Medical Xpress

Dendritic cells stimulate cancer-cell growth

November 17 2006

Since their discovery at Rockefeller University some 30 years ago, dendritic cells have been recognized as key players on the immune-system team, presenting antigens to other immune cells to help them respond to novel insults. Now, Rockefeller scientists have shown that dendritic cells also have other, non-immune actions, and may in fact directly modify the biology of some types of cancer cells.

The results, reported recently in the *Journal of Experimental Medicine*, begin to clarify how the complex microenvironment of tumors promotes or inhibits their growth, which could be useful for devising novel cancer treatments.

“Tumors reside in a very complex environment that includes many, many kinds of cells,” says Madhav Dhodapkar, head of Rockefeller’s Laboratory of Tumor Immunology and Immunotherapy. “Cancer is not a disease just of the cancer cell, but of that cell in the context of everything else around it.” Dendritic cells, in particular, are abundant in myeloma and other tumors. They are attracted by chemical signals secreted by tumor cells, and were suspected of modulating the immune system so that it tolerates tumors instead of attacking them.

Dhodapkar’s research focuses on multiple myeloma, the unchecked proliferation of plasma cells in bone marrow. These immune cells are the final developmental stage of B cells, and are tuned to respond to specific antigens. The team, including Anjli Kukreja, a postdoc in the lab, used specialized culture systems to explore how individual components of the microenvironment influence cancer development. Ordinarily, only about

one tumor cell out of a hundred forms a colony in these cultures, but when the scientists introduced progressively more dendritic cells, the number of colonies progressively increased, ultimately multiplying by a factor of more than 10. They also saw increased growth in lymphoma and breast cancer cultures, but not in glioma, a brain cancer. Previous research had found that macrophages, a cousin of dendritic cells, directly affect tumor-cell growth, but the effect had never been observed with dendritic cells.

The dendritic cells also caused some tumor cells to go “backward” in development, resuming production of a chemical marker that had been shut off as they progressed from B cells to plasma cells. “These data suggest that the differentiation state of myeloma cells may be plastic, and capable of change in response to the microenvironment,” Dhodapkar explains. “This plasticity could be important in understanding how tumors develop.”

The researchers also identified two chemical signaling pathways by which the dendritic cells influence tumor cells, suggesting that complementary molecules on the surfaces of the two types of cells act only when the cells are in direct contact.

The supporting role of dendritic cells in tumors is also providing new insights into treatment. In a followup study in the *British Journal of Haematology*, Dhodapkar's team reports that a well-known myeloma drug, bortezomib, disrupts the interaction between tumor and dendritic cells in culture, and also kills the problematic dendritic cells. “In myeloma we are learning that both tumors and their environment need to be targeted for effective therapies,” he says.

Citation: Journal of Experimental Medicine 203(8): 1859-1865 (August 2006)
British Journal of Haematology Online: October 24, 2006

Source: Rockefeller University