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The role of RNF20 in lung cancer metastasis

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Lung cancer is the second most commonly diagnosed cancer but remains the leading cause of cancer-related death globally. Therefore, a better understanding of the molecular mechanisms responsible for lung cancer initiation and progression is crucial for attenuating the risk of cancer-related deaths.
In our present study, we uncover that RNF20, an E3 ligase that specifically monoubiquitylates histone H2B at lysine 120, serves as a tumor suppressor in lung cancer. We found that mice with a single allele depletion of RNF20 has a higher incidence of lung tumor formation, with morphological characteristics of adenocarcinoma and small-cell lung cancer, indicating that RNF20 loss promotes lung cancer initiation. Consistent with these data, we observed that RNF20 expression level is significantly lower in human lung cancer tissues compared to normal lung tissues. Furthermore, its expression level is negatively associated with lung cancer stage and patients' overall survival rate. Mechanistically we found that RNF20 haploinsufficiency results in defective DNA repair and accumulation of DNA damage. Further, RNF20 loss results in significantly decreased p53 and Rb expression in both mouse and cell culture models. Moreover, RNF20 depletion induces epithelial-mesenchymal transition (EMT) and facilitates cell migration and proliferation. RNA-seq analysis of epithelial and neuroendocrine cells from lung tissues revealed that RNF20 loss induces cell cycle-associated gene expression, while repressing genes involved in cell adhesion and extracellular matrix organization.
Altogether, our data demonstrate that RNF20 functions as a tumor suppressor in lung cancer development and progression.