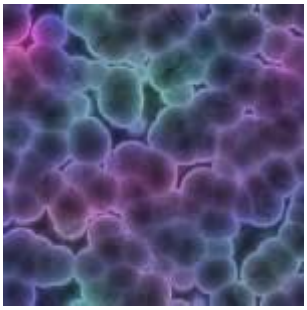
Levels of PD-L1 Expression on target cells helps to establish viral latency



During HIV infection, cytotoxic T lymphocytes (CTL) are able to eliminate virally infected cells at the acute stage of infection. However, due to the persistent nature of the infection, CTL become dysfunctional and display an “exhausted” phenotype. The inhibitory receptor PD-1 plays a central role in this phenotype as it is able to inhibit the cytotoxic function of T cells during chronic infections – and most likely contributes to viral persistence.

In the October edition of PloS Pathogens, Akhmetzyanova and Drabczyk show that that PD-L1, the ligand for the PD-1 receptor, can be up-regulated on retrovirus infected cells and that “the cells with the highest expression of PD-L1 escaped from cytotoxic T cell killing”. The authors used a murine Friend retrovirus model (Friend virus, FV) to show that FV-infected cells expressing very high levels of PD-L1 accumulated during infection and that these cells established a reservoir of viral persistence.

The authors state that “PD-L1high infected target cells accumulated during the course of infection, formed the reservoir of virus persistence, and subsequently mediated a negative feedback on cytotoxic T cells via the PD-1 receptor that ultimately resulted in functional exhaustion of these cells.” These results importantly show a link between PD-L1

expression and immune escape leading to the formation of a viral reservoir. Does this provide a clue to new strategies for eliminating viral reservoirs during HIV infection? An anti-PD-L1 approach, perhaps.

Akhmetzyanova, I. et al. 2015. PD-L1 Expression on Retrovirus-Infected Cells Mediates Immune Escape from CD8+ T Cell Killing. *PLOS*.