

Editorial

Transforming growth factor beta (TGF β) signaling pathway is one of the key players during embryogenesis and maintaining tissue homeostasis [1]. Activated TGF β binds to its receptor and regulates transcription, translation, miRNA biogenesis, protein synthesis and post-translational modifications through canonical SMAD and non-SMAD pathways ultimately mediating cell proliferation, differentiation, apoptosis, adhesion, invasion and cellular micro-environment [2-4]. Alterations in TGF β signaling lead to tumor initiation and progression. For over three decades of research since its discovery, researchers found that TGF β has diverse and contrasting functions as tumor suppressor and tumor promoter [5,6]. One of the key mechanisms by which TGF β elicits its tumor suppressive functions is by simultaneously inhibiting the CDK functions and eliminating proliferative drivers [7]. However, it has to be noted that TGF β is not a universal proliferation regulator and exerts its anti-proliferative actions depending upon the context [6]. It has been shown that it is a powerful growth inhibitor in cells that lack either p15Ink4b or the c-Myc response alone and results in effective evasion of cytostasis upon combined loss of these two genes [8-11]. Cancer cells that bypass the anti-proliferative effect of TGF β take advantage of its immunosuppressive, pro-angiogenic and epithelial-mesenchymal transdifferentiation in order to establish and gain control over the surrounding cellular environment [12-14]. Evidence from several animal studies implicated that it has also a role in bone and lung metastasis [15,16].

Several studies showed that TGF β can have potent tumor suppressive properties in early stages of cancer but switches to tumor promoting nature at later stages [17-19]. Therefore therapies targeting TGF β should be cautious as the timing of the treatment is very critical. However, the precise molecular mechanisms determining when the TGF β switches from a tumor suppressor to promoter poses a great challenge in the field. Recent studies have showed that host immune cells play a critical role in switching the activity of TGF β [20,21]. Genetic abrogation of TGF β signaling specifically in myeloid cells resulted in reduction of bone and lung metastasis in an in vivo mouse model system [20,21]. These two studies have unequivocally suggested that specific targeting of TGF β signaling in myeloid cells reduces tumor metastasis.

Currently, multiple drugs have been developed targeting TGF β . The three major approaches that took into consideration while designing the drugs include: prevention of TGF β synthesis (using antisense molecules), inhibition of binding to cell membrane receptor (using neutralizing monoclonal antibodies or trapping TGF β ligand with soluble receptors), and inhibition of receptor mediated signaling (TGF β receptor kinase inhibitors) [6]. As mentioned Hata A, Davis M (2009) Control of microRNA biogenesis by TGFbeta signaling pathway-A novel role of Smads in the nucleus. *Cytokine Growth Factor Rev* 20: 517-521.

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