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The Role of the cytokine IL-33 and its receptor ST2 in promoting colon carcinogenesis.

The cytokine IL-33 and its receptor ST2 have been implicated in many inflammatory diseases. Inflammation is recognised as a hallmark of cancer. Little is known about the role of ST2 and IL-33 in cancer. Recent research has indicated that IL-33 and ST2 may be involved in tumour growth and metastasis (Jovanovic et al. 2011, Gillibert-Duplantier et al. 2011). We are interested in colon cancer as IL-33 and ST2 is elevated in ulcerative colitis a key risk factor for the development of colon cancer. In non-cancer cells expression is induced by TNF-α. It is not known how the IL-33/ST2 pathway is regulated in cancer cells. The ST2/IL-33 pathway activates a Th2 immune response. We aim to stimulate ST2 using IL-33 to examine how the tumour microenvironment is affected. IL-4, IL-5 and IL-13 are produced during a Th2 response. A Th2 response can be pro-tumour. IL-13 has been shown to polarise macrophages towards an M2 pro-tumour phenotype. TNF-α will be used to determine if this can stimulate the IL-33/ST2 pathway, as it does in non-cancer cells. We will examine ST2 activation in colon cancer cells using a variety of cytokines including Th2 cytokines IL-4,IL-5 and IL-13. IL-4 has been shown to increase expression of ST2 in non-cancer cells. IL-33 will be used to stimulate the ST2 receptor and the cytokine profile compared to that of ST2 knock out cells. Macrophages from ST2 knock-out mice will be stimulated with IL-13 to determine if they can polarise towards an M2 pro-tumour phenotype.

Gillibert-Duplantier, J. et al., 2011. Gene expression profiling identifies sST2 as an effector of ErbB2-driven breast carcinoma cell motility, associated with metastasis. Oncogene, 2, pp.1–9. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22105364.

Jovanovic, I. et al., 2011. ST2 deletion enhances innate and acquired immunity to murine mammary carcinoma. European journal of immunology, 41(7), pp.1902–1912. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21484786.