Suppressed T-cell activation by IFN-gamma-induced expression of PD-L1 on renal tubular epithelial cells.

BACKGROUND: The interaction of the T-cell molecule PD-1 (programmed death-1) with its ligands PD-L1 and PD-L2 represents a known mechanism of T-cell inhibition. PD-1 is homologous to CD28 while the PD-1 ligands share homology with the B7 family of co-stimulatory molecules.

METHODS: We have studied surface expression and transcript levels of PD-L1 and PD-L2 on murine renal tubular epithelial cells (TEC) by flow cytometric analysis and reverse transcription-polymerase chain reaction. Western blot analysis was used to confirm protein expression of PD-L1. We also tested the functional role of PD-L1 and PD-1 in antigen presentation. Furthermore, we stained mouse kidney transplants with rejection for the expression of the PD-1 ligands. RESULTS: We found that PD-L1 but not PD-L2 was weakly expressed on unstimulated TEC. Upon stimulation with IFN-gamma, a dose-dependent upregulation of PD-L1 expression was observed. Blockade of the PD-L1/PD-1 pathway with monoclonal antibodies in antigen presentation assays uncovered an inhibitory role of this ligand system in Th1 and Th2 cell activation. Staining for PD-L1 was strong in proximal and distal tubules in mouse kidney transplants with rejection, whereas staining of normal kidneys and syngenic mouse kidney transplants did not reveal PD-L1 expression. PD-L2 was not observed in normal or rejected mouse kidneys.

CONCLUSIONS: These data...
demonstrate that PD-L1 is an inducible renal tubular epithelial antigen that negatively regulates T-cell responses elicited by IFN-gamma-stimulated TEC. We speculate that the PD-1/PD-L1 pathway may play a role in protecting the epithelium from immune-mediated tubulointerstitial injury.