Identification of prognostic noncoding RNA-mediated networks disclose PTTG3P/FOXM1/BUB1B oncogenic signaling pathway in lung adenocarcinoma

Yuh-Shan Jou, Ph.D.

Institute of Biomedical Sciences, Academia Sinica

Prognostic noncoding RNA (ncRNA) based network prediction is necessary to understand unrevealed functions and mechanisms of ncRNAs for serving as theranostic targets to improve therapeutic intervention in cancers. Here, we established a systemic pipeline to uncover prognostic ncRNAs and explore pathological mechanisms based on lung adenocarcinoma (LUAD), the predominant subtype of the most common cause of human cancer death worldwide. After *in silico* and experimental validations involving evaluations of prognostic value in multiple cohorts, we prioritized PTTG3P pseudogene from other prognostic ncRNAs (MIR497HG, HSP078, TBX5-AS1, LOC100506990, C14orf64) for mechanistic studies. Up-regulation of PTTG3P shortened the metaphase to anaphase transition in mitosis, increased cell viability after cisplatin or paclitaxel treatment, sustained tumor growth leading to poor survival in lung orthotopic models, as well as being associated with poor survival rate in LUAD patients who received chemotherapy in TCGA cohort. Our results further indicated that PTTG3P as an ncRNA might collaborate with transcription factor FOXM1 to regulate the transcriptional activity of mitotic kinase BUB1B to facilitate tumor growth and its chemo-resistance leading to poor outcomes of LUAD patients. Together, we established a systematic strategy to uncover driving prognostic ncRNAs and confirmed that up-regulated PTTG3P/ FOXM1/BUB1B axis could be the theranostic target for LUAD patients, which could be applied to pan-cancer studies.