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Virtual Screening for the Discovery of New Anticoagulants

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Introduction

The discovery of novel anticoagulants without side effects is one of the main problems of haemostasis. Ever since the discovery of the anticoagulant properties of hirudin from the leech saliva, the increasing relevance of thromboembolic diseases has encouraged a continuous search for new compounds with anticoagulant activity, which have led to the development of the new commercially available anticoagulants [1]. One of the targets for prophylaxis and treatment of thromboembolic diseases is the plasma anticoagulant antithrombin. This protein circulates in blood in a metastable conformation, in which the reactive centre loop is partially inserted and is only activated by heparin and heparan sulfate glycosaminoglycans on the injured sub endothelium [2]. Accordingly sulfated polysaccharide heparin chains with different size, from unfractionated to the essential pentasaccharide, have been used with more or less success in anticoagulant therapy and thromboprophylaxis [3]. In the last decades new molecules able to bind antithrombin have been identified. The strategies used in this search have been based mainly on the synthesis or chemical modification of existing drugs, or in the application of natural compounds with similar properties to those currently used [2]. Examples for such compounds are lignins and flavonoids [1,4], highly sulfated small organic ligands that seem to have similar properties to heparins.

Therefore, the discovery of novel or improved drugs for given diseases or special groups of patients, is a very slow and expensive process. Nevertheless, recent results demonstrate the discovery using Virtual Screening (VS) of a novel molecular scaffold [5], different to the previous ones based on heparin. Using this alternate approach, a large database of millions of chemical compounds is screened in-silico and affinity-ranking is used to identify at least some weakly-binding molecules for further refinement. Aided by ever-increasing computational power [3,6,7], VS is an appealing and cost-effective approach to tap into the wealth of available structural information [8,9]. Consequently, novel and enhanced VS methodologies, conveniently exploited in innovative drug discovery strategies can lead to significant and quantifiable developments.

References

1. Paikin, JS, Eikelboom JW, Cairns JA, Hirsh J (2010) New antithrombotic agents-insights from clinical trials. Nat Rev Cardiol 7: 498-509.
2. de Agostini AI, Watkins SC, Slayter HS, Youssoufian H, Rosenberg RD (1990) Localization of anticoagulantly active heparan sulfate proteoglycans in vascular endothelium: antithrombin binding on cultured endothelial cells and perfused rat aorta. J Cell Biol 111: 1293-1304.
3. Harenberg J, Wehling M (2008) Current and future prospects for anticoagulant therapy: inhibitors of factor Xa and factor IIa. Semin Thromb Hemost 34: 39-57.
4. Gunnarsson GT, Desai UR (2004) Hydropathic interaction analyses of small organic activators binding to antithrombin. Bioorg Med Chem 12: 633-640.
5. Navarro-Fernandez J, Pérez-Sánchez H, Martínez-Martínez I, Meliciani I, Guerrero JA, et al. (2012) In silico discovery of a compound with nanomolar affinity to antithrombin causing partial activation and increased heparin affinity. J Med Chem 55: 6403-6412.
6. Pérez-Sánchez H, Wenzel W (2011) Optimization methods for virtual screening on novel computational architectures. Curr Comput Aided Drug Des 7: 44-52.
7. Guerrero GD, Pérez-Sánchez HE, Cecilia JM, García JM (2012) Parallelization of Virtual Screening in Drug Discovery on Massively Parallel Architectures. 20th Euromicro International Conference on Parallel, Distributed and Network-based Processing, Germany.
8. Henry BL, Connell J, Liang A, Krishnasamy C, Desai UR (2009) Interaction of antithrombin with sulfated, low molecular weight lignins: opportunities for potent, selective modulation of antithrombin function. J Biol Chem 284: 20897-20908.
9. Ghosh S, Nie A, An J, Huang Z (2006) Structure-based virtual screening of chemical libraries for drug discovery. Curr Opin Chem Biol 10: 194-202.

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