

PhD defence Jef Hens

In vitro assessment of allogeneic NK cell responses against HIV-1 infected T cells

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Dit is de omschrijving

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Abstract

The human immune-deficiency virus 1 (HIV-1) is spread worldwide and causes an infection leading to AIDS which, to date, cannot be cured. In search for a better understanding of the virus, scientists investigate the virus by inspecting infected individuals. Especially people that are exposed to HIV-1 but remain seemingly uninfected are crucial for understanding how the virus can be controlled naturally. In general, it is believed that the earlier the virus is controlled, the slower the infection will progress. Recent research even indicates that events during the transmission of HIV-1 could make these individuals resistant to infection. More specifically, immune responses were suggested to obstruct the viral threat by eliminating the cells derived from the HIV-1 infected sexual partner. These immune responses were believed to be exerted by Natural killer (NK) cells, triggered by a mechanism called "missing-self". To further explore this hypothesis, we assessed the elimination of (non-self) cells derived from the sexual partner when encountered by (self) NK cells, and whether the missing-self mechanism could trigger this or not.

In my PhD, it became clear that the missing-self mechanism enabled the elimination of non-self cells by NK cells. However, NK cells were unable to eliminate the non-self cells when they were infected with HIV-1. Other factors such as MIC-A/B expressed on the HIV-1 infected cells did seem to have an impact on elimination by missing-self NK cell responses. These results show a rather limited impact of the missing-self mechanism on the specific elimination of HIV-1 infected cells. Nevertheless, the results also show that MIC-A/B might be an interesting target when looking at NK cell responses against HIV-1 infected cells. Interestingly, the strength of the missing-self response varied between the different subtypes of NK cells, demonstrating the need for more extensive investigation of the missing-self principle. Especially missing-self responses triggered by KIR2DL1 on NK cells were seen to elicit a strong response. In general, the missing-self mechanism activates the NK cells against non-self cells, whereas NK cell activation against HIV-1 infected cells was rather limited in missing-self conditions.