Aurora Kinases: Potential Therapeutic Targets in K-Ras-Induced Lung Cancer

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K-Ras-induced lung cancer is a very common disease, for which there are currently no effective therapies. Intense efforts are underway to identify K-Ras targets that play a crucial role in oncogenesis. We have previously shown that K-Ras-induced lung tumorigenesis is potentiated by the transcription factor NF-κB; and recently others have shown that the Aurora kinases, not only play a significant role in tumorigenesis, but also can activate NF-kB. Therefore we hypothesized that Aurora A and/or B are important targets of K-Ras in lung cancer. To test this hypothesis, we first determined how K-Ras levels in lung cells affect Aurora kinase expression. For that purpose we used three different cell-based models: (1) an immortalized primary lung epithelial cell line and its isogenic K-Ras-transformed counterpart, (2) a lung cancer cell line engineered to express K-Ras inducibly, and (3) K-Ras positive cancer cell lines with K-Ras inhibition by RNAi. In all cases, K-Ras expression positively correlated with Aurora A/B expression. Next we used genetic and pharmacological approaches to inactivate Aurora A or B in the abovementioned cells to investigate how Aurora kinase inhibition affects oncogenic properties in vitro. Treatment with a dual Aurora A and B inhibitor reduced cell growth, the ability of cells to form colonies, blocked the cell cycle at G1 and reduced viability. RNAi-mediated knockdown of Aurora A or B resulted in diminished viability and proliferation. In conclusion, our results support our hypothesis and suggest Aurora kinase inhibition as a novel therapeutic approach in K-Ras-induced lung cancer.

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