THE RETINOBLASTOMA GENE: ITS ROLE IN RETINAL TUMORS AND NON-OCULAR TUMORS

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Tumors form through loss of adequate growth control. This growth control can be achieved in two ways. Inappropriate activation of growth stimulatory pathways define the nature of dominant oncogenes. These pathways have been preliminarily defined by two dozen or so dominant oncogenes. There is an alternative pathway that is also able to bring about deregulated growth. It is also possible to form tumors by inactivating growth limiting genes. Our work has focused on the isolation and characterization of these growth limiting genes that are termed recessive oncogenes. This term refers to the fact that both copies of these genes must be inactivated for tumor formation. We isolated the first of the recessive oncogenes. It is termed the retinoblastoma gene, "Rb gene", because it was first noted to be inactivated in retinoblastomas. Since then we have found that it is a vital step in the function of several other tumors. It is virtually always inactivated also in osteosarcomas, soft tissue sarcomas and small cell lung cancer.
The second recessive oncogene to be identified is the p53 gene. Both p53 and the Rb gene encoded nuclear phosphoproteins that regulate the cells progression through the cell cycle. We have found that reintroduction of both of these genes on expression constricts can severely limit cell growth. The current working model is that there are several dozen recessive oncogenes that are important for controlling the growth of separate organs. Combinations of these genes make tissue specific requirements for growth. Our goal is to better understand how these recessive oncogenes and dominant oncogenes cooperate functionally to bring about cancer.

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