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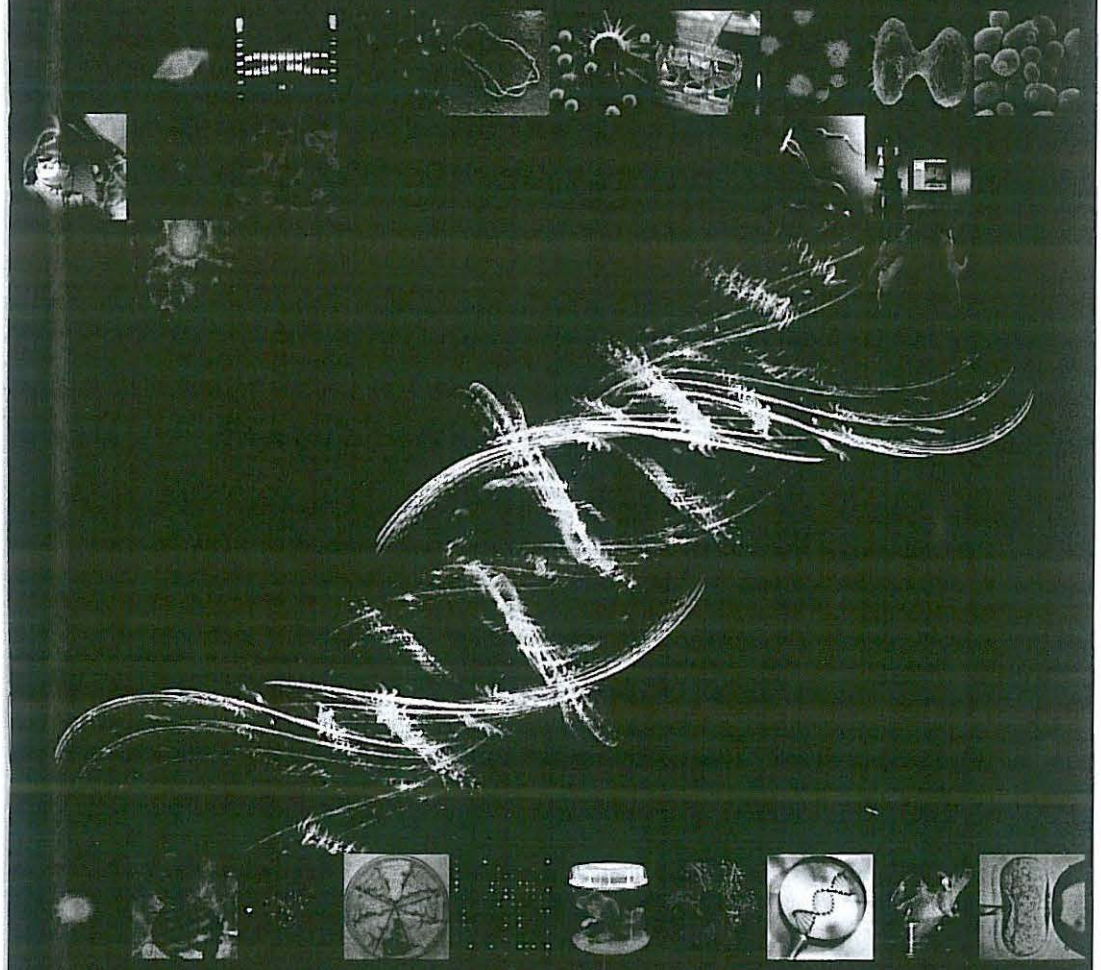

PROGRAMA E RESUMOS

Aula Magna, Universidade de Trás-os-Montes e Alto Douro, Vila Real

ADNGB - Alunos do Núcleo de Genética e Biotecnologia

Farnesoid X Receptor: Docking Model Validation

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Farnesoid X receptor (FXR) is a protein that was shown to be involved in controlling numerous metabolic pathways that include: maintaining bile acid, lipid and glucose homeostasis, preventing intestinal bacterial infection and modulating liver regeneration and tumorigenesis [1]. The different roles played by FXR highlight potential new opportunities for using FXR as a drug target for different diseases [2]. In this work we validate the use of FXR as a target for virtual docking simulation experiments.

We used the docking software Autodock 4 as it is acknowledged to be one of the most widely used in docking simulations [3]. The FXR 3 -D structure used (PDB code: 1OSH) in this study is co-crystallized with Fexaramine, a known high affinity agonist. Before the docking experiment, Fexaramine was removed from the structure. A docking experiment was then performed using Fexaramine as ligand and the docking results showed that the predicted binding mode essentially matches the Fexaramine present in the experimental FXR 3-D structure, with a RMSD (Root Mean Standard Deviation) of less than 1 Å on average, a cluster of 49 in 50 runs and a minimum binding energy of -14,39 kcal/mol. We also evaluate the FXR against other known agonists. These results validate the use of the FXR 3D structure as a good target for virtual docking experiments with other potential ligands.

[1] Y. Zhang, and P.A. Edwards, FEBS Lett. 582 (2008) 10-8. | [2] Y.D. Wang, W.D. Chen, D.D. Moore, and W. Huang, Cell Res. (2008), doi: 10.1038/cr.2008.289. | [3] G.M. Morris, D.S. Goodsell, R.S. Halliday, R. Huey, W.E. Hart, R.K. Belew, and A.J. Olson, Journal of Computational Chemistry. 19 (1998) 1639-1662.