

Implants mimic infection to rally immune system against tumors

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Bioengineers at Harvard University have shown that small plastic disks impregnated with tumor-specific antigens and implanted under the skin can reprogram the mammalian immune system to attack tumors.

The research -- which ridded 90 percent of mice of an aggressive form of melanoma that would usually kill the rodents within 25 days -- represents the most effective demonstration to date of a cancer vaccine.

Harvard's David J. Mooney and colleagues describe the research in the current issue of the journal *Nature Materials*.

"Our immune systems work by recognizing and attacking foreign invaders, allowing most cancer cells -- which originate inside the body -- to escape detection," says Mooney, Gordon McKay Professor of Bioengineering in Harvard's School of Engineering and Applied Sciences. "This technique, which redirects the immune system from inside the body, appears to be easier and more effective than other approaches to cancer vaccination."

Most previous work on cancer vaccines has focused on removing immune cells from the body and reprogramming them to attack malignant tissues. The altered cells are then reinjected back into the body. While Mooney says ample theoretical work suggests this approach should work, in experiments more than 90 percent of the reinjected cells have died before having any effect.

The implants developed by Mooney and colleagues are slender disks measuring 8.5 millimeters across. Made of an FDA-approved biodegradable polymer, they can be inserted subcutaneously, much like the implantable contraceptives that can be placed in a woman's arm.

The disks are 90 percent air, making them highly permeable to immune cells. They release cytokines, powerful attractants of immune-system messengers called dendritic cells.

These cells enter an implant's pores, where they are exposed to antigens specific to the type of tumor being targeted. The dendritic cells then report to nearby lymph nodes, where they activate the immune system's T cells to hunt down and kill tumor cells throughout the body.

"Much as an immune response to a bacterium or virus generates long-term resistance to that particular strain, we anticipate our materials will generate permanent and body-wide resistance against cancerous cells, providing durable protection against relapse," says Mooney, a core member of the recently established Wyss Institute for Biologically Inspired Engineering at Harvard.

The implants could also be loaded with bacterial or viral antigens to safeguard against an array of infectious diseases. They could even redirect the immune system to combat autoimmune diseases such as type 1 diabetes, which occurs when immune cells attack insulin-producing pancreatic cells.

"This study demonstrated a powerful new application for polymeric biomaterials that may potentially be used to treat a variety of diseases by programming or reprogramming host cells," Mooney and his co-authors write in *Nature Materials*. "The system may be applicable to other situations in which it is desirable to promote a destructive immune response (for example, eradicate infectious diseases) or to promote

tolerance (for example, subvert autoimmune disease)."

Source: Harvard University

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