SOUTHWESTERN NEWS

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UT SOUTHWESTERN RESEARCHERS DEVELOP NEW METHOD OF DELIVERING VACCINES

DALLAS – Dec. 28, 2001 – Researchers at UT Southwestern Medical Center at Dallas have developed a quicker, more cost-efficient method of delivering dendritic cell-based vaccines – a discovery that moves anti-tumor vaccines closer to a practical reality.

Until now, the conventional method to develop these vaccines involved extracting dendritic cells, which initiate immune responses to bacteria, viruses and cancer cells, from the body, then culturing and expanding the cells in a petri dish, loading them with tumor-associated antigens – substances the immune system recognize on cancer cells – and finally administering them through a vaccine.

Dr. Akira Takashima, professor of dermatology at UT Southwestern, reported in today's *Nature Biotechnology* that this expensive and time-consuming process has prevented broader clinical applications for dendritic cell-based vaccines.

In the UT Southwestern study, Takashima developed and tested a new procedure in mice that enabled researchers to manipulate dendritic cells in the skin rather than in a petri dish. This new process streamlines the conventional method from 10 days to 24 hours.

Dendritic cells are specialized white blood cells that signal T lymphocytes, critical components of the immune system, to multiply and initiate an immune response. The epidermis, or outermost layer of normal skin, contains immature dendritic cells known as Langherhans cells.

Upon exposure to a topical chemical called a hapten, Langerhans cells mature and migrate from the epidermis to draining lymph nodes. Small molecules called chemokines attract the trafficking cells and help mediate this process.

"Lymphatic endothelial cells produce a chemokine known as MIP-3ß , which binds to a corresponding receptor called CCR7. Langerhans cells utilize CCR7 to migrate from the epidermis to draining lymph nodes," said Takashima. "We incorporated this chemokine into a polymer rod so that it could be released in a controlled fashion."

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The researchers created an artificial trap for Langerhans cells by implanting under the skin a polymer rod synthesized with ethylene-vinyl-acetate to release MIP-3ß. After the rod was implanted, researchers applied hapten to trigger Langerhans-cell migration. The rod temporarily entrapped the Langerhans cells, which eventually homed to the lymph nodes. The procedure resulted in accumulation of Langerhans cells around the rod, Takashima said.

In a second experiment, a polymer rod releasing a tumor-associated antigen was then implanted under the skin.

"We thought these Langerhans cells would carry the tumor-associated antigen to the draining lymph nodes and initiate protective immunity against tumor development. Our subsequent experiments with several tumor models have, indeed, demonstrated the preclinical efficacy of this strategy. We believe that our *in situ* Langerhans-cell vaccine format represents a breakthrough in the tumor vaccines field, thus moving it toward practical medicine," said Takashima.

Dr. Tadashi Kumamoto, postdoctoral researcher in dermatology at UT Southwestern, was also involved in the study, which was supported by grants from the National Institutes of Health.