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118

Antiproliferative Efficacy of a Focused Library of Tyrosine-Kinase Inhibitors

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Background: Inhibition of false proliferative signals is one of the major targets of drug development, today. Tyrosine kinase enzymes (TK) are considered among the key molecular targets in this respect. Our aim was to characterise the antiproliferative efficacy of a focused library of compounds with known TK inhibitory potential, that are used in Quantitative Structure Relationship (QSAR) predictive models for TK inhibitory action.

Methods: Panc1 pancreatic ductal adenocarcinoma and A431 epidermoid carcinoma cell (overexpressing EGFR) were harvested in standard cell-culture environment (37C, 5% CO_2, 10% FCS). Proliferation assays were based on the Methylene Blue (Oliver M.H. et al. J Cell Sci 1989;92(3):513–518) and MTT methods (Carmichael J. et al. Cancer Res. 1987;47(4):936–942) on 300 compounds with diverse chemical structures but uniform in potent TK inhibitory action. Cell viability was assessed after 6 and 48 hours. Efficacy (=low non-specific toxicity + high rate of apoptosis induction) was judged on the basis of high early viability connected to the maximum viability-loss at 48 h.

Results-Conclusion: 13% of the compounds showed superior than 80% efficacy regarding growths inhibition connected to minimum in vitro toxicity. Verification of apoptosis induction by Flow cytometry will facilitate efficacy of prediction of artificial neural-network based studies with regard to novel molecule design.

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