Pharmacophore modeling and virtual screening to discover cytochrome P450 17 inhibitors among environmental chemicals

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The modulation of endocrine receptors by environmental chemicals is intensively studied. However, the inhibition of cytochrome P450 17 (CYP17) by environmental chemicals is not very well investigated. CYP17 is a central enzyme for steroid synthesis and has a critical role in androgen production in humans. The inhibition of CYP17 has a strong impact on androgen synthesis and on sperm count [1]. It has been known recently that the inhibition of CYP17 is also an important option for the treatment of castration-resistant prostate cancer [2,3,4,5].

In this study, we have generated structure-based and ligand-based pharmacophore models for CYP17 inhibition. These pharmacophore models were used to perform a virtual screening to identify potential CYP17 inhibitors from environmental chemical databases like food contact compounds, food flavoring agents, cosmetic ingredients, industrial chemicals, endocrine disruptors, approved drugs, and pesticides. The most relevant hits will be tested for CYP17 inhibition *via* an enzymatic assay. Molecular docking studies will be performed to propose protein-ligand interactions of the experimentally tested hits.

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