

# The human genital tubercle is steroidogenic organ at early pregnancy

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## Introduction

It is generally accepted that androgens produced by fetal Leydig cells (FLC) control proper masculinization of the male external genitalia. Here, we hypothesized that the human genital tubercle (GT) has potential to synthesize androgens independently of FLC at early pregnancy.

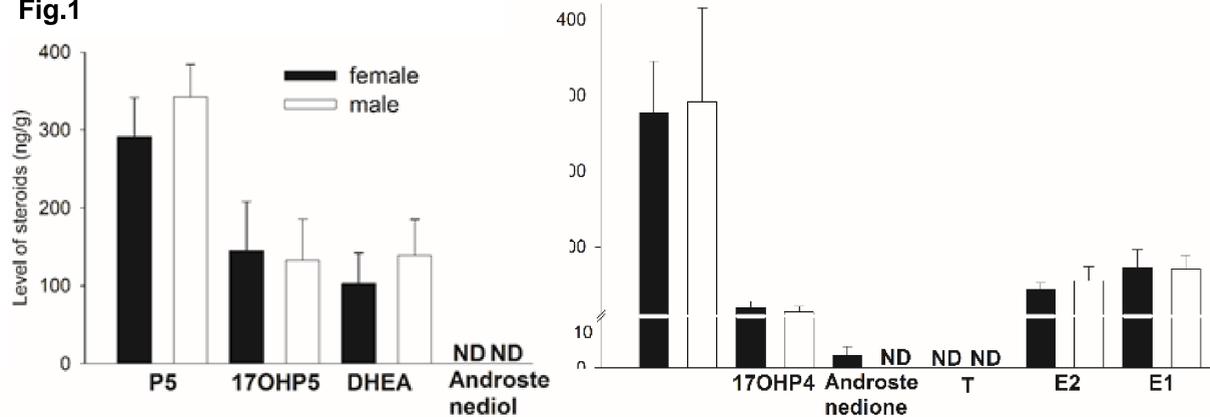
## Methods

Human fetal GT were obtained with ethical permit from aborted fetuses in connection with elective termination of pregnancy during the first trimester (8-12 GW) at Karolinska University Hospital, Stockholm, Sweden. Expression of steroidogenic enzymes at the mRNA level were explored by qPCR and by immunohistochemical method at the protein level.

## Results

We observed that human GT of both genders have capacity to synthesize steroids of the  $\Delta 4$ ,  $\Delta 5$  and alternative pathway of DHT synthesis including the androgen itself (Fig.1). The presence of steroids in the GT was associated with the expression of corresponding steroidogenic enzymes (Fig.2,3). Levels of steroids and the expression of steroidogenic enzymes were similar in the GT from male and female fetuses (Fig.2).

Fig.1



**Fig.1** The tissue levels (ng/g) of steroids in the GT of male and female fetuses at the end of the first trimester. The values shown are means  $\pm$  SE for seven GT isolated from male and female fetuses, respectively at GW9-11. ND – not detectable.

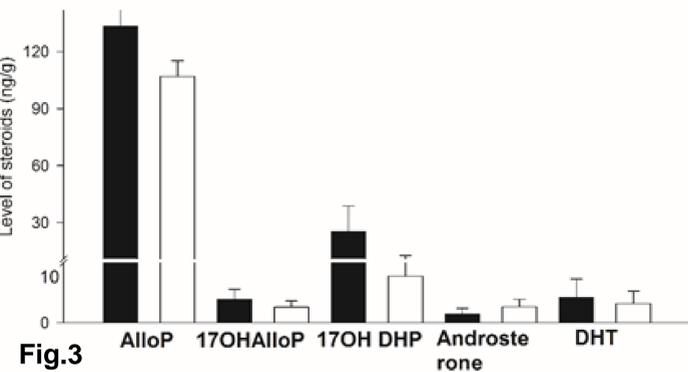
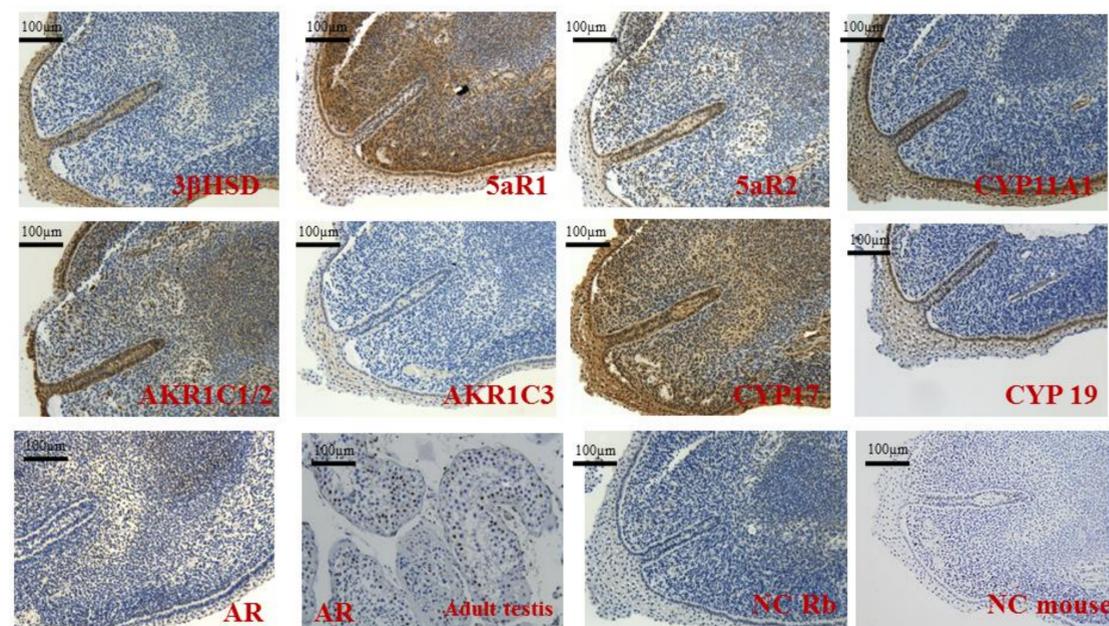
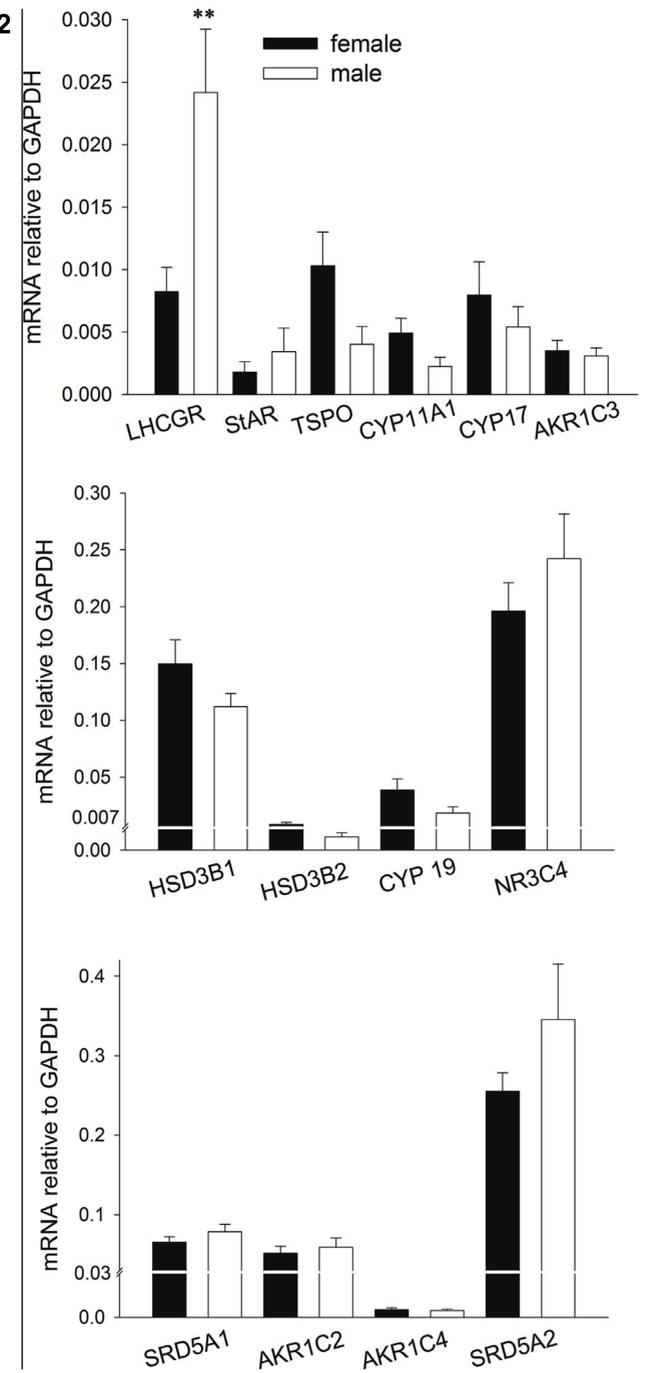


Fig.3



**Fig.3** Immunohistochemical detection of steroidogenic enzymes in human male genital tubercle at GW10 (n=1). Negative control (NC) shows the absence of immunostaining in the presence of non-immune serum IgG of rabbit (NC Rb) and mouse (NCmouse) origin.

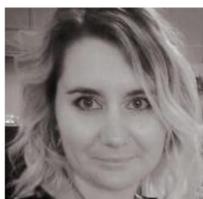
Fig.2



**Fig.2** Sex-dependent differences in the levels of mRNAs encoding steroidogenic genes in the GT of male and female fetuses at GW9-11. The mRNA levels were normalized to GAPDH as a house keeping gene. \*P<0.01 compared to female group.

## Discussion

Altogether, the present study demonstrated that the human GT at early pregnancy is steroidogenic organ with potential to synthesize DHT via the alternative testosterone-independent pathway. We suggest that local production of DHT by the human GT plays an important role in proper formation of the urethra at very early stage of the external genitalia development.



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