

**Title: Interleukin-33 and Innate Lymphocytes are Immune Defense Prognosticators in Recurrent Cancer** (by *Iryna Saranchova*)

**Abstract**

Type 2 innate lymphoid cells (ILC2s) potentiate adaptive immune responses and are the first responders to the pro-inflammatory “alarmin” interleukin 33 (IL-33) in the tissue microenvironment. However, their role in cancer progression is not defined. We demonstrate that metastatic carcinomas express reduced levels of IL-33 compared to syngeneic primary tumours. Metastatic tumours engineered to overexpress IL-33 have significantly reduced growth rates and result in a decreased frequency of circulating metastatic tumour cells. ILC2s mediate this process as metastatic tumours have significantly increased growth rates in mice genetically lacking ILC2s. Parallel studies in humans demonstrate that low tumour expression of IL-33 is a prognosticator associated with reoccurrence of prostate cancer 3.4 years more rapidly than IL-33 high-expressing tumours. These observations indicate that IL-33 can modify metastatic spread of the disease and demonstrate the role of ILC2s in cancer immune surveillance via a retinoid-related orphan receptor alpha (RORα)-IL-33-ILC2 axis.