Expression of TGFβ signaling molecules and genes in loci linked to polycystic ovary syndrome in human fetal and adult tissues

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Altered signaling of androgens, anti-Mullerian hormone and transforming growth factor beta (TGFβ1) during fetal development have all been implicated in the predisposition to polycystic ovary syndrome (PCOS) in later life. There is also a genetic predisposition to PCOS. In fetal ovarian fibroblasts, we have shown that TGFβ1 regulates androgen signalling and expression of seven genes located in genetic loci associated with PCOS (Hum Reprod. 2022, 37:1244-1254). Since PCOS exhibits a myriad of symptoms, it likely involves many organs other than just ovaries. We aimed to identify the relationships between TGFβ signalling molecules and PCOS candidate genes in different human fetal and adult tissues. Using RNA-sequencing data, we examined the expression patterns of TGFβ signalling molecules in human ovary, testis, heart, liver, kidney, brain tissue and cerebellum from 4-20 weeks of gestation and postnatally. We also conducted correlation analysis with expression of PCOS candidate genes. TGFβ signalling molecules were dynamically expressed in most tissues prenatally or/and postnatally. Many relationships were observed. *FBN3*, a PCOS candidate gene involved in TGFβ signaling, was expressed during fetal development in all tissues examined. The PCOS candidate genes *HMGA2*, *YAP1* and *RAD50* correlated significantly ($P < 0.01$) with most TGFβ signalling molecules in at least four fetal tissues; and specifically with *TGFBR1* in six out of the seven tissues examined. This study suggests that crosstalk is likely to occur between genes in loci associated with PCOS and TGFβ signaling molecules in multiple tissues during fetal development. Thus, alteration in TGFβ signaling during fetal development could affect many tissues, potentially contributing to the multiple symptoms and phenotypes of PCOS in later life.