[P4] Chemical space mining for new glucocorticoid receptor agonists

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The glucocorticoid receptor (GR) is a transcription factor that plays a significant role in the regulation of metabolism and immune response. GR belongs to the family of steroid receptors that are known to influence the development and growth of many human cancers, and are thus important targets for therapeutic intervention. Herein, we propose a computational approach for the development of new GR ligands based on the exploration of chemical space. Molpher [1], our exploration algorithm, is used to create GR virtual chemical library by a process called 'molecular morphing' in which small structural changes are incrementally applied on a set of known GR agonists (figure 1). GR agonist set is a maximum diverse subset of compounds compiled from the ChEMBL database and from our high-throughput screening experimental data. The virtual chemical library of potential GR agonists, produced by Molpher, is then projected into the database of commercially available compounds ZINC using structural similarity search. The most promising ZINC hits will be eventually purchased and experimentally characterized.

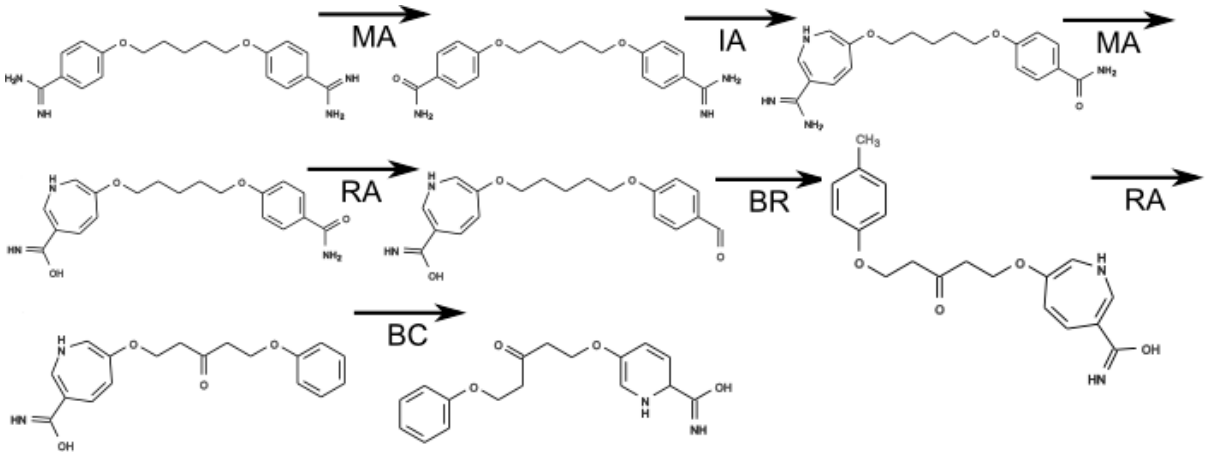

Figure 1 : Schematic illustration of the 'molecular morphing' process.

[1] Hoksza D, Skoda P, Voršilák M, Svozil D. J Cheminform. Mar 21; 6(1)(2014), 7