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Oral presentation

The Molecular and Cellular Basis of Tumor Rejection After Vaccination With Mammary Adenocarcinoma Cells Transduced With the MHC Class II Transactivator CIITA

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CD8+ T cell responses are major players of tumor eradication in various vaccination protocols. However, an optimal stimulation of CD4+ T helper cells is required for both priming and maintenance of the effector CTL response against the tumor. In this study we show that the murine mammary adenocarcinoma cell line TS/A, a highly malignant MHC-II-negative tumor, is rejected in vivo if genetically engineered to express MHC-II molecules by transfer of the MHC-II transactivator CIITA. TS/A-CIITA cells are fully rejected by 93% of the syngeneic recipients and have a significantly lower growth rate in the remaining 7% of animals. Rejection requires CD4+ and CD8+ cells. CD4+ T cells are fundamental in the priming phase, whereas CTLs are the major anti-tumor effectors. All tumor rejecting animals are protected against rechallenge with the parental TS/A tumor. Immunohistochemical data at day 5 post-inoculation showed an higher infiltrate of CD4+ T cells in mice bearing TS/A-CIITA, than in mice bearing the TS/A tumor. Subsequently, from day 7 trough day 10, TS/A-CIITA tumors showed higher number of both CD4+ and CD8+ cells, dendritic cells, together with massive necrosis. The frequency of IFN-α-secreting splenocytes early after inoculations was also assessed by an ex vivo ELISPOT assay. Only the rejecting TS/A-CIITA animals showed an high frequency of IFN-α-secreting cells (between 80 and 120/10^6 splenocytes). Importantly, CD4 and CD8 depletion experiments revealed that at the time of tumor resolution the major cell population recognizing the TS/A-CIITA cells was of CD4 origin. This is the first example of successful tumor vaccination by genetic transfer of CIITA. These results open the way to a possible use of CIITA for increasing both the inducing and the effector phase of the anti-tumor response.