Notch Signaling: A Novel Therapeutic Target for Cancer

Yuefei Yu*

*Division of Hematology and Oncology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas, USA

Notch signaling pathway is highly conserved in evolution in the signal transduction pathway, in which it regulates stem-cell maintenance, cell proliferation, differentiation and apoptosis in almost all the tissues and organs. Notch signaling plays a critical role in cell fate decision in many developmental systems. Notch-mediated signaling can expand and cure molecular differences between adjacent cells, and ultimately determine the fate of cells. Notch receptors are type I transmembrane heterodimeric receptors that widely exist in all known animal cells. There are four Notch receptors (Notch1-4), three Delta-like ligands (Dll1, Dll3, and Dll4), and two ligands of the Jagged family (Jag1 and Jag2) in mammals [1].

Aberrant Notch signaling has been implicated in the uncontrolled growth of malignant cells, which might function as an oncogene. The further understanding of Notch signaling in normal development and malignant transformation may open up a new avenue for developing novel cancer therapeutics. The first evidence for the involvement of Notch signaling in cancer came from T-cell acute lymphoblastic leukemia (T-ALL). The progress in the characterization of the mechanisms that mediate the oncogenic activity of Notch signaling make it possible to develop new anti-Notch therapies in the treatment of T-ALL. The high prevailing of Notch1 mutations in T-ALL makes it an ideal target for small molecules therapy. In the gross, Notch signaling could be inhibited at several levels: ligand binding, endocytosis, proteolysis or transcriptional activity [2]. A multi-subunit protease, γ-secretase, is critical in the processing of Notch. γ-secretase inhibitors (GSIs), the small molecules, are considered to be the most promising therapeutic agents, which could block the growth of T-ALL cells. Now GSIs are widely used to inhibit the Notch signaling in basic research and clinical trials. It has been reported that the combination of GSI with intravenous chemotherapy had a good antitumor activity in several conventional chemotherapy or radiation therapy [8]. Furthermore, the recent reports have described the involvement of aberrant Notch signaling in the pathogenesis of solid tumors and tumor angiogenesis, implying a new role for anti-Notch signaling in human cancer therapeutics.

References


*Corresponding author: Yuefei Yu, Division of Hematology and Oncology, Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas, USA, Tel: 806-559-9076; E-mail: yuefei.yu@ttuhsc.edu

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and endothelial cells promotes angiogenesis by VEGF activation of the Notch/Dll4 pathway. Carcinogenesis 34: 667-677.

