Beta-Catenin Transcription Function is Essential for Müllerian Duct Regression

Evelyn A. Carrion, Rachel D. Mullen, Jace A. Aloway, Richard R. Behringer

Department of Genetics, MD Anderson Cancer Center, and University of Saint Thomas

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Introduction:

- Mouse embryos initially have precursor tissues for both male and female reproductive tracts. Müllerian ducts are a pair of embryonic structures that give rise to the female reproductive tract. Wolffian ducts give rise to the male reproductive tract. During male sex differentiation, Müllerian duct regression eliminates the female precursor tissue.

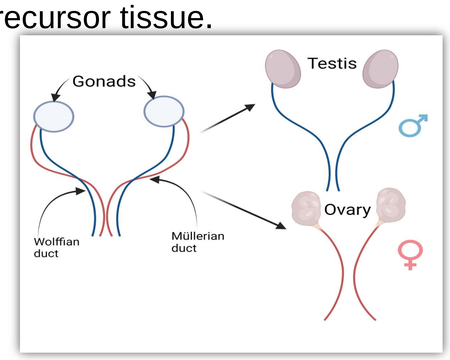

Figure 1. Mammalian reproductive tract differentiation in males and females.

- Beta-catenin protein is required for Müllerian duct regression (Kobayashi et al. 2011).

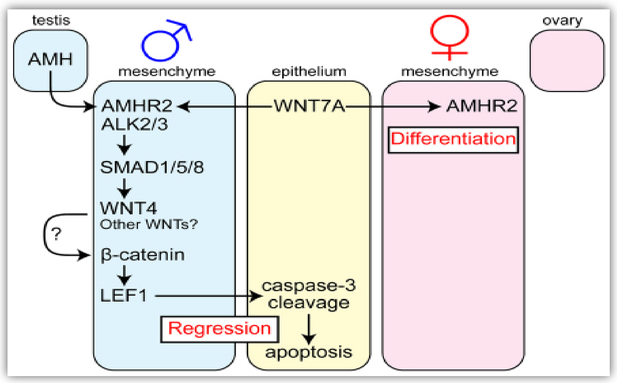

Figure 2. The Müllerian duct regression pathway (from Kobayashi et al. 2011).

Background:

- In the presence of Wnt glycoproteins, beta-catenin can avoid phosphorylation and degradation and then be transported into the nucleus where it binds with transcription factors that activate the expression of target genes.
- Beta-catenin has two separate functions in the cell: transcriptional activator and membrane-cytoskeleton linker protein (Zhurinsky et al. 2000).

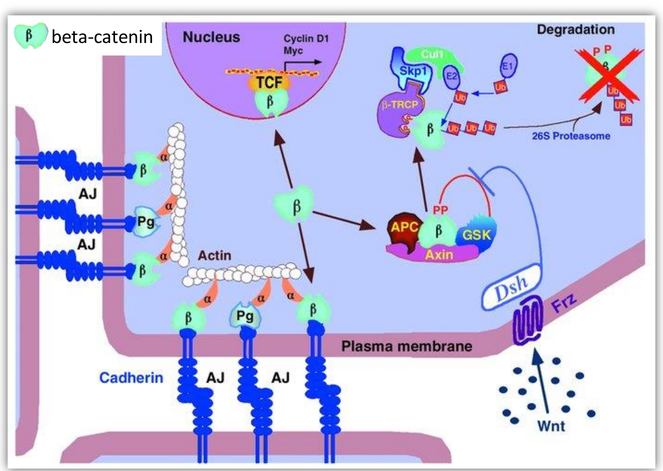

Figure 3. Beta-catenin function in adhesion and transcription (adapted from Zhurinsky et al. 2000).

Hypothesis: The transcription function of beta-catenin is necessary for Müllerian duct regression.

Methods:

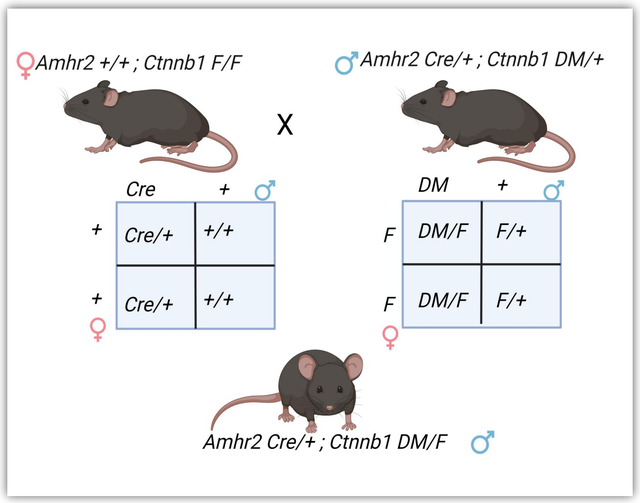

Figure 4.
Cross to obtain desired genotype of mutant who will have no beta catenin with transcription function.

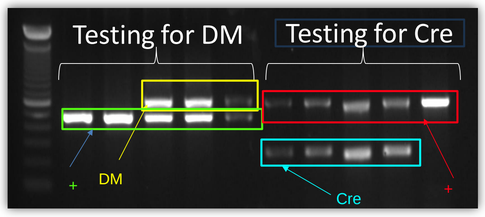

Figure 5.
PCR genotyping. DM (Double mutation), Green + (Wild-type Beta-catenin), Red + (internal control), Cre (Amhr2 Cre/+).

Mutation Description:

- The beta-catenin double mutation *(Ctnnb1 DM)* allele replaces Aspartic Acid with Alanine at position 164 and has a deletion of the C-terminus.
- CTNNB1 DM mutated protein lacks transcriptional function BUT retains adhesion function (Valenta et al. 2011).

Results

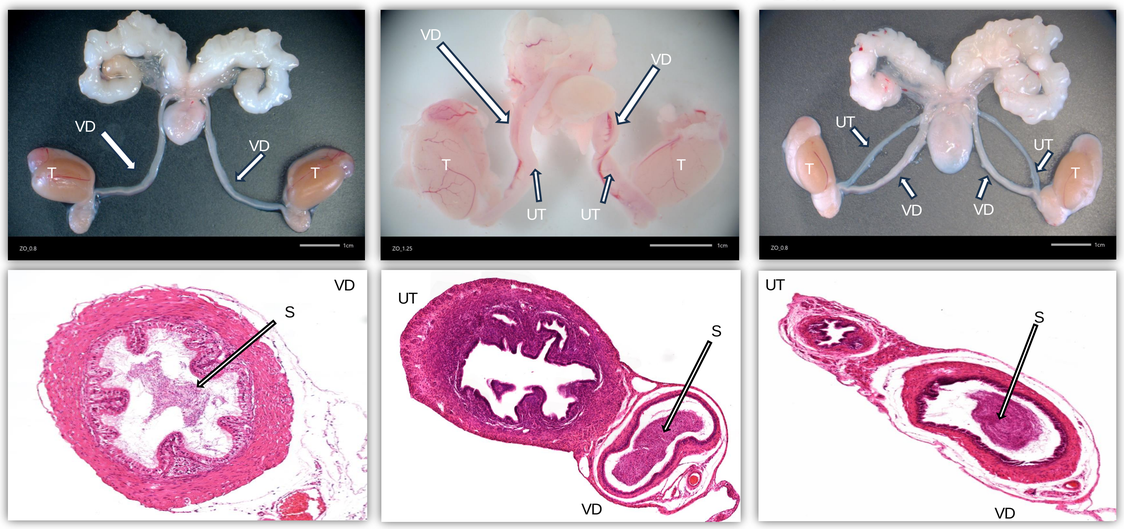

Figure 6.
Morphological imaging. Hematoxylin and eosin staining of section of tissue from Uterus and Vas deferens. VD (Vas deferens), UT (Uterus), T (Testis), and S (Sperm).

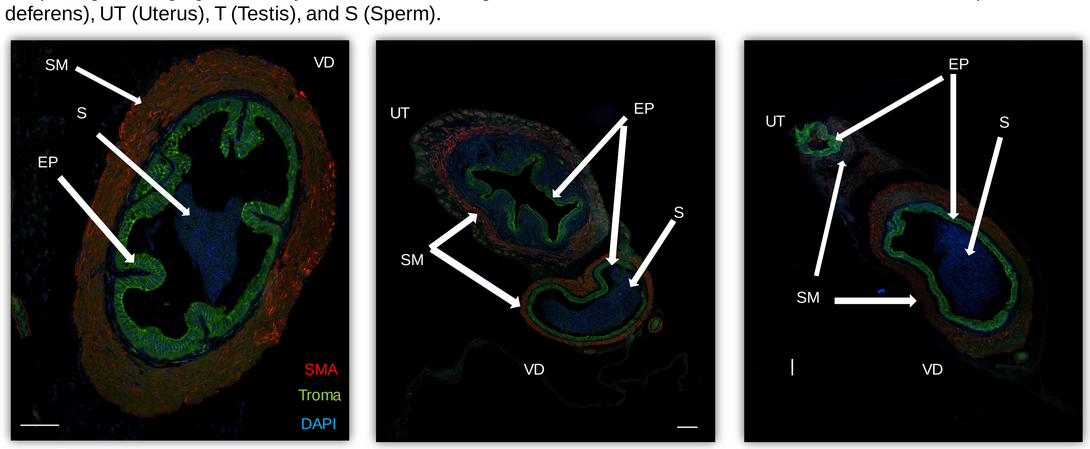

Figure 7.
Immunofluorescent staining of section of tissue from Uterus and Vas deferens. VD (Vas deferens), UT (Uterus) , S (Sperm), EP (epithelium), SM (smooth muscle), DAPI stains for nucleus, Troma stains for epithelium cells, and SMA(Smooth muscle actin stains for smooth muscle.

Conclusion

- Mice with beta-catenin transcription mutation are born with both female and male reproductive tracts, therefore transcription is the necessary function of beta-catenin needed for Müllerian duct regression.
- The uterus for the beta-catenin mutant versus the *Amhr2 lacZ/lacZ* mutant is significantly different in size, that could be due to the fact that beta-catenin is involved in uterus grow.

Future Work

- Investigate the function of beta-catenin in the uterus growth pathway.
- Observe a beta-catenin DM mutation in a female mouse organism.
- Fluorescence staining for AMH and AMHR2 to show beta-catenin DM mutation does not disrupt these proteins.

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- BioRender