Design and synthesis of reversine-like molecules as Aurora B kinase inhibitors

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First synthesized in 2004 by the group of Peter G. Schultz [1], reversine is a 2,6-diamino substituted purine showing a potent inhibition on Aurora B, a protein kinase overexpressed in a variety of solid tumors. Due to its relevance in the cell cycle regulation, Aurora B represents a good target for anti-cancer drug development, so that reversine can be used as a promising lead compound for new potential antitumor agents[2].

Recently we have designed a series of reversine analogs by docking calculation having Aurora B kinase as specific target (Figure 1). The synthesis of new selected molecules bearing structural modifications in 2 and 6 positions has been carried out, focusing on the improvement of both the synthetic strategy (also using microwave-assisted reactions) and the products purification.

The presence of different tautomeric forms for each analog is also under investigation.

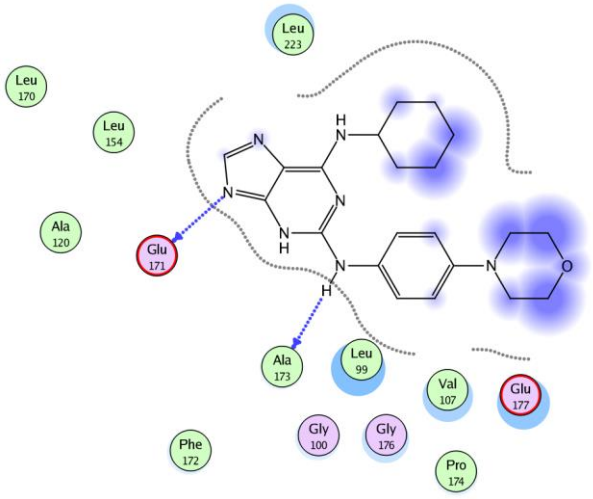

Figure 1: Molecular structure of reversine and 2D-view of its interactions with Aurora kinase B (2VGO pdb file) by AutoDock Vina calculation.

[1] S.Chen , Q. Zhang, X. Wu, P. G. Schultz and S. Ding, *J.Am.Chem.Soc*. **126** (2004) 410–411.
[2] A. M. D'Alise, G.Amabile, M. Iovino, F.P. Di Giorgio, M. Bartiromo, F.Sessa, F.Villa, A. Musacchio and R.Cortese, *Mol. Cancer Ther*. **7** (2008) 1140-1149.