

Structure of Guinea Pig 11 β Steroid Dehydrogenase 1 with Glycyrrhetic Acid

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11 β steroid dehydrogenase 1 (11 β HSD1) catalyzes the conversion of glucocorticoid cortisone to cortisol, amplifying the local concentration of cortisol in select tissues. Increasing evidence in the literature implicates 11 β HSD1 in the metabolic syndrome consisting of diabetes, visceral obesity, and hyperlipidemia[1]. In addition, inhibition of 11 β HSD1 ameliorates hyperglycemia and increases insulin sensitivity in diabetic animal models[2]. 11 β HSD1 is thus a target for drug intervention in diabetes. We present the structure of Guinea Pig 11 β HSD1 with Glycyrrhetic Acid, a natural product inhibitor. We also discuss the mechanism of 11 β HSD1 in relation to other steroid dehydrogenases and the implications of the structure for structure based drug design.

[1]Masuzaki H., Paterson J., Shinyama H., Morton N., Mullins J., Seckl J., Flier J., *Science*, 2001, **294**, 2166. [2] Alberts P., Nilsson C., Selen G., Engblom L.O., Edling N.H., Norling S., Klingstrom G., Larsson C., Forsgren M., Ashkzari M., Nilsson C.E., Fiedler M., Bergqvist E., Ohman B., Bjorkstrand E., Abrahmsen L.B., *Endocrinology*, 2003, **144**, 4755.

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