Antitumor T cell responses in bladder cancer are directed against a limited set of antigens and are modulated by regulatory T cells and routine treatment approaches.

Abstract:
Regulatory T cells (Tregs) play a key role in cancer immune escape. We identified target antigens of spontaneous tumor-specific T cell responses in urothelial carcinoma (UC) and evaluated their modulation by treatment and Treg. We determined Treg target antigens in UC. Fifty-six UC and 13 control patients were prospectively enrolled. Blood was drawn before and after routine treatment. Changes in Treg frequency were measured by fluorescence cytometry and the T effector cell (Teff) response against a set of nine tumor-associated antigens (TAAs) was monitored with an interferon-gamma ELISpot. Antigen specificity of Treg was determined by their increased capacity to inhibit after TAA-specific activation the proliferation of an autologous T cell population. The highest difference in the overall response rate for the total T cell population was observed for epidermal growth factor receptor (EGFR) (UC: 23% and controls: 0%). After depleting Treg, also new york esophageal (NYES)O1 (19 and 0%) and MUC20 (27 and 0%) were more frequently recognized in UC patients. In metastasized patients, the TAA-directed T cell response was augmented by Treg depletion. Tumor resection seemed to diminish Treg
suppression of TAA-specific immunity, whereas chemotherapy had no effect. We demonstrated the existence of TAA-specific Treg in UC, which share antigen specificities with Teff. The coexistence of TAA-specific Treg and Teff was very rare. Treg frequencies in the peripheral blood were not changed by therapy. In summary, we identified potentially immunologically relevant TAA in UC. TAA-specific T cell responses against these antigens are suppressed by Treg. We identified TAA-specific Treg in UC patients, which do not cooccur with TAA-specific Teff.