FEATURES

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Gene Regulatory Networks Governing Lung Specification

Scott A. Rankin and Aaron M. Zorn

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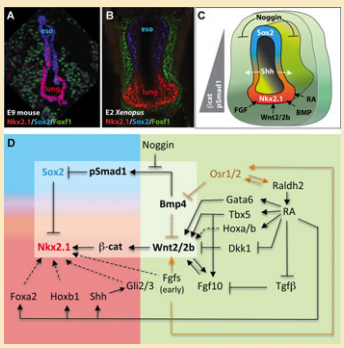

The epithelial lining of the respiratory system originates from a small group of progenitor cells in the ventral foregut endoderm of the early embryo. Research in the last decade has revealed a number of paracrine signaling pathways that are critical for the development of these respiratory progenitors. In the post genomic era the challenge now is to figure out at the genome wide level how these different signaling pathways and their downstream transcription factors interact in a complex "gene regulatory network" (GRN) to orchestrate early lung development. The prospective reviews current understanding of the GRN governing lung specification. The authors identify key knowledge gaps and describe emerging opportunities that will soon provide an unprecedented understanding of lung development.

Factors Affecting the Nuclear Localization of β-Catenin in Normal and Malignant Tissue

Rhys G. Morgan, Jenna Ridsdale, Alex Tonks, and Richard L. Darley

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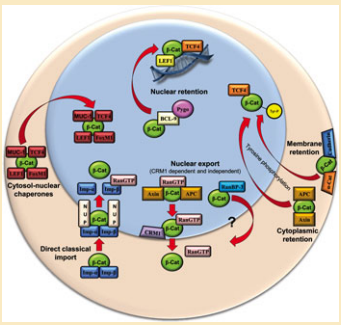

The canonical Wnt signaling pathway has been the focus of intensive research because of its frequent dysregulation in human cancers. Much of the research has been directed towards the aberrant expression and/or activity of the central mediator of the pathway, β-catenin. In particular, the nuclear localization of β-catenin and subsequent inappropriate activation of TCF/LEF-mediated transcription appears to be an important process in both the establishment and maintenance of cancer stem cells. However, the exact mechanisms controlling β-catenin nuclear localization in both normal and malignant cells are poorly understood. The prospect article brings together the many mechanisms previously reported to regulate the nuclear localization of β-catenin and explains how they are relevant to cancer.

Journal of Cellular Biochemistry

3-Dimensional Tissue Is Formed From Cancer Cells In Vitro on Gelfoam®, But Not on Matrigel™

Yasunori Tome, Fuminari Uehara, Sumiyuki Mii, Shuya Yano, Lei Zhang, Naotoshi Sugimoto, Hiroki Maehara, Michael Bouvet, Hiroyuki Tsuchiya, Fuminori Kanaya, and Robert M. Hoffman

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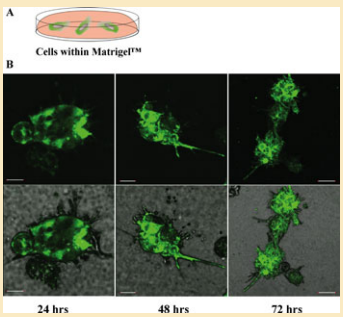
Cell and tissue culture can be performed on different substrates such as on plastic, in Matrigel™, and on Gelfoam® sponge matrix. Each of these substrates consists of a very different surface, ranging from hard and inflexible, a gel, and a sponge-matrix, respectively. Folkman and Moscona found that cell shape was tightly coupled to DNA synthesis and cell growth. Therefore, the flexibility of a substrate is important for cells to maintain their optimal shape. Human osteosarcoma cells, stably expressing a fusion protein of α_v integrin and green fluorescent protein (GFP), grew as a simple monolayer without any structure formation on the surface of a plastic dish. When the osteosarcoma cells were cultured within Matrigel™, the cancer cells formed colonies but no other structures. When the cancer cells were seeded on Gelfoam®, a sponge gel matrix, the cells formed three-dimensional tissue-like structures. The behavior of 143B osteosarcoma cells in Gelfoam® culture is remarkably different from those of these cells in monolayer culture or in Matrigel™. Tissue-like structures were observed only in Gelfoam® culture. The data suggest a flexible structural substrate such as Gelfoam® provides a more in vivo-like culture condition than monolayer culture or Matrigel™ and that Matrigel™ does not result in actual three-dimensional culture.



SUMOylation Attenuates the Transcriptional Activity of the NF-κB Subunit RelB

Julia Leidner, Cornelia Voogdt, Rainer Niedenthal, Peter Möller, Uta Marienfeld, and Ralf B. Marienfeld

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The NF-κB subunit RelB is known to act either as an activator or repressor of NF-κB-dependent gene expression. Despite accumulating reports describing the functional variability of RelB, the molecular mechanisms underlying these divergent functions are still unknown. One potential explanation could be a functional reprogramming of RelB by different post-translational modifications. SUMOylation of RelB might be one of these post-translational modifications rendering the function of the NF-κB transcription factor RelB. In vivo SUMOylation analyses using either the UBC9-fusion-directed SUMOylation method or endogenous proteins from Namalwa B cells revealed that RelB is modified by either SUMO1 or SUMO2 attachment at various sites. Functional studies suggest that SUMOylation converts RelB into a transcriptional repressor. For instance, a SUMO1-RelB fusion protein mimicking RelB-SUMOylation displayed a reduced transcriptional activity in comparison to wild type RelB. Consistently, inactivation of specific SUMOylation sites in the central part of RelB augmented the transcription activity of the corresponding RelB mutant. Taken together, the data suggest that SUMOylation might be a potential molecular mechanism involved in reprogramming RelB, thus contributing to its functional diversity.