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Molecular Discovery Could Point the Way to New Treatment for Androgen Excess

Posted on Thursday 28th May 2009

Scientists at the University of Birmingham have uncovered a novel cause of androgen excess that may help to improve diagnosis and lead to the development of more effective treatment options for the condition polycystic ovary syndrome that affects between 5-15% of women.

Researchers have discovered that a mutation in an enzyme responsible for deactivating the steroid dehydroepiandrosterone (DHEA) is sufficient to cause the over production of androgens in females.

In humans, dehydroepiandrosterone (DHEA) is the most abundant steroid in circulation, and is the main source for androgen synthesis in women. While DHEA can be converted directly to androgens, modification of this steroid by addition of a sulfate group can switch it to an inactive form, DHEAS, which cannot be directly converted to androgens.

Two enzymes, PAPSS1 and PAPSS2, are responsible for this process. In findings published today in the *New England Journal of Medicine*, a research group led by Prof Wiebke Arlt reveals that mutations in the PAPSS2 gene are sufficient to cause androgen excess in the female body. They do this by reducing the ability of the body to switch DHEA to its inactive form (DHEAS), thereby creating an increased pool of steroids available for conversion to androgens, including testosterone.

Prof Arlt explains: "*Our observations highlight the crucial role of DHEA sulfation as a gatekeeper to human androgen synthesis by demonstrating that impaired DHEA sulfation increases the DHEA pool available for conversion to active androgens, thus causing androgen excess.*"

Androgens are produced naturally in the body of both men and women. Levels in women are typically lower and are regulated and balanced with female hormones. However, in some cases a woman's body can produce too much, known as androgen excess. Androgen excess is a main symptom of the polycystic ovary syndrome (PCOS). Symptoms of PCOS include acne, excessive hair growth, irregular periods and weight gain. PCOS is also associated with an increased risk of diabetes and high blood pressure.

Prof Arlt concludes: "*Our findings open up the possibility for future therapeutic advancements where the circulating pool of DHEA can be targeted and reduced in order to control the disorder.*"

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Further Media Information – Prof Wiebke Arlt is available for interview. Please contact Anna Mitchell on 0121 414 6029 / 07920 593946.

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