Human enzyme breaks down potentially toxic nanomaterials

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An international study based at the University of Pittsburgh provides the first identification of a human enzyme that can biodegrade carbon nanotubes—the superstrong materials found in products from electronics to plastics—and in laboratory tests offset the potentially damaging health effects of being exposed to the tiny components, according to findings published online in *Nature Nanotechnology*.

The results could open the door to the use of carbon nanotubes as a safe drug-delivery tool and also could lead to the development of a natural treatment for people exposed to nanotubes, either in the environment or the workplace, the team reported. The researchers found that carbon nanotubes degraded with the human enzyme myeloperoxidase (hMPO) did not produce the lung inflammation that intact nanotubes have been shown to cause. Furthermore, neutrophils, the white blood cells that contain and emit hMPO to kill invading microorganisms, can be directed to attack carbon nanotubes specifically.

"The successful medical application of carbon nanotubes rely on their effective breakdown in the body, but carbon nanotubes also are notoriously durable," said lead researcher Valerian Kagan, a professor and vice chair in the Department of Environmental and Occupational Health in Pitt's Graduate School of Public Health. "The ability of hMPO to biodegrade carbon nanotubes reveals that this breakdown is part of a natural inflammatory response. The next step is to develop methods for stimulating that inflammatory response and reproducing the biodegradation process inside a living organism."

Kagan and his research group led the team of more than 20 researchers from four universities along with the laboratory groups of Alexander Star, an assistant professor of chemistry in Pitt's School of Arts and Sciences, and Judith Klein-Seethharaman, an assistant professor of structural biology in Pitt's School of Medicine. Additional Pitt researchers included Yulia Tyurina, a Pitt assistant professor of environmental and occupational health in the Graduate School of Public Health, and Donna Stolz, an associate professor of cell biology and physiology in Pitt's medical school; other researchers are from Sweden's Karolinska Institute, Trinity College in Ireland, the National Institute for Occupational Safety and Health, and West Virginia University.

Carbon nanotubes are one-atom thick rolls of graphite 100,000 times smaller than a human hair yet stronger than steel. They are used to reinforce plastics, ceramics, or concrete; are excellent conductors of electricity and heat; and are sensitive chemical sensors. However, a nanotube's surface also contains thousands of atoms that could react with the human body in unknown ways. Tests on mice have shown that nanotube inhalation results in severe lung inflammation coupled with an early onset of fibrosis. The tubes' durability raises additional concern about proper disposal and cleanup. In 2008, Star and Kagan reported in Nano Letters that carbon nanotubes deteriorate when exposed to the plant enzyme horseradish peroxidase, but their research focused on cleanup after accidental spills during manufacturing or in the environment.

For the current study, the researchers focused on human MPO because it works via the release of strong acids and oxidants—similar to the chemicals used to break down carbon nanotubes. They first incubated short, single-walled nanotubes in an hMPO and hydrogen peroxide solution—the hydrogen peroxide sparks and sustains hMPO activity—for 24 hours, after which the structure and bulk of the tube had completely degenerated. The nanotubes degenerated even faster when

sodium chloride was added to the solution to produce hypochlorite, a strong oxidizing compound known to break down nanotubes.

After establishing the effectiveness of hMPO in degrading carbon nanotubes, the team developed a technique to prompt neutrophils to attack nanotubes by capturing them and exposing them to the enzyme. They implanted a sample of nanotubes with antibodies known as immunoglobulin G (IgG), which made them specific neutrophil targets. After 12 hours, 100 percent of IgG nanotubes were degraded versus 30 percent of those without IgG. The researchers also tested the ability of macrophages, another white blood cell, to break down nanotubes, but after two days, only 50 percent of the tubes had degenerated.

In subsequent laboratory tests, lung tissue exposed to the degraded nanotubes for seven days exhibited negligible change when compared to unexposed tissue. On the other hand, tissue exposed to untreated nanotubes developed severe inflammation.

Provided by University of Pittsburgh