Novel genes involved in pathophysiology of gonadotropin-dependent adrenal tumors in mice - DTU Orbit (07/10/2018)

Novel genes involved in pathophysiology of gonadotropin-dependent adrenal tumors in mice

Specific inbred strains and transgenic inhibin-α Simian Virus 40 T antigen (inhα/Tag) mice are genetically susceptible to gonadectomy-induced adrenocortical neoplasias. We identified altered gene expression in prepubertally gonadectomized (GDX) inhα/Tag and wild-type (WT) mice. Besides earlier reported Gata4 and Lhcgr, we found up-regulated Esr1, Prlr-rs1, and down-regulated Grb10, Mmp24, Sgcd, Rerg, Gnas, Nfatc2, Gnhr, Igf2 in inhα/Tag adrenal tumors. Sex-steroidogenic enzyme genes expression (Srd5a1, Cyp19a1) was up-regulated in tumors, but adrenal-specific steroidogenic enzyme (Cyp21a1, Cyp11b1, Cyp11b2) down-regulated. We localized novel Lhcgr transcripts in adrenal cortex parenchyma and in non-steroidogenic A cells, in GDX WT and in intact WT mice. We identified up-regulated Esr1 as a potential novel biomarker of gonadectomy-induced adrenocortical tumors in inhα/Tag mice presenting with an inverted adrenal-to-gonadal steroidogenic gene expression profile. A putative normal adrenal remodeling or tumor suppressor role of the down-regulated genes (e.g. Grb10, Rerg, Gnas, and Nfatc2) in the tumors remains to be addressed.

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