Steroid binding to metabolic enzyme

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The human cytochrome P450 enzymes are responsible for metabolizing a variety of substances—from lipids (fats) and steroid hormones to drugs and toxic chemicals.

One such enzyme, P450 17A1, generates androstenedione and dehydroepiandrosterone (DHEA), involved in the production of sex hormones. How the enzyme binds to its substrates has remained a mystery until now.

Using kinetics and modeling techniques, F. Peter (Fred) Guengerich, Ph.D., and colleagues Clayton Wilkey, Sarah Glass and Michael Reddish, Ph.D., determined that the dominant mode of binding is via conformational selection rather than induced fit.

Their findings, reported in the *Journal of Biological Chemistry*, show that P450 enzymes exist in different conformational states and then bind drugs or chemicals presented to them.

Understanding how P450 17A1 binds to its substrates may aid in designing drugs to treat sexual dysfunction, for example, as well as prostate cancer.

More information: F. Peter Guengerich et al. Conformational selection dominates binding of steroids to human cytochrome P450 17A1, *Journal of Biological Chemistry* (2019). DOI: 10.1074/jbc.RA119.008860