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Title: Regulatory T, B cells and inflammation: Do they play an important role in lung cancer?

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Body: Increasing evidences indicate that regulatory T cells (Treg) and regulatory B cells (Breg) have the potent ability to suppress host immune responses and maintain peripheral tolerance, thus inhibiting antitumor immunity in the tumor microenvironment. Intratumoral and circulating Treg and Breg may play a significant role in the pathogenesis of lung cancer. We cocultured peripheral blood mononuclear cell (PBMC), which were from healthy donor, with A549 cell, a human alveolar adenocarcinoma cell line. Frequencies of Tregs and Bregs were measured by flow cytometry with antibodies against CD4, CD25, CD127, CD19, CD24, CD27 and IL-10 before, and after coculturing. We also used different doses of LPS as A549 stimulus to see whether the inflammatory tumor microenvironment would alter levels of Tregs and Bregs. After cocultured with A549, levels of CD19+CD24hiCD27+ Bregs in PBMC were significantly augmented while level of CD4+CD25+CD127- Tregs was obviously decreased. After cocultured with LPS-pre-stimulated A549, both the levels of Tregs and Bregs in PBMC were augmented, which amplified the immunosuppressive capacity. In addition, the FCM detection displayed an increase of IL-10, a mainly functional cytokine of Breg-mediated suppression. The mRNA expression of IFN-γ and TGF-β were significantly increased in the PBMC cocultured with A549 or the LPS-pre-stimulated A549. In addition, the mRNA expression of RANTES and MIP-α in the A549 also increased. Levels of Tregs and Bregs decreased when TLR4 on A549 and NF-κB pathway were blocked. Level of Bregs increased in lung cancer microenvironment. Inflammatory tumor microenvironment regulates levels of Tregs and Bregs in lung cancer.