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Specialisation of the adrenal reticularis for DHEA synthesis explains human reproductive ageing

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The explanation of why women from about age 37 have an accelerated rate of reproductive decline and increasing rates of trisomic offspring has been elusive. The observation that disturbances of the fidelity of mitosis occurs in peripheral blood lymphocytes at the same ages has suggested that the mediator of the problems with meiosis do not originate from the oocytes and possibly not even from the ovary. Similar, accelerated rates of decline in meiosis are not observed in most animal models and the phenomenon is probably linked to the evolution of menopause. The evolution of menopause is now known to be linked to evolution within the CYP17A1 gene (cytochrome P45c17 enzyme) and the concurrent co-localisation of P450c17 and CytB5 in a specialised region of the adrenal cortex reticularis (AR) so that it only synthesises the steroid hormone DHEA. During development, the AR cells arise from the mesonephros along with the Sertoli cells in males and theca (ovarian cells) in females, which all share the ability to synthesise DHEA. DHEA is readily converted into DHEA-S and this is well known to stimulate the peroxisome proliferator PPAR α , which is a major regulator of many genes including fatty acid metabolism. Ageing of cells in the human AR occurs relatively early. No TERT activity (telomere elongation) has been detected in the adrenal cortex and cells cease replication by about age 40 in both males and females. This seems to particularly affect the AR which ceases DHEA synthesis at the same time. As reproduction declines and after menopause, DHEA is only synthesised by the ovarian theca cells. A model of female reproductive ageing is presented that proposes that changes in meiosis and mitosis occur as a result of changes in the lipid composition of cellular membranes secondary to loss of DHEA synthesis by the AR. Clinical interventions that successfully reverse age-related infertility with DHEA supplementation support this model.

Biography

Judy Ford joined the University of South Australia in March 2006 in a new position of Research Education Adviser for Science, Engineering and Technology. Her major role is to deliver workshops and give support to PhD students as they develop the scientific and transferable skills necessary to become successful and independent professionals. She also undertakes her own health (ageing) related research in conjunction with the Centre for Regional Engagement. Her research interest lies in understanding the critical changes that underlie ageing, especially with relevance to reproduction and cancer.

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