

[P15] Similarity between biosynthetic enzymes and druggable proteins captured by 3D-computing approach

Noé Sturm^{1,2}, Ronald J. Quinn² and Esther Kellenberger¹

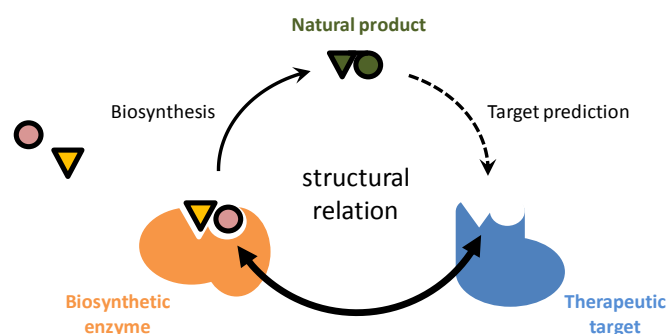
¹Laboratoire d'innovation thérapeutique, Medalis Drug Discovery Center, UMR7200 CNRS-Université de Strasbourg, F-67400 Illkirch

²Eskitis Institute, Griffith University, Brisbane, QLD 4111, Australia

Natural products are made by nature through interaction with biosynthetic enzymes. They also exert their effect as drugs by interaction with proteins.¹ To address the question “Does recognition of the natural product by biosynthetic enzymes translate to recognition of the therapeutic target?”, we have compared the active site of five flavonoid biosynthetic enzymes (FBE) to 8 077 druggable binding sites in the Protein Database (release 2012 of the sc-PDB)² using two unrelated 3D-based methods, SiteAlign and Shaper.^{3,4}

Virtual screenings retrieved proteins able to bind flavonoids, in particular protein kinases. The total number of proteins found similar to FBE however varied greatly depending on the query FBE site as well as the method used for the comparison. In agreement with manual 3D-alignment of kinase ATP-binding site with FBE active site,⁵ we observed that flavonoid binding is not primary driven by shape complementarity, yet rather by recognition of common anchoring points.

Aiming at the identification of new target for other natural products, we are now collecting and annotating all biosynthetic enzymes in the Protein Database.



Bibliography :

Bibliography:

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