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Investigation of proliferation and cytotoxicity capacity of cytokine-induced killer cells: Omics strategy

Wenju Wang
Yan'an Hospital of Kunming City, China

Clinical trials of Cytokine-Induced Killer (CIK) cells based immunotherapy against cancer are widely performed in China. However, the mechanism of CIK cell proliferation and acquisition of cytolytic function against tumor have not been well elucidated yet. We compared the proliferation and tumor toxic capacity between CIK_{IL-2} and CIK_{IL-15}. By employing microarray, we analyzed miRNA expression profiles of PBMCs, CIK_{IL-2} and CIK_{IL-15}. Moreover, RNA-seq was performed to identify differentially expressed genes between CIK_{IL-2} and CIK_{IL-15}. The results indicated that CIK_{IL-15} showed improved cell proliferation capacity compared to CIK_{IL-2}. However, CIK_{IL-2} has exhibited greater tumor cytotoxic effect than CIK_{IL-15}. Bioinformatic analysis indicated that miR-143-3p/miR-145-5p was miRNA cluster which may positively regulated cell proliferation. In contrast, miR-340-5p/miR-340-3p cluster may negatively regulate cell proliferation via induction apoptosis, which may cause decreased cell proliferation capacity of CIKIL-2. Importantly, we found that repressed miR-193a-5p may regulate the expressions of inhibitory receptor KLRD1 which may restrict cytotoxic function of CIK. Employing deep sequencing, a total of 374 differentially expressed genes (DEGs) were identified. Among DEGs in CIK_{IL-15}, Wnt signaling and cell adhesion were significant GO terms and pathways which related with their functions. In CIK_{IL-2}, type I interferon signaling and cytokine-cytokine receptor interaction were significant GO terms and pathways. We found that inhibitory signal from interaction between CTLA4 and CD80 may be responsible for the weak proliferation capacity of CIK_{IL-2}. Our findings have provided new insights into mechanisms of CIK cells production and tumor cytotoxic function.

Biography

Wenju Wang has completed his PhD from Peking Union Medical College and Postdoctoral studies from Institute of Zoology, Chinese Academy of Science. He is an Associate Professor of Cancer Immunotherapy at Yan'an Hospital of Kunming City and Yunnan Cell Biology & Clinical Translation Research Center. Currently, his researches focus on developing novel antigen-specific immune cells against tumors.

wangwenju_vip@hotmail.com

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