Medical Xpress

To spread, skin cancer attacks immune dendritic cells

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(PhysOrg.com) -- Dendritic cells are the sentinels of the immune system. When they're alert and on guard, they will marshal the body's immunosoldiers, T cells, to battle at the sight of harmful pathogens. But some diseases, such as cancer, are able to escape their watchful eye. By knocking out or beguiling dendritic cells, they slip the defenses of the immune system and sack the unsuspecting body. New research shows that one of the most common types of skin cancer has learned such a trick, finding a way to disable apparently healthy dendritic cells, which then allow cancer cell nests to spread around them without calling T cells to the fight.

The work was led by Michelle Lowes, an assistant professor of clinical investigation in the Laboratory for Investigative Dermatology at Rockefeller University, and John Carucci, associate professor of dermatology and director of Mohs Micrographic and Dermatologic Surgery at Weill Cornell Medical College. Their research shows that dendritic cells taken from squamous cell carcinomas have most of the known genetic and physiologic hallmarks of their able-bodied fellows in healthy skin tissue. But they do not behave the same at all, says Carucci, a former postdoc in the lab of Rockefeller professor Ralph M. Steinman, who discovered dendritic cells in 1973. "They are impotent," he says. "They just can't be turned on."

Curucci is an expert in surgical treatment of aggressive carcinomas and an immunologist who focuses on tumor biology. Lowes, whose usual focus is psoriasis, an inflammatory skin disorder in which dendritic cells

are implicated, helped Carucci and colleagues adapt her methods for the detailed study of dendritic cells in squamous cell carcinoma. It is the second most common type of skin cancer, afflicting about 250,000 people in the United States in 2007. The work, funded by a Dana Foundation grant supporting collaborative immunological research likely to lead to clinical treatments, involved genetic and biochemical testing of dendritic cell samples from carcinoma nests, bordering tissue and healthy skin.

Under normal circumstances, mature dendritic cells present pathogens to T cells, stimulating the production of an army of T cells specialized to neutralize the threat. Certain kinds of immunoregulatory proteins called cytokines are known to normally increase dendrtic cells' ability to muster that army. But Lowes and Carucci found that dendritic cells from the squamous cell carcinomas, although appearing mature and ready, could not be boosted with a cytokine cocktail to do much of anything at all. Similar-looking dendritic cells from healthy skin responded positively to the booster, and dendritic cells from skin bordering the cancer nests fell somewhere in between. The researchers do not yet know why; they're investigating that now. "First we need to find out what switched the dendritic cells off, then we'll look at how to turn them on," Lowes says. "If you can stimulate the right T cell response, you could mount a robust antitumor response," says Carucci. "If we can do that, we might actually be able to treat so-called inoperable cancers. This could truly have some clinical applications."

The research was published last month in the *Journal of Investigative Dermatology.*

Provided by Rockefeller University (news : web)