ESTROGEN ACTIONS ON FOLLICLE FORMATION AND EARLY FOLLICLE DEVELOPMENT

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Estradiol 17 beta (E2) effects late follicular development whilst primordial follicle formation and early activation are thought to be independent of E2. To test this hypothesis we compared numbers of primordial and primary follicles in wildtype and E2 deficient ArKO mice, and the immunohistochemical staining or mRNA expression of Mullerian inhibiting substance (MIS), Wilms tumour 1 (WT-1), and growth differentiation factor (GDF9), known to effect early follicular differentiation. Proliferating cell nuclear antigen (PCNA) staining was a marker of proliferative index. The effects of E2 replacement for 3 wk in 7 wk old ArKO and wildtype mice on these parameters were also tested. We used unbiased, assumption-free stereological methods for quantification of early follicular numbers in the mouse ovary (1). ArKO mice had reduced numbers of primordial and primary follicles compared to wildtype (63%, $p<0.001$ and 60%, $p=0.062$ of Wt respectively). This reduction was not corrected by E2 treatment, suggesting that E2 effects the initial formation or activation of primordial follicles. There was a significant increase in the diameters of the oocytes in primordial follicles of ArKO mice compared to wildtype. There were no differences in the immunostaining of MIS, WT-1 and PCNA in primordial and primary follicles between wildtype and ArKO mice. The only difference was as a consequence of Sertoli and Leydig cells in ovaries of ArKO mice. GDF9 mRNA expression was markedly increased in ArKO ovaries. E2 treatment restored the ovarian follicular morphology, and consequently the immunostaining patterns, but had no effect on early follicle numbers. In conclusion, E2 has a role in controlling the size of the oocyte and primordial follicle pools in mice. *Supported by NH&MRC RegKey #241000 and 198705.*

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