FEATURES

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HIFs, Angiogenesis, and Cancer

967

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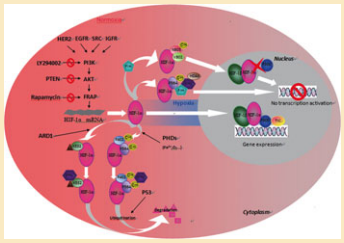
Tumor hypoxia was first described in the 1950s by radiation oncologists as a frequent cause of failure to radiotherapy in solid tumors. Today, it is evident that tumor hypoxia is a common feature of many cancers and the master regulator of hypoxia, hypoxia-inducible factor-1 (HIF-1), regulates multiple aspects of tumorigenesis, including angiogenesis, proliferation, metabolism, metastasis, differentiation, and response to radiation therapy. Although the tumor hypoxia response mechanism leads to a multitude of downstream effects, it is angiogenesis that is most crucial and also most susceptible to molecular manipulation. The delineation of molecular mechanisms of angiogenesis has revealed a critical role for HIF-1 in the regulation of angiogenic growth factors. In this article, what has been described about HIF-1 is reviewed: its structure, its regulation, and its implication for cancer therapy and the focus on its role in angiogenesis and cancer.



Genetic and Molecular Control of Osterix in Skeletal Formation

975

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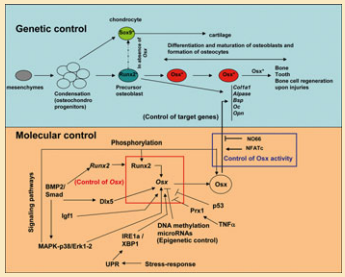
Osteoblast differentiation is a multi-step process where mesenchymal cells differentiate into osteoblast lineage cells including osteocytes. Osterix (Osx) is an osteoblast-specific transcription factor which activates a repertoire of genes during differentiation of pre-osteoblasts into mature osteoblasts and osteocytes. The essential role of Osx in the genetic program of bone formation and in bone homeostasis is well established. *Osx* mutant embryos do not form bone and fail to express osteoblast-specific marker genes. Inactivation of *Osx* in mice after birth causes multiple skeletal phenotypes including lack of new bone formation, absence of resorption of mineralized cartilage, and defects in osteocyte maturation and function. Since *Osx* is a major effector in skeletal formation, studies on Osx gained momentum over the last 5–7 years and implicated its important function in tooth formation as well as in healing of bone fractures. This review outlines mouse genetic studies that establish the essential role of Osx in bone and tooth formation as well as in healing of bone fractures. The recent advances in regulation of *Osx* expression, which is under control of a transcriptional network, signaling pathways, and epigenetic regulation is also discussed. Finally, important findings on the positive and negative regulation of Osx's transcriptional activity through protein–protein interactions in expression of its target genes during osteoblast differentiation is summarized. In particular, the identification of the histone demethylase NO66 as an Osx-interacting protein, which negatively regulates Osx activity opens further avenues in studying epigenetic control of Osx target genes during differentiation and maturation of osteoblasts.



Journal of Cellular Biochemistry

New Insights Into the Role of Runx1 in Epithelial Stem Cell Biology and Pathology 985

Cornelia Johanna Franziska Scheitz and Tudorita Tumbar

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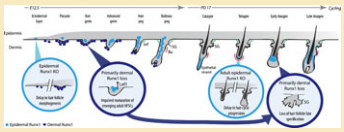

The transcription factor Runx1 has been studied in leukemia and blood for decades, but recently it has been also implicated in epithelial biology and pathology. Particularly in mouse skin Runx1 modulates Wnt signaling levels thereby regulating timely induction of hair follicle specification, proper maturation of the emerging adult hair follicle stem cells in embryogenesis, and timely stem cell (SC) activation during adult homeostasis. Moreover, Runx1 acts as a tumor promoter in mouse skin squamous tumor formation and maintenance, likely by repressing p21 and promoting Stat3 activation. Similarly, Runx1 is essential for oral epithelium tumorigenesis mediated in mice by Ras, and for growth of three kinds of human epithelial cancer cells. In contrast, Runx1 has a tumor suppressor function in the mouse intestine and shows tumor subtype specific behavior in human breast cancer. Multiple studies revealed Runx1 SNPs to be associated with human cancers and autoimmune disease. With this information as background, the field is poised for functional and mechanistic studies to elucidate the role of Runx1 in formation and/or progression of epithelial-based human disease.

Advance in Research of microRNA in *Caenorhabditis elegans* 994

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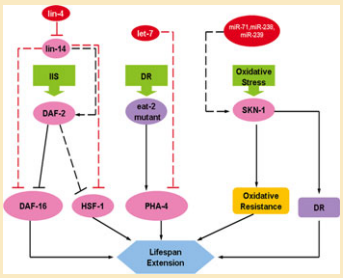

microRNA (miRNA) is a family of small, non-coding RNA first discovered as an important regulator of development in *Caenorhabditis elegans* (*C. elegans*). Numerous miRNAs have been found in *C. elegans*, and some of them are well conserved in many organisms. Though, the biologic function of miRNAs in *C. elegans* was largely unknown, more and more studies support the idea that miRNA is an important molecular for *C. elegans*. In this review, the research progress of miRNAs in *C. elegans* related with development, aging, cancer, and neurodegenerative diseases and compared the function of miRNAs between *C. elegans* and human is revisited.