The role of mitochondrial energy metabolism in adrenal hyperandrogenism: mechanisms and clinical implications

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The role of mitochondria in steroid synthesis is well established, but the specific effects of mitochondrial energy metabolism on adrenal androgen production are largely unknown. My preliminary data in an adrenal cell model show that defects in oxidative phosphorylation and mitochondrial pyruvate transport lead to adrenal hyperandrogenism. I propose that mitochondrial energy metabolism plays a critical role in directing adrenal steroidogenesis toward androgen excess that needs to be further elucidated. I will use the established H295R cell model to perform an in-depth analysis of steroid output, metabolic flux dependencies and transcriptional adaptations. In parallel, I will evaluate adrenocortical steroid profiles in children with primary mitochondrial disease (PMD) to characterize the occurrence of adrenal hyperandrogenism. This proposal aims to determine the impact of mitochondrial metabolism on adrenal androgen production, to define metabolic vulnerabilities for future treatment of hyperandrogenic diseases, and to establish the rationale for testing adrenocortical function in children with PMD.