**ABSTRACT**

CD229/SLAMF3 is a transmembrane glycoprotein primarily found on mature T cells, B cells, myeloid cells, macrophages, and thymocytes. The functions of CD229 remain uncertain. Data from CD229 knockout mice indicate that CD229 is uniquely involved in enhancing T cell activation. However, co-ligation of CD229 and T cell receptor (TCR) using anti-CD229 (mAb) and anti-CD3 antibodies has been demonstrated to inhibit T cell activation. We expressed the mouse CD229 extracellular domain (aa 48-454) with a poly-Histidine tag in the NS0 mouse myeloma cell line and investigated the functions of purified recombinant CD229 in mouse CD3+ cells in vitro. Concurrent ligation of CD229 and TCR with immobilized CD229-His protein and anti-CD3 antibody significantly enhanced cell proliferation and IFN-γ secretion in mouse CD3+ splenocytes in a dose-dependent manner. Furthermore, pre-treatment of CD3+ splenocytes with polyclonal anti-CD229 completely abolished the co-stimulatory actions of CD229-His. This suggests that CD229-His co-stimulates T cells through CD229 receptors on T cell surfaces. Moreover, ligation of CD229 with CD229-His in CD3+ cells led to ERK1/2 phosphorylation in response to anti-CD3 stimulation. Taken together, these results suggest that CD229 acts as a homophilic co-stimulatory molecule and is able to up-regulate T cell activation.

**RESULTS**

**SUMMARY**

- Treatment of mouse CD3+ splenocytes with recombinant mouse CD229 (rmCD229) induces cell proliferation and IFN-γ secretion in a dose-dependent manner.
- Pre-treatment of CD3+ splenocytes with a polyclonal anti-CD229 antibody abolishes rmCD229-induced cell proliferation and IFN-γ production.
- Stimulation of CD3+ splenocytes with anti-CD3 and rmCD229 results in ERK1/2 phosphorylation.
- These data strongly suggest that CD229 acts as a homophilic molecule capable of up-regulating T cell activation.

**REFERENCES**


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