*Nature Reviews Immunology* | AOP, published online 11 March 2011; doi:10.1038/nri2961

TUMOUR IMMUNOLOGY

# TSLP drives human tumour progression

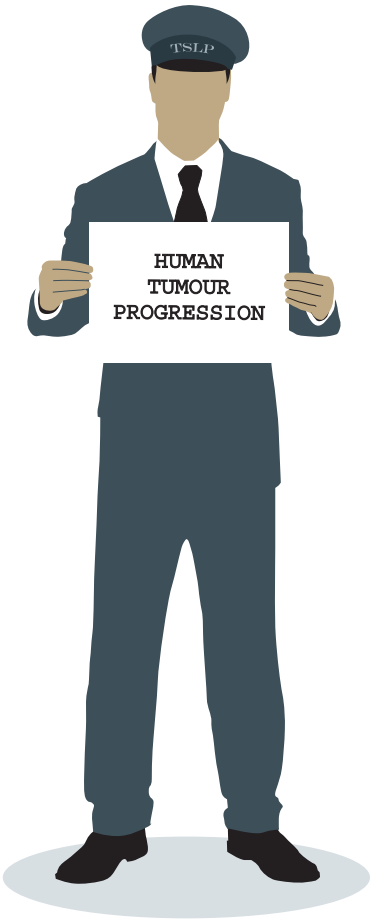
Chronic inflammation associated with $CD4^+$ T helper 2 ($T_H2$) cell polarization can promote cancer progression. Two independent studies report that thymic stromal lymphopoietin (TSLP) expression in the tumour microenvironment contributes to tumour growth following intratumoural $T_H2$ cell differentiation.

TSLP induces inflammatory $T_H2$ cells — which produce interleukin-13 (IL-13) and tumour necrosis factor (TNF) but no IL-10 — through myeloid dendritic cell (DC) activation. De Monte *et al.* showed that stimulation of human pancreatic cancer-associated fibroblasts (CAFs) with tumour-derived factors, such as TNF and IL-1β, results in increased secretion of TSLP, whereas Pedroza-Gonzalez *et al.* report constitutive TSLP production by human breast cancer cells. TSLP-containing supernatant from pancreatic CAFs induced high expression of the TSLP receptor and $T_H2$-type chemoattractants by myeloid DCs. Moreover, myeloid DCs treated with breast cancer tumour supernatant exhibited an activated phenotype and drove inflammatory $T_H2$ cell differentiation in an OX40 ligand-dependent manner. Using a TSLP-specific neutralizing antibody, the two groups demonstrated that tumour-derived TSLP directly affects the ability of myeloid DCs to prime inflammatory $T_H2$ cells.

Interestingly, the phenotype of myeloid DCs that infiltrate pancreatic or breast cancer tumours was found to be similar to that of *in vitro* TSLP-treated myeloid DCs, suggesting a TSLP-mediated mechanism of inflammatory $T_H2$ cell differentiation in cancer. This is of physiological relevance, as an increase in the ratio of $T_H2$ to $T_H1$ cells in the pancreatic tumour stroma was shown to be associated with disease progression. Furthermore, using humanized mice with breast cancer tumours, Pedroza-Gonzalez *et al.* demonstrated that the administration of antibodies that neutralize TSLP or its receptor decreases the secretion of $T_H2$ cell-associated cytokines by tumour-infiltrating T cells and blocks tumour growth.

Thus, these two studies identify a role for TSLP in tumour progression through the activation of a myeloid DC-induced inflammatory $T_H2$ cell response. Based on their findings, the authors suggest that targeting TSLP or its receptor may be of therapeutic value in the treatment of pancreatic or breast cancer.

*Maria Papatriantafyllou*




**ORIGINAL RESEARCH PAPERS** Pedroza-Gonzalez, A. *et al.* Thymic stromal lymphopoietin fosters human breast tumor growth by promoting type 2 inflammation. *J. Exp. Med.* 21 Feb 2011 (doi:10.1084/jem.20102131) | De Monte, L. *et al.* Intratumor T helper type 2 cell infiltrate correlates with cancer-associated fibroblast thymic stromal lymphopoietin production and reduced survival in pancreatic cancer. *J. Exp. Med.* 21 Feb 2011 (doi:10.1084/jem.20101876)