Knockdown of the oncoprotein, SS18–SSX1, Suppresses Cell Growth and Metastasis in the Protein Kinase B-Dependent Signaling Pathway in Synovial Sarcoma

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Background: Synovial sarcoma (SS) is a malignant soft tissue tumor characterized by a unique translocation t (X;18), generating synovial sarcoma translocation (SS18) oncoprotein, such as SS18-synovial sarcoma X (SSX)1 and SS18–SSX2. Although SS18-SSX1 plays a critical role in the formation of SS, the detailed molecular mechanisms underlying the oncogenic potential of SS18-SSX1 are not entirely clear.

Methods:

Results: Inhibition of SS18-SSX1 with a lentiviral vector effectively decreased cell proliferation, colony formation, cell invasiveness, and tubule formation by the SS cell line HS-SYN-II. Mechanistic investigations suggested that down-regulation of SS18-SSX1 significantly suppresses the expression of phosphorylated-protein kinase B (p-AKT), phosphorylated-extracellular-signal-regulated kinases (p-ERK)1⁄2, vascular endothelial growth factor, matrix metalloproteinase (MMP)-2, and MMP-9 as detected by Western blotting. Further studies of the identified perturbed pathways revealed that the AKT pathway is involved in SS18-SSX1-mediated cell invasiveness.

Knockdown of SS18-SSX1 *in vivo* inhibited proliferation and invasive activity of SS cells in a mouse xenograft tumor model.

Conclusions: Our findings suggest that SS18-SSX1 is a direct oncogenic target for therapeutic intervention and that SS18-SSX1 activated ERK and phosphatidylinositol-4,5-bisphosphate 3-kinase/AKT pathways and SS18-SSX1-enhanced cell invasion is dependent on the AKT pathway.