REGIONAL CENTRE FOR BIOTECHNOLOGY
Journal Club

Aurora kinases A and B are up-regulated by Myc and are essential for maintenance of the malignant state

Jürgen den Hollander et al.(2010) Blood, 116, 1498-1505.

Deepak Singh

Wednesday, February 6, 2013
4:00 pm
Seminar Room

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Myc oncoproteins promote continuous cell growth, in part by controlling the transcription of key cell cycle regulators. Here, we report that c-Myc regulates the expression of Aurora A and B kinases (Aurka and Aurkb), and that Aurka and Aurkb transcripts and protein levels are highly elevated in Myc-driven B-cell lymphomas in both mice and humans. The induction of Aurka by Myc is transcriptional and is directly mediated via Eboxes, whereas Aurkb is regulated indirectly. Blocking Aurka/b kinase activity with a selective Aurora kinase inhibitor triggers transient mitotic arrest, polyploidization, and apoptosis of Myc-induced lymphomas. These phenotypes are selectively bypassed by a kinase inhibitor-resistantAurkb mutant, demonstrating that Aurkb is the primary therapeutic target in the context of Myc. Importantly, apoptosis provoked by Aurk inhibition was p53 independent, suggesting thatAurka/Aurkb inhibitors willshow efficacy in treating primary or relapsed malignancies having Myc involvement and/or loss of p53 function.