学 位 論 文 の 要 約

三 重 大 学

所 属	三重大学大学院医学系研究科 甲 生命医科学専攻 病態解明医学講座 新生児医学分野	氏 名	須 麗清

主論文の題名

Cord blood $CD4^+CD25^+$ regulatory T cells fail to inhibit cord blood NK cell functions due to insufficient production and expression of TGF-beta 1

（臍帯血 CD4,CD25 陽性の制御性 T 細胞は TGF-β1 の産生及び発現不足のため NK 細胞を抑制できない）

Liqing Xu, Shigeki Tanaka, Motoki Bonno, Masaru Ido, Masatoshi Kawai, Hatsumi Yamamoto, Yoshihiro Komada

Cellular Immunology 2014; 290: 89-95

主論文の要約

Introduction

In neonatal period, innate immune system plays a major role in infectious diseases and natural killer (NK) cells are important cellular components like other cells in innate immunity. Although NK cells have numerous activating and inhibitory receptors on their surface and are functionally controlled by ligands for these receptors, recent studies of NK cell regulation reported the interaction of $CD4^+CD25^+$ regulatory T (Treg) cells and NK cells.

Background

Treg cells are known to modulate NK cell function, but the immunological mechanism of cord Treg (cTreg) cells to regulate cord NK (cNK) cells is not fully clarified.

Objectives

The purpose of this study is to clarify the mechanism whereby cTreg cells modulate cNK cells.

Methods

The immunoregulatory function of cTreg cells, adult $CD4^+CD25^+$ Treg (aTreg) cells and soluble TGF-beta1 to NK cells were evaluated. After various cultures

of purified NK cells with or without autologous Treg cells, the expression of early activation marker CD69, production of IFN-gamma and TNF-alpha, cytotoxicity of NK cells were analyzed by flowcytometory and ELISA and Multiplex assay using luminex technology.

Results

Cord Treg cells represented significantly weaker potential to inhibit CD69 expression, cytokine production and cytotoxicity of cNK cells than adult. However, rhTGF-beta1 inhibited CD69 expression, cytokine production and cytotoxicity of both cNK and aNK cells. Since the relative percentage of $FoxP3^+$ cells, which is relevant to the potent suppressive function in cTreg cells, was higher than that of adult, the function of $FoxP3^+$ Treg cells might be responsible for explaining the suppressive potential of cTreg cells. Consequently, cTreg cells secreted lower concentrations of sTGF-beta1 than aTreg cells. The quantity of mTGF-beta1 on cTreg cells was also insufficient compared with adult.

Consideration

The rhTGF-beta1 inhibited CD69 expression, cytokine production and cytotoxicity of both cord and aNK cells. These data revealed that rhTGF-beta1 were responsible for reducing NK cell activity and are consistent with a former report that a sufficient dose of rhTGF-beta1 suppresses rhIL-2 induced adult and cord NK cell activation. Cord Treg cells secreted lower concentrations of sTGF-beta1 in the culture supernatant than aTreg cells secreted. The expression of mTGF-beta1 increased quickly on both cord and adult Treg cells with rhIL-2 activation as previously described. The quantity of mTGF-beta1 on cTreg cells was insufficient to suppress the activity of cord NK cells compared with aTreg cells in our study.

Conclusion

The reduced inhibitory effect of cTreg cells on cNK cells can be ascribed to reduced mTGF-beta1 expression and sTGF-beta1 secretion.