# WNT4 Balances Development vs Disease in Gynecologic Tissues and Women's Health

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The WNT family of proteins is crucial in numerous developmental pathways and tissue homeostasis. WNT4, in particular, is uniquely implicated in the development of the female phenotype in the fetus, and in the maintenance of müllerian and reproductive tissues. WNT4 dysfunction or dysregulation can drive sex-reversal syndromes, highlighting the key role of WNT4 in sex determination. WNT4 is also critical in gynecologic pathologies later in life, including several cancers, uterine fibroids, endometriosis, and infertility. The role of WNT4 in normal decidualization, implantation, and gestation is being increasingly appreciated, while aberrant activation of WNT4 signaling is being linked both to gynecologic and breast cancers. Notably, single-nucleotide polymorphisms (SNPs) at the WNT4 gene locus are strongly associated with these pathologies and may functionally link estrogen and estrogen receptor signaling to upregulation and activation of WNT4 signaling. Importantly, in each of these developmental and disease states, WNT4 gene expression and downstream WNT4 signaling are regulated and executed by myriad tissue-specific pathways. Here, we review the roles of WNT4 in women's health with a focus on sex development, and gynecologic and breast pathologies, and our understanding of how WNT4 signaling is controlled in these contexts. Defining WNT4 functions provides a unique opportunity to link sex-specific signaling pathways to women's health and disease.