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Letter to the Editor

Letter to the Editor From Hoekstra: "Adrenal Abcg1 Controls Cholesterol Flux and Steroidogenesis"

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Dear Editor,

A recent study by Liimatta et al published in *Endocrinology* reported that adrenal-specific deficiency of the cholesterol efflux transporter ATP-binding cassette transporter G1 (ABCG1) in mice is associated with moderately enhanced secretion of the steroid hormone corticosterone (1). This finding contrasts our earlier observation that total body ABCG1 deficiency in mice is associated with mild glucocorticoid insufficiency (2). Liimatta et al suggest that this discrepancy is related to a potential effect of global ABCG1 deficiency on the secretion of corticotropin-releasing hormone or adrenocorticotropic hormone. However, we anticipate that other factors are actually underlying the difference in study outcomes. Our findings are derived from mice that were subjected to treatment with adrenocorticotropic hormone to maximally stimulate the adrenal glucocorticoid output, while Liimatta et al have obtained blood specimens from mice in the nonstressed (low-steroidogenic) state. As a result, corticosterone levels in wild-type control mice in the study of Liimatta et al were much lower than those measured in our experimental setting (~350 nmol/L = ~122 ng/mL vs 600 ng/mL). Furthermore, it remains questionable whether ABCG1 function was really eliminated from the adrenocortical cells that produce corticosterone in the mouse model of Liimatta et al as the CYP11B2 promoter was used to drive expression of the Cre recombinase needed for ABCG1 gene targeting. CYP11B2 is present in adrenocortical cells that produce aldosterone (but not corticosterone) located in the adrenal zona glomerulosa and, to a lesser extent, zona fasciculata (3). Within the zona fasciculata, CYP11B1-expressing cells are actually essential for the formation of corticosterone from its precursor deoxycorticosterone (4). Inspection of the representative pictures of the ABCG1 immunohistochemical staining provided in Fig. 1C in the manuscript by Liimatta et al shows that ABCG1 protein expression is fully eliminated from the zona glomerulosa. However, blue spots representing ABCG1-expressing cells are still clearly visible in the zona fasciculata within adrenal sections of mice with CYP11B2-driven ABCG1 deficiency. Follow-up studies in which the CYP11B1 promoter is utilized as the driver of the Cre recombinase expression and the adrenocortical cell-specific ABCG1 gene targeting are thus warranted.

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Disclosures

The author has nothing to disclose.

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