

Natural killer cell subsets display helper and suppressor effects in modulating host viral responses *in vivo*

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Natural Killer (NK) cells play important effector roles in viral resistance. Here we show that NK cell subsets exist based on Ly49 or KIR receptor expression that exert diverse and potent immunoregulatory effects on host viral responses in a manner consistent with licensing or education. Using both MCMV and influenza mouse models and tracking both resistance via viral titers and antigen-specific T cell responses by tetramer staining we demonstrate that depletion of different NK cell subsets exerted markedly different effects on the host response. Licensed NK cells acted as NK effector/suppressor cells due to their ability to mediate innate resistance to viral challenge whereas the unlicensed population exhibited NK helper functions. The NK helper population promoted dendritic cell expansion in the regional lymph nodes and both CD4 and CD8 antigen-specific responses. Furthermore, the different NK cell subsets could be distinguished by the cytokine profile where the NK effector subset produced greater amounts of interferon-gamma and the NK helper subset produced large amounts of GM-CSF which was responsible for the dendritic cell expansion. Upon viral rechallenge after vaccination corroborated the protective effects of the NK helper subset on antigen-specific T cell responses. Similar subset characteristics were found in human NK cell subsets as well indicating these different subsets may have significant effects on host viral responses and vaccine effects.

Biography

William J Murphy received his PhD in Immunology from UT Southwestern Medical Center in 1989 and did his Post-doctoral fellowship at the National Cancer Institute. He became Director of Basic Research at the NCI-Frederick in 2000. He is currently Acting Chair of Dermatology and Professor of Internal Medicine at the UC Davis School of Medicine. He has over 250 publications in the fields of immunotherapy, *in vivo* modeling and hematopoietic stem cell transplantation.

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