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The study is featured in the current issue of the Journal of Clinical Investigation.

A cancer cellâ€™s â€œhyperexcitabilityâ€ is a critical feature of disease. Thus, the ability of cancer cells to be â€œpromiscuousâ€ and grow rapidly in large numbers despite signaling failures of molecular activators of cell signaling has been implicated in tumour aggressiveness. â€œHowever, as yet there is no successful means of regulating cellular hyperexcitability,â€ said senior study author Gayathri Chadalapaka, PhD, associate professor in molecular medicine at UCSF.

To demonstrate that selective transcription factors can trigger tumor cell hyperexcitability, Chadalapaka and her colleagues used high sensitivity cellular proteasome assays on human anaplastic lymphoma kinase (ALK) tumors. The ASP assay revealed that selectors could change the ability of a cellâ€™s DNA content to promote the expression of certain signal transduction proteins with the ability to promote proteasome activity.

The authors then identified three selectors that could lead to the hyperexcitability of tumors. They showed that ALK4 could dampen cell hyperexcitability, and added that ALK4 inhibiting transcription factors CD133A, CD133B and CD133CS could induce tumor hyperthermia, cooling the tumor cell nucleus and thus reducing tumor growth and prognosis. Chadalapaka cautioned that further studies are needed to test these selectorsâ€™ anti-tumor effects in vitro and in animal models.

Seep Sreevalsan, PhD, who was the lead author of the study, and fellow investigators also at UCSF as well as at the University of Edinburgh in the UK, collaborated on the study.

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A Black And White Photo Of A Black And White Cat