Increasing the ex vivo antigen-specific IFN-γ production in subpopulations of T cells and NKp46+ cells by anti-CD28, anti-CD49d and recombinant IL-12 costimulation in cattle vaccinated with recombinant proteins from Mycobacterium avium subspecies paratuberculosis - DTU Orbit (09/11/2017)

Increasing the ex vivo antigen-specific IFN-γ production in subpopulations of T cells and NKp46+ cells by anti-CD28, anti-CD49d and recombinant IL-12 costimulation in cattle vaccinated with recombinant proteins from *Mycobacterium avium* subspecies *paratuberculosis*

T cells, which encounter specific antigen (Ag), require additional signals to mount a functional immune response. Here, we demonstrate activation of signal 2, by anti-CD28 mAb (aCD28) and other costimulatory molecules (aCD49d, aCD5), and signal 3, by recombinant IL-12, enhance Ag-specific IFN-γ secretion by CD4, CD8, γδ T cells and NK cells. Age matched male jersey calves, experimentally infected with Mycobacterium avium subsp. paratuberculosis (MAP), were vaccinated with a cocktail of recombinant MAP proteins or left unvaccinated. Vaccine induced ex vivo recall responses were measured through Ag-specific IFN-γ production by ELISA and flow cytometry. There was a significant increase in production of IFN-γ by T cell subsets or NKp46+ cells cultured in the presence of Ag and aCD28/aCD49d. The increase was accompanied by an increase in the integrated median fluorescence intensity (iMFI) of activated T cells. Addition of rIL-12 induced a significant additive effect leading to a maximum increase in responder frequency of Ag-specific T cell subsets or NKp46+ cells with a heavy bias toward IFN-γ production by CD4 T cells. We provide the first description of using aCD28/aCD49d costimulation to potentiate an Ag-specific increase in the production of IFN-γ in bovine immunology. The study also shows the degree of signaling in T cells is regulated by the costimulatory environment.

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