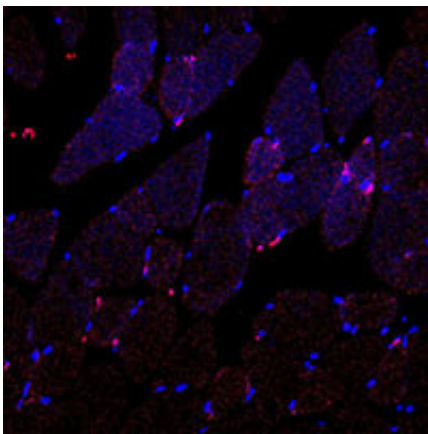


Scientists develop a biodegradable nanoparticle that effectively resolves inflammation

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Collagen IV-targeted polymeric nanoparticles (shown in pink) are home to injured tissue, post-injection, in the blood. Credit: Farokhzad Lab

(Phys.org) —Inflammation is the body's natural defense mechanism against invading organisms and tissue injury. In acute inflammation, the pathogen or inflammatory mediators are cleared away and homeostasis is reached, however in chronic inflammatory states, this resolving response is impaired, leading to chronic inflammation and tissue damage. It is now widely believed that an impaired resolution of inflammation is a major contributing factor to the progression of a number of devastating diseases such as atherosclerosis, arthritis, and neurodegenerative diseases, in addition to cancer. Since the level of inflammation in these

diseases is very high—targeted therapeutic solutions are required to help keep inflammation contained.

A new study from researchers at Brigham and Women's Hospital (BWH), Columbia University Medical Center, Icahn School of Medicine at Mount Sinai, and Massachusetts Institute of Technology presents the development of tiny nanomedicines in the sub 100 nm range (100,000 times smaller than the diameter of a human hair strand) that are capable of encapsulating and releasing an inflammation-resolving peptide drug. The authors showed that these nanoparticles are potent pro-resolving nanomedicines, capable of selectively homing to sites of [tissue injury](#) in mice, and releasing their therapeutic payload in a controlled manner over time. Uniquely, these nanoparticles are designed to target the extracellular microenvironment of inflamed tissues. The particles then slowly release their potent inflammation-resolving payload such that it can diffuse through the [inflamed tissue](#). There the drug binds to receptors on the [plasma membrane](#) of activated white blood cells and causes them to become more quiescent.

This study will be electronically published in *Proceedings of the National Academy of Sciences* the week of March 18, 2013.

"The beauty of this approach is that it takes advantage of nature's own design for preventing inflammation-induced damage, which, unlike many other anti-inflammatory strategies, does not compromise host defense and promotes tissue repair," said Ira Tabas, MD, PhD, physician-scientist at Columbia University Medical Center and co-senior author of this study.

"The development of self-assembled targeted nanoparticles which are capable of resolving inflammation has broad application in medicine including the treatment of atherosclerosis," said Omid Farokhzad, MD, physician-scientist at BWH, and a co-senior author of this study.

Polymers consisting of three chains attached end-to-end were developed as building blocks for the engineering of self-assembled targeted nanoparticles; one chain enabled the entrapment and controlled release of the therapeutic payload, in this case a peptide which mimics the pro-resolving properties of the Annexin A1 protein. Another chain conferred stealth properties to the nanoparticles, enabling their long-circulation after systemic administration. Yet a third chain gave homing capability to the nanoparticles to target the collagen IV protein to the vascular wall. As such these nanoparticles are capable of selectively sticking to injured vasculature allowing their therapeutic anti-inflammatory cargo to be released where it is needed to effectively promote inflammation resolution in a deliberate and targeted manner.

"These targeted polymeric nanoparticles are capable of stopping neutrophils, which are the most abundant form of [white blood cells](#), from infiltrating sites of disease or injury at very small doses. This action stops the neutrophils from secreting further signaling molecules which can lead to a constant hyper-inflammatory state and further disease complications," said Nazila Kamaly, PhD, a postdoctoral fellow at BWH and co-lead author of this study.

"[Nanoparticles](#) that selectively bind to injured vasculature could have a profound impact in prevalent diseases, such as atherosclerosis, where damaged or comprised vasculature underlie the pathology. This work offers a novel targeted nanomedicine to the burgeoning field of inflammation-resolution, a field previously pioneered by BWH's Dr. Charles Serhan," said Gabrielle Fredman, PhD, a post-doctoral fellow at Columbia University Medical Center and co-lead author of this study.

These new developments have led the researchers to start investigating the potential of these pro-resolving nanomedicines for their effects on shrinking atherosclerotic plaques, and these studies are currently underway.

More information: The paper is titled, "Development and in vivo efficacy of targeted polymeric inflammation-resolving nanoparticles."

Provided by Brigham and Women's Hospital

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