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Development of multi-pathway inhibitor screening system to combat the existing combinations of signaling dysregulations in gastric cancer

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Despite being the leading cause of cancer death, targeted therapy for gastric cancer is yet to be established. Through a comprehensive signaling profiling in gastric cancer cell lines, we have identified the activation of multiple oncogenic signaling pathways in all cell lines in an unbiased manner. In parallel, this observation is also found true in primary tumors by integrative functional genomics investigation. This warrants the need for developing therapeutic agents capable of targeting multiple oncogenic signaling processes. Wnt/β-catenin signaling pathway is one of the frequently dysregulated signaling in gastric cancers and first, we developed a gastric cancer cellular assay system for Wnt pathway modulator screening and identified several molecules capable of inhibiting Wnt/β-catenin signaling pathway. The identified compounds were further screened for their other pathway targeting potential by mRNA profiling and signaling activity profiling. We have identified a class of molecules capable of inhibiting STAT3, IRF1, MAPK, NOTCH and RXR signaling apart from inhibiting Wnt/β-catenin-Myc-E2F signaling cascade. Signaling pathway focused analysis of gastric cancer transcriptome reveals that Wnt, STAT3, IRF1, MAPK, NOTCH and RXR signaling pathways are indeed highly deregulated in majority of gastric tumors and indicates the possible candidacy of the identified compounds for targeted gastric cancer therapeutics. The talk will describe the features of our comprehensive signaling profiling approach, advantages of the developed screening system and the outcome of our investigation towards developing combinatorial and targeted gastric cancer therapeutics.

Biography

Kumaresan Ganesan has completed his Ph.D. from Madurai Kamaraj University, India and did his postdoctoral studies at University of Texas M.D. Anderson Cancer Centre, Texas and National Cancer Centre, Singapore. At present, he is Associate Professor of Department of Genetics, School of Biological Sciences, Madurai Kamaraj University, India. He is leading the cancer genomics group and dissecting the complex transcriptional regulations in stomach, liver and breast cancers by integrative functional genomics approaches. He has developed pathway focused screening system and identified potential therapeutic candidates for targeted and combinatorial cancer therapeutics. He has published more than 15 papers in reputed journals and is the principal investigator of several Cancer Genomics research projects.

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