

Networking the Signaling Pathways in Stem Cells and Cancer

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Abstract

The cellular phenotypes are regulated with the signaling pathways consist of molecular interactions. Network of several signaling pathways activates the stem cells and cancer to transit the cellular phenotypes. The molecules in the signaling pathway are epigenetically regulated upon the stimulation, which leads to dynamic changes in cell types such as differentiation of stem cells or malignancy of cancer cells. Considering that the disease status is involved in signaling pathway alteration, the investigation in epigenetic changes to find the targets of therapeutics are clinically of importance.

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Mediators of Signaling Pathways

The stimulation with extracellular substances such as chemicals or molecules in vesicles, and intercellular adhesion molecules start the signaling transduction in the cells. The receptors receive the stimulation and transduce the information to down-stream regulators mainly with conformational changes. The cascade of signaling occurs with phosphorylation of the molecules mediated by several kinases towards nucleus. Vesicles containing microRNA internalize through the membranes and mediate the signaling inside the cells. Some receptors such as nuclear receptors internalize and directly activate the nucleic signaling. Transcription factors bind to DNA and regulate the expression of genes, which leads to the activation of other signaling pathways. Epigenetic regulation such as methylation and acetylation of DNA modulate the gene transcription, followed by the consequences as cell proliferation or differentiation.

Signaling Pathways in Stem Cells

In stem cells, signaling for self-renewal and differentiation balance the cellular phenotypes. Wnt signaling pathway, Hedgehog signaling pathway and Notch signaling pathway are activated in stem cells [1]. For maintaining the stem cells, several molecules such as Nanog, Sox2, and Oct4 (Pou5f1) are important and these molecules are regulated as the consequence of the signaling pathway activation. Cross-talks of several signaling pathways modify the cellular phenotypes in the feedback mechanism, which emphasizes the significance of networking of signaling pathways in stem cells.

Signaling Pathways in Cancer

In general, proliferation signaling is activated and apoptosis

signaling is reduced in cancer. The therapeutic targets for cancer include EGF signaling, since the EGF signaling is usually activated in cancer. Another strategy to target cancer is PD1 inhibition with antibodies to regain the anti-cancer immunity with immune cells. The signaling pathways to activate and modulate the immune cells may be of clinical importance for cancer medication. For cancer phenotype identification, gene expression profiling in activated signaling pathways are useful and concise. The diagnosis with microRNA in the blood is practical in clinical setting, and the microRNA signaling pathway will elucidate the cancer metastasis signaling pathways and networking of cancer signaling pathways.

Mapping of Signaling Pathways

The expression of the molecules in the signaling pathways is regulated in epigenetic alterations. The mapping of the molecules in terms of the expression and interaction with the other signaling pathways is essential for elucidating the whole picture of signaling pathway networks. Overlapping of timing and location of several signaling pathways in the cells are important for the cross-talk of the signaling pathways. The epigenetic regulation in the signaling pathway network would require the further investigation to target the cancer and stem cell signaling for therapeutics.

References

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