

## CHARACTERIZATION OF ACTIVATED TUMOR-INFILTRATING B LYMPHOCYTES

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Tumor-infiltrating B-lymphocytes (TIL-B), expressing CD19<sup>+</sup> or CD20<sup>+</sup>, have been identified in several cancers. Although their presence frequently correlates with a positive clinical outcome, their heterogeneity and function are not well characterized.

*Aim:* To characterize the differentiation and activation status of TIL-B in lung and kidney tumors, and define their function.

*Methods:* PBMCs and TILs were isolated from same patients of lung or kidney cancer, and then stained for B cell differentiation and activation markers using flow cytometry (e.g. CD19, CD20, CD24, CD25, CD38, CD69, CD80, CD86, IgD) (n=5-10). In addition, B cells of cancer patients were *in vitro* cultured in simulating conditions (e.g. with sCD40L/IL-4) (n=5-7).

*Results:* Most circulating B cells were IgD<sup>+</sup> cells, including 5% transitional memory CD24<sup>++</sup> CD38<sup>++</sup> cells, while lung and kidney TIL-B were equally further differentiated, being IgD<sup>-</sup> (60-70%) (p<0.05). In addition, more CD69<sup>+</sup> and CD86<sup>+</sup> cells, and fewer CD95<sup>+</sup> expression is observed amongst IgD<sup>-</sup> TIL-B than circulating PBMCs (p<0.05), indicating the presence of recently activated B cells in the tumor. Increased activation is also supported by the presence of cytokine-producing cells and by the modulated expression of chemokine receptors (CXCR4, CCR6 and CCR10). In addition, we observed an enhanced expression of CD25, CD69, CD80 and CD86 (p<0.05), as activation markers, and the production of cytokines like TNF on *in vitro* cultured B cells.

*Conclusions:* B cells infiltrating tumors are more differentiated and activated when compared to circulating B cells in the same patient. Tumor-infiltrating B cells can be activated and expanded *in vitro*. Understanding the tumor-infiltrating B cells and standardizing method to expand competent B cells would promote the development of adoptive cell therapies against cancer.