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Review

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ACCEPTED MANUSCRIPT

Cytochrome b5: novel roles in steroidogenesis

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Abstract

Cytochrome b₅ (cyt-b₅) is essential for the regulation of steroidogenesis and as such has been implicated in a number of clinical conditions. It is well documented that this small activity 17.20-lvase of P450 hemoprotein augments the cytochrome 17αhydroxylase/17,20-lyase (CYP17A1). Studies have revealed that this augmentation is accomplished by cyt-b₅ enhancing the interaction between cytochrome P450 reductase (POR) and CYP17A1. In this paper we present evidence that cyt-b₅ induces a conformational change in CYP17A1, in addition to facilitating the interaction between CYP17A1 and POR. We also review the recently published finding that $cyt-b_5$ allosterically augments the activity of 3 β -hydroxysteroid dehydrogenase/ Δ^5 - Δ^4 isomerase (3 β HSD), a non cytochrome P450 enzyme, by increasing the enzymes affinity for its cofactor, NAD⁺. The physiological importance of this finding, in terms of understanding adrenal androstenedione production, is examined. Finally, evidence that cyt-b₅ is able to form homomeric complexes in living cells is presented and discussed.

Keywords: Cytochrome b₅; cytochrome P450 17α-hydroxylase/17,20-lyase; CYP17A1; 3β-hydroxysteroid dehydrogenase/ Δ^5 - Δ^4 isomerase; 3βHSD; steroidogenesis

Abbreviations

3β-hydroxysteroid dehydrogenase/ Δ^5 - Δ^4 isomerase, 3βHSD; 16-hydroxyprogesterone, 16OH-PROG; 17-hydroxypregnenolone, 17OH-PREG; 17-hydroxyprogesterone, 17OH-PROG; androstenedione, A4; cytochrome b₅, cyt-b₅; cytochrome P450 17αhydroxylase/17,20-lyase, CYP17; dehydroepiandrosterone, DHEA; pregnenolone, PREG; progesterone, PROG Download English Version:

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