FGF9 stimulates ovarian progesterone production

A. E. Drummond, M. Dyson, J. K. Findlay

Prince Henry’s Institute, Clayton, VIC, Australia

FGF9, a member of the fibroblast growth factor family (FGF), is known to be a male sex-determining factor involved in testicular cord formation (1). FGF9 knockout males are sex-reversed (2). However, nothing is known about FGF9’s role in folliculogenesis because these mice die at birth (2). We previously reported the presence of FGF9 mRNA and protein in the immature rat ovary (3). In these studies we investigated: (1) the presence of FGF9 receptors (FGFR3) on granulosa cells (GC); and (2) the impact of FGF9 on GC progesterone production.

GC isolated from 21 day old diethylstilboestrol (DES)-treated rats were cultured for either 2 hours (RNA) or 2 days (progesterone) in McCoys 5C with FGF9 (0.1-50ng/ml) ± FSH (100ng/ml). Progesterone was measured in conditioned media by radioimmunoassay. RNA was extracted from the granulosa cells and reverse-transcribed for PCR. Specific primers for P450 side chain cleavage (SCC) amplified a 329 bp cDNA fragment. GAPDH was used for data normalisation. The FGF9 receptor FGFR3, was immunolocalised on formalin-fixed, paraffin-embedded sections of immature rat ovary.

FGFR3 protein was localised only to GC of the ovary. Progesterone production by cultured GC was significantly elevated by FGF9, consistent with the presence of FGFR3. Relative to a maximally stimulating dose of FSH, FGF9 increased progesterone production 10-fold. In preliminary studies, FGF9 increased the expression of P450 SCC mRNA by cultured GC revealing a mechanism by which FGF9 increases progesterone production. These data suggest a role for FGF9 not just in testicular formation, but in the regulation of ovarian steroidogenesis. **Supported by the NH&MRC of Australia (Regkey 241000 & 198705).**