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The identification of anti-cancer molecular targets of COX-2 inhibitor Nimesulide

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Abstract

Non-steroidal anti inflammatory drugs which were primarily used for the treatment inflammation and pain have also shown anti-cancer activity in many studies. The mechanism of action of NSAIDs in cancer may involve cyclooxygenase (COX) dependent or independent pathways. According to studies, COX-2 is overexpressed in several cancers such as prostate, breast, nonsmall-cell lung, colon, and pancreas. Nimesulide is an NSAID with COX-2 inhibitory activity and investigations show that it could induce apoptosis in cancer. Previously, a library of compounds was synthesized using Nimesulide as a lead compound. However, they displayed different molecular targets: tubulin and heat shock protein 27 (HSP27). Since Nimesulide does not interfere with any of these proteins, the targets of it in cancer remain unclear. Therefore, it is necessary to identify the original anti-cancer targets of Nimesulide in order to understand the structure activity relationship that lead to target switching in the Nimesulide derivatives. For this purpose, a six carbon linker and biotin conjugated Nimesulide probe was designed and synthesized. A human prostate cancer cell line, LnCap, was used to perform protein pull-down assay in order to analyze the proteins that bind to the Nimesulide probe. This study provides insight into the structural interactions that are important for the anti-cancer activity which can be used to synthesize more potent analogs with the original target of Nimesulide.

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