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Immunomodulatory molecules in glioblastoma multiforme tissues and primary cells

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Immune modulation in the glioma microenvironment, which can play a pivotal role for outcomes of autologous DC-tumor vaccine adjuvant therapy (ADCTA) of glioblastoma multiforme (GBM). Our clinical investigation had been completed clinical studies of ADCTA Phase II trials in GBM patients, which can effectively prolong survivals via generating anti-tumor immune-activities by ADCTA. However, some GBM patients in the ADCTA trial represented strong immunosuppressive responses, which are considered as a key obstacle for the immunotherapeutic strategy. GBM-mediated immunomodulation is thought to be regulated by various immune factors, such as IL-10, TGF- β . Recently, glioblastoma stem cell (GSC) has been shown abilities to impair immune responses, modulate the microenvironment and differentiate into tumor-derived endothelial cells. In the present study, we found that Foxp3 could play a critical role in GBM cells. We had established the experimental foundation for this approach and enable a functional test of tumor-associated Foxp3 that may influence the activities of metastasis and/or tumor immunosuppression in GBM cells. High level of FOXP3 expression in tissues of GBM patients was exhibited a decreasing trend of survival. Primary GSCs were characterized into two subtypes, PN-GSC (CD133+) and MES-GSC (CD133-). In tumor-sphere cultures, FOXP3 was induced and expressed higher in PN-GSC than in MES-GSC.

It resulted in different morphology between two subtypes after 24 hours. In the meanwhile, tumor-related immunosuppressive molecules, IDO and TGF-beta, were induced in cultured PN-GSC. Furthermore, we have found an immunosuppressive molecule (PDL-1) associated with the survival of patients, which underwent the ADCTA immunotherapy. These results may help establish immediately feasible ADCTA modulations for GBM and other tumors, as well as to shed light on new mechanistic insights on how Treg function can be regulated.

Biography

Since 2008, Dr. Chiu has been recruited as an assistant professor of the Graduate Institute of Immunology at the China Medical University. He then joined in the field of immune cell-based therapy for malignant gliomas and collaborated with the clinical team in China Medical University Hospital. His interest is to address the molecular and cellular mechanistic explanations of major immune responses, with particular emphasis on understanding the immunomodulatory activity in the glioma immune therapy.

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