Abstract:

Transforming growth factor (TGF-β) is a pleiotropic cytokine, secreted by immune and nonhematopoietic cells. TGF-β is involved in many different critical processes, such as embryonal development, cellular maturation and differentiation, wound healing, and immune regulation. It maintains immune homeostasis by acting as a potent immune suppressor through inhibition of proliferation, differentiation, activation, and effector function of immune cells. Paradoxically, depending on the context, it displays proinflammatory properties by being a potent chemoattractant for neutrophils and promoting inflammation. In addition, it does not only induce differentiation into the anti-inflammatory Treg cells, but also into the proinflammatory Th17 and Th9 cells and inhibits Th22 differentiation. TGF-β has been demonstrated to be involved in multiple pathologies. In infections, it protects against collateral damages caused by the immune system, but it also promotes immune evasion and chronic infections. In autoimmune diseases, a TGF-β dysfunction leads to the loss of tolerance to self-antigens. In cancer, TGF-β is a potent inhibitor of cell proliferation and acts as a tumor suppressor at the beginning of tumorogenesis. However, once the cells become resistant to TGF-β, it mainly supports tumor growth and metastasis by promoting immune evasion and angiogenesis. In asthma, it is assumed to promote allergen tolerance, but plays a detrimental role in irreversible...
remodeling of the airways. Despite the high numbers of TGF-β-targeted pathways, it is a promising drug target for treatment of autoimmunity, cancer, fibrosis, if cell specificity can be achieved. This review summarizes the progresses that have been accomplished on the understanding of TGF-β's signaling in the immune homeostasis and its role in pathogenesis.