Huretro Medical &Life Science Seminar, AY2025

Experimental Targeting of the Splicing Machinery: Inhibiting Aberrant Splicing & Regulators for Cancer Control

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Venue: Seminar room (2F)

Joint Research Center for Human Retrovirus Infection

Alternative splicing increases proteomic diversity by producing multiple mRNA or protein isoforms from a single gene. Dysregulation of this process can generate aberrant splice variants that drive cancer development. Growing evidence shows that splicing errors in key oncogenes often stem from abnormal activity of splicing factors, SRSFs, which are regulated by upstream kinases such as SRPKs and CLKs. Inhibitors of these kinases, including SRPIN340 and SPHINX31 (SRPK inhibitors) and TG003 (CLK inhibitor), are useful tools for exploring splicing-based therapeutic strategies. In our study, we identified oncogenic splice variants that promote tumor progression. Functional assays using gene silencing and isoform overexpression demonstrated their essential roles in cancer cell growth and survival. Moreover, genetic and pharmacological inhibition of splicing factors and their regulatory kinases produced strong anti-cancer effects in cholangiocarcinoma, melanoma, and glioma. Overall, our findings underscore the critical role of alternative splicing in cancer and support splicing-targeted interventions as a promising therapeutic approach.

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