The roles of lncRNAs in cancer malignancies and autophagy regulation

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LncRNAs represent the emerging class of macromolecules that elicit profound impacts on diverse biological processes and disease states. Targeting disease-relevant lncRNAs is therefore a new and promising strategy in precision medicine. We identify lncRNA *Smyca* for its association with poor prognosis of many cancer types. *Smyca* potentiates metabolic reprogramming, migration, invasion, cancer stemness, metastasis and chemoresistance. Mechanistically, *Smyca* enhances TGF-□/Smad signaling by acting as a scaffold for Smad3/4 complex and a guide for its promoter recruitment, and serves as a Smad target to further amplify and prolong TGF-□ signaling. Additionally, *Smyca* potentiates c-Myc signaling by guiding Myc/Max complex to its target genes. Through co-activating TGF-□ and Myc pathways, *Smyca* synergizes the Warburg effect elicited by both pathways but evades the anti-proliferative effect of TGF-□. Targeting *Smyca* by nanoparticle-assisted gapmer antisense oligonucleotides delivery prevents metastasis and chemoresistance, two major causes of cancer patient mortality. With respect to autophagy regulation, we identify the function of lncRNA *BCRP3* as a RNA activator of VPS34 complex. With this mechanism, *BCRP3* promotes autophagy/aggrephagy to support cell viability and proliferation in response to proteotoxic stresses.