The Morphological Progress of Müllerian Duct Fusion in Mice

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Introduction

- Early mammalian embryonic development in both sexes involves the formation of two pairs of urogenital ducts termed the Wolffian (WD) and Müllerian ducts (MD).
- It is known that the two MD will fuse to form the uterine corpus, and it is thought that the degree of fusion leads to the variation of uterus morphology [1].

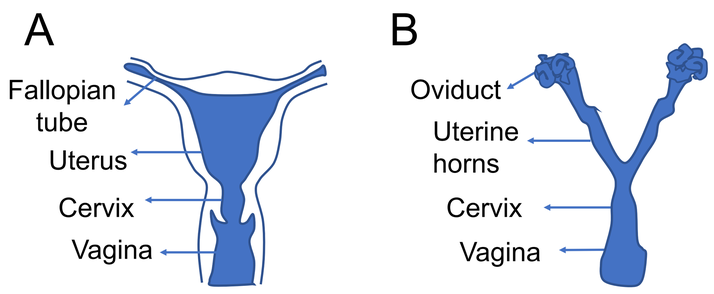
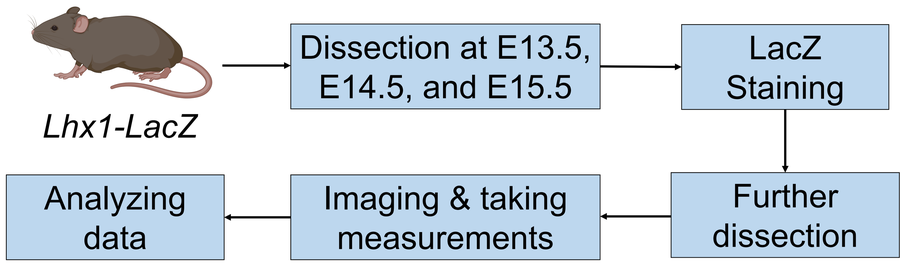


Figure 1: Different uterine morphology
(A) Simplex uterus in human (B) Bicornuate uterus in mice

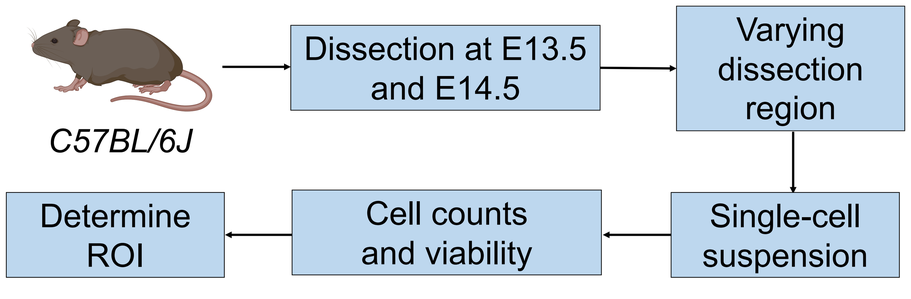
- Several observed uterine variations are the result of MD fusion failure [2]. However, there is a gap in our knowledge with regards to the MD fusion with little research investigating this process.
- Here, we choose mice as our research organism and focus on (1) characterizing the timing, position, and morphological landmarks during the fusion process and (2) determining the region of interest (ROI) for single cell RNA sequencing.

Methods

- Determining the timing, position, and morphological landmarks of the MD fusion:



- Determining ROI for single cell RNA sequencing:



Result

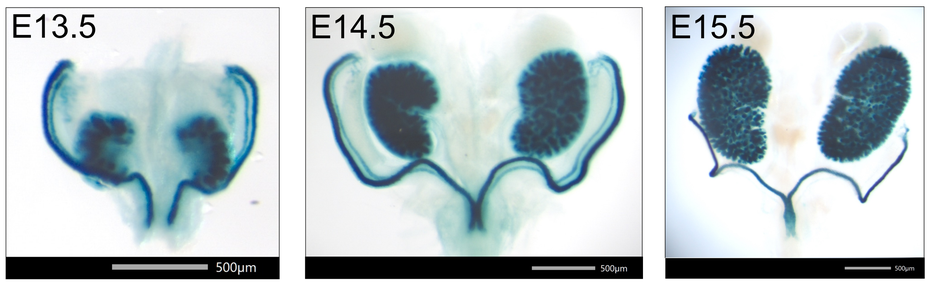


Figure 2: Representative images of the MD ducts.
Scale bar, 500 μm.

Figure 3: The MD growth and fusion model. Oviduct-region MD don't proliferate. Uterine-region MD proliferate at different rates over time.

Time	Feature in model	Average (μm)	SD (μm)
E13.5	Total vertical length	865	61
	Green	1262	101
	Red	307	95
	Distance between red features (top, mid, bottom)	173, 123, 107	16, 16, 25
E14.5	Total vertical length	1255	237
	Green	1565	358
	Dark Red	828	271
	Purple	243	35
E15.5	Total vertical length	1278	253
	Green	1297	191
	Dark Red	1041	237
	Purple	466	34

Table 1: Measured length of different MD features

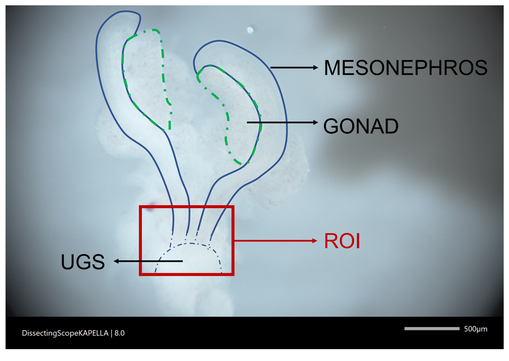


Figure 4: The identified ROI for single cell transcriptome analysis.

Conclusion

We have confirmed that the MD fusion window is between E13-E14.5. We have determined the lengths of the developing Müllerian ducts and the physical relationships between the two ducts before, during and after fusion. We have defined the regions of interest of the fusing MD for single cell transcriptome analysis. These studies should lead to a cell and molecular understanding of MD fusion for uterine morphogenesis.

Future Direction

To validate the MD growth and fusion model, immunofluorescent staining with markers for various cellular processes such as proliferation, apoptosis, shape change, fate change, and migration will need to be performed.
Single cell transcriptome analysis will be performed on the determined ROI to shed light on the underlying molecular mechanism of MD fusion.

Acknowledgement

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References

[1] Kobayashi and Behringer. Nat Rev Genet 4. 2003 PMID. 14631357
[2] Chan et al. Hum Reprod Update. 2011 PMID. 21705770.