Biologic used by athletes could also ease nerve pain from chemo, diabetes

May 23 2023, by Sarah Avery

Credit: Pixabay/CC0 Public Domain

Autologous conditioned serum (ACS)—a biologic therapy that famous athletes swear by to treat arthritis and sports injuries—also shows benefit for the kind of neurological pain caused by chemotherapy or diabetes.

In a study using rodents, Duke Health researchers found that a spinal injection of the conditioned serum eased limb pain for far longer than typical analgesics. They also showed that this long-lasting pain relief results from a process outside the anti-inflammatory effects previously ascribed to ACS—an insight that could enhance and expand the therapy 's use.

The findings are published online in the journal *Brain, Behavior, and Immunity*.

"This treatment just seemed to be more effective and longer lasting than other biologic therapies," said lead author Thomas Buchheit, M.D., associate professor in Duke's Department of Anesthesiology and director of the Duke Regenerative Pain Therapies Program.

ACS is produced from a person's own blood, which is then processed in a centrifuge to remove the blood cells and concentrate the anti-inflammatory proteins. While not FDA approved, the therapy is offered at Duke as well as a handful of other centers in the United States, and for years has been extoled by athletes who undergo injections for cartilage injuries.

Buchheit and co-senior author Ru-Rong Ji, Ph.D., began to collaborate to better understand the long-lasting drivers of pain relief with ACS. Ji is professor in the departments of Anesthesiology, Neurobiology and Cell Biology at Duke, and has expertise in the molecular and cellular mechanisms underlying pain; he is also director of the Center for Translational Pain Medicine.

The research team additionally tapped the expertise of co-senior author Tony Jun Huang, Ph.D., professor of Mechanical Engineering & Material Science, who focuses on the micro-particles in fluids for biomedical diagnostics and therapeutics.

The Duke team used human, rat and mouse ACS fluid to test its effectiveness as a therapy for neuropathy. The serums were injected in both mice and rats after the animals had undergone a regimen of the chemotherapy drug paclitaxel, which is used to treat breast, ovarian and lung cancers. The most common side effect of paclitaxel is numbness and tingling in the hands and feet.

Not only did the therapy alleviate the animals' nerve pain, but its effect lasted several weeks—well beyond the hours or days provided by normal pain medicines.

"That prompted us to examine what was driving this long-lasting effect, because it could not be explained by the typical anti-inflammatory properties that we associate with ACS," Buchheit said.

Specifically, the benefits of ACS have largely been attributed to the abundance of growth proteins and anti-inflammatory cytokines isolated in the serum. Cytokines are signaling proteins that help regulate inflammation. But these proteins would only produce short-lived results, not the long-term benefits seen in the study and experienced in real-world clinical situations.

Instead, the Duke researchers found that exosomes appear to be the component that gives ACS its durability. These tiny vesicles contain a host of molecules that fight inflammation, including micro-RNAs, and they become highly activated through the conditioning and incubation process of ACS.

"Our finding is that exosomes—small packages of information that cells such as immune cells share—are responsible for the long-term pain-relieving effects of ACS," Ji said. "By describing this newly identified mechanism for how ACS provides extended pain relief, we can explore a number of additional therapeutic uses. We are greatly interested in

continuing our work to investigate exosome profiles in ACS to further define the mechanisms behind this pain relief therapy."

More information: Thomas Buchheit et al, Intrathecal administration of conditioned serum from different species resolves Chemotherapy-Induced neuropathic pain in mice via secretory exosomes, *Brain, Behavior, and Immunity* (2023). DOI: 10.1016/j.bbi.2023.04.013

Provided by Duke University