UC SANTA BARBARA

THE Current

January 7, 2015
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Special Delivery

Inflammation is a normal and often beneficial response to injury or infection. The swelling, heat and even pain are the body's attempts to protect its soft tissue, remove offending objects, substances or microbes and initiate healing. However, persistent inflammation is often indicative of more serious conditions and can lead to problems of its own, including impaired healing, loss of function or even tissue death.

"Many diseases result in inflammation," said Samir Mitragotri, professor of chemical engineering at UC Santa Barbara and director of the campus's Center for Bioengineering. Whether inflammation is a byproduct of the disease or the inflammation *is* the disease, it is a common indicator of a problem with the system. "If we could target the common denominator, whether the inflammation is coming from cancer or arthritis, we could deliver the drug there," said Mitragotri, who specializes in targeted drug delivery.

By taking advantage of natural body processes, researchers at UC Santa Barbara and MIT have developed a method of targeting inflamed tissues, creating a way to treat both the inflammation and its underlying cause.

"It's a cell-mediated approach to targeted drug delivery," said UCSB grad student researcher Aaron Anselmo, lead author of a study in the current issue of the Journal of Controlled Release.

Key to this technology is the utilization of monocytes, the type of white blood cell known for its ability to penetrate into deep sections of tissue. Under normal circumstances, the job of these monocytes is to circulate in the blood and respond to biochemical signals that indicate inflammation — a sign of injury or infection. Once at the site, these monocytes transform into macrophages, cells that reside in the affected tissues to engulf and digest foreign material.

Working with the expertise of chemical engineering and materials science researchers at MIT, including graduate researcher Jonathan Gilbert and professors Robert Cohen and Michael Rubner, the UCSB researchers developed an approach based on “cellular backpacks” — flat, disc-shaped polymeric particles that could, in the near future, hold therapeutic agents that can be released at the site of the inflammation. These polymeric discs are coated on one side with a single layer of an antibody that can bind to receptors on the monocyte’s surface.

To prevent the cellular backpack from being engulfed and devoured by the very cell that is transporting it, the researchers chose a flexible particle that is nonspherical in shape, which, according to the study, has proved to be more durable and resistant to phagocytosis than a rigid spherical particle. The shape and flexibility gives the backpack the ability to bind strongly while resisting phagocytosis to hitchhike onto monocytes and reach the inflamed tissue.

In-vitro and in-vivo tests have proved that cellular backpacks are successful in attaching to and being transported by monocytes to target areas without impairing the monocytes’ natural functions, said Anselmo. Further studies will include research into how much drug can be loaded into the cellular backpacks. Ideally, Anselmo said, the cellular backpacks loaded with drugs would be injected into the bloodstream, whereupon they would attach to these traveling monocytes and hitchhike to the target region. At the inflamed site, the particles would simultaneously degrade and release their drugs.

The development of effective cellular backpacks has broad potential, say the researchers.

“Basically the main benefit is that you can deliver the drug in a more effective dose,” Mitragotri said. Take for example the case of chemotherapy, which often has a narrow therapeutic range: Too little and the treatment is not effective, too much and it can be lethal. Because chemo travels through the bloodstream and affects all the tissues it comes in contact with, dosages are restricted at least in part based on

the deleterious effect it has on other, unafflicted organs and their functions. Not only can targeted therapy ensure other body systems remain unaffected, Mitragotri explained, but it could allow for higher doses of drug to the site, which could decrease treatment time.

About UC Santa Barbara

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