

Modulation Of Endometrial HOXA10 And Other Markers Of Endometrial Receptivity By Human Chorionic Gonadotropin (Hcg) As A Function Of Uterine Age

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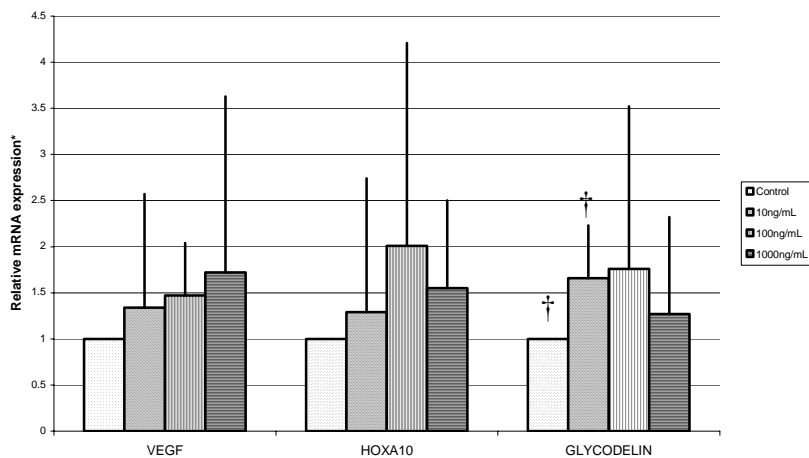
Objective: *In vitro* evaluation of endometrial receptivity (ER) remains elusive and is limited by cell culture which disrupts physiologic interactions between stroma, glands, and epithelium. We have previously confirmed the utility of the endometrial explant culture system as a model for studying ER. Using this model, we sought to characterize the endometrial response to hCG, as influenced by uterine age, using receptivity markers including HOXA10, vascular endothelial growth factor (VEGF), and glycodeclin.

Materials and Methods: Endometrial biopsy was performed in 9 prospective recipients of egg donation. Subjects (42 ± 8 years) received estradiol (E₂) and progesterone (P₄) with a biopsy performed on day 7 of P₄. Samples were cut into 1mm³ pieces and cultured in DMEM/F-12 with E₂ and P₄, without (control) or with hCG (10, 100, 1000ng/mL), on Millicell-CM inserts for 24 hours. Explant viability was assessed using immunohistochemistry (IHC). Semi-quantitative PCR was performed using an internal control gene to evaluate relative mRNA expression of HOXA10, VEGF, and glycodeclin.

Results: Explant viability was confirmed on IHC by histology and proliferation staining. A non-significant, dose-dependent increase was observed in VEGF ($p=0.24$), HOXA10 ($p=0.07$), and glycodeclin ($p=0.11$) in response to increasing hCG. HOXA10 trended towards a statistically significant increase between hCG of 10 and 100ng/mL (1.29 ± 1.45 vs 2.21 ± 2.01 ; $p < 0.08$). Glycodeclin demonstrated a statistically significant increase between control and 10ng/mL hCG (1.00 vs 1.66 ± 0.57 ; $p < 0.05$). Age was inversely associated with HOXA10 (-0.09 ± 0.03 mRNA expression/year of age, $p < 0.01$) and positively associated with VEGF (0.04 ± 0.02 mRNA expression/year of age, $p < 0.05$).

Conclusions:

1. The endometrial explant culture system is a promising model for the study of ER as it maintains interactions between stroma, glands, and epithelium.
2. HOXA10, VEGF, and glycodeclin all demonstrated a dose-response increase in mRNA expression in response to hCG, though statistical significance was not achieved.
3. Increasing expression of ER markers in response to hCG supports the role of hCG as a candidate protein for blastocyst-endometrial communication.
4. Statistically significant associations between age and expression of receptivity markers provides the first evidence that, among recipients of egg donation, uterine age may play a role in ER on a molecular level.



* relative to an internal control gene, GAPDH

† $P < 0.05$