RP, Hourigan CS, Kim TK, Komrokji R, Kuchroo VK, List AF, Loghavi S, Majeti R, Odenike O, Patnaik MM, Platzbecker U, Roboz GJ, Sallman DA, Santini V, Sanz G, Sekeres MA, Stahl M, Starczynowski DT, Steensma DP, Taylor J, Abdel-Wahab O, Xu ML, Savona MR, Wei AH, Zeidan AM.Blood Rev. 2023 Jul;60:101072. doi: 10.1016/j.blre.2023.101072. Epub 2023 Mar 11.PMID: 36934059 Review.</p>	<p>Finding consistency in classifications of myeloid neoplasms: a perspective on behalf of the International Workshop for Myelodysplastic Syndromes. Zeidan AM, Bewersdorf JP, Buckstein R, Sekeres MA, Steensma DP, Platzbecker U, Loghavi S, Boultonwood J, Bejar R, Bennett JM, Borate U, Brunner AM, Carraway H, Churpek JE, Daver NG, Della Porta M, DeZern AE, Efficace F, Fenaux P, Figueroa ME, Greenberg P, Griffiths EA, Halene S, Hasserjian RP, Hourigan CS, Kim N, Kim TK, Komrokji RS, Kuchroo V, List AF, Little RF, Majeti R, Nazha A, Nimer SD, Odenike O, Padron E, Patnaik MM, Roboz GJ, Sallman DA, Sanz G, Stahl M, Starczynowski DT, Taylor J, Xie Z, Xu M, Savona MR, Wei AH, Abdel-Wahab O, Santini V.Leukemia. 2022 Dec;36(12):2939-2946. doi: 10.1038/s41375-022-01724-9. Epub 2022 Oct 20.PMID: 36266326 No abstract available.</p>
<p>Adipose-Derived Stromal Cell-Based Therapies for Radiation-Induced Fibrosis. Berry CE, Abbas DB, Lintel HA, Churukian AA, Griffin M, Guo JL, Cotterell AC, Parker JBL, Downer MA, Longaker MT, Wan DC.Adv Wound Care (New Rochelle). 2022 Dec 9. doi: 10.1089/wound.2022.0103. Online ahead of print.PMID: 36345216</p>	<p>RUNX1 loss renders hematopoietic and leukemic cells dependent on IL-3 and sensitive to JAK inhibition. Fan AC, Nakauchi Y, Bai L, Azizi A, Nuno KA, Zhao F, Köhnke T, Karigane D, Cruz-Hernandez D, Reinisch A, Khatri P, Majeti R.J Clin Invest. 2023 Oct 2;133(19):e167053. doi: 10.1172/JCI167053.PMID: 37581927</p>	<p>MYC-driven synthesis of Siglec ligands is a glycoimmune checkpoint. Smith BAH, Deutzmann A, Correa KM, Delaveris CS, Dhanasekaran R, Dove CG, Sullivan DK, Wisnovsky S, Stark JC, Pluvinaige JV, Swaminathan S, Riley NM, Rajan A, Majeti R, Felsher DW, Bertozzi CR.Proc Natl Acad Sci U S A. 2023 Mar 14;120(11):e2215376120. doi: 10.1073/pnas.2215376120. Epub 2023 Mar 10.PMID: 36897988</p>	<p>An agenda to advance research in myelodysplastic syndromes: a TOP 10 priority list from the first international workshop in MDS. Stahl M, Abdel-Wahab O, Wei AH, Savona MR, Xu ML, Xie Z, Taylor J, Starczynowski D, Sanz GF, Sallman DA, Santini V, Roboz GJ, Patnaik MM, Padron E, Odenike O, Nazha A, Nimer SD, Majeti R, Little RF, Gore S, List AF, Kutchroo V, Komrokji RS, Kim TK, Kim N, Hourigan CS, Hasserjian RP, Halene S, Griffiths EA, Greenberg PL, Figueroa M, Fenaux P, Efficace F, DeZern AE, Della Porta MG, Daver NG,</p>
<p>Immune Surveillance of Acute Myeloid Leukemia Is Mediated by HLA-Presented Antigens on Leukemia</p>		<p>Reprogramming Cancer into Antigen-Presenting</p>	

Churpek JE, Carraway HE, Brunner AM, Borate U, Bennett JM, Bejar R, Boultonwood J, Loghavi S, Bewersdorf JP, Platzbecker U, Steensma DP, Sekeres MA, Buckstein RJ, Zeidan AM.Blood Adv. 2023 Jun 27;7(12):2709-2714. doi: 10.1182/bloodadvances.2022008747.PMID: 36260702 No abstract available.

TP53-Mutated Myelodysplastic Syndrome and Acute Myeloid Leukemia: Biology, Current Therapy, and Future Directions. Daver NG, Maiti A, Kadia TM, Vyas P, Majeti R, Wei AH, Garcia-Manero G, Craddock C, Sallman DA, Kantarjian HM.Cancer Discov. 2022 Nov 2;12(11):2516-2529. doi: 10.1158/2159-8290.CD-22-0332.PMID: 36218325 Review.

Single-cell genomics in AML: extending the frontiers of AML research. Ediriwickrema A, Gentles AJ, Majeti R.Blood. 2023 Jan 26;141(4):345-355. doi: 10.1182/blood.2021014670.PMID: 35926108

Michelle Monje
Glioma synapses recruit mechanisms of adaptive plasticity. Taylor KR, Barron T, Hui A, Spitzer A, Yalçin B, Ivec AE, Geraghty AC, Hartmann GG, Arzt M, Gillespie SM, Kim YS, Maleki Jahan S, Zhang H, Shamardani K, Su M, Ni L, Du PP, Woo PJ, Silva-Torres A, Venkatesh HS, Mancusi R, Ponnuswami A, Mulinyawe S, Keough MB, Chau I, Aziz-Bose R, Tirosh I, Suvà ML, Monje M.Nature. 2023 Nov;623(7986):366-374. doi: 10.1038/s41586-023-06678-1. Epub 2023 Nov 1.PMID: 37914930

Neuron-oligodendroglial interactions in health and malignant disease. Taylor KR, Monje M.Nat Rev Neurosci. 2023 Oct 19. doi: 10.1038/s41583-023-00744-3. Online ahead of print.PMID: 37857838 Review.

Distinguishing features of long COVID identified through immune profiling. Klein J, Wood J, Jaycox JR, Dhodapkar RM, Lu P, Gehlhausen JR, Tabachnikova A, Greene K, Tabacof L, Malik AA, Silva Monteiro V, Silva J, Kamath K, Zhang M, Dhal A, Ott IM, Valle G, Peña-Hernández M, Mao T, Bhattacharjee B, Takahashi T, Lucas C,

Song E, McCarthy D, Breyman E, Tosto-Mancuso J, Dai Y, Perotti E, Akduman K, Tzeng TJ, Xu L, Geraghty AC, Monje M, Yildirim I, Shon J, Medzhitov R, Lutchmansingh D, Possick JD, Kaminski N, Omer SB, Krumholz HM, Guan L, Dela Cruz CS, van Dijk D, Ring AM, Putrino D, Iwasaki A.Nature. 2023 Nov;623(7985):139-148. doi: 10.1038/s41586-023-06651-y. Epub 2023 Sep 25.PMID: 37748514

Tumors on different wavelengths. Shamardani K, Monje M.Cancer Cell. 2023 Sep 11;41(9):1541-1543. doi: 10.1016/j.ccell.2023.07.009. Epub 2023 Aug 30.PMID: 37652004

A combined immunopeptidomics, proteomics, and cell surface proteomics approach to identify immunotherapy targets for diffuse intrinsic pontine glioma. Pandey K, Wang SS, Mifsud NA, Faridi P, Davenport AJ, Webb AI, Sandow JJ, Ayala R, Monje M, Cross RS, Ramarathinam SH, Jenkins MR, Purcell AW.Front Oncol. 2023 Aug 11;13:1192448. doi: 10.3389/fonc.2023.1192448. eCollection 2023.PMID: 37637064

Epigenetic neural glioblastoma enhances synaptic integration and predicts therapeutic vulnerability. Drexler R, Khatri R, Sauvigny T, Mohme M, Maire CL, Ryba A, Zghaibeh Y, Dührsen L, Salviano-Silva A, Lamszus K, Westphal M, Gempt J, Wefers AK, Neumann J, Bode H, Hausmann F, Huber TB, Bonn S, Jütten K, Delev D, Weber KJ, Harter PN, Onken J, Vajkoczy P, Capper D, Wiestler B, Weller M, Snijder B, Buck A, Weiss T, Keough MB, Ni L, Monje M, Silverbush D, Hovestadt V, Suvà ML, Krishna S, Hervey-Jumper SL, Schüller U, Heiland DH, Hänzelmann S, Ricklefs FL.bioRxiv. 2023 Aug 7:2023.08.04.552017. doi: 10.1101/2023.08.04.552017. Preprint.PMID: 37609137

CAR T cell therapies for diffuse midline glioma. Thomas BC, Staudt DE, Douglas AM, Monje M, Vitanza NA, Dun MD.Trends Cancer. 2023 Oct;9(10):791-804. doi: 10.1016/j.trecan.2023.07.007. Epub 2023 Aug 3.PMID: 37541803 Review.

A Phase I Trial of Panobinostat in Children with Diffuse Intrinsic Pontine Glioma: A Report from the

Pediatric Brain Tumor Consortium (PBTC-047). Monje M, Cooney T, Glod J, Huang J, Peer CJ, Faury D, Baxter P, Kramer K, Lenzen A, Robison NJ, Kilburn L, Vinitsky A, Figg WD, Jabado N, Fouladi M, Fangusaro J, Onar-Thomas A, Dunkel IJ, Warren KE.Neuro Oncol. 2023 Aug 1:noad141. doi: 10.1093/neuonc/noad141. Online ahead of print.PMID: 37526549

Remote neuronal activity drives glioma progression through SEMA4F. Huang-Hobbs E, Cheng YT, Ko Y, Luna-Figueroa E, Lozzi B, Taylor KR, McDonald M, He P, Chen HC, Yang Y, Maleki E, Lee ZF, Murali S, Williamson MR, Choi D, Curry R, Bayley J, Woo J, Jalali A, Monje M, Noebels JL, Harmanci AS, Rao G, Deneen B.Nature. 2023 Jul;619(7971):844-850. doi: 10.1038/s41586-023-06267-2. Epub 2023 Jun 28.PMID: 37380778

Haploinsufficiency of NFKBIA reshapes the epigenome antipodal to the IDH mutation and imparts disease fate in diffuse gliomas. Bredel M, Espinosa L, Kim H, Scholtens DM, McElroy JP, Rajbhandari R, Meng W, Kollmeyer TM, Malta TM, Quezada MA, Harsh GR, Lobo-Jarne T, Solé L, Merati A, Nagaraja S, Nair S, White JJ, Thudi NK, Fleming JL, Webb A, Natsume A, Ogawa S, Weber RG, Bertran J, Haque SJ, Hentschel B, Miller CR, Furnari FB, Chan TA, Grosu AL, Weller M, Barnholtz-Sloan JS, Monje M, Noushmehr H, Jenkins RB, Rogers CL, MacDonald DR, Pugh SL, Chakravarti A.Cell Rep Med. 2023 Jun 20;4(6):101082. doi: 10.1016/j.xcrm.2023.101082.PMID: 37343523

The neuroscience of cancer. Mancusi R, Monje M.Nature. 2023 Jun;618(7965):467-479. doi: 10.1038/s41586-023-05968-y. Epub 2023 Jun 14.PMID: 37316719 Review.

Glioblastoma remodelling of human neural circuits decreases survival. Krishna S, Choudhury A, Keough MB, Seo K, Ni L, Kakaizada S, Lee A, Aabedi A, Popova G, Lipkin B, Cao C, Nava Gonzales C, Sudharshan R, Egladyous A, Almeida N, Zhang Y, Molinaro AM, Venkatesh HS, Daniel AGS, Shamardani K, Hyer J, Chang EF, Findlay A, Phillips JJ, Nagarajan S, Raleigh DR, Brang D, Monje M, Hervey-Jumper SL.Nature. 2023 May;617(7961):599-607. doi: 10.1038/s41586-023-

06036-1. Epub 2023 May 3.PMID: 37138086

Kinase-Modulated Bioluminescent Indicators Enable Noninvasive Imaging of Drug Activity in the Brain. Wu Y, Walker JR, Westberg M, Ning L, Monje M, Kirkland TA, Lin MZ, Su Y.ACS Cent Sci. 2023 Mar 20;9(4):719-732. doi: 10.1021/acscentsci.3c00074. eCollection 2023 Apr 26.PMID: 37122464

Cancer neuroscience: State of the field, emerging directions. Winkler F, Venkatesh HS, Amit M, Batchelor T, Demir IE, Deneen B, Gutmann DH, Hervey-Jumper S, Kuner T, Mabbott D, Platten M, Rolls A, Sloan EK, Wang TC, Wick W, Venkataramani V, Monje M. Cell. 2023 Apr 13;186(8):1689-1707. doi: 10.1016/j.cell.2023.02.002.PMID: 37059069 Review.

Tumor inflammation-associated neurotoxicity. Mahdi J, Dietrich J, Straathof K, Roddie C, Scott BJ, Davidson TB, Prolo LM, Batchelor TT, Campen CJ, Davis KL, Gust J, Lim M, Majzner RG, Park JR, Partap S, Ramakrishna S, Richards R, Schultz L, Vitanza NA, Wang LD, Mackall CL, Monje M.Nat Med. 2023 Apr;29(4):803-810. doi: 10.1038/s41591-023-02276-w. Epub 2023 Apr 6.PMID: 37024595 Review.

Generation and multi-dimensional profiling of a childhood cancer cell line atlas defines new therapeutic opportunities. Sun CX, Daniel P, Bradshaw G, Shi H, Loi M, Chew N, Parackal S, Tsui V, Liang Y, Koptyra M, Adjumain S, Sun C, Chong WC, Fernando D, Drinkwater C, Tourchi M, Habarakada D, Sooraj D, Carvalho D, Storm PB, Baubet V, Sayles LC, Fernandez E, Nguyen T, Pörksen M, Doan A, Crombie DE, Panday M, Zhukova N, Dun MD, Ludlow LE, Day B, Stringer BW, Neeman N, Rubens JA, Raabe EH, Vinci M, Tyrrell V, Fletcher JI, Ekert PG, Dumevska B, Ziegler DS, Tsoli M, Syed Sulaiman NF, Loh AHP, Low SY, Sweet-Cordero EA, Monje M, Resnick A, Jones C, Downie P, Williams B, Rosenbluh J, Gough D, Cain JE, Firestein R.Cancer Cell. 2023 Apr 10;41(4):660-677.e7. doi: 10.1016/j.ccell.2023.03.007. Epub 2023 Mar 30.PMID: 37001527

Remote neuronal activity drives glioma infiltration via Sema4f. Huang-Hobbs E, Cheng YT, Ko Y, Luna-Figueroa

E, Lozzi B, Taylor KR, McDonald M, He P, Chen HC, Yang Y, Maleki E, Lee ZF, Murali S, Williamson M, Choi D, Curry R, Bayley J, Woo J, Jalali A, Monje M, Noebels JL, Harmanci AS, Rao G, Deenen B.bioRxiv. 2023 Mar 16:2023.03.15.532832. doi: 10.1101/2023.03.15.532832. Preprint.PMID: 36993539 Updated.

Cancer hallmarks intersect with neuroscience in the tumor microenvironment. Hanahan D, Monje M.Cancer Cell. 2023 Mar 13;41(3):573-580. doi: 10.1016/j.ccell.2023.02.012. PMID: 36917953 Review.

Neuronal-Activity Dependent Mechanisms of Small Cell Lung Cancer Progression. Savchuk S, Gentry K, Wang W, Carleton E, Yalçın B, Liu Y, Pavarino EC, LaBelle J, Toland AM, Woo PJ, Qu F, Filbin MG, Krasnow MA, Sabatini BL, Sage J, Monje M, Venkatesh HS.bioRxiv. 2023 Jan 20:2023.01.19.524430. doi: 10.1101/2023.01.19.524430. Preprint.PMID: 36711554

Multifocal demyelinating leukoencephalopathy and oligodendroglial lineage cell loss with immune effector cell-associated neurotoxicity syndrome (ICANS) following CD19 CAR T-cell therapy for mantle cell lymphoma. Nie EH, Ahmadian SS, Bharadwaj SN, Acosta-Alvarez L, Threlkeld ZD, Frank MJ, Miklos DB, Monje M, Scott BJ, Vogel H.J Neuropathol Exp Neurol. 2023 Jan 20;82(2):160-168. doi: 10.1093/jnen/nlac121. PMID: 36592076

The landscape of tumor cell states and spatial organization in H3-K27M mutant diffuse midline glioma across age and location. Liu I, Jiang L, Samuelsson ER, Marco Salas S, Beck A, Hack OA, Jeong D, Shaw ML, Englinger B, LaBelle J, Mire HM, Madlener S, Mayr L, Quezada MA, Trissal M, Panditharatna E, Ernst KJ, Vogelzang J, Gatesman TA, Halbert ME, Palova H, Pokorna P, Sterba J, Slaby O, Geyeregger R, Diaz A, Findlay IJ, Dun MD, Resnick A, Suvà ML, Jones DTW, Agnihotri S, Svendlund J, Koschmann C, Haberler C, Czech T, Slavic I, Cotter JA, Ligon KL, Alexandrescu S, Yung WKA, Arrillaga-Romany I, Gojo J, Monje M, Nilsson M, Filbin MG.Nat Genet. 2022 Dec;54(12):1881-1894.

doi: 10.1038/s41588-022-01236-3. Epub 2022 Dec 5.PMID: 36471067

Adaptive and maladaptive myelination in health and disease. Knowles JK, Batra A, Xu H, Monje M.Nat Rev Neurol. 2022 Dec;18(12):735-746. doi: 10.1038/s41582-022-00737-3. Epub 2022 Nov 14.PMID: 36376595 Review.

Hiro Nakauchi

Preparation of mechanically patterned hydrogels for controlling the self-condensation of cells. Matsuzaki T, Kawano Y, Horikiri M, Shimokawa Y, Yamazaki T, Okuma N, Koike H, Kimura M, Kawamura R, Yoneyama Y, Furuichi Y, Hakuno F, Takahashi SI, Nakabayashi S, Okamoto S, Nakauchi H, Taniguchi H, Takebe T, Yoshikawa HY.STAR Protoc. 2023 Jul 28;4(3):102471. doi: 10.1016/j.xpro.2023.102471. Online ahead of print.PMID: 37515762

Functional calcium-responsive parathyroid glands generated using single-step blastocyst complementation. Kano M, Mizuno N, Sato H, Kimura T, Hirochika R, Iwasaki Y, Inoshita N, Nagano H, Kasai M, Yamamoto H, Yamaguchi T, Suga H, Masaki H, Mizutani E, Nakauchi H.Proc Natl Acad Sci U S A. 2023 Jul 11;120(28):e2216564120. doi: 10.1073/pnas.2216564120. Epub 2023 Jun 28.PMID: 37379351

Chemically defined cytokine-free expansion of human haematopoietic stem cells. Sakurai M, Ishitsuka K, Ito R, Wilkinson AC, Kimura T, Mizutani E, Nishikii H, Sudo K, Becker HJ, Takemoto H, Sano T, Kataoka K, Takahashi S, Nakamura Y, Kent DG, Iwama A, Chiba S, Okamoto S, Nakauchi H, Yamazaki S.Nature. 2023 Mar;615(7950):127-133. doi: 10.1038/s41586-023-05739-9. Epub 2023 Feb 22.PMID: 36813966

Physioxia improves the selectivity of hematopoietic stem cell expansion cultures. Igarashi KJ, Kucinski I, Chan YY, Tan TK, Khoo HM, Kealy D, Bhadury J, Hsu I, Ho PY, Niizuma K, Hickey JW, Nolan GP, Bridge KS, Czechowicz A, Gottgens B, Nakauchi H, Wilkinson AC.Blood Adv.

2023 Jul 25;7(14):3366-3377. doi: 10.1182/bloodadvances.2023009668.PMID: 36809781

Removal of sperm tail using trypsin and pre-activation of oocyte facilitates intracytoplasmic sperm injection in mice and rats. Torikai K, Shimizu K, Nagatomo H, Kasai M, Kato-Itoh M, Kamada Y, Shibasaki I, Jeon H, Kikuchi R, Wakayama S, Suchy F, Nakauchi H, Wakayama T, Mizutani E.J Reprod Dev. 2023 Feb 8;69(1):48-52. doi: 10.1262/jrd.2022-065. Epub 2022 Dec 16.PMID: 36529517

Roel Nusse

The Lasker-Koshland Special Achievement Award in Medical Science awarded to Piet Borst. Nusse R, Shapiro L.Proc Natl Acad Sci U S A. 2023 Sep 26;120(39):e2311130120. doi: 10.1073/pnas.2311130120. Epub 2023 Sep 21.PMID: 37732755

APEX2-Mediated Proximity Labeling of Wnt Receptor Interactors Upon Pathway Activation. Rim EY, Nusse R.MicroPubl Biol. 2023 May 15;2023:10.17912/micropub.biology.000817. doi: 10.17912/micropub.biology.000817. eCollection 2023.PMID: 37260921

Intermittent fasting induces rapid hepatocyte proliferation to restore the hepatostat in the mouse liver. Sarkar A, Jin Y, DeFelice BC, Logan CY, Yang Y, Anbarchian T, Wu P, Morri M, Neff NF, Nguyen H, Rulifson E, Fish M, Kaye AG, Martínez Jaimes AM, Nusse R.Elife. 2023 Jan 31;12:e82311. doi: 10.7554/eLife.82311.PMID: 36719070

Aaron Newman

Single-cell mapping identifies MSI+ cells as a common origin for diverse subtypes of pancreatic cancer. Rajbhandari N, Hamilton M, Quintero CM, Ferguson LP, Fox R, Schürch CM, Wang J, Nakamura M, Lytle NK, McDermott M, Diaz E, Pettit H, Kritzik M, Han H, Cridebring D, Wen KW, Tsai S, Goggins MG, Lowy AM, Wechsler-Reya RJ, Von Hoff DD, Newman AM, Reya T.Cancer Cell. 2023 Nov 13;41(11):1989-2005.e9. doi: 10.1016/j.ccell.2023.09.008. Epub 2023 Oct 5.PMID: 37802055

Diversity of intratumoral regulatory T cells in B-cell

non-Hodgkin lymphoma. Spasevska I, Sharma A, Steen CB, Josefsson SE, Blaker YN, Kolstad A, Rustad EH, Meyer S, Isaksen KT, Chellappa S, Kushekhar K, Beiske K, Før Sund MS, Spetalen S, Holte H, Ostenstad B, Brodt-korb M, Kimby EK, Olweus J, Taskén K, Newman AM, Lorenz S, Smeland EB, Alizadeh AA, Huse K, Myklebust JH.Blood Adv. 2023 Sep 11:bloodadvances.2023010158. doi: 10.1182/bloodadvances.2023010158. Online ahead of print.PMID: 37695745

CD4 T cells and toxicity from immune checkpoint blockade. Earland N, Zhang W, Usmani A, Nene A, Bacchiocchi A, Chen DY, Sznol M, Halaban R, Chaudhuri AA, Newman AM.Immunol Rev. 2023 Sep;318(1):96-109. doi: 10.1111/imr.13248. Epub 2023 Jul 25.PMID: 37491734 Review.

p53 governs an AT1 differentiation programme in lung cancer suppression. Kaiser AM, Gatto A, Hanson KJ, Zhao RL, Raj N, Ozawa MG, Seoane JA, Biegging-Rolett KT, Wang M, Li I, Trope WL, Liou DZ, Shrager JB, Plevritis SK, Newman AM, Van Rechem C, Attardi LD.Nature. 2023 Jul;619(7971):851-859. doi: 10.1038/s41586-023-06253-8. Epub 2023 Jul 19.PMID: 37468633

Profiling Cellular Ecosystems at Single-Cell Resolution and at Scale with EcoTyper. Steen CB, Luca BA, Alizadeh AA, Gentles AJ, Newman AM.Methods Mol Biol. 2023;2629:43-71. doi: 10.1007/978-1-0716-2986-4_4.PMID: 36929073

High-resolution alignment of single-cell and spatial transcriptomes with CytoSPACE. Vahid MR, Brown EL, Steen CB, Zhang W, Jeon HS, Kang M, Gentles AJ, Newman AM.Nat Biotechnol. 2023 Nov;41(11):1543-1548. doi: 10.1038/s41587-023-01697-9. Epub 2023 Mar 6.PMID: 36879008

A spatial map of human macrophage niches reveals context-dependent macrophage functions in colon and breast cancer. Matusiak M, Hickey JW, Luca B, Lu G, Kidziński L, Zhu S, Colburg DRC, Phillips DJ, Brubaker SW, Charville GW, Shen J, Nolan GP, Newman AM, West RB, van de Rijn M.Res Sq. 2023 Jan

10:rs.3.rs-2393443. doi: 10.21203/rs.3.rs-2393443/v1. Preprint.PMID: 36711732

Aberrant corticospinal tract characteristics in prodromal PD: A diffusion tensor imaging study. Pimer LJ, Leslie RA, Phillips G, Newman AJ, Rusak B, Rolheiser TM, Schoffer K, Khan MN, McKelvey JR, Robertson HA, Good KP.Clin Park Relat Disord. 2022 Dec 19;8:100182. doi: 10.1016/j.prdoa.2022.100182. eCollection 2023.PMID: 36632053

Lucy O’Brien

Basal stem cell progeny establish their apical surface in a junctional niche during turnover of an adult barrier epithelium. Galenza A, Moreno-Roman P, Su YH, Acosta-Alvarez L, Debec A, Guichet A, Knapp JM, Kizilyaprak C, Humbel BM, Kolotuev I, O’Brien LE.Nat Cell Biol. 2023 May;25(5):658-671. doi: 10.1038/s41556-023-01116-w. Epub 2023 Mar 30.PMID: 36997641

Tissue Homeostasis and Non-Homeostasis: From Cell Life Cycles to Organ States. O’Brien LE.Annu Rev Cell Dev Biol. 2022 Oct 6;38:395-418. doi: 10.1146/annurev-cell-bio-120420-114855. Epub 2022 Jul 18.PMID: 35850152 Review.

Anthony Oro

A Spatiotemporal and Machine-Learning Platform Accelerates the Manufacturing of hPSC-derived Esophageal Mucosa. Yang Y, McCullough CG, Seninge L, Guo L, Kwon WJ, Zhang Y, Li NY, Gaddam S, Pan C, Zhen H, Torkelson J, Glass IA; Birth Defects Research Laboratory; Charville G, Que J, Stuart J, Ding H, Oro A.bioRxiv. 2023 Oct 26:2023.10.24.563664. doi: 10.1101/2023.10.24.563664. Preprint.PMID: 37961271

Epigenetic regulation of p63 blocks squamous-to-neuroendocrine transdifferentiation in esophageal development and malignancy. Zhang Y, Karagiannis D, Liu H, Lin M, Fang Y, Jiang M, Chen X, Suresh S, Huang H, She J, Shi F, Yang P, El-Rifai W, Zaika A, Oro AE, Rustgi AK, Wang TC, Lu C, Que J.bioRxiv. 2023 Sep 11:2023.09.09.556982. doi: 10.1101/2023.09.09.556982. Preprint.PMID:

37745439 Acquisition of drug resistance in basal cell nevus syndrome tumors through basal to squamous cell carcinoma transition. Jussila AR, Haensel D, Gaddam S, Oro AE.bioRxiv. 2023 Jul 27:2023.07.26.550719. doi: 10.1101/2023.07.26.550719. Preprint.PMID: 37546976

Integrated single-cell chromatin and transcriptomic analyses of human scalp identify gene-regulatory programs and critical cell types for hair and skin diseases. Ober-Reynolds B, Wang C, Ko JM, Rios EJ, Aasi SZ, Davis MM, Oro AE, Greenleaf WJ.Nat Genet. 2023 Aug;55(8):1288-1300. doi: 10.1038/s41588-023-01445-4. Epub 2023 Jul 27.PMID: 37500727

Skin basal cell carcinomas assemble a pro-tumorigenic spatially organized and self-propagating Trem2+ myeloid niche. Haensel D, Daniel B, Gaddam S, Pan C, Fabo T, Bjelajac J, Jussila AR, Gonzalez F, Li NY, Chen Y, Hou J, Patel T, Aasi S, Satpathy AT, Oro AE.Nat Commun. 2023 May 10;14(1):2685. doi: 10.1038/s41467-023-37993-w.PMID: 37164949

A scalable, GMP-compatible, autologous organotypic cell therapy for Dystrophic Epidermolysis Bullosa. Neumayer G, Torkelson JL, Li S, McCarthy K, Zhen HH, Vangipuram M, Jackow J, Rami A, Hansen C, Guo Z, Gaddam S, Pappalardo A, Li L, Cramer A, Roy KR, Nguyen TM, Tanabe K, McGrath PS, Bruckner A, Bilousova G, Roop D, Bailey I, Tang JY, Christiano A, Steinmetz LM, Wernig M, Oro AE.bioRxiv. 2023 Mar 1:2023.02.28.529447. doi: 10.1101/2023.02.28.529447. Preprint.PMID: 36909618

GRHL2 and AP2a coordinate early surface ectoderm lineage commitment during development. Collier AE, Piekos SN, Liu A, Pattison JM, Felix F, Bailetti AA, Sedov E, Gaddam S, Zhen H, Oro AE.iScience. 2023 Feb 3;26(3):106125. doi: 10.1016/j.isci.2023.106125. eCollection 2023 Mar 17.PMID: 36843855

LY6D marks pre-existing resistant basosquamous

tumor subpopulations. Haensel D, Gaddam S, Li NY, Gonzalez F, Patel T, Cloutier JM, Sarin KY, Tang JY, Rieger KE, Aasi SZ, Oro AE.Nat Commun. 2022 Dec 6;13(1):7520. doi: 10.1038/s41467-022-35020-y.PMID: 36473848

Matthew Porteus

Epitope-engineered human hematopoietic stem cells are shielded from CD123-targeted immunotherapy. Marone R, Landmann E, Devaux A, Lepore R, Seyres D, Zuin J, Burgold T, Engdahl C, Capoferri G, Dell’Aglio A, Larrue C, Simonetta F, Rositzka J, Rhiel M, Andrieux G, Gallagher DN, Schröder MS, Wiederkehr A, Sinopoli A, Do Sacramento V, Haydn A, Garcia-Prat L, Divsalar C, Camus A, Xu L, Bordoli L, Schwede T, Porteus M, Tamburini J, Corn JE, Cathomen T, Cornu TI, Urlinger S, Jeker LT.J Exp Med. 2023 Dec 4;220(12):e20231235. doi: 10.1084/jem.20231235. Epub 2023 Sep 29.PMID: 37773046

Molecular dynamics of genome editing with CRISPR-Cas9 and rAAV6 virus in human HSPCs to treat sickle cell disease. Xu L, Lahiri P, Skowronski J, Bhatia N, Lattanzi A, Porteus MH.Mol Ther Methods Clin Dev. 2023 Jul 27;30:317-331. doi: 10.1016/j.omtm.2023.07.009. eCollection 2023 Sep 14.PMID: 37637384

High-efficiency transgene integration by homology-directed repair in human primary cells using DNA-PKcs inhibition. Selvaraj S, Feist WN, Viel S, Vaidyanathan S, Dudek AM, Gastou M, Rockwood SJ, Ekman FK, Oseghale AR, Xu L, Pavel-Dinu M, Luna SE, Cromer MK, Sayana R, Gomez-Ospina N, Porteus MH.Nat Biotechnol. 2023 Aug 3. doi: 10.1038/s41587-023-01888-4. Online ahead of print.PMID: 37537500

Combined lineage tracing and scRNA-seq reveals unexpected first heart field predominance of human iPSC differentiation. Galdos FX, Lee C, Lee S, Paige S, Goodyer W, Xu S, Samad T, Escobar GV, Darsha A, Beck A, Bak RO, Porteus MH, Wu SM.Elife. 2023 Jun 7;12:e80075. doi: 10.7554/eLife.80075.PMID: 37284748

Comparative analysis of CRISPR off-target discovery tools following ex vivo editing of CD34+ hematopoi-

etic stem and progenitor cells. Cromer MK, Majeti KR, Rettig GR, Murugan K, Kurgan GL, Bode NM, Hampton JP, Vakulskas CA, Behlke MA, Porteus MH.Mol Ther. 2023 Apr 5;31(4):1074-1087. doi: 10.1016/j.ymthe.2023.02.011. Epub 2023 Feb 15.PMID: 36793210

CRISPR-Cas9-AAV versus lentivector transduction for genome modification of X-linked severe combined immunodeficiency hematopoietic stem cells. Brault J, Liu T, Liu S, Lawson A, Choi U, Kozhushko N, Bzhilyanskaya V, Pavel-Dinu M, Meis RJ, Eckhaus MA, Burkett SS, Bosticardo M, Kleinstiver BP, Notarangelo LD, Lazzarotto CR, Tsai SQ, Wu X, Dahl GA, Porteus MH, Malech HL, De Ravin SS.Front Immunol. 2023 Jan 4;13:1067417. doi: 10.3389/fimmu.2022.1067417. eCollection 2022.PMID: 36685559

Kristy Red Horse

CXCL12 regulates coronary artery dominance in diverse populations and links development to disease. Rios Coronado PE, Zanetti D, Zhou J, Naftaly JA, Prabala P, Kho PF, Martínez Jaimes AM, Hilliard AT, Pyarajan S, Dochtermann D; Million Veteran Program; Chang KM, Winn VD, Pasca AM, Plomondon ME, Waldo SW, Tsao PS, Clarke SL, Red-Horse K, Assimes TL.medRxiv. 2023 Oct 27:2023.10.27.23297507. doi: 10.1101/2023.10.27.23297507. Preprint.PMID: 37961706

Sox7-positive endothelial progenitors establish coronary arteries and govern ventricular compaction. Chiang IK, Humphrey D, Mills RJ, Kaltzis P, Pachauri S, Graus M, Saha D, Wu Z, Young P, Sim CB, Davidson T, Hernandez-Garcia A, Shaw CA, Renwick A, Scott DA, Porrello ER, Wong ES, Hudson JE, Red-Horse K, Del Monte-Nieto G, Francois M.EMBO Rep. 2023 Oct 9;24(10):e55043. doi: 10.15252/embr.202255043. Epub 2023 Aug 8.PMID: 37551717

Dedifferentiation and Proliferation of Artery Endothelial Cells Drive Coronary Collateral Development in Mice. Arolkar G, Kumar SK, Wang H, Gonzalez KM, Kumar S, Bishnoi B, Rios Coronado PE, Woo YJ, Red-Horse K, Das S.Arterioscler Thromb Vasc Biol. 2023 Aug;43(8):1455-1477. doi: 10.1161/ATVBA-

HA.123.319319. Epub 2023 Jun 22.PMID: 37345524

Maria Grazia Roncarolo

AML/T cell interactomics uncover correlates of patient outcomes and the key role of ICAM1 in T cell killing of AML.
Sayitoglu EC, Luca BA, Boss AP, Thomas BC, Freeborn RA, Uyeda MJ, Chen PP, Nakau-chi Y, Waichler C, Lacayo N, Bacchetta R, Ma-jeti R, Gentles AJ, Cepika AM, Roncarolo MG.bioRxiv. 2023 Sep 23:2023.09.21.558911. doi: 10.1101/2023.09.21.558911. Preprint.PMID: 37790561

SATB1 Chromatin Loops Regulate Megakaryocyte/ Erythroid Progenitor Expansion by Facilitating HSP70 and GATA1 Induction.
Wilkes MC, Chae HD, Scanlon V, Cepika AM, Went-worth EP, Saxena M, Eskin A, Chen Z, Glader B, Grazia Roncarolo M, Nelson SF, Sakamoto KM.Stem Cells. 2023 Jun 15;41(6):560-569. doi: 10.1093/stmc-ls/sxad025.PMID: 36987811

Type 1 regulatory T cell-mediated tolerance in health and disease.
Freeborn RA, Strubbe S, Roncarolo MG.Front Immunol. 2022 Oct 28;13:1032575. doi: 10.3389/fimmu.2022.1032575. eCollection 2022.PMID: 36389662 Review.

Epigenetic and immunological indicators of IPEX disease in subjects with FOXP3 gene mutation.
Narula M, Lakshmanan U, Borna S, Schulze JJ, Holmes TH, Harre N, Kirkey M, Ramachandran A, Tagi VM, Barzaghi F, Grunebaum E, Upton JEM, Hong-Diep Kim V, Wysocki C, Dimitriades VR, Weinberg K, Weinacht KG, Gernez Y, Sathi BK, Schelotto M, Johnson M, Olek S, Sachsenmaier C, Roncarolo MG, Bacchetta R.J Allergy Clin Immu-nol. 2023 Jan;151(1):233-246.e10. doi: 10.1016/j.jaci.2022.09.013. Epub 2022 Sep 21.PMID: 36152823

Vittorio Sebastiano
Monolayer platform to generate and purify primor-dial germ-like cells in vitro provides insights into human germline specification.
Vijayakumar S, Sala R, Kang G, Chen A, Pablo MA, Adebayo AI, Cipriano A, Fowler JL, Gomes DL, Ang LT, Loh KM, Sebastiano V.Nat Commun. 2023 Sep

14;14(1):5690. doi: 10.1038/s41467-023-41302-w. PMID: 37709760

Biomarkers of aging for the identification and evalu-ation of longevity interventions.
Moqri M, Herzog C, Poganik JR; Biomarkers of Ag-ing Consortium; Justice J, Belsky DW, Higgins-Chen A, Moskalev A, Fuellen G, Cohen AA, Bautmans I, Widschwendter M, Ding J, Fleming A, Mannick J, Han JJ, Zhavoronkov A, Barzilai N, Kaeberlein M, Cummings S, Kennedy BK, Ferrucci L, Horvath S, Verdin E, Maier AB, Snyder MP, Sebastiano V, Gladyshev VN.Cell. 2023 Aug 31;186(18):3758-3775. doi: 10.1016/j.cell.2023.08.003.PMID: 37657418

Judith Shizuru

Erratum: Anti-CD117 CAR T cells incorporating a safety switch eradicate human acute myeloid leuke-mia and hematopoietic stem cells.
Magnani CF, Myburgh R, Brunn S, Chambovey M, Ponzo M, Volta L, Manfredi F, Pellegrino C, Pascolo S, Miskey C, Sandoval-Villegas N, Ivics Z, Shizuru JA, Neri D, Manz MG.Mol Ther Oncolytics. 2023 Aug 20;30:150. doi: 10.1016/j.omto.2023.08.002. eCollection 2023 Sep 21.PMID: 37654971

Anti-CD117 CAR T cells incorporating a safety switch eradicate human acute myeloid leukemia and hematopoietic stem cells.
Magnani CF, Myburgh R, Brunn S, Chambovey M, Ponzo M, Volta L, Manfredi F, Pellegrino C, Pasco-lo S, Miskey C, Ivics Z, Shizuru JA, Neri D, Manz MG.Mol Ther Oncolytics. 2023 Jul 19;30:56-71. doi: 10.1016/j.omto.2023.07.003. eCollection 2023 Sep 21.PMID: 37583386

Improved outcomes for relapsed/refractory Hodgkin lymphoma after autologous transplantation in the era of novel agents.
Spinner MA, Sica RA, Tamaresis JS, Lu Y, Chang C, Lowsky R, Frank MJ, Johnston LJ, Miklos DB, Muff-ly LS, Negrin RS, Rezvani AR, Shiraz P, Shizuru JA, Weng WK, Binkley MS, Hoppe RT, Advani RH, Arai S.Blood. 2023 Jun 1;141(22):2727-2737. doi: 10.1182/blood.2022018827.PMID: 36857637

Tom Südhof

Correction: Distinct neurexin-cerebellin complexes control AMPA- and NMDA-receptor responses in a

circuit-dependent manner.
Dai J, Liakath-Ali K, Golf SR, Südhof TC.Elife. 2023 Nov 9;12:e94305. doi: 10.7554/eLife.94305.PMID: 37943030

Neutral lysophosphatidylcholine mediates α-synucle-in-induced synaptic vesicle clustering.
Lai Y, Zhao C, Tian Z, Wang C, Fan J, Hu X, Tu J, Li T, Leitz J, Pfuetzner RA, Liu Z, Zhang S, Su Z, Burré J, Li D, Südhof TC, Zhu ZJ, Liu C, Brunger AT, Diao J.Proc Natl Acad Sci U S A. 2023 Oct 31;120(44):e2310174120. doi: 10.1073/pnas.2310174120. Epub 2023 Oct 26.PMID: 37883437

Piconewton Forces Mediate GAIN Domain Dissocia-tion of the Latrophilin-3 Adhesion GPCR.
Zhong BL, Lee CE, Vachharajani VT, Bauer MS, Südhof TC, Dunn AR.Nano Lett. 2023 Oct 25;23(20):9187-9194. doi: 10.1021/acs.nano-lett.3c03171. Epub 2023 Oct 13.PMID: 37831891

Correction: Synaptic neurexin-1 assembles into dy-namically regulated active zone nanoclusters.
Trotter JH, Hao J, Maxeiner S, Tsetsenis T, Liu Z, Zhuang X, Südhof TC.J Cell Biol. 2023 Oct 2;222(10):e20181207608242023c. doi: 10.1083/jcb.20181207608242023c. Epub 2023 Sep 4.PMID: 37665610 No abstract available.

Efficient generation of functional neurons from mouse embryonic stem cells via neurogenin-2 ex-pression.
Liu Y, Wang J, Südhof TC, Wernig M.Nat Protoc. 2023 Oct;18(10):2954-2974. doi: 10.1038/s41596-023-00863-2. Epub 2023 Aug 18.PMID: 37596357 Review.

Combinatorial expression of neurexins and LAR-type phosphotyrosine phosphatase receptors in-structs assembly of a cerebellar circuit.
Sclip A, Südhof TC.Nat Commun. 2023 Aug 17;14(1):4976. doi: 10.1038/s41467-023-40526-0. PMID: 37591863

Neuronal γ-secretase regulates lipid metabolism, linking cholesterol to synaptic dysfunction in Alzhei-mer’s disease.
Essayan-Perez S, Südhof TC.Neuron. 2023 Oct

18;111(20):3176-3194.e7. doi: 10.1016/j.neu-ron.2023.07.005. Epub 2023 Aug 4.PMID: 37543038

Postsynaptic synucleins mediate endocannabinoid signaling.
Albarran E, Sun Y, Liu Y, Raju K, Dong A, Li Y, Wang S, Südhof TC, Ding JB.Nat Neurosci. 2023 Jun;26(6):997-1007. doi: 10.1038/s41593-023-01345-0. Epub 2023 May 29.PMID: 37248337

Author Correction: Teneurins assemble into presyn-aptic nanoclusters that promote synapse formation via postsynaptic non-teneurin ligands.
Zhang X, Lin PY, Liakath-Ali K, Südhof TC.Nat Commun. 2023 May 23;14(1):2957. doi: 10.1038/s41467-023-38713-0.PMID: 37221212 No abstract available.

Cerebellin-neurexin complexes instructing synapse properties.
Südhof TC.Curr Opin Neurobiol. 2023 Aug;81:102727. doi: 10.1016/j.conb.2023.102727. Epub 2023 May 18.PMID: 37209532 Review.

Astrocytic Neuroligins Are Not Required for Synapse Formation or a Normal Astrocyte Cytoarchitecture.
Golf SR, Trotter JH, Nakahara G, Südhof TC.bioRxiv. 2023 Apr 10:2023.04.10.536254. doi: 10.1101/2023.04.10.536254. Preprint.PMID: 37090508

A combinatorial code of neurexin-3 alternative splic-ing controls inhibitory synapses via a trans-synaptic dystroglycan signaling loop.
Trotter JH, Wang CY, Zhou P, Nakahara G, Südhof TC.Nat Commun. 2023 Mar 30;14(1):1771. doi: 10.1038/s41467-023-36872-8.PMID: 36997523

Neurexin-2 restricts synapse numbers and restrains the presynaptic release probability by an alternative splicing-dependent mechanism.
Lin PY, Chen LY, Zhou P, Lee SJ, Trotter JH, Südhof TC.Proc Natl Acad Sci U S A. 2023 Mar 28;120(13):e2300363120. doi: 10.1073/pnas.2300363120. Epub 2023 Mar 24.PMID: 36961922

Piconewton forces mediate GAIN domain dissocia-tion of the latrophilin-3 adhesion GPCR.

Zhong BL, Lee CE, Vachharajani VT, Südhof TC, Dunn AR.bioRxiv. 2023 Jan 13;2023.01.12.523854. doi: 10.1101/2023.01.12.523854. Preprint.PMID: 36711622 Updated.

Engineered adhesion molecules drive synapse organization. Hale WD, Südhof TC, Huganir RL.Proc Natl Acad Sci U S A. 2023 Jan 17;120(3):e2215905120. doi: 10.1073/pnas.2215905120. Epub 2023 Jan 13.PMID: 36638214

Neurexin-2: An inhibitory neurexin that restricts excitatory synapse formation in the hippocampus. Lin PY, Chen LY, Jiang M, Trotter JH, Seigneur E, Südhof TC.Sci Adv. 2023 Jan 6;9(1):eadd8856. doi: 10.1126/sciadv.add8856. Epub 2023 Jan 6.PMID: 36608123

The autism risk factor CHD8 is a chromatin activator in human neurons and functionally dependent on the ERK-MAPK pathway effector ELK1. Haddad Derafshi B, Danko T, Chanda S, Batista PJ, Litzenburger U, Lee QY, Ng YH, Sebin A, Chang HY, Südhof TC, Wernig M.Sci Rep. 2022 Dec 27;12(1):22425. doi: 10.1038/s41598-022-23614-x. PMID: 36575212

Irv Weissman
Prospective isolation of neural stem and progenitor cells from the developing human brain. Liu DD, He JQ, Uchida N, Weissman IL, Sinha R.STAR Protoc. 2023 Oct 27;4(4):102674. doi: 10.1016/j.xpro.2023.102674. Online ahead of print. PMID: 37897731

Immune Surveillance of Acute Myeloid Leukemia Is Mediated by HLA-Presented Antigens on Leukemia Progenitor Cells. Nelde A, Schuster H, Heitmann JS, Bauer J, Maringer Y, Zwick M, Volkmer JP, Chen JY, Stanger AMP, Lehmann A, Appiah B, Märklin M, Rücker-Braun E, Salih HR, Roerden M, Schroeder SM, Häring MF, Schlosser A, Schetelig J, Schmitz M, Boerries M, Köhler N, Lengerke C, Majeti R, Weissman IL, Rammensee HG, Walz JS.Blood Cancer Discov. 2023 Nov 1;4(6):468-489. doi: 10.1158/2643-3230.BCD-23-0020.PMID: 37847741

Stem-Cell Aging and Pathways to Precancer Evolution. Jamieson CHM, Weissman IL.N Engl J Med. 2023 Oct 5;389(14):1310-1319. doi: 10.1056/NEJM-ra2304431.PMID: 37792614 Review. No abstract available.

Cell-type-specific aging clocks to quantify aging and rejuvenation in neurogenic regions of the brain. Buckley MT, Sun ED, George BM, Liu L, Schaum N, Xu L, Reyes JM, Goodell MA, Weissman IL, Wyss-Coray T, Rando TA, Brunet A.Nat Aging. 2023 Jan;3(1):121-137. doi: 10.1038/s43587-022-00335-4. Epub 2022 Dec 19.PMID: 37118510

A Combination of Distinct Vascular Stem/Progenitor Cells for Neovascularization and Ischemic Rescue. Zhao L, Lee AS, Sasagawa K, Sokol J, Wang Y, Ransom RC, Zhao X, Ma C, Steininger HM, Koepke LS, Borrelli MR, Brewer RE, Lee LLY, Huang X, Ambrosi TH, Sinha R, Hoover MY, Seita J, Weissman IL, Wu JC, Wan DC, Xiao J, Longaker MT, Nguyen PK, Chan CKF.Arterioscler Thromb Vasc Biol. 2023 Jul;43(7):1262-1277. doi: 10.1161/ATVBA-HA.122.317943. Epub 2023 Apr 13.PMID: 37051932

Multiple Forms of Neural Cell Death in the Cyclical Brain Degeneration of A Colonial Chordate. Anselmi C, Caicci F, Bocci T, Guidetti M, Priori A, Giusti V, Levy T, Raveh T, Voskoboynik A, Weissman IL, Manni L.Cells. 2023 Mar 29;12(7):1041. doi: 10.3390/cells12071041.PMID: 37048113

Purification and characterization of human neural stem and progenitor cells. Liu DD, He JQ, Sinha R, Eastman AE, Toland AM, Morri M, Neff NF, Vogel H, Uchida N, Weissman IL.Cell. 2023 Mar 16;186(6):1179-1194.e15. doi: 10.1016/j.cell.2023.02.017.PMID: 36931245

Radiotherapy in combination with CD47 blockade elicits a macrophage-mediated abscopal effect. Nishiga Y, Drainas AP, Baron M, Bhattacharya D, Barkal AA, Ahrari Y, Mancusi R, Ross JB, Takahashi N, Thomas A, Diehn M, Weissman IL, Graves EE, Sage J.Nat Cancer. 2022 Nov;3(11):1351-1366. doi: 10.1038/s43018-022-00456-0. Epub 2022 Nov 21.PMID: 36411318

Increased macrophage phagocytic activity with TLR9 agonist conjugation of an anti- Borrelia burgdorferi monoclonal antibody. Jahanbani S, Hansen PS, Blum LK, Bastounis EE, Ramadoss NS, Pandrala M, Kirschmann JM, Blacker GS, Love ZZ, Weissman IL, Nemati F, Tal MC, Robinson WH.Clin Immunol. 2023 Jan;246:109180. doi: 10.1016/j.clim.2022.109180. Epub 2022 Nov 14.PMID: 36396013

Marius Wernig
Insights and applications of direct neuronal reprogramming. Schaukowitch K, Janas JA, Wernig M.Curr Opin Genet Dev. 2023 Oct 18;83:102128. doi: 10.1016/j.gde.2023.102128. Online ahead of print.PMID: 37862835 Review.

Integrative analyses highlight functional regulatory variants associated with neuropsychiatric diseases. Guo MG, Reynolds DL, Ang CE, Liu Y, Zhao Y, Donohue LKH, Siprashvili Z, Yang X, Yoo Y, Mondal S, Hong A, Kain J, Meservey L, Fabo T, Elfaki I, Kellman LN, Abell NS, Pershad Y, Bayat V, Etmnani P, Holodniy M, Geschwind DH, Montgomery SB, Duncan LE, Urban AE, Altman RB, Wernig M, Khavari PA.Nat Genet. 2023 Nov;55(11):1876-1891. doi: 10.1038/s41588-023-01533-5. Epub 2023 Oct 19.PMID: 37857935

A cell therapy approach to restore microglial Trem2 function in a mouse model of Alzheimer’s disease. Yoo Y, Neumayer G, Shibuya Y, Mader MM, Wernig M.Cell Stem Cell. 2023 Oct 5;30(10):1392. doi: 10.1016/j.stem.2023.08.011.PMID: 37802040 No abstract available.

Ascl1 and Ngn2 convert mouse embryonic stem cells to neurons via functionally distinct paths. Vainorius G, Novatchkova M, Michlits G, Baar JC, Raupach C, Lee J, Yelagandula R, Wernig M, Elling U.Nat Commun. 2023 Sep 2;14(1):5341. doi: 10.1038/s41467-023-40803-y.PMID: 37660160

Efficient generation of functional neurons from mouse embryonic stem cells via neurogenin-2 expression. Liu Y, Wang J, Südhof TC, Wernig M.Nat Protoc. 2023 Oct;18(10):2954-2974. doi: 10.1038/s41596-

023-00863-2. Epub 2023 Aug 18.PMID: 37596357 Review.

A cell therapy approach to restore microglial Trem2 function in a mouse model of Alzheimer’s disease. Yoo Y, Neumayer G, Shibuya Y, Mader MM, Wernig M.Cell Stem Cell. 2023 Aug 3;30(8):1043-1053.e6. doi: 10.1016/j.stem.2023.07.006.PMID: 37541210

Proteostasis and lysosomal quality control deficits in Alzheimer’s disease neurons. Chou CC, Vest R, Prado MA, Wilson-Grady J, Paulo JA, Shibuya Y, Moran-Losada P, Lee TT, Luo J, Gygi SP, Kelly JW, Finley D, Wernig M, Wyss-Coray T, Frydman J.bioRxiv. 2023 Mar 27:2023.03.27.534444. doi: 10.1101/2023.03.27.534444. Preprint.PMID: 37034684

Augmentation of a neuroprotective myeloid state by hematopoietic cell transplantation. Mader MM, Napole A, Wu D, Shibuya Y, Scavetti A, Foltz A, Atkins M, Hahn O, Yoo Y, Danziger R, Tan C, Wyss-Coray T, Steinman L, Wernig M.bioRxiv. 2023 Mar 12:2023.03.10.532123. doi: 10.1101/2023.03.10.532123. Preprint.PMID: 36945385

A scalable, GMP-compatible, autologous organotypic cell therapy for Dystrophic Epidermolysis Bullosa. Neumayer G, Torkelson JL, Li S, McCarthy K, Zhen HH, Vangipuram M, Jackow J, Rami A, Hansen C, Guo Z, Gaddam S, Pappalardo A, Li L, Cramer A, Roy KR, Nguyen TM, Tanabe K, McGrath PS, Bruckner A, Bilousova G, Roop D, Bailey I, Tang JY, Christiano A, Steinmetz LM, Wernig M, Oro AE.bioRxiv. 2023 Mar 1:2023.02.28.529447. doi: 10.1101/2023.02.28.529447. Preprint.PMID: 36909618

Gerlinde Wernig
Innate immune cell activation causes lung fibrosis in a humanized model of long COVID. Cui L, Fang Z, De Souza CM, Lerbs T, Guan Y, Li I, Charu V, Chen SY, Weissman I, Wernig G.Proc Natl Acad Sci U S A. 2023 Mar 7;120(10):e2217199120. doi: 10.1073/pnas.2217199120. Epub 2023 Feb 27.PMID: 36848564

Upregulation of PD-L1 by SARS-CoV-2 promotes

immune evasion.

Huang HC, Wang SH, Fang GC, Chou WC, Liao CC, Sun CP, Jan JT, Ma HH, Ko HY, Ko YA, Chiang MT, Liang JJ, Kuo CT, Lee TA, Morales-Scheihing D, Shen CY, Chen SY, McCullough LD, Cui L, Wernig G, Tao MH, Lin YL, Chang YM, Wang SP, Lai YJ, Li CW. *J Med Virol.* 2023 Feb;95(2):e28478. doi: 10.1002/jmv.28478.PMID: 36609964

Joanna Wysocka

A genome-wide genetic screen uncovers determinants of human pigmentation.

Bajpai VK, Swigut T, Mohammed J, Naqvi S, Arreola M, Tycko J, Kim TC, Pritchard JK, Bassik MC, Wysocka J. *Science.* 2023 Aug 11;381(6658):eade6289. doi: 10.1126/science.ade6289. Epub 2023 Aug 11.PMID: 37561850

DNA-guided transcription factor cooperativity shapes face and limb mesenchyme.

Kim S, Morgunova E, Naqvi S, Bader M, Koska M, Popov A, Luong C, Pogson A, Claes P, Taipale J, Wysocka J. *bioRxiv.* 2023 May 29:2023.05.29.541540. doi: 10.1101/2023.05.29.541540. Preprint.PMID: 37398193

Co-transcriptional genome surveillance by HUSH is coupled to termination machinery.

Spencley AL, Bar S, Swigut T, Flynn RA, Lee CH, Chen LF, Bassik MC, Wysocka J. *Mol Cell.* 2023 May 18;83(10):1623-1639.e8. doi: 10.1016/j.molcel.2023.04.014. Epub 2023 May 9.PMID: 37164018

The frequency and macromorphological classification of abnormal blood vessel impressions and periosteal appositions of the dura mater in an early modern osteological collection from Poland.

Wysocka J, Cieřlik A. *Int J Paleopathol.* 2023 Jun;41:78-87. doi: 10.1016/j.ijpp.2023.04.001. Epub 2023 Apr 8.PMID: 37031588

Precise modulation of transcription factor levels identifies features underlying dosage sensitivity.

Naqvi S, Kim S, Hoskens H, Matthews HS, Spritz RA, Klein OD, Hallgrímsson B, Swigut T, Claes P, Pritchard JK, Wysocka J. *Nat Genet.* 2023 May;55(5):841-851. doi: 10.1038/s41588-023-01366-2. Epub 2023 Apr 6.PMID: 37024583

Structural elements promote architectural stripe formation and facilitate ultra-long-range gene regulation at a human disease locus.

Chen LF, Long HK, Park M, Swigut T, Boettiger AN, Wysocka J. *Mol Cell.* 2023 May 4;83(9):1446-1461.e6. doi: 10.1016/j.molcel.2023.03.009. Epub 2023 Mar 29.PMID: 36996812

Theory of Mind and Parental Mental-State Talk in Children with CIs.

Pluta A, Krysztofiak M, Zgoda M, Wysocka J, Golec K, Gajos K, Dołyk T, Wolak T, Haman M. *J Deaf Stud Deaf Educ.* 2023 Jun 20;28(3):288-299. doi: 10.1093/deafed/enad004.PMID: 36951492

C. David Allis (1951-2023).

Bernstein E, Dent S, Dou Y, Duncan EM, Hake SB, Strahl BD, Wysocka J. *Mol Cell.* 2023 Feb 16;83(4):497-499. doi: 10.1016/j.molcel.2023.02.002. PMID: 36805122 No abstract available.

C. David Allis (1951-2023).

Bernstein E, Dent S, Dou Y, Duncan EM, Hake SB, Strahl BD, Wysocka J. *Cell.* 2023 Feb 16;186(4):663-667. doi: 10.1016/j.cell.2023.01.031.PMID: 36803594 No abstract available.

Deciphering the multi-scale, quantitative cis-regulatory code.

Kim S, Wysocka J. *Mol Cell.* 2023 Feb 2;83(3):373-392. doi: 10.1016/j.molcel.2022.12.032. Epub 2023 Jan 23.PMID: 36693380