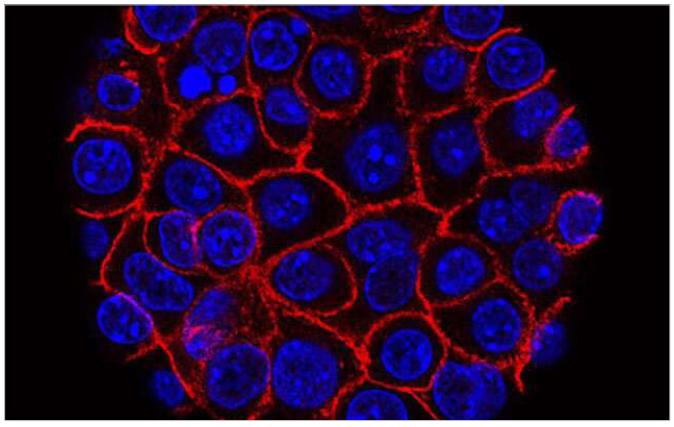
The Study Identifies Biomarker That Could Help to Diagnose Pancreatic Cancer

Researchers from the Queen Mary University of London have identified a protein that could be used to aid in the diagnosis of pancreatic cancer.

Findings from the new study suggest that a protein called pentraxin 3 (PTX3) may be a specific diagnostic biomarker—or biological measure—for pancreatic cancer, with the ability to differentiate pancreatic cancer from other non-cancerous conditions of the pancreas.

The research was published in *npj Precision Oncology* and primarily funded by the Pancreatic Cancer Research Fund, Barts Charity and Cancer Research UK.

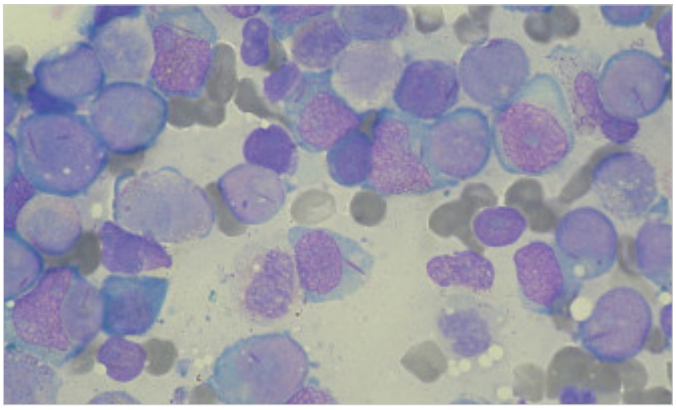


PTX3 levels elevated in patients with pancreatic cancer. In the study, researchers measured PTX3 levels in serum blood samples from patients with pancreatic ductal adenocarcinoma (PDAC) – the most common type of pancreatic cancer—and from healthy volunteers or patients with other non-cancerous conditions of the pancreas and found levels of the protein to be significantly higher in the serum samples of those with PDAC.

Link Between Inflammation and Leukemia

Two recent collaborative publications by CU Cancer Center members provide insights into how chronic inflammation can serve as a key factor in the development of leukemia and other blood cancers.

Eric Pietras, PhD, CU Cancer Center member and assistant professor in the CU School of Medicine Division of Hematology, and James DeGregori, PhD, deputy director of the CU Cancer Center and professor in the Department of Biochemistry and Molecular Genetics, were corresponding authors on both papers.



Both papers provide support for the theory of adaptive oncogenesis, which was developed by DeGregori. The theory stipulates that chronic inflammation (such as the inflammation associated with aging or with chronic disease) reduces the fitness of normal cells, hindering their ability to reproduce and creating space for cells with cancer-causing mutations to proliferate.

The first paper, "PU.1 enforces quiescence and limits hematopoietic stem cell expansion during inflammatory stress," on which Pietras' laboratory technician, James Chavez, B.S., is the primary author, explores the effect of inflammation on the transcription factor PU.1 and its effect in turn on the production of hematopoietic stem cells (HSCs)—the immature cells found in the bone marrow that can develop into blood cells.

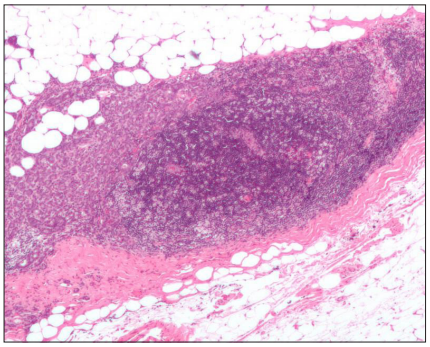
The second paper, "Chronic interleukin-1 exposure triggers selection for Cebpa-knockout multipotent hematopoietic progenitors," co-led by DeGregori and Pietras, also studies the impact of the pro-inflammatory cytokine IL-1 on hematopoietic stem and progenitor cells (HSPCs). The primary author of this study was Kelly Higa, a student in CU's MD/Ph.D. program co-mentored by DeGregori and Pietras.

Study Finds Breast Cancer's Response to Tumor Stiffness May Predict Bone Metastasis

In cases of breast cancer, bone metastasis—when cancer cells spread to new sites in the bone—causes the most breast cancer-related harm and is often incurable in advanced disease. A new study by University of Arizona Health Sciences researchers found that cancer cells become more aggressive when exposed to tissue stiffening and that these changes persist over time.

Tumor stiffening, which develops as diseased breast tissue becomes fibrotic, plays a major role in how breast cancer cells spread throughout the body. The paper, "Breast tumor stiffness instructs bone metastasis via maintenance of mechanical conditioning," published in the journal *Cell Reports*, found that the stiffness of the breast tumor microenvironment can cause changes to cancer cells that make them more aggressively spread to the bone. The resulting changes are maintained as "mechanical memory," which instructs the cancer cells to send signals that lead to the breakdown of bone. Once this happens, patients often suffer debilitating complications like spontaneous fractures.

"Unfortunately, bone metastasis is normally not identified until an advanced state when it's not reversible," said senior author Ghassan Mouneimne, PhD, associate professor of cellular and molecular medicine and cancer biology in the Arizona College of Medicine—Tucson. "What's exciting is one day being able to take a sample from the patient's primary tumor and predict who is at high risk for bone metastasis. Then we could intervene with a prevention strategy that we are now validating in the lab."

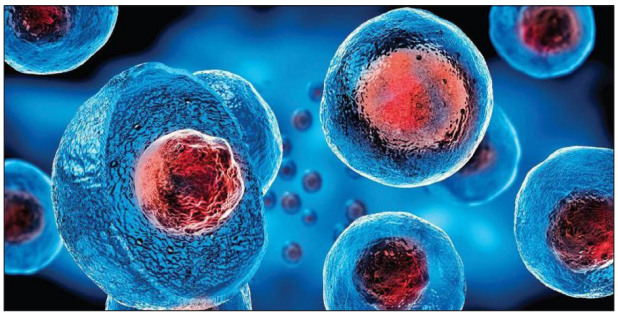


The study, which is the first to demonstrate the concept of mechanical memory during cancer metastasis, developed a novel mechanical conditioning, or "MeCo," score, to quantify the cellular changes. Eventually, researchers hope the MeCo score can be used to help identify breast cancer patients who might benefit from repurposed antifibrotic treatments to prevent bone metastasis.

Stem Cells from the Umbilical Cord Can Help Treat Covid-19 Pneumonia

Stem cells obtained from the placenta and umbilical cord can halt the progression of Covid-19 effectively, a city-based lab has found. Mesenchymal stem cells are cells in our body that are most versatile. These cells can renew themselves by dividing and can differentiate into multiple tissues. "These cells can increase immune response and has proved effective in the treatment of pneumonia induced by Covid-19," Dr Nisha Reddy, a stem cell research consultant at Reelabs, said.

"It has been proved in our clinical trials that diseases of the lungs such as pneumonia, acute lung injury and acute respiratory distress syndrome caused by Covid-19 can be cured effectively with Mesenchymal Stem Cell Therapy if administered at an early stage of the disease when the level of oxygen saturation is between 92 and 85," the researcher said.

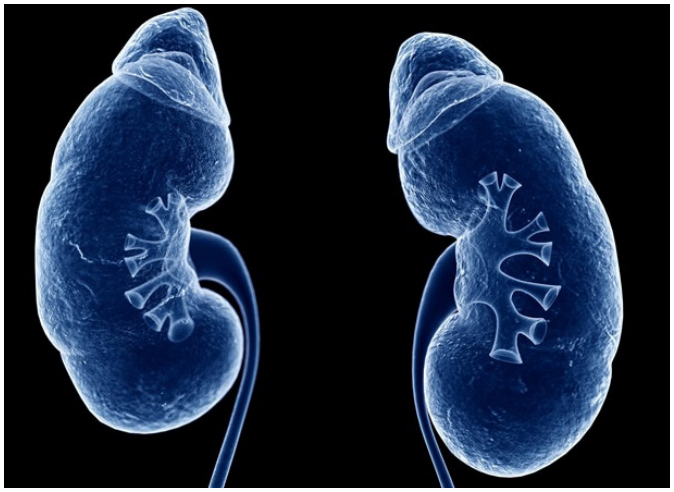


Last year, the stem cell lab obtained permission from the central government for clinical trials. "Mesenchymal stem cells play a positive role mainly in two ways, namely immunomodulatory effects and differentiation abilities. These cells can secrete many types of cytokines by paracrine secretion or make direct interactions with immune cells leading to immunomodulation," said Nisha.

Stem cell therapy can inhibit the over-activation of the immune system and promote endogenous repair by improving the micro-environment. After entering the body through intravenous transfusion, a part of the stem cells accumulates in the lungs, which could improve the pulmonary microenvironment, protect alveolar epithelial cells, prevent pulmonary fibrosis and improve lung function.

Newly Discovered Proteins Protect Against the Progression of Diabetic Kidney Disease

Elevated levels of three specific circulating proteins are associated with protection against kidney failure in diabetes, according to research from the Joslin Diabetes Center that will be published in *Science Translational Medicine.*



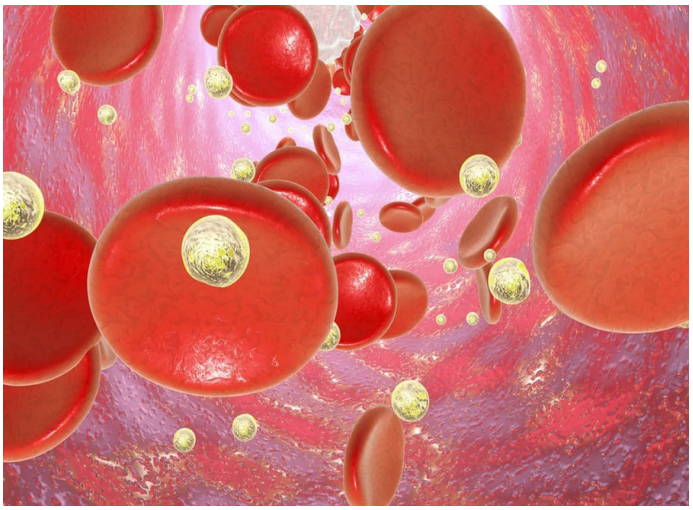
"As well as acting as biomarkers for advancing kidney disease risk in diabetes, the proteins may also serve as the basis for future therapies against progression to the most serious types of kidney disease," said Andrzej S. Krolewski MD, PhD, senior author on the publication, senior investigator at Joslin Diabetes Center and professor of medicine at Harvard Medical School. This would likely include the delay and prevention of end-stage renal disease (ESRD), which is the most serious and advanced stage of diabetic kidney disease.

The study marks a move towards looking for markers associated with protection against rather than the increased individual risk for the rapid progression of diabetic kidney disease. This should more directly derive potential targets for slowing progression since it is based on the thinking that individuals with slow progression will have protective factors of some sort.

"Our research became possible only recently," said Dr Krolewski. "We were able to search for these markers thanks to the development of high-throughput proteomic platforms. More importantly, the availability of biobank specimens that we established many years ago in the Joslin Kidney Study was critical."

New Drug Shows Real Promise Against Celiac Disease

An experimental drug can prevent intestinal damage caused by celiac disease; an early trial has found—raising hopes that it could become the first medication for the serious digestive disorder.



With celiac disease, the immune system attacks the lining of the small intestine when a genetically susceptible person eats gluten—a protein found in wheat, rye and barley.

Right now, the only treatment is "rigorous avoidance of even traces of gluten in the daily diet," said lead researcher Dr Detlef Schuppan. But a lifelong gluten-free diet is difficult to maintain, said Schuppan, a professor at the University Medical Center of Johannes Gutenberg University, in Germany.

Gluten can lurk in many processed foods, from pasta and breakfast cereals to sauces and soups to energy bars and chips.

Beyond being a practical burden, the strict diet is a "social and psychological" one as well, Schuppan noted. And even when patients manage to adhere to it, he said, some can still have intestinal inflammation and symptoms.

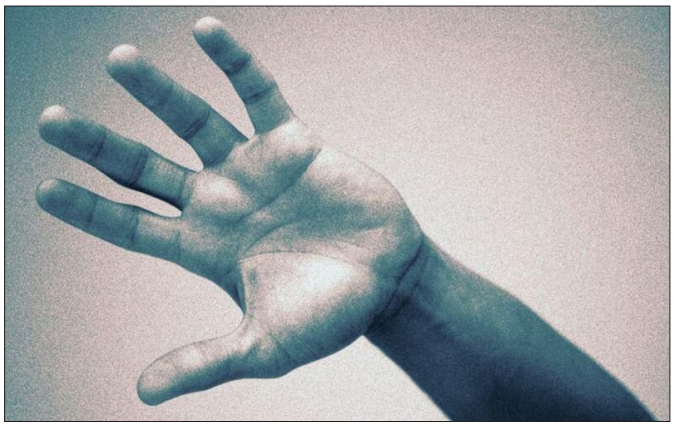
The new study, published in the New *England Journal of Medicine,* looked at whether an experimental drug can prevent that intestinal damage. The drug, dubbed ZED1227, inhibits the activity of an enzyme called transglutaminase 2 (TG2) in the intestines, Schuppan explained. TG2 plays a key role in the autoimmune response that marks celiac.

Inflammation at IP Thumb Joint Common in Psoriatic Arthritis

Patients with psoriatic arthritis (PsA) more often have inflammation at the interphalangeal (IP) joint of the thumb compared to those with undifferentiated inflammatory arthritis (UIA), according to a study published online in the *International Journal of Rheumatic Diseases.*

Ashish J. Mathew, M.B.B.S., D.M., from the Christian Medical College in Vellore, India, and colleagues compared inflammation at the IP joint of the thumb in 42 patients with PsA, 28 with rheumatoid arthritis (RA), 29 with UIA, and 62 psoriasis patients without clinical arthritis who had undergone magnetic resonance imaging (MRI) of the hands. Three independent readers assessed the presence or absence of MRI inflammatory lesions including synovitis, tenosynovitis, and bone marrow edema.

The researchers found that 33.3 per cent of the PsA patients had global MRI inflammation at the IP joint of the thumb compared with 14.3 and 10.3 per cent in RA and UIA, respectively. Of the psoriasis patients without clinical arthritis, 8.1 per cent had subclinical MRI



inflammation. The risk ratios of global MRI inflammation at the IP joint of the thumb were 2.3 (95 per cent confidence interval, 0.86 to 6.36) and 3.2 (95 per cent confidence interval, 1.02 to 10.21) for PsA patients compared with RA and UIA patients, respectively.

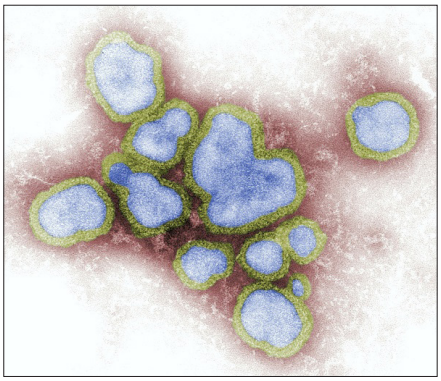
"Our present study has, therefore, validated a bedside clinical observation that can be used for early diagnosis of PsA and differential diagnosis," the authors write.

Vaccines Grown in Eggs Induce Antibody Response Against an Egg-Associated Glycan

Over years of studying antibody responses against the flu in the Wilson lab at the University of Chicago, researchers kept coming up with a strange finding: antibodies that seemed to bind not only to the flu virus but to every virus the lab could throw at them. Since antibodies are usually highly specific to individual pathogens, to maximize their targeted protective response, this pattern was extremely unusual.

Until finally, they realized: The antibodies weren't responding to the viruses, but rather to something in the biological material in which the viruses had been grown. In every case, the virus had been propagated in chicken eggs—more specifically, in a part of the egg called the allantois. The findings were published in *mBio.*

"Growing vaccines in eggs is the old school way of doing things because it's cheap and you can grow a lot of viruses in eggs," said first author Jenna Guthmiller, PhD, a postdoctoral fellow at UChicago. "Now we're finding that these antibodies bind to this glycan—a sugar molecule—found in eggs, which means that people who are getting vaccinated are producing an antibody response against this egg component that's not related to the virus at all."



The fact that vaccines grown in eggs can lead to this off-target antibody response is unexpected, but the implications aren't yet known. It could mean that the immune system diverts resources away from developing protective antiviral antibodies to produce these egg-sugar antibodies instead, which could have implications for vaccine effectiveness.

It's important to note that these antibodies do not bind to known egg allergens, indicating that they likely are not the culprits behind egg allergies, Guthmiller said. "It doesn't seem to be harmful, but it may not be beneficial, and it may be affecting immunity, and that's the important next step."

It took the team years to determine that the antibodies were linked, not to the viruses they were studying, but rather to the eggs in which they were grown. "No joke,

we spent years thinking about this," said Guthmiller. "But once we figured it out, it was straightforward. And we found that it's very specific to the flu vaccine grown in this one compartment, in the allantois. This isn't seen with vaccines grown in other chicken cells."

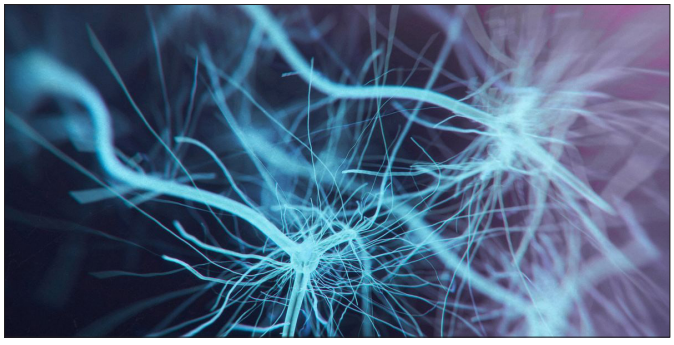
Psychedelic Spurs Growth of Neural Connections Lost in Depression

The psychedelic drug psilocybin, a naturally occurring compound found in some mushrooms, has been studied as a potential treatment for depression for years. But exactly how it works in the brain and how long beneficial results might last is still unclear.

In a new study, Yale researchers show that a single dose of psilocybin given to mice prompted an immediate and long-lasting increase in connections between neurons. The findings are published in the journal *Neuron*.

"We not only saw a 10% increase in the number of neuronal connections, but also they were on average about 10% larger, so the connections were stronger as well," said Yale's Alex Kwan, associate professor of psychiatry and neuroscience and senior author of the paper.

Previous laboratory experiments had shown promise that psilocybin, as well as the anesthetic ketamine, can decrease depression. The new Yale research found that these compounds increase the density of dendritic spines, small protrusions found on nerve cells that aid in the transmission of information between neurons.



Chronic stress and depression are known to reduce the number of these neuronal connections.

Using a laser-scanning microscope, Kwan and first author Ling-Xiao Shao, a postdoctoral associate in the Yale School of Medicine, imaged dendritic spines in high resolution and tracked them for multiple days in living mice. They found increases in the number of dendritic spines and their size within 24 hours of administration of psilocybin. These changes were still present a month later. Also, mice subjected to stress showed behavioral improvements and increased neurotransmitter activity after being given psilocybin.

Review of Acute Migraine Treatments Shows Many Effective, Opioids Not Appropriate

Several pharmacological and nonpharmacological therapies were found to improve pain outcomes in adults with migraines, though the strength of the evidence supporting these treatments varied, according to the findings of a systematic review and meta-analysis published in *JAMA*.

The study aimed to assess the benefits and risks associated with various acute treatments for episodic migraines. Following an extensive literature search, independent reviewers identified and extracted data from 15 systematic reviews, which analyzed evidence on triptans and nonsteroidal anti-inflammatory drugs (NSAIDs), and 115 randomized clinical trials

(n=28,803), which evaluated other interventions.

Pain freedom, pain relief, sustained pain freedom, and adverse events were the main outcomes of the study. The Agency for Healthcare Research and Quality Methods Guide for Effectiveness and Comparative Effectiveness Reviews was used to grade the strength of evidence (SOE).

Compared with placebo, significant improvements in short-term pain outcomes were observed with triptans (high SOE), NSAIDs (moderate SOE), calcitonin gene-related peptide receptor antagonists (rimegepant, ubrogepant; low to high SOE), lasmiditan (5-HT1F receptor agonist; high SOE), dihydroergotamine (moderate to high SOE), ergotamine plus caffeine (moderate SOE), acetaminophen (moderate SOE), antiemetics (chlorpromazine, prochlorperazine, metoclopramide, haloperidol, droperidol; low SOE), butorphanol (low SOE), and tramadol plus acetaminophen (low SOE).