Emerging role of Treg FOXP3 expression in cancer prognosis and autoimmune diseases

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Regulatory T cells (Tregs), were previously named suppressor T cells. Tregs are immunosuppressive cells that generally suppress the induction and proliferation of effector T cells, maintaining tolerance to self-antigens (1). Tregs express CD4, FOXP3, and CD25 (2). Both effector T cells and Tregs express CD4 and CD25, making it difficult to differentiate between them (3). Thus, FOXP3 expression was used to detect suppressor activity (4). Tregs are important in maintaining the immune cell homeostasis by enforcing a dominant negative regulation on other immune cells. Tregs are usually classified into natural Tregs CD4+CD25+ T-developing from thymus and induced Tregs which acquire CD25 (IL-2R alpha) expression outside of the thymus and are induced by inflammation and disease processes, like autoimmunity or cancers (5).

In patients having cancer, Tregs tend to be upregulated, and recruited to the site of the tumor. Studies have proved that Tregs suppress the tumor immunity mediated by the host defense (6). Most tumors induce an immune response in the host by tumor antigens, this causes large numbers of tumor-infiltrating lymphocytes (TILs) to be found in the tumor microenvironment slowing or terminating the tumor development (7). Tregs can make up as much as 20%-30% of the total CD4+ population around the tumor microenvironment (8). High levels of Tregs demonstrated by FOXP3 in the tumor microenvironment indicate poor prognosis in many cancers, like ovarian, breast, renal, and pancreatic cancer (9). In ovarian cancer, high FOXP3 expression was considered as an independent prognostic factor (10). It was also correlated with recurrence in patients of NSCLC at pathologic stage I (11).

On the other hand, in some types of cancer like colorectal carcinoma and follicular lymphoma high levels of Tregs were reported to be associated with good prognosis (12). Treg infiltration into the tumor microenvironment is facilitated by binding of the chemokine receptor CCR4, expressed on Tregs, to its ligand CCL22, which is secreted by many types of tumor cells. While the differentiation and expansion of Tregs is induced by TGF-β (12).

Regarding autoimmune diseases, high FOXP3 expression was correlated with disease activity in autoimmune diseases including lupus nephritis (13), oral lichen planus (14), and in synovial fluid for patients with active rheumatoid arthritis (15). A decrease in the number of Tregs in the peripheral blood of patients following organ transplantation correlates with decreased graft survival (16).

While graft survival following kidney transplant recipients was also improved in patients who maintained Treg levels one year after transplantation, other studies have shown conflicting findings (17).

These studies highlight the promising role of immunohistochemical evaluation of FOXP3 as a routine affordable marker in predicting disease activity of autoimmune diseases and as a prognostic marker for various types of cancer.
carcinoma.

The appearance of FOXP3 expression by immunohistochemistry and flow cytometry is illustrated in Figures 1 (18), 2 and 3.

Conflicts of interest
None to be declared.

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Marwa M Shakweer and Nadia M El-Sheshtawy wrote the manuscript equally.

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