

## GLAX Health Announces the Discovery of Notch Inhibitors for Cancer Therapy. Dr. Rakesh K. Srivastava

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DOVER, DELAWARE, UNITED STATES, September 18, 2022 /EINPresswire.com/ -- GLAX Health Announces the Discovery of Notch Inhibitors for Cancer Therapy. Dr. Rakesh K. Srivastava

What is Notch Signaling Pathway? The Notch signaling pathway is highly evolutionarily conserved, and plays a significant role in cell growth, development, and differentiation, serving key regulatory roles ranging from embryonic development to adult homeostasis. It is a key regulator of immune cell differentiation and is linked to autoimmune diseases, tumorigenesis, and tumor-induced immunomodulation. Abnormal activation of the Notch signaling pathway contributes to almost all of the key features of cancer, including stemness, tumor angiogenesis, and epithelial-mesenchymal transition.



The pathway is comprised of a ligand-expressing cell and a receptor-expressing cell. The canonical ligands are members of the Delta/Serrate/Lag-1 (DSL) family of proteins. The pathway includes 4 receptors (Notch1-4) and 5 ligands (Jagged1 [JAG1], JAG2, delta-like 1 [DLL1], DLL3 and DLL4). The Notch transmembrane receptor glycoproteins function as membrane-bound transcription factors that regulate multiple cellular functions including cell fate determination, differentiation, proliferation, self-renewal, and survival. The Notch receptor contains three domains: the extracellular domain (NECD), the transmembrane domain (NTMD), and the intracellular domain (NICD). The binding of a ligand to a Notch receptor in a neighboring cell induces a conformational change in the receptor, which will undergo regulated intramembrane proteolysis (sequential cleavage by ADAM10/17 and γ-secretase enzymes), liberating NICD. The NICD is translocated to the nucleus and promotes gene transcription. Notch targets several genes such as HES, HEY, PI3K, Akt, NF-kB, PPAR, p21, p27, Cyclins, and Bcl-2. Dysregulated Notch

signaling is implicated in several malignancies such as lymphoid leukemia, breast, ovary, head and neck, cervix, lung, pancreas, colon, and kidney cancer.

Cross-talks between the Notch and other pathways such as Wnt, NF $\kappa$ B, STAT3, WNT, and SHH pathways have been described. Interestingly, inhibition of  $\gamma$ -secretase, which prevents the release of the NICD and its translocation to the nucleus, may be a promising therapeutic target for the treatment of cancer and other diseases.

Dr. Rakesh K. Srivastava (President and CEO of GLAX Health) and his colleagues discovered new drugs that inhibit Notch transcription and cancer cell growth. These drugs are effective in solid tumors and lymphoid leukemia. These drugs also inhibit the growth of cancer stem cells without affecting normal cells.

<u>Dr. Srivastava Rakesh</u> says that Notch inhibitors can be used to eliminate not only cancer cells but also cancer stem cells. Cancer stem cells exhibit the properties of self-renewal and pluripotency. They are responsible for cancer initiation, progression, metastasis, drug resistance, and cancer relapse. Targeted therapies are being used in cancer patients due to better survival and fewer side effects when compared to traditional chemotherapy. Notch inhibitors can also be combined with other chemotherapy and irradiation. Activation of the Notch pathway induces immunosuppression and immunotherapy resistance. Therefore, inhibition of the Notch pathway by these novel drugs can be beneficial for the treatment of various cancers. They not only inhibit cancer cells but also enhance immunotherapy. Dr. Srivastava says future plans are underway to further validate and perform clinical trials in collaboration with global partners.

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