Antioxidant biomaterial promotes healing

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When a foreign material like a medical device or surgical implant is put inside the human body, the body always responds. According to Northwestern University's Guillermo Ameer, most of the time, that response can be negative and affect the device's function.

"You will always get an inflammatory response to some degree," said Ameer, professor of biomedical engineering in Northwestern's McCormick School of Engineering and Applied Science and professor of surgery in the Feinberg School of Medicine. "A problem with commonly used plastic materials, in particular, is that in addition to that inflammatory response, oxidation occurs."

We all need oxygen to survive, but a high concentration of oxygen in the body can cause oxidative reactions to fall out of balance, which modifies natural proteins, cells, and lipids and causes them to function abnormally. This oxidative stress is toxic and can contribute to chronic disease, chronic inflammation, and other complications that may cause the failure of implants.

For the first time ever, Ameer and his team have created a biodegradable biomaterial that is inherently antioxidant. The material can be used to create elastomers, liquids that turn into gels, or solids for building devices that are more compatible with cells and tissues. The research is described in the June 26 issue of *Biomaterials*.

"Plastics can self-oxidize, creating radicals as part of their degradation process," Ameer said. "By implanting devices made from plastics, the oxidation process can injure nearby cells and create a cascade that leads to chronic inflammation. Our materials could significantly reduce the inflammatory response that we typically see."

Ameer created the biomaterial, which is a polyester based on citric acid, by incorporating vitamin C as part of the building blocks. In preliminary experiments, his team coated vascular grafts with the antioxidant biomaterial, and the grafts were evaluated in animals by Ameer's long-time collaborator Melina Kibbe, professor of surgery and the Edward G. Elcock Professor of Surgical Research at Feinberg and a vascular surgeon at Northwestern Memorial Hospital.

As part of the foreign body response, grafts tend to inflame nearby cells and slowly scar over time, which eventually leads to failure. When the antioxidant vascular graft was implanted, however, the scarring was significantly reduced. Ameer's team, funded by a proof-of-concept grant from the Northwestern University Clinical and Translational Sciences Institute, also found that a water-soluble, thermoreversible version of the material sped of the healing of diabetic ulcers. Because the material is biodegradable, it harmlessly is absorbed by the body over time.

"In the past, people have added antioxidant vitamins to a polymer and blended it in," Ameer said. "That can affect the mechanical properties of the material and limit how much antioxidant you can add, so it doesn't work well. What we're doing is different. We're building a material that is already inherently, intrinsically antioxidant."

Ameer said the new biomaterial could be used to create scaffolds for tissue engineering, coat or build safer medical devices, promote healing in regenerative medicine, and protect cells, genes, and viruses during drug delivery. He added that the new biomaterial is easy to make and inexpensive.

"Citric acid is affordable and in pretty much everything we come in contact with on a daily basis—food and beverages, skin and hair products, drugs, etc.," Ameer said. "It's a common, inexpensive raw material to use, and our system can stabilize vitamin C, an antioxidant that we are all familiar with."

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