Letter to Editor

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Letter to the Editor Regarding the NLR Member CIITA: Master Controller of Adaptive and Intrinsic Immunity and Unexpected tool in Cancer Immunotherapy

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ABSTRACT

Keywords: CIITA; NLR; MHC-II; Cancer Immunotherapy; Tumor Antigen Recognition; Antitumor Vaccine Strategies

Editorial

We read the article by Greta Forlani and Mariam Shallak, who introduced the NLR member CIITA as an unexpected tool for assessing adaptive and intrinsic immunity and cancer immunotherapy [1]. CIITA is a founding member of the NLR protein family [2]. The regulation of MHC-II gene expression is largely regulated at the CIITA and MHC-II levels, so it is critical to regulate MHC-II gene expression. This paper reveals the use of CIITA as a tool for inducing MHC-II gene and molecular expression in tumor cells, opening new possibilities for improving the recognition and characterization of tumor antigens and imaging realistic antitumor vaccine strategies. In a recent study in mice, Fabrizio Celesti demonstrated that MHC-II-positive GL261-CIITA tumor cells were rejected or that their growth was significantly reduced after intracranial implantation, further demonstrating the feasibility of this approach [3]. Unfortunately, this paper did not consider the relevant factors affecting CIITA expression. Among these factors, the two most important points are the influence of pathogens on CIITA expression and the regulatory effect of the MHC 2TA gene on CIITA expression, which need to be considered.

The first is related to the inhibition of CIITA expression by pathogens. In this field, Jorge Alfonso Leon Machado suggested that some pathogens can also inhibit CIITA expression, silencing CIITA to achieve the recognition and elimination of the host immune response. Salom and LeibundGut-Landmann further indicated that varicella zoster virus, human cytomegalovirus (CMV), and human parainfluenza virus type 3 (HPIV 3) inhibit IFN- and induced CIITA expression, and the HIV Dart protein can inhibit MHCII expression by interfering with CIITA function in HIV-infected or TAT-transfected fibroblasts and T-cell lines. None of the abovementioned cases of related pathogens affecting CIITA expression are mentioned in this paper [4,5]. If this method cannot be used to effectively cope with the impact of pathogens on CIITA when applied clinically, there is a large risk that this method may be useful. Second, there is growing evidence that failure to express MHCII is due to epigenetic silencing of the MHC 2 TA gene. In Salom'e LeibundGut-Landmann's article, it was clearly proposed that the activation and silencing of the MHC 2 TA gene have positive and negative effects on the expression of CIITA, respectively, and that the expression of CIITA is responsible for driving the activation of the MHCII gene. CIITA is regulated mainly at the transcriptional level of the MHC 2TA gene, so transcriptional control of the MHC 2TA gene determines the expression of CIITA and the expression level of the MHCII gene [4]. USF-1 is a ubiquitous factor needed to activate the MHC 2TA gene pIV, and the intracellular bacterium Chlamydia downregulates the expression of the MHC 2TA gene by inducing USF-1 degradation, thus affecting the function of CIITA and the expression of MHC molecules. Overall, the communication was excellent, opening up new possibilities for exploring the possibility of using CIITA as a tool to induce the expression of MHC-II genes and other molecules in tumor cells to increase the recognition and characterization of tumor antigens and to imagine realistic antitumor vaccine strategies. However, the factors influencing CIITA, especially the two important factors inhibiting CIITA expression, are still lacking, so further experiments are needed to verify CIITA as a tool for improving tumor immunogenicity.

Conflicts of Interest

The authors declare no conflicts of interest.

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