

“Targeting cancer signaling nodes to overcome metastasis and chemotherapy resistance”

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Metastatic or therapy resistant cancers are often considered incurable. Although dysregulated metabolism and kinase signaling have been demonstrated in cancer cells, the precise mechanism remains unclear. We performed transcriptomics screen and identified GDH1 as a critical metabolic factor which provides anti-anoikis and pro-metastatic signals through activating CamKK2 and AMPK that promotes tumor metastasis in lung cancer. Targeting GDH1 with a GDH specific inhibitor R162 attenuated tumor metastasis in mice. We also performed cisplatin synthetic lethal partner screen using kinome shRNA library and identified MAST1 as a promising target to overcome cisplatin resistance. Mechanistically, we demonstrated that cisplatin dissociates cRaf from MEK1 to inhibit the MAPK pathway and identify MAST1 as a main cisplatin resistance driver that replaces cRaf to reactivate the MAPK pathway. Through a drug repurposing study, lestaurtinib was identified as a MAST1 inhibitor. Lestaurtinib effectively inhibits MAST1 kinase activity and cancer cell proliferation in combination with platinum-based compounds including cisplatin and carboplatin.

Biography: Dr.Kang's research has focused on how intricate molecular communication networks evolve to control cell growth, survival, and proliferation in cells, and how disruption of these processes leads to cancer, with a particular focus on the role of cellular protein kinase signaling and metabolic reprogramming in tumorigenesis, tumor metastasis, and chemotherapy resistance in human cancers. The findings have been published in journals including *Cancer Cell*, *Nat Cell Biol*, *Mol Cell*, *J Clin Invest*, and *Oncogene*.

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