**Functional genomics of MRKH syndrome**

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**Introduction**

MRKH syndrome: incomplete development of the female reproductive tract (FRT), 1:4500 women. Genetics of MRKH is unknown. Type I: only FRT is affected. Type II: additional malformations are present, mostly involving the kidney.

**Methods**

Functional genomics: clinic to lab to discover condition-causing genes

- Whole Exome Sequencing
- DNA Microarrays
- Animal models
- Candidate genes
- Functional validation

**Results**

**Uterine hypoplasia**

- Control
- Hnf1b KO

**Kidney agenesis**

- Control
- Hnf1b KO

**Lack of uterine basal lamina**

**Uterus is comprised of nine cell types**

**Conclusions**

This is the first functional genomic analysis for MRKH syndrome achieved by leveraging a top-down approach from patients samples to laboratory benchwork. Identification of Hnf1b led to the development of the first mouse model of MRKH type II: hypoplastic uterus and unilateral kidney agenesis. Single-cell RNA Seq analysis shows specific mechanisms involved in MRKH pathogenesis. This study demonstrates a translational approach to solve complex medical problems and develop new clinical strategies.