FSH SUPPLEMENTATION INCREASES THE GROWTH OF PC-3 HUMAN PROSTATE CANCER CELL XENOGRAFT IN GONADOTROPIN-SUPPRESSED NUDE MICE

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INTRODUCTION:
Gonadotropin-releasing hormone (GnRH) analogues are now the standard hormonal treatment for prostate cancer1. A fundamental difference between GnRH agonist and antagonist treatment is the permanent suppression of both LH and FSH by antagonist (e.g. Degarelix), while a rebound in FSH is associated with agonist (e.g. Leuprolide) treatment (Figs. 1A and B)2,3. The benefits of antagonist include the immediate onset of action and profound long-term suppression of FSH, suggested to be an independent growth factor in prostate cancer.

METHODS:
Nude male intact mice (IM; N=20) and gonadectomised mice (GM; N=20) were inoculated with 2×10⁶ PC-3 human prostatic cancer cells. Half of the mice (N=10/group) received degarelix at a dose of 30 mg/kg body weight subcutaneously in a slow-release formula. In another experiment (N=10/group), degarelix treatment was supplemented with recombinant human FSH at 10 IU/kg/day using i.p. ALZET osmotic minipumps. Tumour growth was monitored over a 4-week period by external inspection and caliper measurement.

RESULTS:
1. Degarelix suppressed growth of PC-3 cells in IM and GM male nude mice

2. Inhibition of PC-3 xenografts growth by degarelix

3. FSH treatment increased tumour size in IM with and without degarelix treatment

4. Degarelix decreased reproductive organ weights of intact mice

5. Tumour xenografts but not original PC-3 cells expressed gonadotropin receptors

CONCLUSIONS:
2. FSH treatment increases tumour weights in both control and degarelix treated mice.
3. Cultured PC-3 cells do not express FSHR and LHR, but both receptors are expressed in tumours.
4. Similar findings in both groups of mice indicates that testicular function is not involved in growth of the androgen receptor-negative PC-3 cells.
5. The findings suggest that the suppression of both gonadotropins by GnRH antagonist treatment may offer an advantage over GnRH agonist (only LH is permanently suppressed) in the treatment of prostate cancer.

References:

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