Three members of transmembrane-4-superfamily, tm4sf1, Tm4sf4, and tm4sf5, as emerging anticancer molecular Targets against cancer phenotypes and chemoresistance

ABSTRACT

There are six members of the transmembrane 4 superfamily (TM4SF) that have similar topology and sequence homology. Physiologically, they regulate tissue differentiation, signal transduction pathways, cellular activation, proliferation, motility, adhesion, and angiogenesis. Accumulating evidence has demonstrated, among six TM4SF members, the regulatory roles of transmembrane 4 L6 domain family members, particularly TM4SF1, TM4SF4, and TM4SF5, in cancer angiogenesis, progression, and chemoresistance. Hence, targeting derailed TM4SF for cancer therapy has become an emerging research area. As compared to others, this review aimed to present a focused insight and update on the biological roles of TM4SF1, TM4SF4, and TM4SF5 in the progression, metastasis, and chemoresistance of various cancers. Additionally, the mechanistic pathways, diagnostic and prognostic values, and the potential and efficacy of current anti-TM4SF antibody treatment were also deciphered. It also recommended the exploration of other interactive molecules to be implicated in cancer progression and chemoresistance, as well as potential therapeutic agents targeting TM4SF as future perspectives. Generally, these three TM4SF members interact with different integrins andreceptors to significantly induce intracellular signaling and regulate the proliferation, migration, and invasion of cancer cells. Intriguingly, gene silencing or anti-TM4SF antibody could reverse their regulatory roles deciphered in different preclinical models. They also have prognostic and diagnostic value as their high expression was detected in clinical tissues and cells of various cancers. Hence, TM4SF1, TM4SF4, and TM4SF5 are promising therapeutic targets for different cancer types preclinically and deserve further investigation.