Role of Wilms' Tumor 1 in Sex Development

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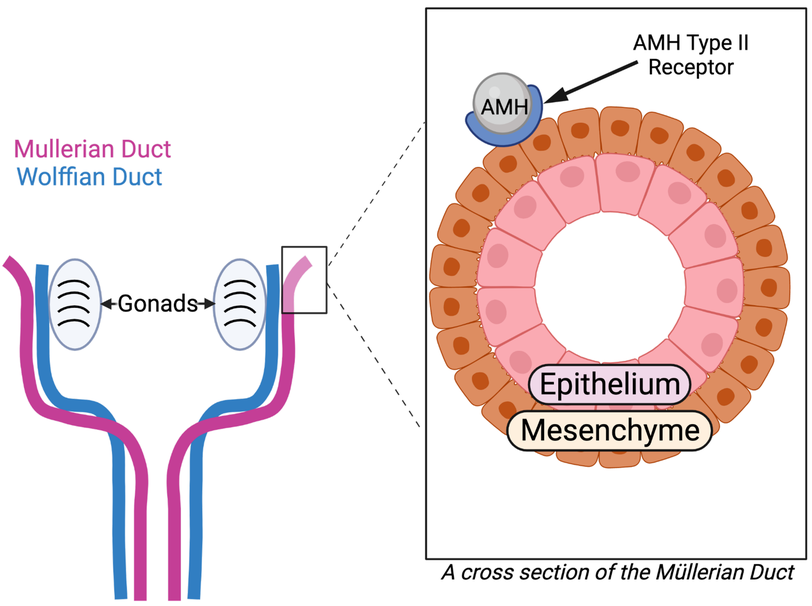
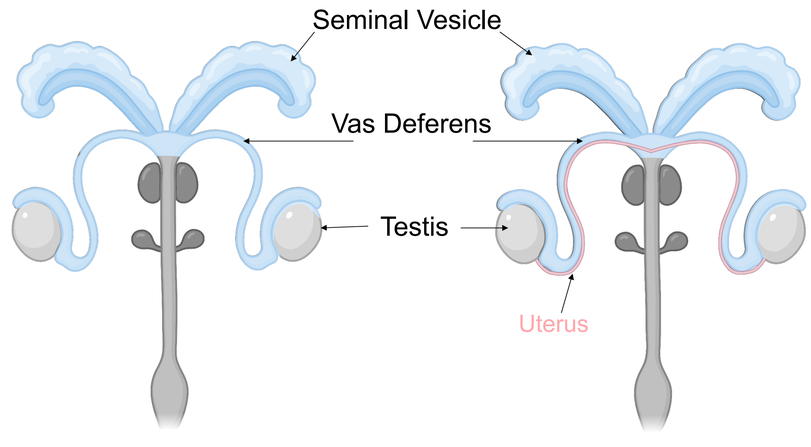
Introduction

Embryos develop two epithelial ducts, the Wolffian and Müllerian ducts. The Wolffian Duct differentiates into the male-specific sex organs. The Müllerian Duct differentiates into the female-specific sex organs. In the male reproductive tract, the gonads develop into testes which produce testosterone and Anti-Müllerian Hormone (AMH).



A cross section of the Müllerian Duct

From the testes, AMH will travel to the Müllerian Duct mesenchyme to signal its receptor, Anti-Müllerian Hormone Type II Receptor (AMHR2). Once AMH & AMHR2 bind, the Müllerian Duct will begin to regress. Ultimately, this will leave the Wolffian Duct which will further develop into the male reproductive system. Mutations in *Amhr2* leads to Persistent Müllerian Duct Syndrome (male with a uterus).



Wilms' Tumor 1 (WT1) is co-expressed with AMHR2 in the Müllerian Duct mesenchyme prior to and during regression.

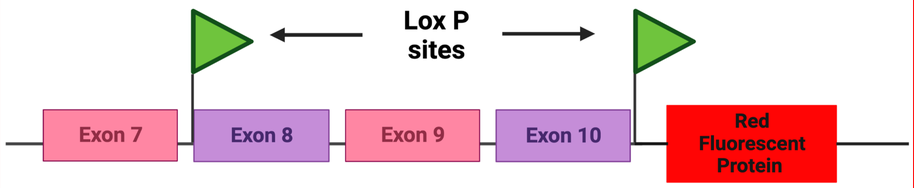
Hypothesis

WT1 is a necessary activator of *Amhr2* in the Müllerian Duct mesenchyme prior to regression.

Methods

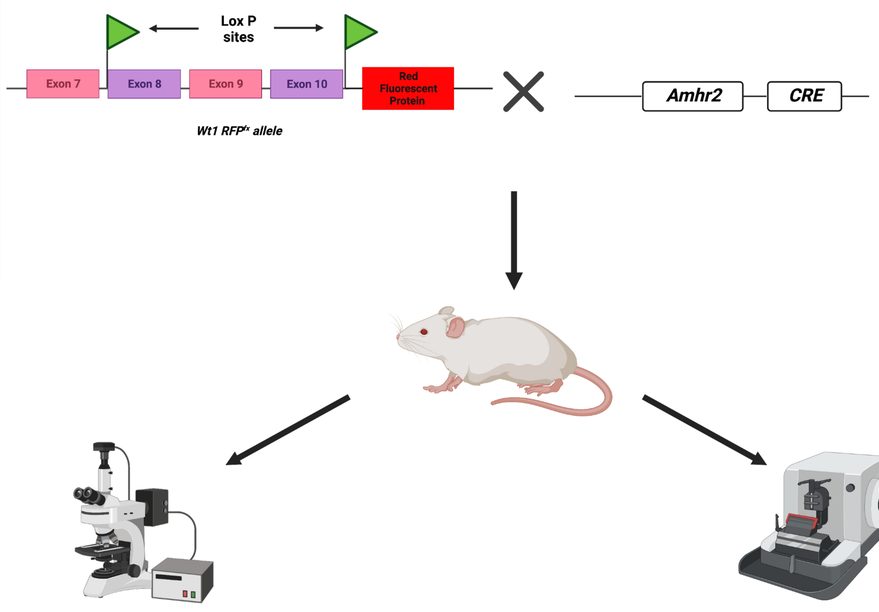
Goal: Block *Amhr2* expression in the Müllerian Duct mesenchyme by knocking out *Wt1*

We used CRE to block WT1 in the Müllerian Duct mesenchyme and prevent expression of *Amhr2*.

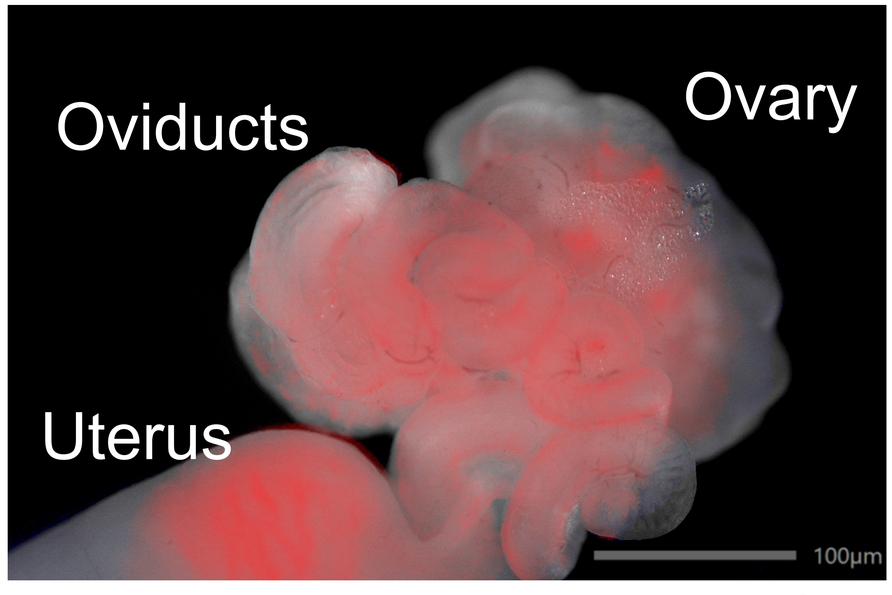


Wt1 RFP^{fx} allele

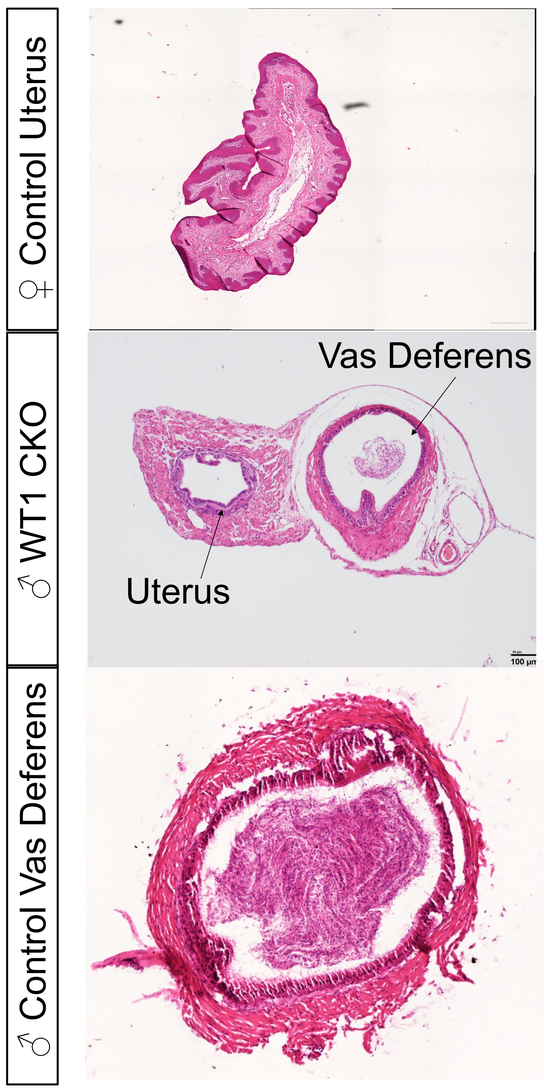
Red Fluorescent Protein (RFP) is activated from the allele to highlight cells that express the recombined WT1 allele.



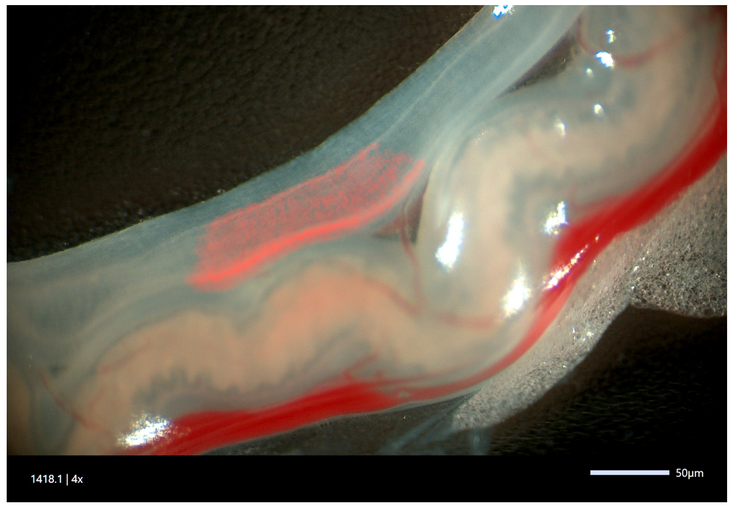
Results



Red Fluorescence in Wt1 RFP$^{\Delta}$/+ Female Reproductive System



Wt1 RFP$^{\Delta}$/+ ♂ Reproductive Tract



Overall, the male knockout mouse has a uterus.

References

1) Klattig, J. *et al.* Wilms' Tumor Protein Wt1 Is an Activator of the Anti-Müllerian Hormone Receptor Gene Amhr2. *Molecular and Cellular Biology* **27,** 4355-4364 (2007).

Acknowledgements

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