GONADOTROPIN RELEASING HORMONE ANTAGONIST TREATMENT INDUCES CELL CYCLE ARREST IN GONADAL SOMATIC CELL AND ADRENOCORTICAL TUMORS

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BACKGROUND

G-coupled protein receptors in tumor tissues have been successfully used as potential targets for cancer therapies. In this study, we used transgenic mice carrying SV40 T-antigen under the inhibit alpha 6kb promoter (inho/Tag) that develop granulosa/Leydig cell tumors by the age of 6-months. Prepubertal gonadectomy results in adrenocortical tumors 5mo after castration. Their gonadal/adrenal tumors and tumor-derived cell lines: BLT1 (Leydig), KK1 (granulosa), Calpha1 (adrenocortical) express gonadotropin releasing hormone (GnRHR) and luteinizing hormone receptors (LHCR). Earlier, we have shown that chemical (by GnRH antagonist) or genetic (crossbreeding with hpg mice) ablation of GnRH could prevent gonadal/adrenocortical tumorigenesis in inho/Tag mice. Furthermore, GnRH antagonist treatment blocked the adrenocortical tumor progression in these mice. Hereby, we studied GnRH antagonist Cetrorelix acetate (CTX) induced mechanism of tumor suppression in gonadal and adrenocortical tumors in vitro and in vivo.

MATERIALS AND METHODS

TREATMENT STRATEGY:
Vehicle
Cetrorelix
Cetrorelix + hCG
hCG

Vehicle
Cetrorelix
Cetrorelix + hCG
hCG

E2
P4
FSH
LH

Treat Blr: CTX= 10μM
CTX+hCG= 10μM+ 10ng/ml
hCG= 10ng/ml

In vitro

RESULTS

IN VIVO

CONCLUSIONS

1. GnRH antagonist Cetrorelix acetate (CTX) treatment induced cell cycle arrest in G0/G1 phase, resulting in significantly decreased cell viability and proliferation in all the studied tumor cell types vs. vehicle.
2. Treatment with human chorionic gonadotropin (hCG) without or with CTX, did not affect the gonadal somatic/adrenocortical tumor progression in inho/Tag mice.

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