

Novel model of osteosarcoma

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In the June 15th issue of G&D, Dr. Stuart Orkin (HHMI, Dana-Farber Cancer Institute, Children's Hospital Boston) and colleagues present a new mouse model of osteosarcoma.

Osteosarcoma is the most common type of malignant bone cancer, and one of the most lethal: The 5-year survival rate is only about 60%, and this statistic drops steeply once the cancer spreads. Osteosarcoma results from the dysregulated growth of osteoblasts (the cells that form the bone matrix). It primarily develops near the ends of the femur, tibia or humerus, and is usually diagnosed during adolescence, when the long bones of the body are undergoing rapid growth.

While the precise causes of osteosarcoma are unknown, it is evident that two tumor suppressor genes – p53 and Rb – are involved, as children with familial mutation syndromes affecting either of these genes have higher incidences of osteosarcoma.

Dr. Orkin's team has developed a novel experimental system to model the genetics of human osteosarcoma. The researchers generated a strain of transgenic mice lacking specifically the p53 and Rb genes in an early osteoblast progenitor cell population. All mutant animals rapidly developed osteosarcomas, with clinical, histo-cytological and molecular features closely recapitulating the human disease.

The scientists concluded that p53 loss is essential for the development of osteosarcoma, and that while Rb gene mutation acts synergistically with p53 loss to facilitate carcinogenesis, loss of Rb, alone, is not sufficient to

induce osteosarcomagenesis.

Ultimately, this high-fidelity animal model will further elucidate the genetic contributions to osteosarcoma, and enable researchers to rationally design and test new therapies. Dr. Orkin is hopeful that "our work will stimulate translational efforts to develop novel therapies for this devastating bone tumor".

Source: Cold Spring Harbor Laboratory

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