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Characterization of porcine T lymphocyte responses to swine influenza virus infection

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With significant concern that domesticated swine populations may serve as a source for novel influenza virus strains that could infect people, swine influenza viruses (SIVs) have been examined under increased scrutiny over the last decade for their zoonotic potential. In order to understand the development of novel strains in swine, it is necessary to understand the host responses to infection which are intricately linked to the pathogenesis of infection and natural selection of antigenic variants. Although several studies have investigated the impact of antibody response on viral pathogenesis, T lymphocyte responses to swine influenza virus have been poorly studied. In the present study, we evaluated the phenotypes of T cells mobilized in the blood and lungs during acute infection in pigs. Four-week-old pigs were infected by intranasal and intratracheal inoculation with an H1N1 (A/Sw/IA/00239/04) virus strain. Increase in T cell mobilization in the blood was evident as early as 2 days post infection (d p.i) which continued to increase at 5 d p.i. Interestingly, expansion of total circulating cytotoxic T lymphocytes [CD3(+)γδ(-)CD4(-)CD8(+)] contributed to the increase in T cells, such that the ratio of absolute numbers of CD4:CD8 αβ T lymphocytes increased at 5 d p.i. In addition, greater numbers of T cell were observed with the increase in total cellularity in SIV-infected lungs at 5 d p.i. Phenotypically, T cells in the lung were characterized by increases in proportions of single positive CD4(+) and CD8(+)αβ T cells and double positive (DP) αβ T cells [CD3(+)γδ(-)CD4(+)CD8(+)]. Although the increase in total numbers of αβ single positive T lymphocyte populations did not attain significance, the total numbers of DP αβ T cells increased significantly with SIV infection. Among the γδ T lymphocytes in the lung, only single positive CD8 cells [CD4(-)CD8(+)]or double negative [CD4(-)CD8(-)] populations were observed with no significant change in the total numbers of γδ T cells. These data indicate a predominant presence of cytotoxic lymphocytes in the lung at 5 d p.i. Using a short-term *ex-vivo* stimulation assay, interferon-gamma production was detected in CD8(+) T cells. Further experiments are underway to determine antigenic specificities of T cell subpopulations to infection and lymphocyte activation profiles to heterosubtypic swine influenza antigen. The results of this study provide new insights into the nature of T lymphocyte responses to SIV, which could be applied to elucidate their role in herd immunity and their contribution to virus evolution and transmission.