

**PHARMA HIGHLIGHTS** ISSUE 37 | OCTOBER 2017

## PPI use alters microbiome, damages liver



New research shows that taking a proton-pump inhibitor (PPI) for acid reflux alters your gut microbiome to promote liver disease. To make matters worse, people with chronic liver disease are already more likely to take a PPI. These findings are rather startling when you consider that PPIs are one of the most commonly prescribed medications in the world.

The group used mice to study the effect of suppressing stomach acid (as a result of PPI use) on three types of chronic liver disease - alcoholic liver disease, nonalcoholic fatty-liver disease, and nonalcoholic steatohepatitis. When they blocked stomach acid production with a PPI (or other methods), they found more Enterococcus in the animals' stools, suggesting that the PPI altered the gut microbiome in some way. Likewise, blocking the production of stomach acid exacerbated all three types of liver disease. In a separate experiment, the researchers colonized mice with extra Enterococcus faecalis, a common gut microbe. Doing so increased both steatohepatitis and alcohol-induced liver disease in the animals - pointing to a direct link between gut microbes and liver disease.

Finally, they looked for a connection between PPI use, alcohol use, and cases of alcoholic liver disease. From a group of over 4,800 people diagnosed with chronic alcohol abuse, 21% actively used PPIs, while 63% had never used them. Interestingly, PPI users had a greater 10-year risk for developing alcoholic liver disease than people who didn't use PPIs - 20.7% versus 12.4%. As in the mice, PPI use also increased the amount of Enterococcus in the stools of these patients.

Source: UC San Diego News, Nature Communications

## Multi-Purpose Immune Cells Heal Diabetic Wounds

People with type 2 diabetes are particularly prone to ulcers on the bottom of the foot, which can increase the risk of death and often result in a major amputation. Ulcers take months to heal, but a new discovery could hasten wound recovery.

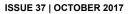
From Massachusetts General Hospital, scientists found that mature B cells, the immune cells of the adaptive immune response that work alongside T cells and produce antibodies, can greatly improve how wounds - chronic like diabetic ulcers and acute - heal over time. Lead author of the new study, Ruxandra Sîrbulescu, PhD, says that the new findings open up an "exciting path to a new treatment for chronic wounds, such as diabetic foot ulcers."

Neuropathy such as damaged nerves and vascular disease are partly responsible for the susceptibility of diabetic people to chronic wounds, namely foot ulcers. It is also responsible for the loss of sensation on skin resulting due to the lack of skin's access to oxygen and nutrients, both essential for healthy tissue healing. The lack thereof results due to limited blood flow to the skin, ultimately



resulting in less than ideal wound healing in diabetic patients.

"Having a novel therapeutic that is based on the immediate isolation of a patient's own cells, with minimal manipulation, will represent an attractive option for the wound care field," explained senior author Mark Poznansky, MD, PhD. Source: Wound Repair and Regeneration







## The Skin's Power to Regulate Blood Pressure and Heart Rate

Some people may forget that the skin is the human body's largest organ, and it has many diverse functions. Researchers now realize that regulating blood pressure and heart rate is one of those functions, and a collaboration between University of Cambridge and Karolinska Institute scientists breaks down the intricate details of how the skin is involved in regulating blood flow through small vessels.

It is not exactly clear, but scientists do know that things like high altitude, pollution, smoking, and obesity can all influence changes. Whatever the specific cause, increases in blood pressure can quickly become dangerous if left



untreated, leading to heart attack, stroke, and other cardiovascular diseases when blood flow through small vessels, like those in the skin, changes. By examining the skin instead of other organs classically studied in the context of blood pressure - brain, heart and kidneys - the present study yields unique findings.

Whatever the reason, when a tissue is oxygen deficient, the body redirects blood flow as a response. This is a mechanism highly regulated by a family of proteins called "HIF." So when the team of researchers began their study of the skin and blood pressure, they started with HIF.

First, researchers watched how mice, genetically modified as unable to produce particular HIF proteins in the skin, responded to low oxygen conditions. They observed a so-called "feedback loop" between the skin and the cardiovascular system. "By working with mice, we were able to manipulate key genes involved in this loop," Johnson explained. They saw that when mice lacked one of two HIF skin proteins, HIF-1 $\alpha$  or HIF-2 $\alpha$ , the response to low oxygen levels changed compared to mice sufficient with both proteins, impacting heart rate, blood pressure, and skin temperature. Researchers also looked at the response of normally, genetically-unaltered mice to oxygen starvation. Losing HIF proteins had an enormous influence on the initiation and duration of this process.

Source: eLife

## **Treating Chronic Pain With Cognitive Behavior Therapy**

In the short term, pain after surgery or an injury is often treated with opioid medications. However, with the rates of drug abuse and overdoses on the rise many doctors, and patients alike, are hesitant to use narcotics because of the risk of dependence. One therapy for chronic pain that is often ignored is cognitive behavioral therapy or CBT.

Part of the reason CBT isn't always considered is patient reluctance. Pain is unpleasant, and many patients don't want to risk losing the relief drugs can provide. Sometimes there are insurance issues as well since most insurance companies will cover prescription medication but many do not offer coverage for mental health services like CBT. There is a time factor as well. A patient who takes a pill for pain relief gets immediate relief. CBT takes longer, and many patients don't have a high level of confidence in it.

Source: Journal of Psychiatric Practice, Psychology Today, Clinical Pain Advisor



Many patients who have chronic pain do not have tissue damage or other injuries or conditions. The pain is real, but the cause of it is likely related to chemical and electrical signals from the brain to the nerves. In patients like this, CBT could be helpful because the goal is to change the way patients perceive pain. In changing how a patient feels about pain and reacts to it, the brain can reset, in a way, and that adjustment can lower pain scores. Interesting, isn't it?