Mast cells and steroidogenesis in human fetal adrenal

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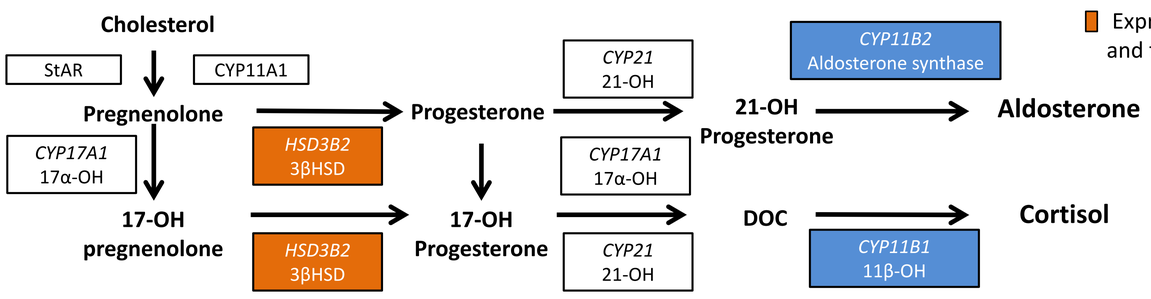
INTRODUCTION

Mast cells, present in human adult adrenal gland, may control mineralocorticoid synthesis and secretion especially in aldosterone-producing adenomas via the serotonin pathway.

As cell-to-cell interactions involving immune cells are implicated in human organogenesis and as similarities exist between tumors and normal human fetal development, the role of mast cells may be hypothesized in fetal adrenal development. Recently, we demonstrated the presence of mast cells in human adrenal development from 18 WG (weeks of gestation) in the adrenal subcapsular layer.



SRB1 (Scavenger receptor class B type I); StAR (Steroidogenic acute regulatory protein); CYP11A1 (cytochrome P450 11A1); 17α-OH (17α-hydroxylase); 3βHSD (3β-hydroxysteroid dehydrogenase); 21-OH (21-hydroxylase); 11β-OH (11β-hydroxylase)

AIM OF THE STUDY

To investigate the steroidogenesis enzymes and the serotonin pathway during the adrenal development in correlation to the mast cell specific protease, tryptase expression.

MATERIAL AND METHODS

Human tissue collection

Human fetal tissue (*n*=28) from 16 to 41 WG were collected from medical and surgical terminations of pregnancy

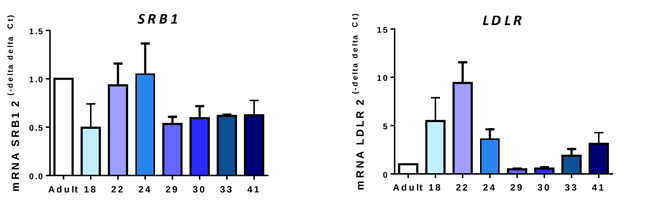
Methods

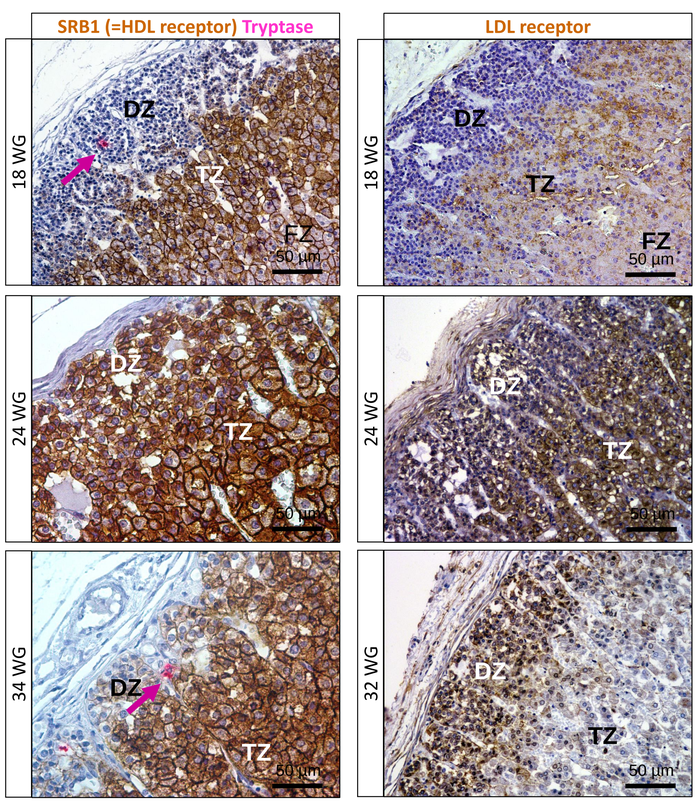
Immunochemical studies were performed on 28 paraffin-embedded adrenal glands at 16-40 weeks of gestation (WG). Moreover, steroidogenic enzymes mRNAs were quantified at 18, 22, 24, 29, 30, 33 and 41 WG and compared to adult tissue.

We studied HDL and LDL cholesterol receptors, steroidogenic enzymes and serotonin signaling pathway actors.

RESULTS

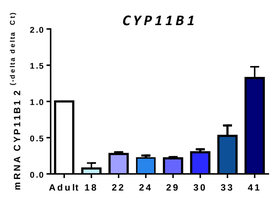
HDL AND LDL RECEPTORS

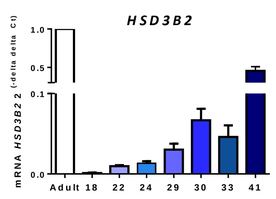


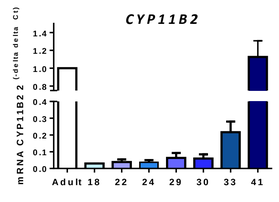


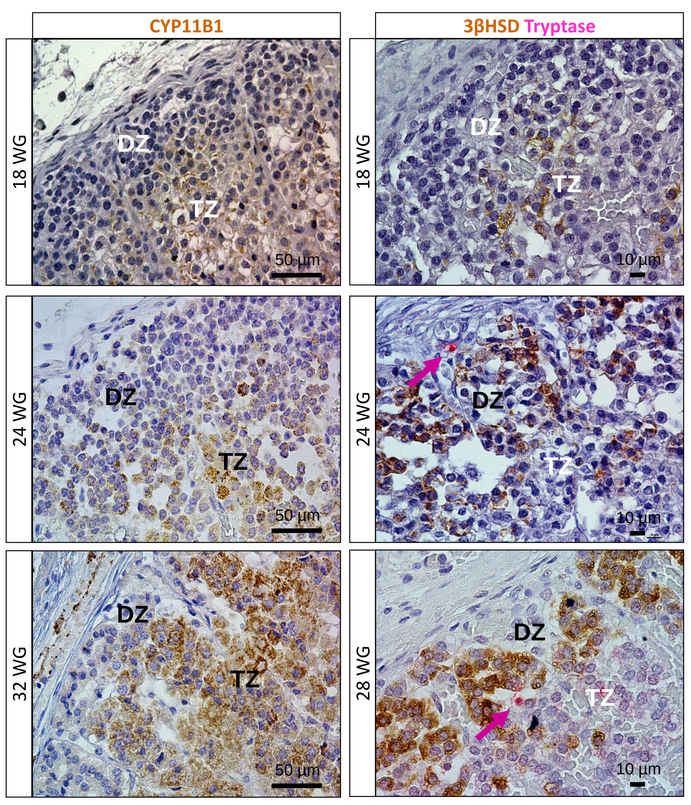
HDL and LDL receptors are initially localized in both the TZ (transitional zone) and FZ (fetal zone), and then extend from 24 WG to the DZ (definitive zone), probably indicative of the onset of steroidogenic activity.

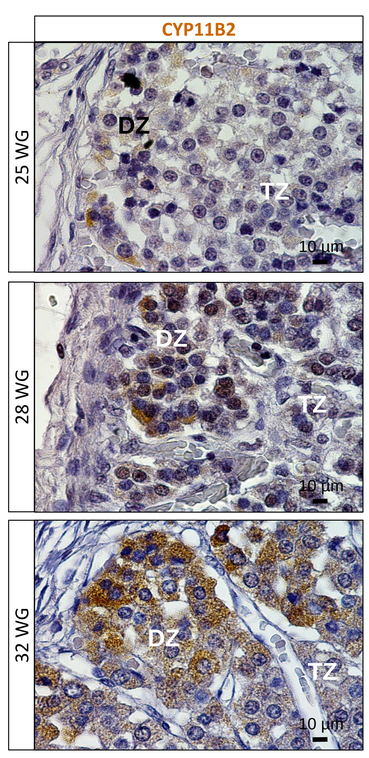
STEROIDOGENIC ENZYMES EXPRESSION







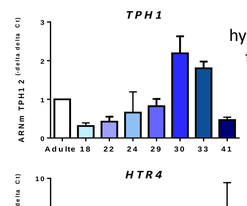




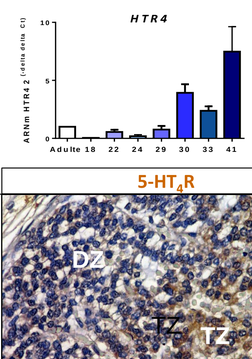
3βHSD and CYP11B2 both required for aldosterone synthesis, are present in the DZ, close to mast cells, 3βHSD being first detected from 18 WG whereas CYP11B2 is detected quite later from 24-25 WG with significant increase of its expression from 32-33 WG.

CYP11B1 required from cortisol synthesis was detected earlier from the first stages studied in the TZ and FZ only, away from mast cells.

SEROTONIN PATHWAY



(Tryptophan hydroxylase type 1), the rate-limiting enzyme that catalyzes 5-HT synthesis



TPH1 and *5-HT$_4$R* are both expressed in the fetal adrenal, with increased expression from 30 WG.

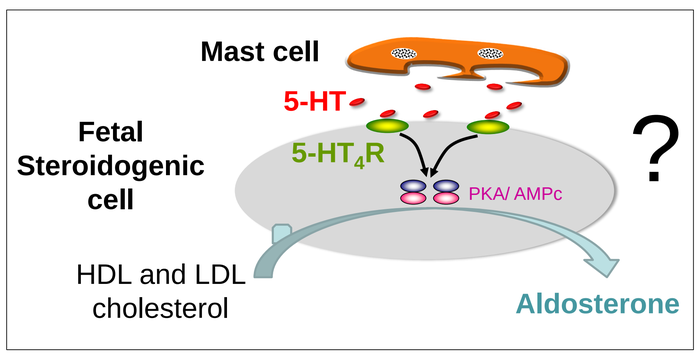
5-HT$_4$R is localized in the DZ, close to mineralocorticoid-producing cells and mast cells.

CONCLUSION

❑ **Mast cells, TPH1/5HT$_4$R are present in the developing human adrenal gland with a possible spatiotemporal correlation with expression of the steroidogenic enzymes required for aldosterone biosynthesis (3βHSD and CYP11B2).**

❑ **Therefore, our results could suggest a paracrine regulation of the fetal aldosterone synthesis involving the mast cells/serotonin pathway. Further studies are now required to confirm this hypothesis.**

❑ **In addition, we showed that CYP11B2 is expressed quite late during the gestation, suggesting an aldosterone production from the third trimester only.**



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