Tumor suppressors: enhancers or suppressors of regeneration?

Journal: Development

Publication Year: 2013

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PubMed link: 23715544

Funding Grants: Molecular Mechanisms of Reprogramming towards Pluripotency

Public Summary:
Regeneration of complex tissues and organs after injury requires extensive cellular proliferation that is precisely regulated and executed in concert with differentiation and patterning mechanisms that preserve the organization of tissues within an organ. How this occurs with high fidelity, on both large and small scales, is matched in sophistication and complexity only by organ generation during development. Neoplasia represents a loss of control or absence of these processes of proliferation or differentiation, respectively. Tumor suppressor genes, initially identified because they are inactivated in mammalian tumors, were subsequently shown experimentally to protect against neoplastic transformation, and are now known to have a long evolutionary history with the ability to regulate diverse and fundamental cellular processes, including growth and division, genome maintenance, differentiation, metabolism and death. Many tumor suppressor genes play crucial roles during normal development and postnatal life that are more likely to explain why they evolved than does their role in protection from tumors. The pervasiveness of tumor suppressor gene function extends to include the context of tissue regeneration. The diverse functions of the tumor suppressors discussed in this Hypothesis article defy the simple model that tumor suppressors restrict proliferation, are therefore anti-regeneration, and can be bluntly targeted to enhance regeneration. Instead, from the available regeneration data reviewed here along with known functions in relevant contexts such as development and postnatal metabolic regulation, we conclude that tumor suppressors in general support regenerative processes.

Scientific Abstract:
Tumor suppressors are so named because cancers occur in their absence, but these genes also have important functions in development, metabolism and tissue homeostasis. Here, we discuss known and potential functions of tumor suppressor genes during tissue regeneration, focusing on the evolutionarily conserved tumor suppressors pRb1, p53, Pten and Hippo. We propose that their activity is essential for tissue regeneration. This is in contrast to suggestions that tumor suppression is a trade-off for regenerative capacity. We also hypothesize that certain aspects of tumor suppressor pathways inhibit regenerative processes in mammals, and that transient targeted modification of these pathways could be fruitfully exploited to enhance processes that are important to regenerative medicine.