学位論文抄録

Functional development of natural killer cells and its modification by hepatitis C viral infection

（ＮＫ細胞の機能分化とＣ型肝炎ウイルス感染による機能変化）

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Abstract of the Thesis

Background/Aims: Chronic hepatitis C virus (HCV) infection has been reported to modulate the immune response in several ways; however the modulation of innate immunity has not been clearly understood. We aimed to assess the impact of HCV infection on NK cells regarding frequency, phenotyping, subset distribution, cytotoxic and cytokine secretion function, as well as IFN-α and Ribavirin therapeutic effects on NK cells.

Methods: Fresh PBMCs were isolated from 29 chronic HCV infected patients PBMC, before receiving treatment and followed up 10 patients at finishing, and 24 weeks after finishing treatment, and analyzed surface staining of NK receptors, intracellular staining for Perforin (PFN), and surface expression of CD107a degranulation marker and intracellular IFN-γ stimulated with K562 cells.

Results: Significant reduction of total NK frequency and $CD56^{dim}16^{+}$ subset were observed in chronic HCV patients. In contrast, $CD56^{dim}16^{-}$ subset was expanded but expression of functional markers (NKp30, NKp46, NKG2A, NKG2D, and CD94) was decreased. IFN-γ expression with K562 stimulation was severely suppressed but cytotoxicity measured by CD107a expression was maintained. These adverse effects were reversed after the treatment with Pegylated IFN-α and Ribavirin.

Conclusion: HCV infection severely affects NK frequency and subset distribution, as well as NCRs, activation receptors, suppression of PFN and cytokine expression, however degranulation is maintained. These compromising effects can be reversed by antiviral treatment. HCV effect on NK cell function might predispose to disease chronicity.