IMMUNOTHERAPY

TSLP fuels inflammation in breast and pancreatic tumors

Inflammation can drive tumor growth, but details on the crosstalk between cancer and immune cells are often elusive. Now, findings from two independent studies point at the crucial role of the protein thymic stromal lymphopoietin (TSLP) in attracting T-helper (T_H)2 cells to breast and pancreatic tumors. In both cases, T_H 2 cells drive T_H 2-type inflammation in the tumor and seem to aggravate the disease.

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Maria Pia Protti and her colleagues from the San Raffaele Scientific Institute in Milan, Italy, analyzed 69 clinical pancreatic tumor samples and observed that high amounts of T_H 2 cells in the tumor correlated with patient mortality. Investigating the underlying mechanism they found that fibroblasts in the tumor microenvironment secreted TSLP. This protein acted on local dendritic cells, which then activated T_H 2 cells that were primed towards tumor antigens and homed to the tissue. “This is the first formal demonstration that T_H 2-type inflammation in human pancreatic cancer has an active role in tumor progression,” explains Protti.

In a similar study, Anna Karolina Palucka from Baylor Institute for Immunology (Dallas, TX) and a team of American and Japanese researchers studied a panel of 99 clinical breast cancer samples. Palucka and

colleagues demonstrated that levels of T_H 2 inflammatory cytokines, such as interleukin (IL)-13, and levels of TSLP-activated dendritic cells were higher in breast tumors than in surrounding tissues. In their study, however, the source of TSLP was the cancer cells, rather than tumor-infiltrating fibroblasts. Accordingly, the investigators detected TSLP in supernatants from five different breast cancer cell lines and in 35 of 38 primary breast tumor samples. Administration of antibodies directed against TSLP or against TSLP-activated dendritic cells reduced tumor development in a xenograft mouse model.

The two studies suggest that blockade of TSLP might be a new strategy for the treatment of patients with breast or pancreatic cancer. As TSLP is known for its role in inflammation, efforts to block TSLP pharmaceutically are already underway, which could speed up the translation of these findings into clinical practice.

For Palucka and her team, the next steps are to unravel “the mechanisms allowing TSLP release from cancer cells and ... [to study] the impact of IL-13 on cancer cells.”

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Original articles De Monte, L. *et al.* Intratumor T helper 2 cell infiltrate correlates with cancer-associated fibroblast thymic stromal lymphopoietin production and reduced survival in pancreatic cancer. *J. Exp. Med.* doi:10.1084/jem.20101876 | Pedroza-Gonzalez, A. *et al.* Thymic stromal lymphopoietin fosters human breast tumor growth by promoting type 2 inflammation. *J. Exp. Med.* doi:10.1084/jem.20102131 (2011)