

Small Molecule XIAP Inhibitor (B64017)

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Challenge

Apoptosis is a highly conserved process regulating the balance between cell death and proliferation for the maintenance of tissue homeostasis. Insufficient apoptosis can lead to the development and progression of cancer. Most chemotherapeutic drugs kill cancer cells by inducing apoptosis. Importantly, tumour cells which are capable of evading programmed cell death often become chemoresistant.

Inhibitor of apoptosis proteins (IAPs) are a group of antiapoptotic proteins that inhibit caspases, central players in the apoptotic cascade. XIAP, the most potent and well characterized member of the IAP family is an inhibitor of caspase-3, -7 and -9. Many human malignancies express elevated XIAP-levels thus leading to apoptosis resistance. Therefore, targeting XIAP is a promising strategy to overcome apoptosis resistance. In this context, small molecule XIAP inhibitors are attractive antitumor drug candidates.

Technology

Through virtual screening of commercially available databases several compounds were identified as novel XIAP inhibitors. These compounds, which showed no cytotoxicity on their own, were tested in a human leukaemia cell line stably overexpressing XIAP for their ability to overcome the cells' chemoresistance. The most effective molecules increased apoptosis-induction through the chemotherapeutic drug etoposide from approximately 10% to above 60% apoptotic cells. In order to develop the full therapeutic potential of our XIAP inhibitors, we currently work on the underlying apoptosis signalling mechanisms, NMR binding studies, and towards an *in vivo* proof of principle.

Commercial Opportunity

On behalf of the LMU the Bayerische Patentallianz GmbH offers an exclusive, worldwide patent license or the option in combination with a cooperation contract.

Developmental Status

In vitro

Patent Situation

Priority Year: 2007

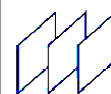
DE EP US PCT (all countries)

national phases active in all major countries and patent regions

Further Reading

Fulda S. Future Drugs 2007, 1255-1264

Vucic D and Fairbrother WJ, Clin Cancer Res 2007, 13(20): 5995-6000



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