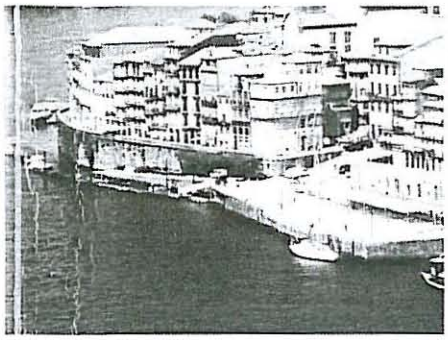

2nd Iberic Meeting on Medicinal Chemistry:

G Protein-Coupled Receptors and Enzymes in Drug Discovery

Porto, Portugal
12 – 15 June, 2011

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Program and Abstracts

VEGFR2 selective residue flexibility enriches AutoDock Vina docking results

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VEGFR2 (Vascular Endothelial Growth Factor Receptor 2) is a recognized anti-cancer protein target with already one known inhibitor, soranefib, in the market for therapeutic use.[1] Protein-ligand docking tools can be used in order to find potential new VEGFR2 inhibitors. However, the quality of docking results can be affected by the simplification of treating protein structures as rigid entities. Selective residue flexibility is a recent option available on several molecular docking tools, including AutoDock Vina used in this work,[2] where only selected residues are allowed to be flexible. This approach is promising as it attempts to provide a more realistic protein environment while preventing an escalation of the computer power need. In this study four residues were selected from the catalytic site of the VEGFR2 structure (PDB: 1YWN): GLU883, LYS866, CYS917 and ASP1044. Each residue was individually made flexible and, for benchmarking, docking experiments were performed using the DUD (Directory of Useful Decoys) dataset. The DUD dataset is composed of 88 VEGFR2 ligands and 2906 decoys compounds, and the virtual screening of all compounds was performed using MOLA software[3] for parallel computing, in a cluster of 14 computer nodes, and AutoDock Vina for molecular docking. The best overall docking result was obtained by flexibilizing the GLU883 residue, with a marked increase in distinguishing VEGFR2 ligands from decoys, when compared with the rigid docking results. The pay-off was a manageable 51% increase on the computer processing time needed. This study proves that carefully flexibilization of key aminoacid residues can improve the predictive power of docking without an unmanageable increase in computer processing time.

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References

1. Eichholz, A., Merchant, S. and Gaya, A. M., *Journal of Onco Targets and Therapy*, **2010**, *3*, 69-82.
2. Trott, O. and Olson, A.J., *Journal of Computational Chemistry*, **2010**, *31*, 455-461.
3. Abreu, R.M.V., Froufe, H.J.C., Queiroz, M.-J.R.P. and Ferreira, I.C.F.R, *Journal of Cheminformatics*, **2010**, *2*, 10.








Certificate

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