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PANCREATIC CANCER

γδ T cells support PDAC

A distinct population of γδ T cells are the dominant lymphocyte subset in human pancreatic ductal adenocarcinoma (PDAC), according to new research. These cells support oncogenesis by suppressing effector T-cell activation, suggesting the potential for novel pancreatic cancer immunotherapies.

The progression of PDAC is associated with immune-suppressive inflammation and a deficiency of effector T cells, stemming in part from leukocyte crosstalk within the tumour microenvironment. γδ T cells have shown contrasting effects on tumorigenesis in different cancers but the exact role of this T-cell subset in PDAC was unknown. Now, following an interest in these cells from work in liver regeneration, George Miller and colleagues specifically examined intrapancreatic γδ T cells.

"Our first preliminary experiment was very provocative. We discovered that γδ T cells were the majority T-cell subset in many human pancreas tumours," reports Miller. The deletion or depletion of γδ T cells, or inhibition of their recruitment, protected against PDAC *in vivo*, causing increased infiltration and activation of antitumour T cells. Furthermore, γδ T cells inhibited effector T cells though direct cellular interactions — PDAC-infiltrating γδ T cells in mice and humans showed high expression of PDL1, the ligand for the immune checkpoint protein PD1. Blockade of PDL1 also protected against PDAC *in vivo*, but only when γδ T cells were present, suggesting that γδ T cells regulate effector T-cells in PDAC and are key sources of checkpoint ligands.

"That γδ T cells mediate T-cell suppression via expression of PDL1 is also novel as the PDL1–PD1 axis was thought to be mediated by tumour cell or myeloid cell interactions with effector T cells," explains Miller. These findings suggest that the development of biologics targeting γδ T cells could be an attractive strategy for pancreatic cancer immunotherapy. The researchers also plan to investigate the potential suppressive roles of γδ T cells in other types of cancer.

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ORIGINAL ARTICLE Daley, D. *et al.* γδ T cells support pancreatic oncogenesis by restraining αβ T cell activation. *Cell* http://dx.doi.org/10.1016/j.cell.2016.07.046 (2016)