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Alternative splicing of the androgen receptor in PCOS with ovulatory dysfunction

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Androgen receptor is essential for healthy developing follicle, while excess intra-ovarian androgens impair follicle growth. Hyperandrogenism is the main characteristic of polycystic ovary syndrome (PCOS), a highly prevalent endocrine disorder and major threat to women's health. However, the etiology of hyperandrogenism is poorly understood. We describe the specific transcription of two AR splice variants, insertion (ins) and deletion (del) isoforms, in granulosa cells (GCs) of women with PCOS. Wild-type (wt) AR existed in each individual; surprisingly its transcription is comparable between PCOS and control group. Women with AR ins or del isoforms showed distinct hyperandrogenism, attenuated androgen metabolism, enhanced androgen synthesis and altered expression corresponding enzymes, aromatase and steroid 17 α -hydroxylase, in GCs, particularly the former. *In vitro* over-expression of different AR variants in primarily cultured human GCs not only confirmed the *in vivo* results, but also revealed notable change of expression of folliculogenesis, steroidogenesis and ovarian structure modeling-related genes. Its underlying mechanism is an inferior ability of nuclear shuttle and DNA binding, including U1 androgen response element (ARE) of *CYP19A1* gene, of AR as nuclear receptor. In conclusion alternative splicing of AR in GCs is a cause of hyperandrogenism leading to follicular arrest in PCOS.

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Polycystic ovary syndrome and infertility: An updated overview

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Polycystic ovary syndrome, or PCOS, is the most common cause of female infertility related to the infertility anovulation. It is well known that many of the symptoms of PCOS are present before a girl has her first menstrual period and 5-10% of females age 18 to 44 are affected by PCOS in some way. PCO syndrome results from a combination of factors, including genes and environmental features. Many women are not aware that they have PCOS until they follow a diagnostic procedure on infertility or menstrual and ovulation irregularities such as amenorrhea or oligomenorrhea, heavy and anovulatory periods. The PCOS symptoms at 70% is hirsutism, severe acne, that does not respond to conventional treatments or that remains in spite of treatment, very oily skin and patches of thickened, dark brown or black skin, and 70-95% cysts on the ovaries. The hormone levels are out of balance in women with PCOS and they have, in fact, higher than normal levels of androgens and may have lower than normal levels of estrogen. The high levels of androgens can cause problems with ovarian follicle growth and development, make immature follicles on the ovaries forming large lumps or cysts. The current treatments for PCOS includes lifestyle changes, such as eating a lower calorie diet, losing weight, and getting more physical activity, oral contraceptives, antiandrogens and insulin sensitizing agents. Women with PCOS to succeed pregnancy are treated with clomiphene citrate, metformin, gonadotropins and can also try other forms of assistive reproductive technology, such as egg donation and in vitro fertilization. The surgical procedure, laparoscopic ovarian drilling, sometimes is also used. Nowadays, the PCOS related infertility, in most cases coexists with many well established male and female infertility factors, as the result for the inquiry of an infertility algorithm investigation and a step by step way of management and infertility treatment.

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