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Guest Editors

Dr Ronald A DePinho

Dr DePinho has been a leader in the use of the mouse to dissect the molecular mechanisms and biological processes governing the genesis and maintenance of tumorigenesis. His studies on the Myc oncoprotein have led to insights into how physical and functional interactions among members of the Myc superfamily (Myc, Max and Mad) regulate the growth and development of normal and neoplastic cells. The demonstration that Mad family members act to repress transcription and suppress cancer *in vivo*, along with his discovery of the mSin3 co-repressor complex and its link to chromatin regulators, have defined a mechanistically distinct tumor suppressor pathway. His analysis of the functional relationship between Rb and p53 and, more recently, p16INK4a and p19ARF proteins, have demonstrated an intimate link between pathways that control cell cycle entry and those that regulate apoptosis. Dr DePinho and his colleagues have also led efforts to understand the role of telomerase in cancer, development and aging, and how telomere dynamics inter-relate to DNA damage and recombination pathways. More recently, he and his colleagues have constructed inducible cancer models that have permitted an *in vivo* analysis of the complex symbiotic host-tumor cell communications that are central to tumor maintenance.

Dr Tyler Jacks

Dr Jacks has been a leader in the use of gene targeting in cancer research. Over the past ten years, he and his laboratory have developed mouse strains with mutations in several cancer-associated genes. The characterization of these strains has led to the development of animal models of human familial cancer syndromes, numerous discoveries regarding the roles of these genes in normal development and novel insights into the relationship between gene function in embryogenesis and tumorigenesis. Dr Jacks has also pioneered the use of cells derived from such mutant strains as a means of addressing gene function *in vitro*. This approach has been utilized successfully to demonstrate altered cell cycle characteristics in cells lacking members of the pRB family, p53 or p21 function and enhanced growth/differentiation factor sensitivity in cells mutant for Nf1. Of particular clinical importance, Dr Jacks and his colleagues have discovered that certain p53-deficient cells are resistant to apoptosis in response to exposure to DNA-damaging agents and other conditions. This discovery led to their demonstration that the effectiveness of a broad range of chemotherapeutic agents could be modulated by the p53 status of tumor cells, both *in vitro* and *in vivo*. Moreover, Dr Jacks and colleagues have shown that p53-dependent apoptosis can eliminate abnormal cells in the developing embryo and during tumor progression, results that help account for the high frequency of p53 mutation in human cancer. Current research in the Jacks laboratory is focused on the refinement of several mouse tumor models, the process of functional overlap and its implications for development and tumorigenesis, and the mechanism of p53-dependent apoptosis.