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Pre-treatment with FSH Enhances the Ability of a LHRH-Lytic Peptide Conjugate (EP-100) to Target and Destroy Human Pancreatic Cancer Cells

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We hypothesize that pre-treatment with FSH will enhance the ability of a LHRH-lytic peptide conjugate (EP-100) to target and destroy pancreatic cancer cells by increasing LHRH receptor gene expression.

### Hypothesis

- To determine, in vitro study whether pre-treatment with FSH increases the cytotoxicity of EP-100 in PANC-1 cells.
- To determine if pre-treatment of nude mice bearing PANC-1 cancer cell xenografts with FSH enhances the ability of EP-100 to target and destroy these cells.

### Methods

**Quantitative Real Time RT-PCR:** Total RNA was subjected to two-step SYBR Green real time RT-PCR using LHRH receptor and β-actin gene specific primers. Relative quantification of LHRH receptor mRNA was performed by standard curve method. The graph represents relative fold expression of LHRH receptor gene in PANC-1 cells.

**Cell Viability Assay:** Cell viability was determined using the MTT reagent method which is a colorimetric assay. The absorbance at 590 nm is directly proportional to the number of live cells. The cell viability is represented as % control.

**In vivo:** PANC-1 tumor xenografts were generated in athymic BALB/c female nude mice and were randomly distributed into the following groups (n=11): 1) Baseline controls, sacrificed at the beginning of the treatment (2) Vehicle treated controls (3) FSH treated (3 µg/day), i.c. for 3 days (4) EP-100 treated (0.02 mg/kg), i.v. (5) EP-100 treated (0.2 mg/kg), i.v. (6) EP-100 pre-treated with FSH (3 µg/day), i.c. for 3 days prior to EP-100 (7) EP-100 treated (0.2 mg/kg), i.v. pre-treated with FSH (3 µg/day), i.c. for 3 days prior to EP-100. Treatments (except FSH) were administered by tail vein injections given once a week for three weeks. Mice were necropsied one week following the last injection. Body weights, tumor weights and volumes (length x width x height) were recorded and photographs of all the tumors were taken. At necropsy tissues were removed, weighed and fixed for histopathological studies.

### Results

**In Vitro**

FSH increased the amount of LHRH receptor gene expression in PANC-1 cells by 3-fold and pre-treatment with FSH enhanced the cytotoxicity of EP-100.

**In Vivo**

Pre-treatment with FSH significantly increased the efficacy of EP-100 in vivo at 0.02 mg/kg and 0.2 mg/kg compared to baseline.

- FSH pre-treatment may be useful in treating pancreatic cancer with LHRH-lytic peptide conjugates.

### Conclusions

FSH increased the amount of LHRH receptor gene expression in PANC-1 cells by 3-fold and pre-treatment with FSH enhanced the cytotoxicity of EP-100.

**References**