AI-guided identification and validation of a target for differentiation therapy in colon cancer

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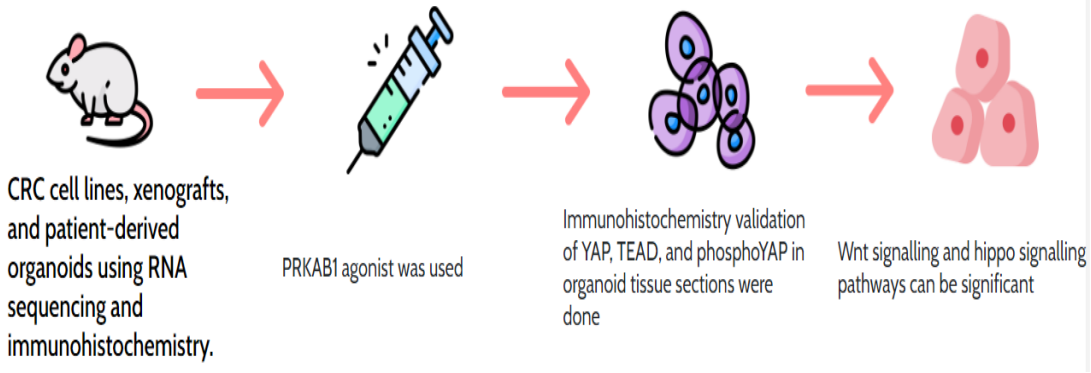
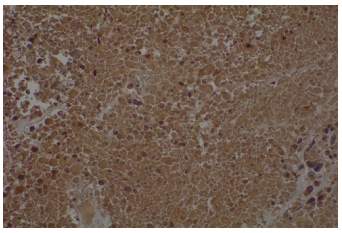
Graphical Abstract

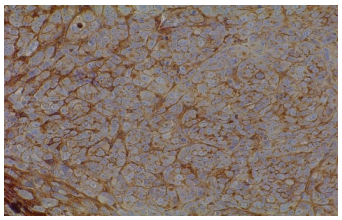


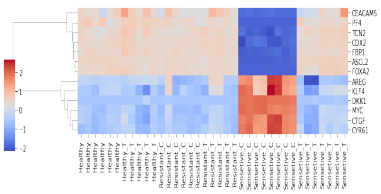
Project Description:

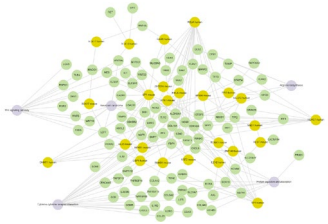
This study investigates the mechanism of action of a PRKAB1 agonist drug identified by artificial intelligence methods, in enhancing differentiation in colorectal cancer (CRC). Preliminary findings suggest CDX2 reinstatement as a key factor. To elucidate this process, researchers analyzed differentially expressed genes in CRC cell lines, xenografts, and patient-derived organoids using RNA sequencing and immunohistochemistry. Transcriptomics data analysis revealed significant changes along the stemness-differentiation axis. Integrated transcription factor and functional enrichment analysis implicated Wnt and Hippo signaling pathways. Immunohistochemistry validation of YAP, TEAD, and phosphoYAP in organoid tissue sections supported these findings. The study sheds light on the molecular mechanisms underlying the drug's potential therapeutic effects in CRC, highlighting CDX2 reinstatement and Wnt and Hippo signaling signaling pathway modulation as crucial factors.

Products/ Instruments/ Results/ Outreach Activities









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Name of the Funding Agency
Science & Engineering Research Board (SERB)

Name of the Scheme
Science & Engineering Research Board International Research experience (SIRE)

Sanctioned Amount (in Rupees)
Rs. 18,12,014

Duration of the Project (years)
0.6