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Unlocking the Secrets of Cancer Stem Cells with γ-Secretase Inhibitors: A Novel Anticancer Strategy

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Abstract

The dysregulation of Notch signaling is associated with a wide variety of different human cancers. Notch signaling activation mostly relies on the activity of the γ-secretase enzyme that cleaves the Notch receptors and releases the active intracellular domain. It is well-documented that γ-secretase inhibitors (GSIs) block the Notch activity, mainly by inhibiting the oncogenic activity of this pathway. To date, several GSIs have been introduced clinically for the treatment of various diseases, such as Alzheimer's disease and various cancers, and their impacts on Notch inhibition have been found to be promising. Therefore, GSIs are of great interest for cancer therapy. The objective of this review is to provide a systematic review of in vitro and in vivo studies for investigating the effect of GSIs on various cancer stem cells (CSCs), mainly by modulation of the Notch signaling pathway. Various scholarly electronic databases were searched and relevant studies published in the English language were collected up to February 2020. Herein, we conclude that GSIs can be potential candidates for CSC-targeting therapy. The outcome of our study also indicates that GSIs in combination with anticancer drugs have a greater inhibitory effect on CSCs.

Keywords: Notch signaling; cancer stem cells; cancer treatment; γ-secretase; γ-secretase inhibitors.

Figures

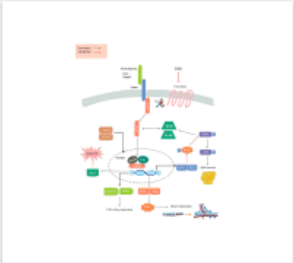

Figure 1 Molecular mechanisms underlying the anticancer...

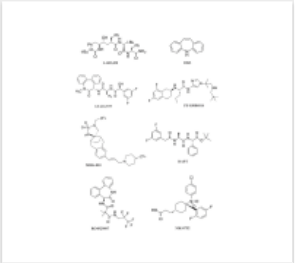

Figure 2 Chemical structure of selected γ-secretase...

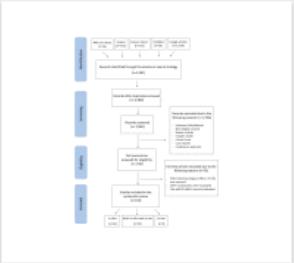

Figure 3 Chemical structure of selected γ-secretase...

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