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A new lung cancer mouse model

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Lung cancer is the leading cause of cancer mortality worldwide. Lung squamous cell carcinoma (SCC), a major type of human lung cancer, has not well been recapitulated in mice. Here, we report that kinase-dead IKK α knock-in mice develop spontaneous lung SCCs associated with IKK α downregulation and marked pulmonary inflammation. In an epigenetic manner, IKK α reduction upregulated the expression of p63, Trim29, and keratin 5 (K5), which serve as diagnostic markers for human lung SCCs. IKK α^{low} K5⁺p63^{hi} cell expansion and SCC formation were accompanied by inflammation-associated deregulation of oncogenes, tumor suppressors, and stem cell regulators. Reintroducing transgenic K5.IKK α , depleting macrophages, and reconstituting irradiated mutant animals with WT bone marrow (BM) prevented SCC development, suggesting that BM-derived IKK α -mutant macrophages promote the transition of IKK α^{low} K5⁺p63^{hi} cells to tumor cells. This mouse model resembles human lung SCCs, sheds light on the mechanisms underlying lung malignancy development, and identifies targets for therapy of lung SCCs.

Biography

Yinling Hu did her undergraduate degree in Chinese Academy of Medical Science and received PhD from University of Melbourne at Australia. She was a Postdoctoral fellow in Michael Karins laboratory, University of California at San Diego from 1996 to 2001. She began to establish her laboratory as an Assistant Professor at Science Park Research Division, M.D. Anderson Cancer Center in November 2001 and came to NCI-Frederick as a Principal Investigator in September 2008..

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