CD3+CD56+ Natural Killer-Like T Cells in HIV(+) Patients With Acute Hepatitis C

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Background: In Western Europe and the US approximately 30% of HIV (+) patients are co-infected with the hepatitis C virus (HCV), which has become a major cause of morbidity and mortality in HIV(+) patients.

We recently showed that natural killer cells are able to recognize HCV-containing target cells via the NK cell receptors NKG2D- and NKp46 and to effectively block HCV replication in vitro. Moreover, we presented first data suggesting NK cells to critically affect outcome of acute hepatitis C in HIV(+) patients.

CD3+CD56+ natural killer-like T cells represent a subset of T lymphocytes that also express natural killer cell receptors. Here, we studied phenotype and function of CD3+CD56+ natural killer-like T cells in HIV(+) patients with acute hepatitis C.

Methodology: 36 HIV(+) patients with acute hepatitis C, including 13 patients with spontaneous clearance and 23 patients that subsequently developed chronic hepatitis C, were studied. As a control HIV mono-infected patients (n=8), HIV(+) patients with chronic hepatitis C (n=12), HIV(-) patients with chronic HCV infection (n=8) as well as 12 healthy individuals were analyzed. Peripheral NKT cells (CD3+CD56+) were phenotypically analyzed by flow-cytometry. IFN-γ secretion and anti-HCV activity of NKT cells were analyzed using the HuH7A2 HCV replicon system.

Results: Frequency of CD3+CD56+ NK-like T cells did not differ significantly between the study groups.

However, we observed a significant higher expression of the maturation markers CD27, CD127, and CD161 on CD3+CD56+ NK-like T cells in healthy controls than in HIV mono-infected patients and HIV patients with an acute HCV infection, respectively.

Interestingly, CD3+CD56+ NK-like T cells from HIV patients with acute hepatitis C displayed a higher expression of CD69, indicating a more activated status as compared to healthy controls. Of note, a high CD69 expression was associated with spontaneous clearance of acute hepatitis C, suggesting a role for CD3+CD56+ NK-like T cells in anti-HCV immune responses.

Accordingly, we found IL12/IL15-activated CD3+CD56+ NK-like T cells to effectively block HCV replication in an IFN-γ dependent fashion. However, CD3+CD56+ NK-like T cells from HIV patients with acute HCV infection displayed a significantly impaired capacity to secrete IFN-γ compared to both HIV mono-infected as well as healthy individuals.

Conclusions: Our results indicate that CD3+CD56+ NK-like T cells have the potential to block HCV replication but are functionally impaired in HIV(+) patients with acute hepatitis C.