Synthesis, *in silico* and *in vitro* Evaluation of Novel Oxazolopyrimidines as Promising Anticancer Agents

Yevheniia Velihina, Thomas Scattolin, Denys Bondar, Stepan Pil'o, Nataliya Obernikhina, Olesksiy Kachkovskyi, Ivan Semenyuta, Isabella Caligiuri, Flavio Rizzolio ... See all authors

First published: 09 October 2020 | https://doi.org/10.1002/hlca.202000169 | Citations: 3

Dedicated to Prof. *Antonio Togni* on the occasion of his 65th birthday and retirement

Abstract

New potential bioactive oxazolopyrimidines have been synthesized using two main approaches: the pyrimidine ring annulation on a functionalized oxazole and the benzoyl bromide trimerization followed by rearrangement and formation of the oxazolo[5,4-*d*]pyrimidine scaffold. The docking analyzes have shown that 7-piperazine substituted oxazolo[4,5-*d*]pyrimidines **8a–8c** could be potential VEGFR2 inhibitors with high free energy of ligand–protein complex formation (ΔG: −10.1, −9.6, −9.8 kcal/mol, respectively). *In vitro* antitumor assays confirmed theoretical predictions that oxazolo[4,5-*d*]pyrimidines **8a–8c** containing positively charged piperazine moiety should demonstrate significantly higher cytotoxic effects. 4-[5-(4-Chlorophenyl)-2-phenyl[1,3]oxazolo[4,5-*d*]pyrimidin-7-yl]piperazin-1-ium trifluoroacetate (**8c**) exhibited a slightly higher antiproliferative effect (IC_{50}=0.21 μM) than doxorubicin (IC_{50}=0.36 μM) on MDA-MB-231 cell line and has relatively good results on OVCAR-3 (IC_{50}=1.7 μM) and HCT-116 (IC_{50}=0.24 μM) cells.