Medical Xpress

Modified immune cells seek and destroy melanoma

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In this issue of the *Journal of Clinical Investigation*, researchers led by Scott Pruitt at Duke University and Merck Research Laboratories report on a human clinical trial in which modified dendritic cells, a component of the immune system, were tested in patients with melanoma. All cells express a complex known as the proteasome, which acts as the garbage disposal for the cell. There are two types of proteasomes: constitutive proteasomes (cPs), which are found in normal tissues, and immunoproteasomes (iPs), which are found in stressed or damaged cells. In a damaged cell, the iP generates protein fragments that are displayed on the surface of the distressed cells, triggering recognition by dendritic cells and subsequent destruction by the immune system.

Most cancers, including melanoma, exclusively express cPs, making it impossible for them to express the protein fragments that are recognized by the immune system. To make it easier for the immune system to find cancer cells, Pruitt and colleagues engineered a specific type of immune cell, known as a dendritic cell, that recognizes protein fragments of cancer specific antigens made by cPs. The engineered dendritic cells were then injected into patients that were in remission from melanoma.

The trial consisted of 4 patients that were vaccinated with regular dendritic cells, 3 patients that received cells that underwent a control treatment, and 5 patients that received dendritic cells that recognized cancer-made protein fragments. Vaccination with all three types of dendritic cells elicited an immune response, which peaked after 3-4 vaccinations with dendritic cells. Patients that received the specially

modified dendritic cells had a longer lasting immune response and fewer circulating melanoma cells. Of the two patients that had active disease, treatment with modified dendritic cells resulted in a partial clinical response in one and a complete clinical response in the other.

These results suggest that modification of dendritic cells so that they recognize cP-produced tumor antigens enhances immune recognition of melanoma cells.

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