SL-11. MDM2-p53

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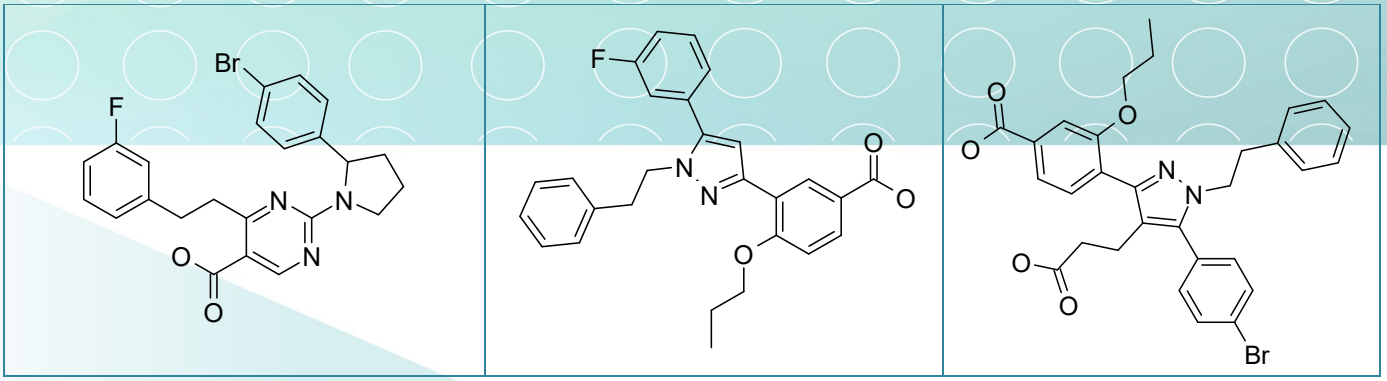
MDM2/p53 is a protein-protein interaction (PPI) which regulates a variety of cellular pathways involved in the onset and development of cancer. MDM2 is a negative regulator of tumor suppression protein p53 thus making MDM2 an attractive target for anticancer therapeutics. Structurally MDM2 has several deep hydrophobic binding pockets that fit α-helical p53. Therefore, synthetic small molecule alpha-helix mimetic scaffolds provide a very promising strategy for designing inhibitors of MDM2 and other α-helix mediated PPIs.

At ASINEX, we performed *in silico* analyses of common structural futures of known MDM2 antagonists to build up a predictive pharmacophore model [1]. Several α-helix mimetic scaffolds were selected as p53 backbone mimetics and p53 binding epitope mimetics [2,3]. The *in vitro* potency of compounds was confirmed in a fluorescence polarization assay, with the IC50s ranging from 1 to 10 µM.



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Formats	Supplementary Information
80 compounds per plate 0.1 mg; 1 mg; 2 mg dry film/powder 0.1 µmol; 1 µmol DMSO solutions	IC_{50} [Mdm2/p53] Solubility data in PBS SL#11_MDM2_p53_05-16.sdf

References:

1. *J Med Chem.* 2015 Feb 12;58(3):1038-52. doi: 10.1021/jm501092z
2. *Med. Chem. Commun*., 2013, 4, 1597-1603 doi: 10.1039/C3MD00211J
3. *Chem Biol Drug Des*. 2014 Nov;84(5):585-92. doi: 10.1111/cbdd.12351

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