

## Adrenal Metabolic Changes and Elevated Steroidogenesis in Obesity and Diabetes Affecting Salt Sensitivity

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### Summary

**Aim:** Obese diabetic patients are known to exhibit salt-sensitive hypertension. db/db mice, a model of obese diabetes mellitus, are also known to be susceptible to salt-sensitive hypertension due to a lack of increased urinary salt excretion upon salt loading. db/db mice have been reported to show higher levels of aldosterone in the blood, suggesting a link to salt sensitivity. But the mechanism of increased adrenal steroid hormone synthesis in obese diabetic pathology is not clear. Perilipin 1, a peri-lipid droplet protein, is involved in both maintenance and degradation of lipid droplets, and is also thought to regulate cholesterol, a substrate of steroid hormones, in the adrenal gland, but its function is not yet understood. In this study, we hypothesized that increased adrenal steroid hormone synthesis underlies salt sensitivity in db/db mice and aimed to elucidate the mechanism and explore therapeutic strategies.

**Methods:** We cultured Y1 adrenal carcinoma cells under hyperglycemic conditions and observed their hormone production capacity and mRNA changes compared to normoglycemic conditions. In addition, we will overexpress and suppress perilipin-1 expression in Y1 cells. We decrease blood glucose levels in db/db mice by administering SGLT2 inhibitors and examine gene expression including perilipin-1 in the adrenal gland.

**Results:** Increased steroid hormone production in Y1 cells under hyperglycemic conditions was observed. Overexpression of perilipin 1 increased hormone production, suggesting metabolic changes such as fatty acids in the cells. db/db mice treated with SGLT2 inhibitor showed decreased blood glucose levels, decreased adrenal perilipin 1 expression and changes in fatty acid synthase, similar to cell experiments.

**Discussion:** Perilipin 1 is involved not only in lipid droplet stabilization but also in metabolic regulation in adrenocortical cells and in the synthesis of steroid hormones. SGLT2 inhibitors may affect salt-sensitive hypertension by regulating perilipin 1 expression through lowering blood glucose level and suppressing steroid hormone synthesis.