Preliminary Communication

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Immunotherapy

Is there any relationship between gene expression of tumor antigens and CD4+ T cells in multiple myeloma?

Aim: The present study aimed at correlating the expression of cancer/testis antigens (CTAs) with the expression of genes related to tumor-infiltrating T cells. **Materials & methods:** *MAGE-C1/CT-7*, *MAGEA3/6*, *NY-ESO-1*, *LAGE-1* and *GAGE* expression were evaluated in 46 bone marrow multiple myeloma (MM) aspirates by RT-PCR. Expression of *FOXP3*/*CTLA4* and *RORyt*, as markers for Tregs and Th17 cells, respectively, was investigated by quantitative PCR. **Results:** *MAGEC1/CT7* was expressed in 66% of MM samples. We did not find correlation between the presence of single CTA and expression of *CTLA4* or *RORyt* neither expression of CD4+ T-cell markers and the number of CTA simultaneously expressed in the tumor. However, we did observe a correlation between the percentage of plasma cells and the number of CTAs expressed in the patients' bone marrow. **Conclusion:** Although CTAs and immunomodulatory CD4+ T cells represent potential targets for immunotherapy in MM, we did not find association among expression of such genes in MM.

Keywords: cancer/testis antigen • multiple myeloma • Th17 • Treg

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Background

The identification of antigens expressed predominantly or exclusively by tumor cells has led to the implementation of clinical trials aiming at inducing or amplifying immune response to these targets in cancer patients [1]. In this context, cancer/testis antigens (CTAs) have been widely studied in various types of malignancies based on their tumor-restricted expression and immunogenicity. CTAs are considered promising targets for the development of antineoplastic immune therapies using, for example, autologous dendritic cells *ex vivo* sensitized by these antigens [2]. A study conducted by our group showed that *MAGEC1/CT7*, *MAGEA3/6*, *LAGE-1* and *NY-ESO-1* are good candidates for the immunotherapy in MM since 85% of MM patients evidence expression of at least one of these CTA in their bone marrow (BM) [3]. Furthermore, the expression of *MAGEC1/CT7*, the *GAGE* family of genes, and the number of CTAs simultaneously expressed by their myeloma cells seemed to have an unfavorable impact on the patients' overall survival [3].

Cytotoxic T lymphocyte-associated antigen 4 (CTLA4) is a coinhibitory molecule expressed by activated T cells and a subset of Tregs with a primary importance in maintaining immune homeostasis by downregulating T-cell costimulatory pathways and contributing to tolerance to self antigens [4]. The suppressive activity of Tregs is associated with the overexpression of *FOXP3*, a member of the forkhead/winged helix family, which acts as a transcriptional repressor. *FOXP3* expression in cancer cells have been correlated with poor antitumor effector response [5]. It is important to note that Treg depletion can increase antitumor immune effects [6], making this CD4+ T-cell subset a very interesting target for cancer immunotherapy. Conversely, Treg depletion carries an increasing risk of autoimmunity and self-tissue damage [6]. Th17 cells are another recently described CD4+ T-cell subset with immunoregulatory properties and these cells

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