NK cells activity in response to HCMV infection

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Human cytomegalovirus (HCMV) causes severe disease in immunocompromised patients. The antiviral immunity controls infections by a complex interplay of immune cells and factors. One such effector cell in the antiviral response is the Natural Killer (NK) cell. The activity of NK cells is balanced by activating and inhibitory signals conveyed through ligands on target cells. NK cells once activated, will release cytotoxic granules which result in the death of the target cell.

Viruses frequently modulate the expression of NK ligands, thereby interfering with NK cell recognition of virally infected cells. To date, six HCMV genes encoding proteins (UL16, UL18, UL40, UL83, UL141 and UL142) and one encoding a microRNA (miR-UL112) have been identified as capable of suppressing NK cell recognition. By understanding the biology of NK cells responses to HCMV infected cells, we will be able to develop more effective preventative and therapeutic approaches against HCMV infection.

An optimal NK cell activation also results from cytokine stimulation and interaction with immune cells and in particular with antigen presenting accessory cells (APCs). We have recently established that infected autologous macrophages could be utilized to quantitatively determine the activity of NK cells. By using this assay, we could demonstrate that HCMV seropositivity increases NK cells activity in unfraction PBMCs in response to infected macrophages. The implications of our findings may have profound influences on HCMV vaccination and therapy. However, the mechanisms for this enhanced NK cell activity remains unclear.

Thus, we want to answer the following questions:

1. Whether NK cells from seropositive donors intrinsically bear a high activity to infected macrophages?

2. Whether other immune cells in PBMCs contribute to the NK cells activity in response to infected macrophages?

3. Whether and what signals from accessory cells are needed for full NK cell activation.