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Protein tyrosine phosphatase PTPN22: An odyssey for tolerance and immunity

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A genetic variant of the protein tyrosine phosphatase PTPN22 is associated with a wide range of autoimmune diseases. We and others have shown that PTPN22 functions as a key regulator of immune homeostasis. In particular, PTPN22 inhibits T-cell receptor signaling and selectively promotes type I interferon responses in myeloid cells. Recent evidence highlights an important role of certain autoimmune susceptibility genetic variants in conferring resistance against certain pathogens. To date, there is little information on role of PTPN22 in response to a viral pathogen. By employing two different strains of lymphocytic choriomeningitis virus (LCMV), we addressed the role of PTPN22 in acute and persistent infection in mice. We found that PTPN22 does not affect viral clearance of the acute LCMV strain. However, PTPN22-/- mice are resistant to chronic infection with LCMV. By following T cell adoptive transfer approaches and performing mixed bone marrow chimeras, we found that intrinsic PTPN22 signals are required for the expansion of antiviral CD8 T cells during acute infection, while extrinsic PTPN22 signals promote CD8 T cell exhaustion. Together, our findings identified a fascinating dual role of PTPN22 as an intrinsic promoter of acute anti-viral CD8 responses, but as a cell-extrinsic repressor of chronic CD8 T cell function.

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