Immunity: Tissue Contribution

Tissue-expressed PD-L1 is important in controlling colon inflammation.

Membrane protein PD-1 and its ligand PD-L1 (B7-H1) are members of the B7/CDD28 families of ligands/receptors. Binding of PD-L1 to its receptor PD-1 leads to inhibition of T-cell activation and proliferation. PD-1 is highly expressed on T cells during chronic viral infections and blunts T-cell responses in conditions of chronic antigen exposure, a process known as T-cell exhaustion. PD-L1 is also upregulated in tumor cells and inhibits anti-tumor T-cell responses. Given the pathological implications of the PD-1-PD-L1 interaction, anti-PD-1 and anti-PD-L1 therapies have the potential clinical application of boosting T-cell function during chronic infections or cancer.

PD-L1 is also expressed by various tissue cells. Recently, Zang and colleagues (PSI NYSGRC) have shown that PD-L1 is expressed by human and mouse intestinal epithelial cells, and explored its role in intestinal inflammation. Although PD-L1-deficient mice had no signs of intestinal inflammation at steady state, they showed increased pathology in experimental models of colitis, due to reduced epithelial integrity in the colon and increased systemic bacterial dissemination. PD-L1 expression on epithelial cells is required for protection against hematopoietic cell-mediated gut inflammation. PD-L1-deficient mice had increased production of tumor necrosis factor-α in the colon and lower expression of interleukin 22, which is known to promote epithelial cell survival and secretion of antibacterial peptides.

These results indicate an important function of PD-L1 expressed by gut epithelial cells in regulating colon inflammation. In conditions of chemically induced damage to the colon epithelium, the lack of PD-L1 signals from the epithelium results in increased inflammation, cell death and bacterial dissemination. The immune cells responsible for these effects in the absence of PD-L1-mediated inhibition remain unknown, although the phenotype is likely to be complex and multifactorial. The microbiota should also play an important role in the process, but the contribution of the gut commensals has not yet been tested in this model.

In conclusion, this study adds to an increasing body of evidence indicating that tissue-expressed PD-L1 can deliver inhibitory signals to immune system cells and contribute to immune tolerance.

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References: