Effectiveness of Neratinib in Inhibiting or Reversing Hepatic Stellate Cell Activation

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Liver Fibrosis is the creation of scar tissue in the liver after it suffers damage, and it can lead to cirrhosis and hepatocellular cancer. There are currently no standard treatments for liver fibrosis. Hepatic Stellate Cells (HSCs) are the main cell type that contributes to liver fibrosis, driving fibrosis when they become activated. The purpose of this project was to investigate a new drug, Neratinib, to test if it can counteract hepatic stellate cell activation, using both a prevention and intervention strategy. LX-2 human hepatic stellate cells were cultured and treated with TGF-beta1, a known activator of HSCs. LX-2 cells received either pre-treatment or post-treatment with Neratinib, and levels of alpha-smooth muscle actin (a-SMA) and PDGF receptor-beta (PDGF-R beta) proteins, markers of HSC activation, were measured by western blotting. TGF-beta1 activated LX-2 cells as expected. Neratinib pre-treatment was effective in preventing the activation of LX-2 cells. Neratinib post-treatment was effective in reversing the activation of LX-2 cells. Therefore, Neratinib was effective in both prevention and intervention, where it can bring about the reversion of the LX-2 cells to a quiescent state. Neratinib could therefore be a promising drug to prevent or treat liver fibrosis in humans.

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