

PD-1 Directed Immunotherapy

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ABSTRACT

Chronic antigen stimulation during persistent infections or cancer leads to T cell exhaustion. Programmed cell death (PD-1) is an inhibitory receptor that attenuates T cell receptor signaling and sustained PD-1 expression by exhausted T cells plays a major role in T cell dysfunction. T cell exhaustion and the role of PD-1 in chronic infection were first described in mice during lymphocytic choriomeningitis virus infection and later shown to occur in several situations of antigen persistence in mice, non-human primates and humans. Importantly, blockade of PD-1 interactions with its ligand (PD-L1) restores function in exhausted T cells. Recently blockade of the PD-1 pathway was used successfully in patients with advanced cancer. In this talk I will discuss the role of PD-1 in regulating T cell differentiation and also discuss combinatorial strategies that enhance PD-1 directed immunotherapy.