Editorial

Transforming growth factor beta (TGF) signaling pathway is one of the key players during embryogenesis and maintaining tissue homeostasis [1]. Activated TGF binds to its receptor and regulates transcription, translation, miRNA biogenesis, protein synthesis and post-translational modi cations through canonical SMAD and non-SMAD pathways ultimately mediating cell proliferation, di erentiation, apoptosis, adhesion, invasion and cellular micro-environment [2-4]. Alterations in TGF signaling lead to tumor initiation and progression. For over three decades of research since its discovery, researchers found that TGF has diverse and contrasting functions as tumor suppressor and tumor promoter [5,6]. One of the key mechanisms by which TGF 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 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 e ective evasion of cytostatis upon combined loss of these two genes [8-11]. Cancer cells that bypass the anti-proliferative e ect of TGF take advantage of its immunosuppressive, pro-angiogenic and epithelial-mesenchymal transdi erentiation 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 can have potent tumor suppressive properties in early stages of cancer but switches to tumor promoting nature at later stages [17-19]. erefore therapies targeting TGF should be cautious as the timing of the treatment is very critical. However, the precise molecular mechanisms determining when the TGF switches from a tumor suppressor to promoter poses a great challenge in the eld. Recent studies have showed that host immune cells play a critical role in switching the activity of TGF [20,21]. Genetic abrogation of TGF signaling speci cally in myeloid cells resulted in reduction of bone and lung metastasis in an in vivo mouse model system [20,21]. ese two studies have unequivocally suggested that speci c targeting of TGF signaling in myeloid cells reduces tumor metastasis.

Currently, multiple drugs have been developed targeting TGF . e three major approaches that took into consideration while designing the drugs include: prevention of TGF synthesis (using antisense molecules), inhibition of binding to cell membrane receptor (using neutralizing monoclonal antibodies or trapping TGF ligand with soluble receptors), and inhibition of receptor mediated signaling (TGF receptor kinase inhibitors) [6]. As ment

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