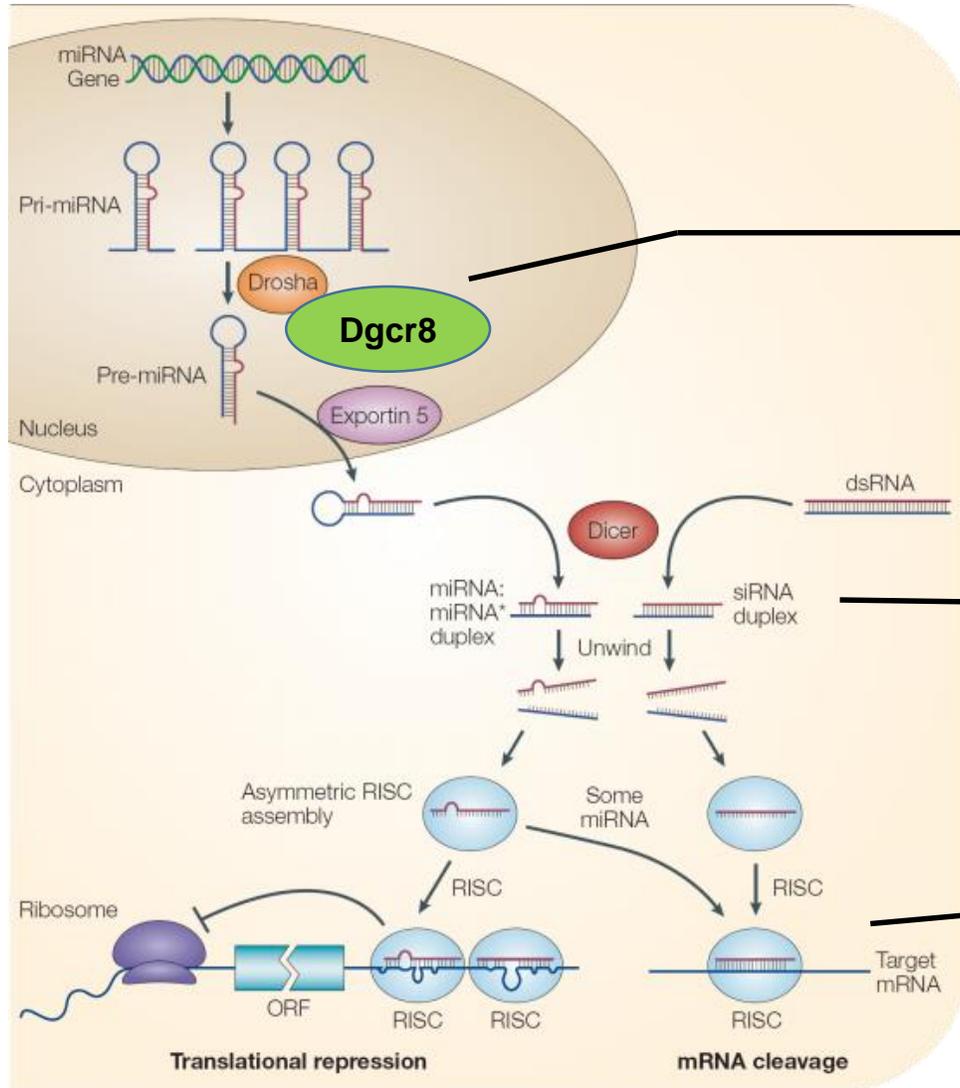


**Deficiency of DGCR8-dependent canonical microRNAs
causes infertility due to multiple spectra of abnormalities
during uterine development in mice**

YEON SUN KIM

**LAB. OF MOLECULAR DEVELOPMENTAL GENETICS
DEPARTMENT OF BIOMEDICAL SCIENCE
CHA UNIVERSITY**

MicroRNA Biogenesis



Cleavage of pri-miRNA
Drosha & Dgcr8

Cleavage of pre-miRNA
Dicer

**Translational repression
& mRNA cleavage**

MicroRNA & Uterus

Molecular Endocrinology

Deletion of Dicer in Somatic Cells of the Female Reproductive Tract Causes Sterility

Endocrinology

Ankur K. Nair,
Derek Y. Han,
and Martin M. Matzuk

Department of Molecular and Human Genetics, Baylor College of Medicine (M.M.M.), and Department of Biology

Dicer1 Is Essential for Female Fertility and Normal Development of the Female Reproductive Tract

Molecular Reproduction & Development

Xiaoman Hong,* Lacey J. ...

Departments of Molecular and Human Genetics (W.B.N.), University of Kansas

Dicer Is Required for Female Reproductive Development and Fertility in the Mouse

Molecular Endocrinology

GABRIEL GONZALEZ AND RICARDO ...

Department of Genetics, The University of Texas at Austin

Dysregulation of Uterine Signaling Pathways in Progesterone Receptor-Cre Knockout of Dicer

Shannon M. Hawkins, Claudia V. Andreu-Vieyra, Tae Hoon Kim, Jae-Wook Jeong, Myles C. Hodgson, Ruihong Chen, Chad J. Creighton, John P. Lydon, Preethi H. Gunaratne, Francesco J. DeMayo, and Martin M. Matzuk

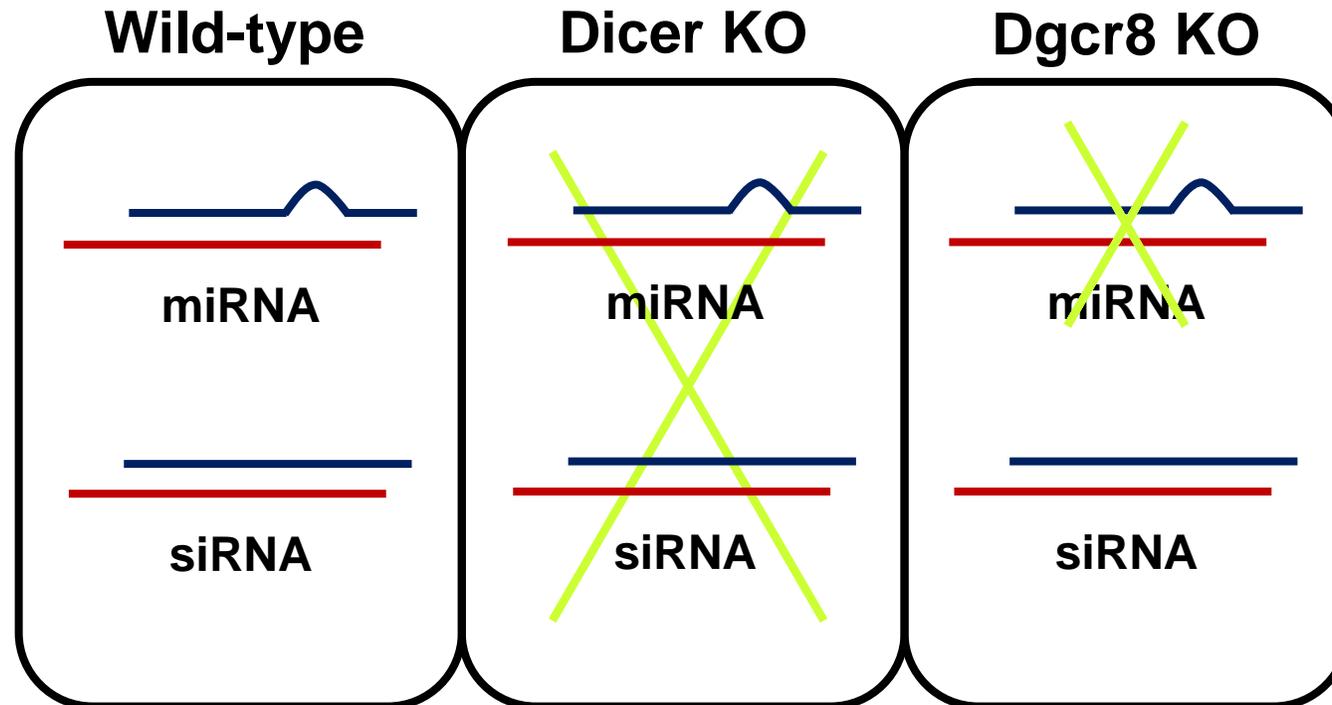
2008

2008

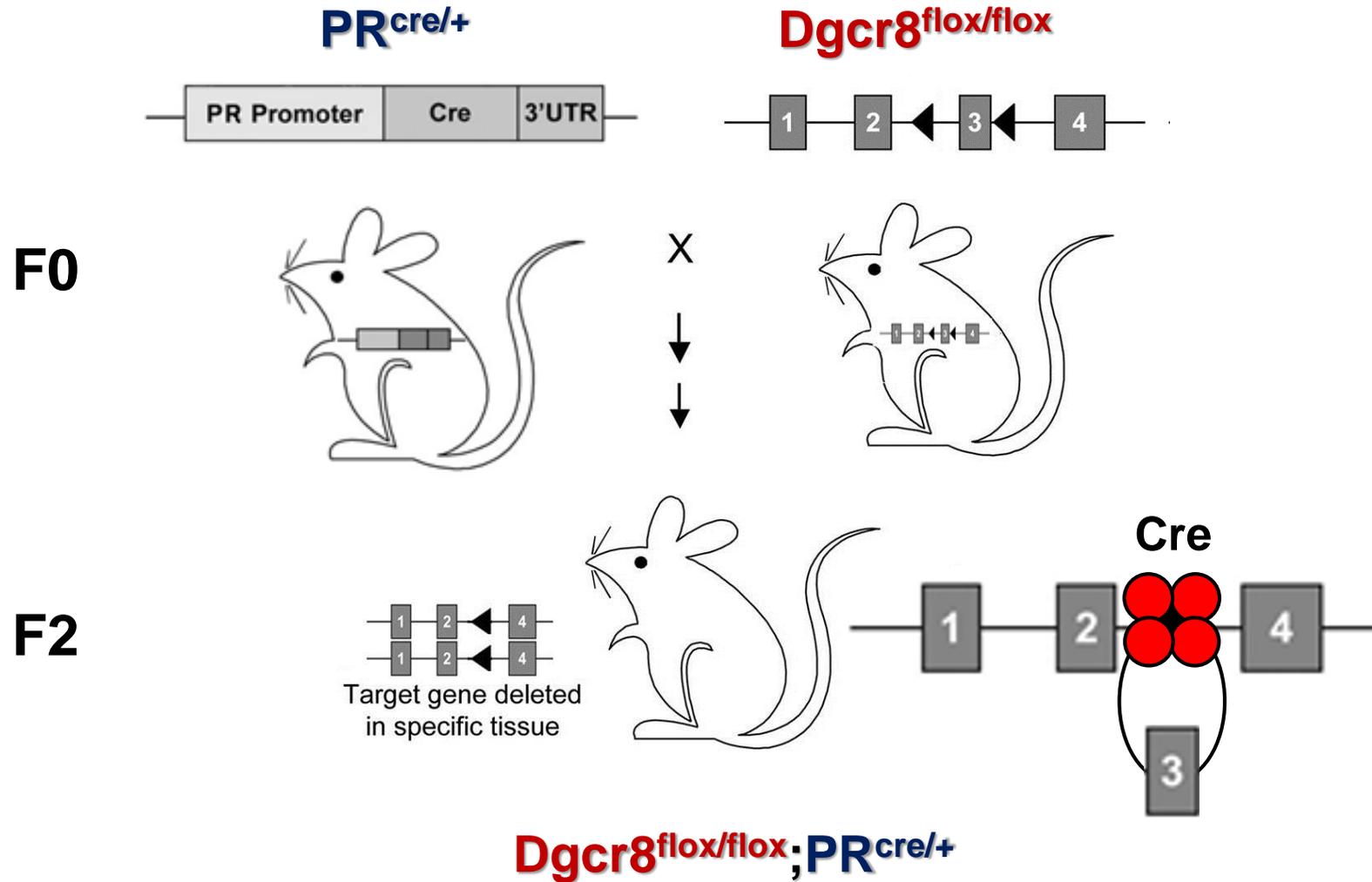
2009

2012

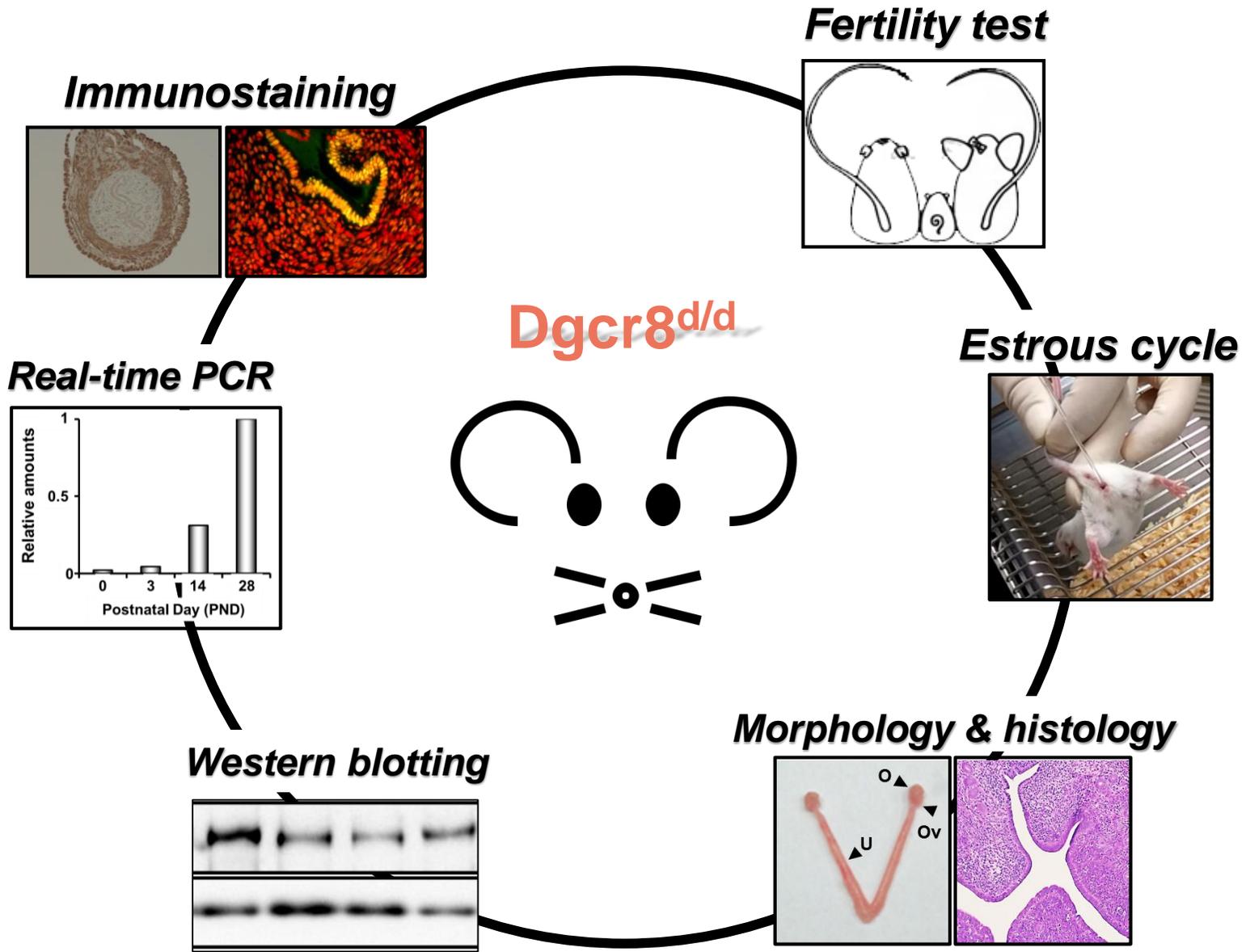
MicroRNA & Uterus



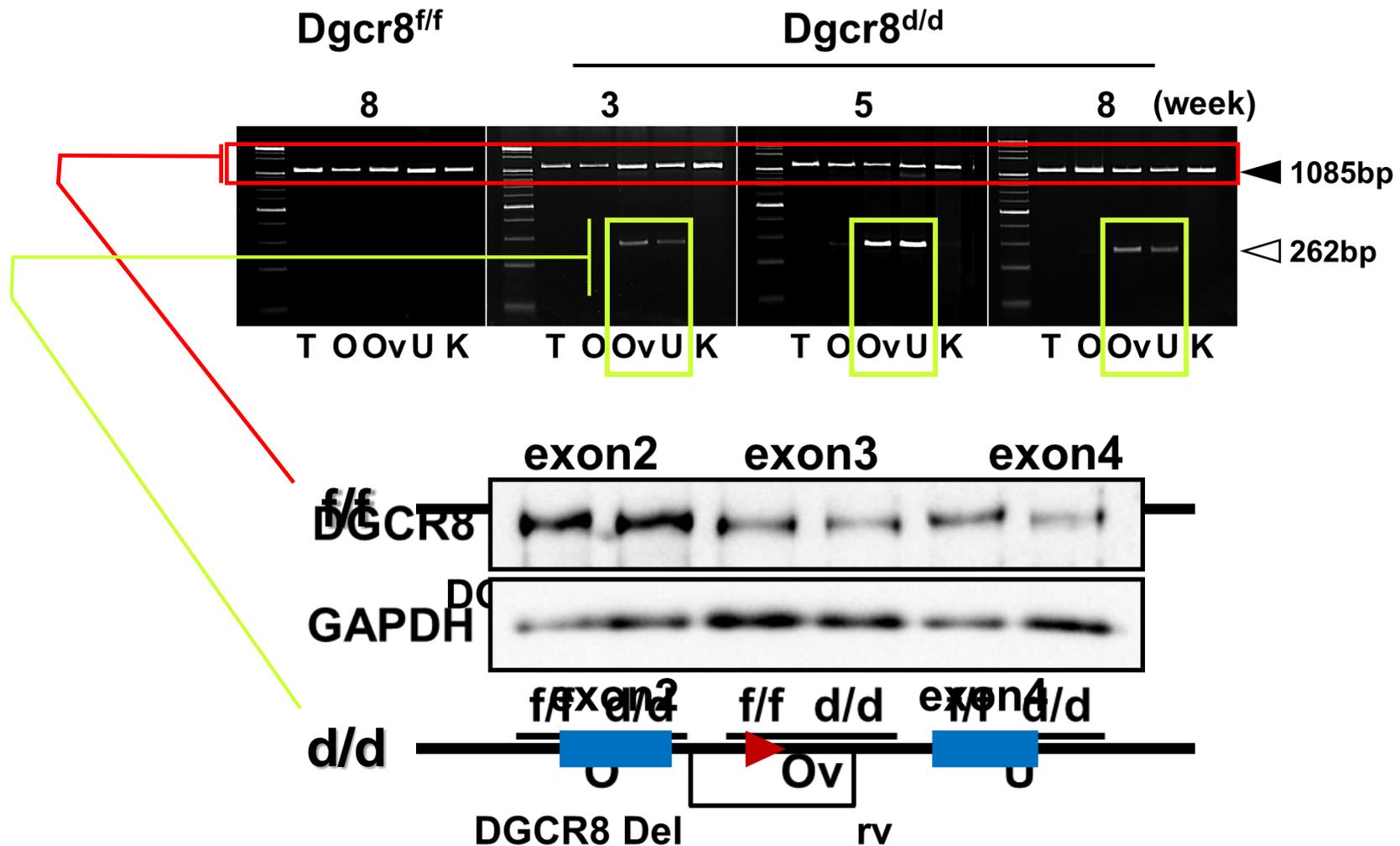
To understand roles of miRNAs in female reproductive tracts



MATERIALS & METHODS

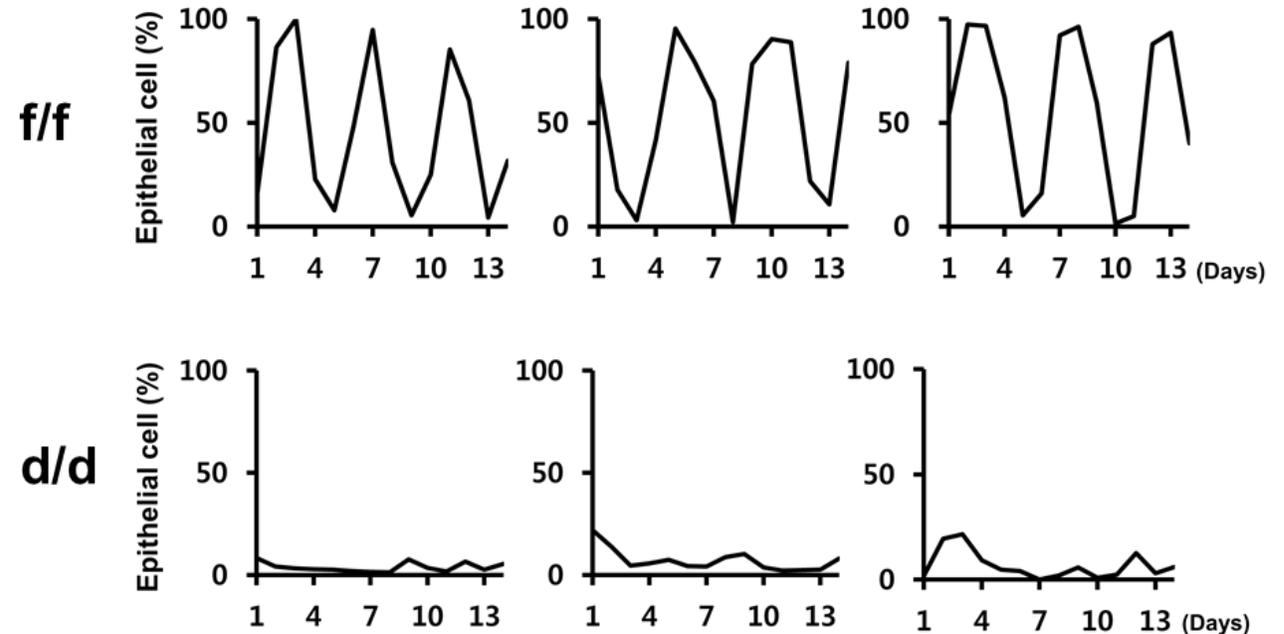
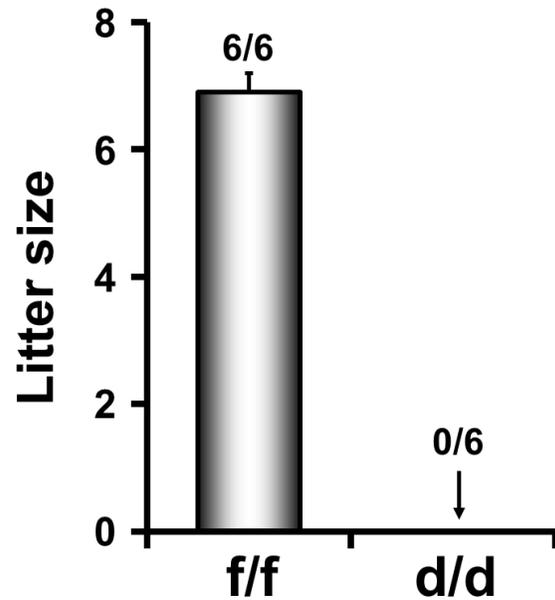


Conditional deletion of *Dgcr8* by PR-Cre in female reproductive tracts



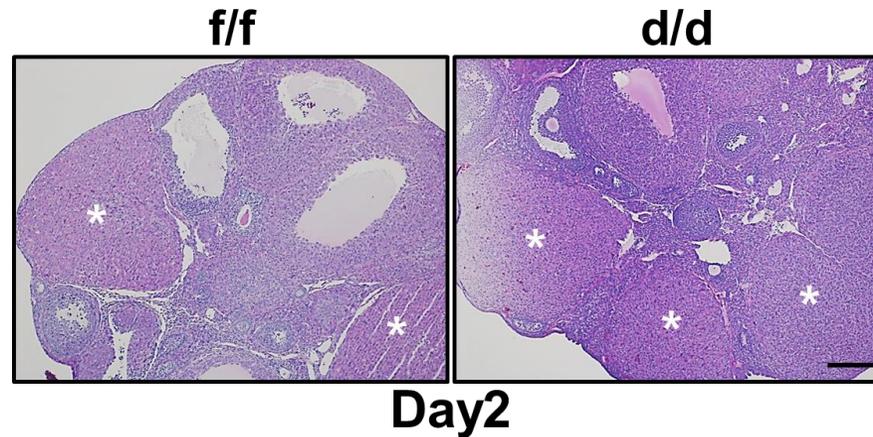
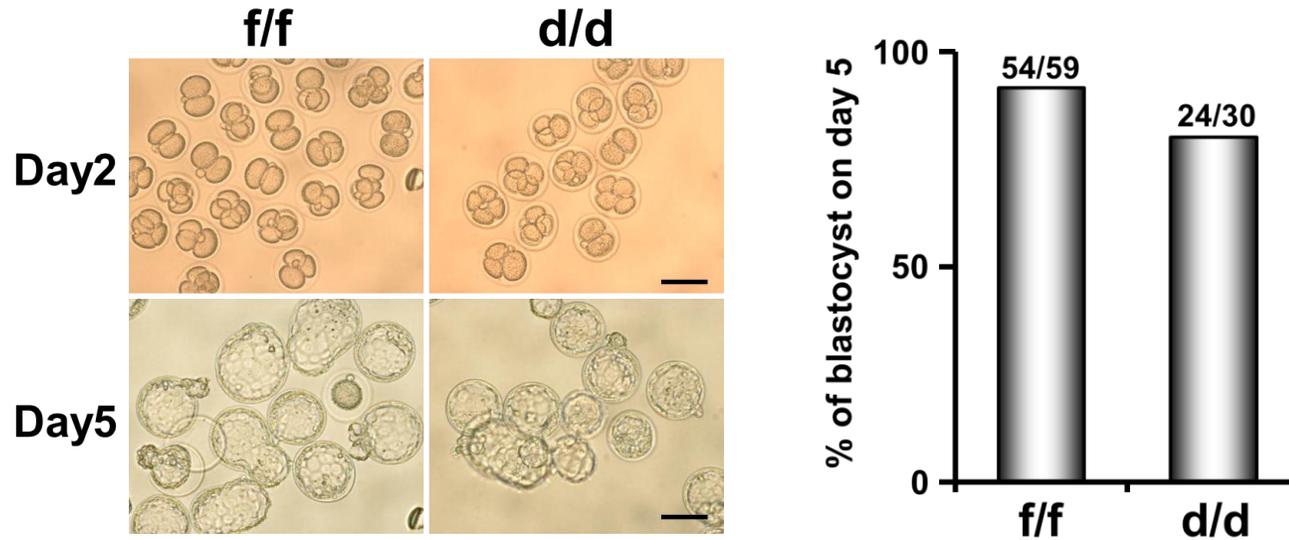
T: Tail; O: Ovary; Ov: Oviduct; U: Uterus; K: Kidney

Dgcr8^{d/d} mice are infertile with acyclic estrous cycle

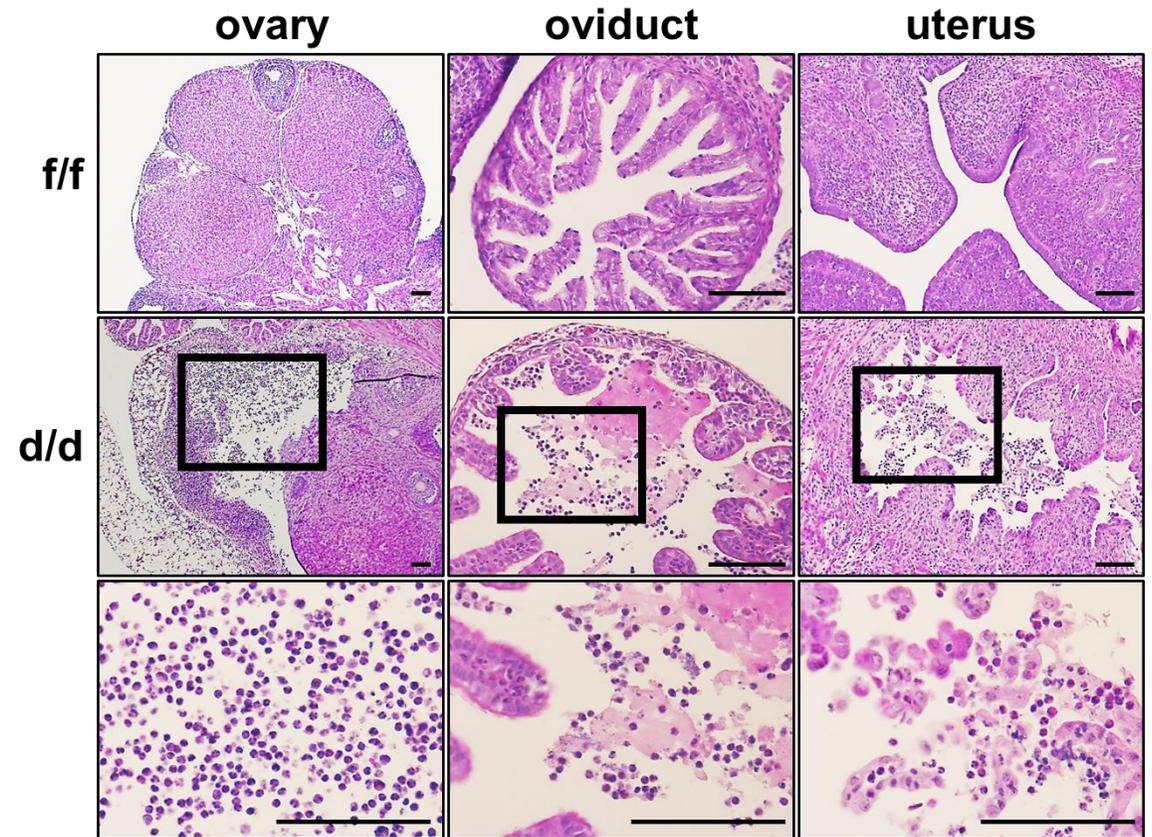
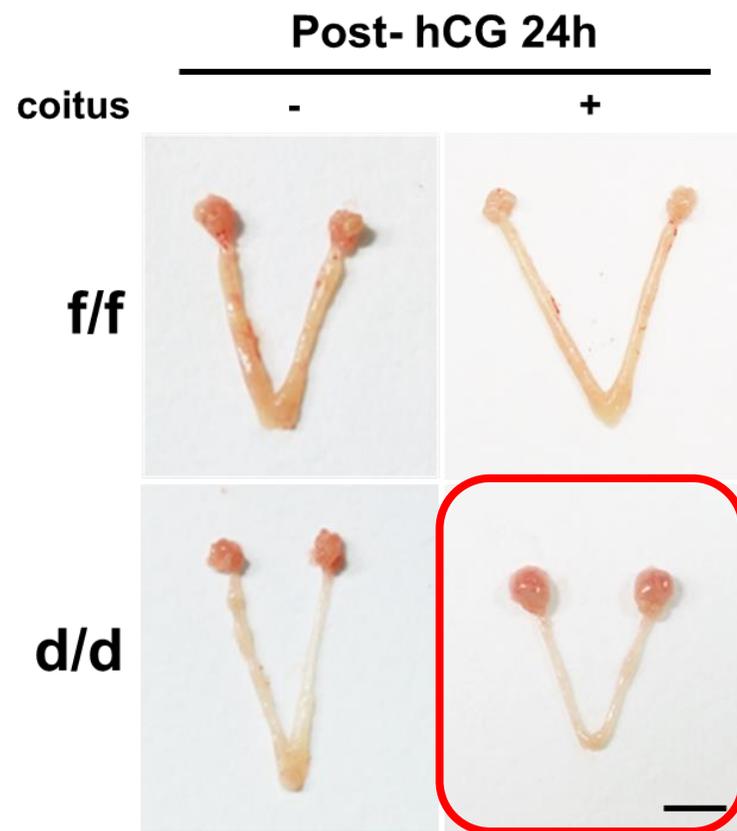


- ***Dgcr8^{d/d} mice have no pups over 2-month period***
- ***Cyclic change of epithelial cell (%) does not occur in *Dgcr8^{d/d} mice****

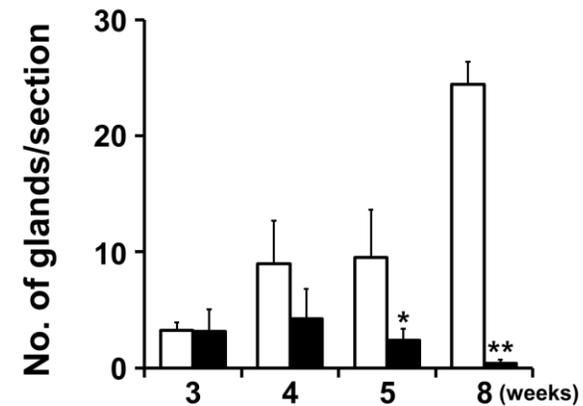
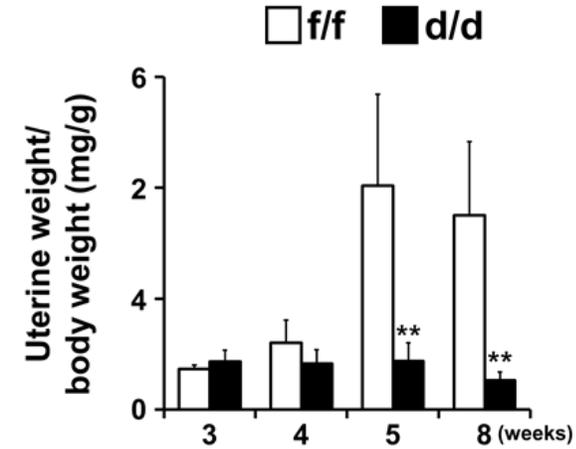
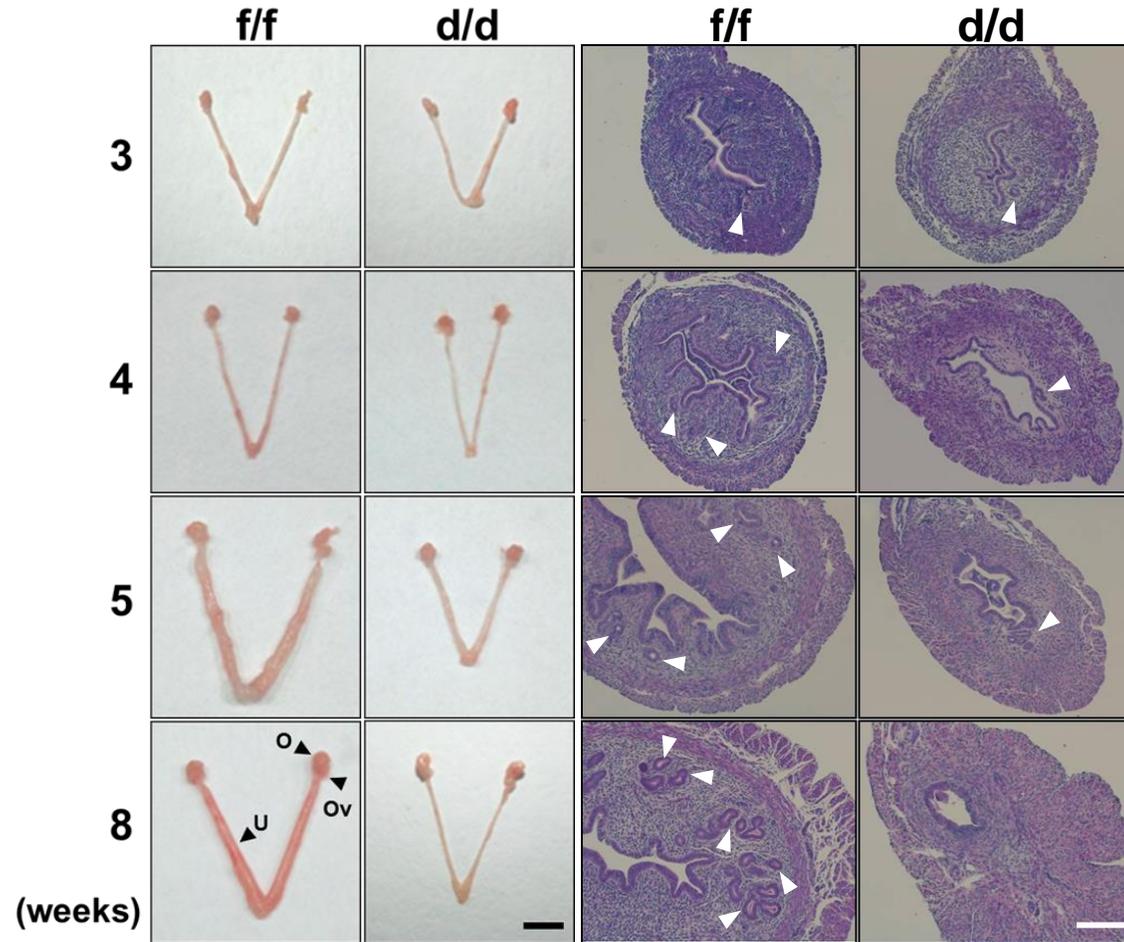
***Dgcr8^{d/d}* mice produce fertilizable oocytes with normal corpus luteum**



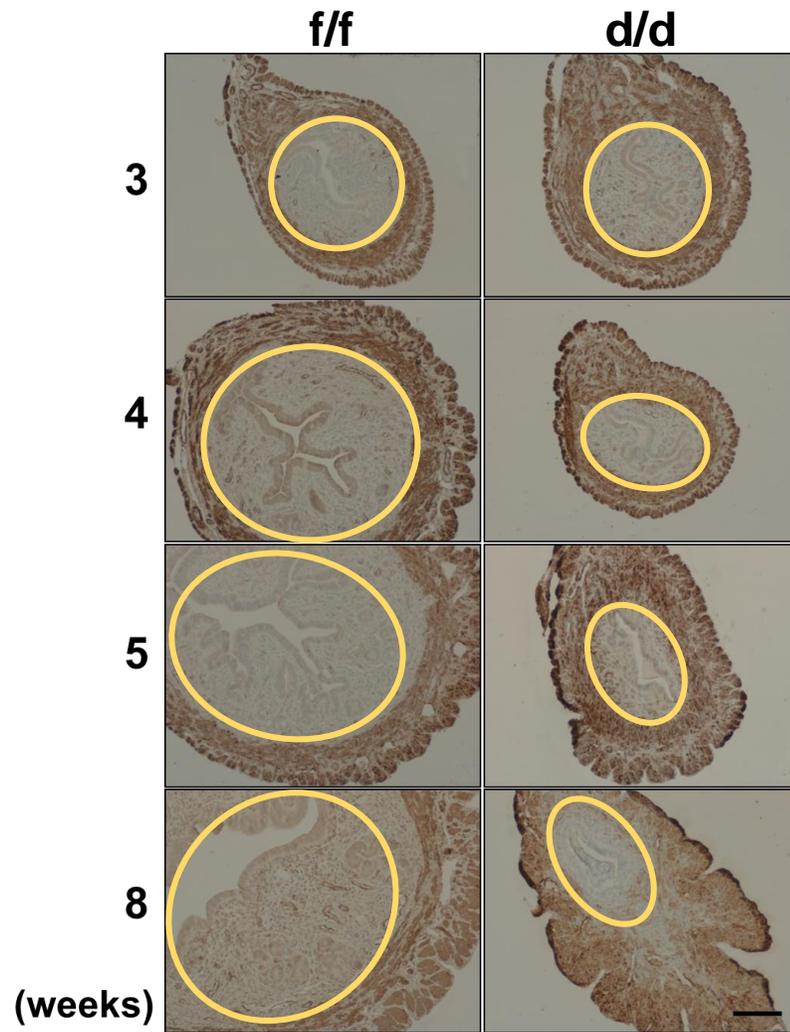
Acute inflammatory infiltration of immune cells occurs in pregnant $Dgcr8^{d/d}$ mice



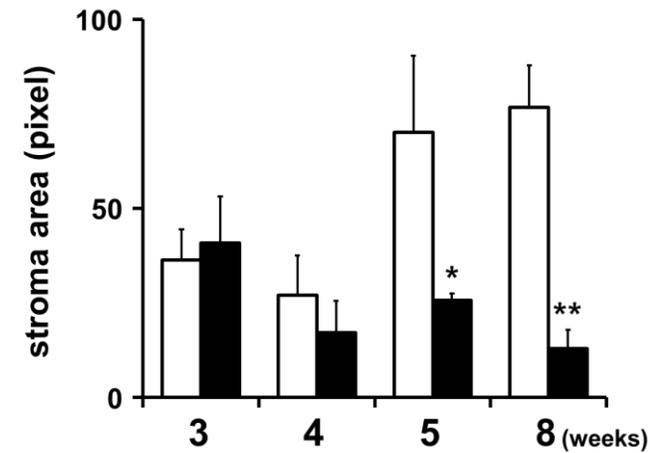
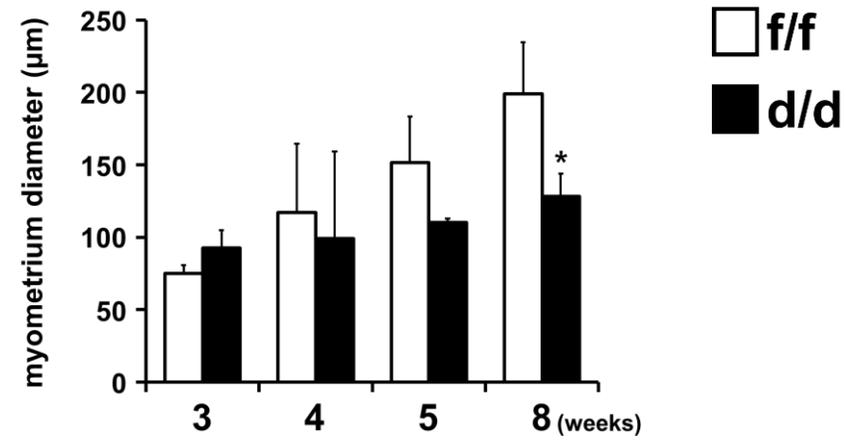
Dgcr8^{d/d} mice have multiple uterine abnormalities



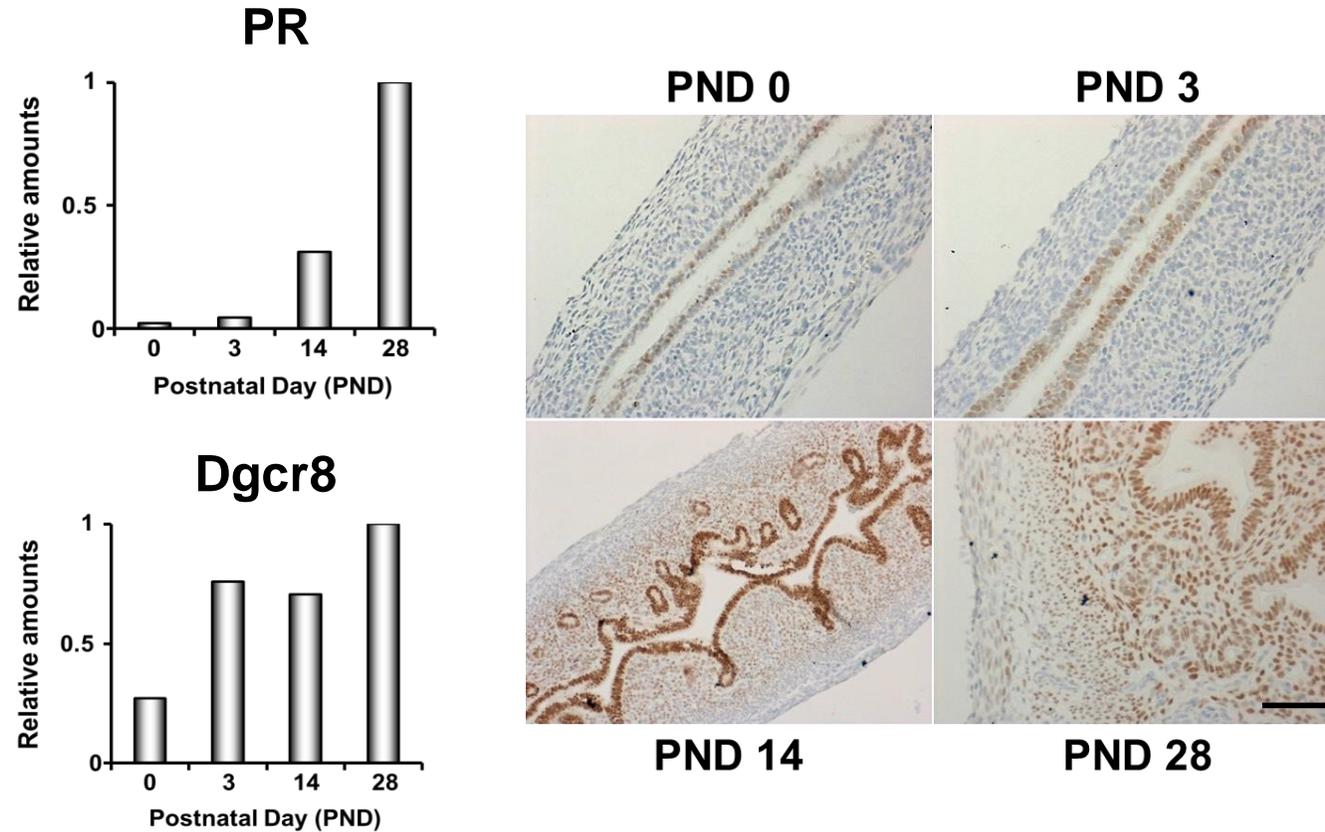
Dgcr8^{d/d} mice have multiple uterine abnormalities



α -SMA

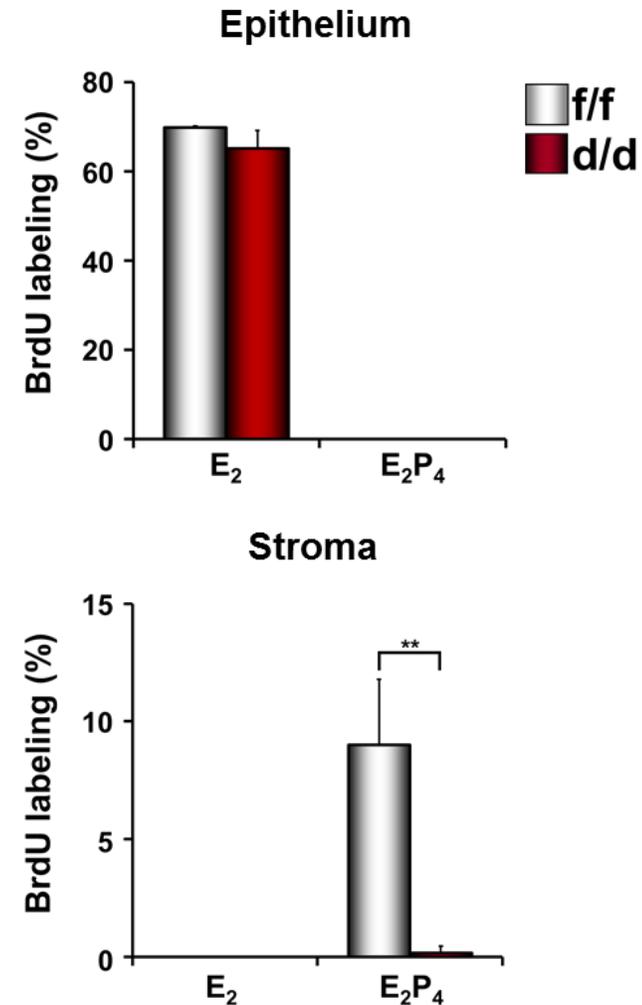
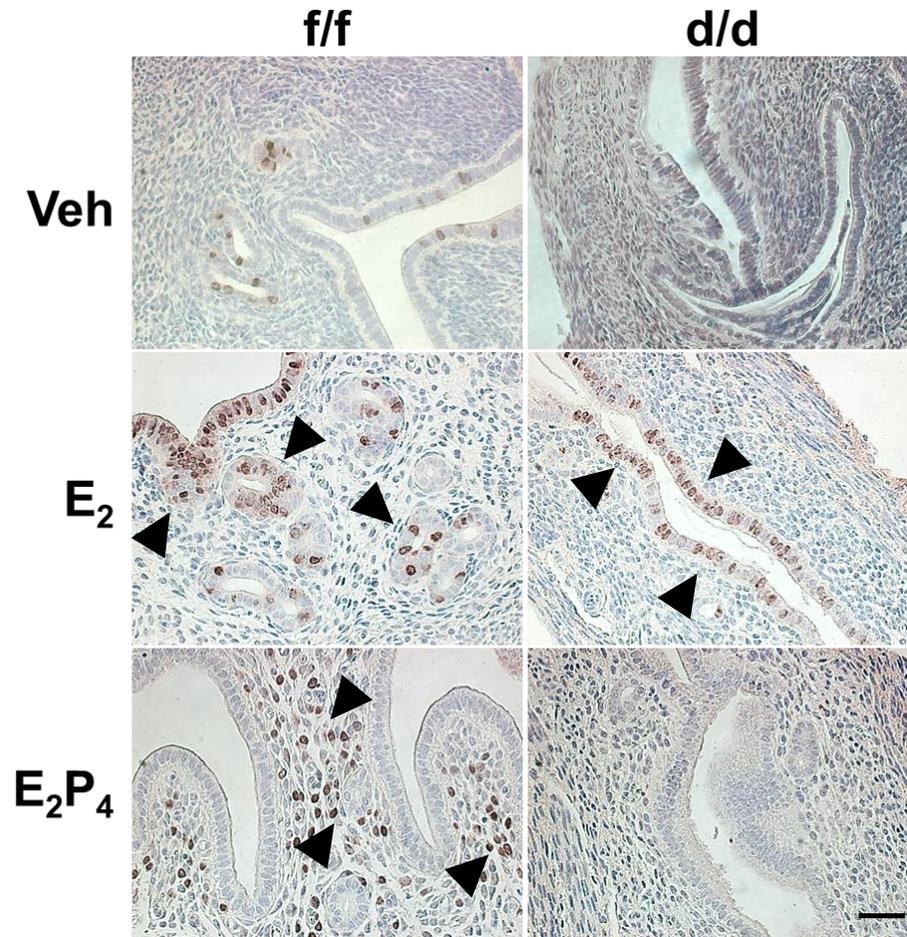


Onset of uterine abnormalities in *Dgcr8*^{d/d} mice coincides with PR expression

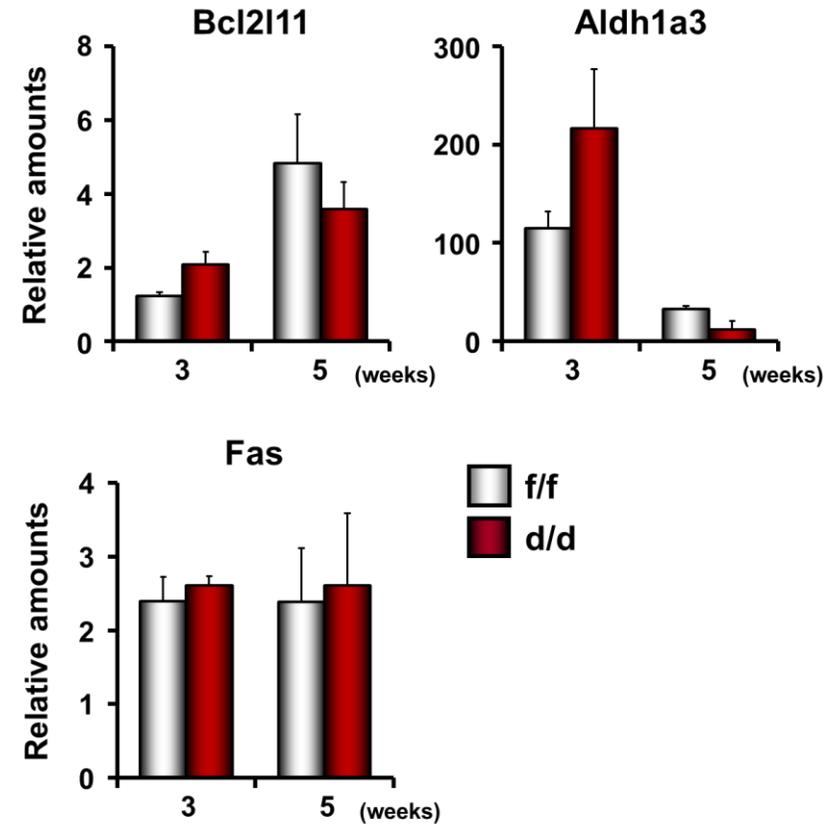
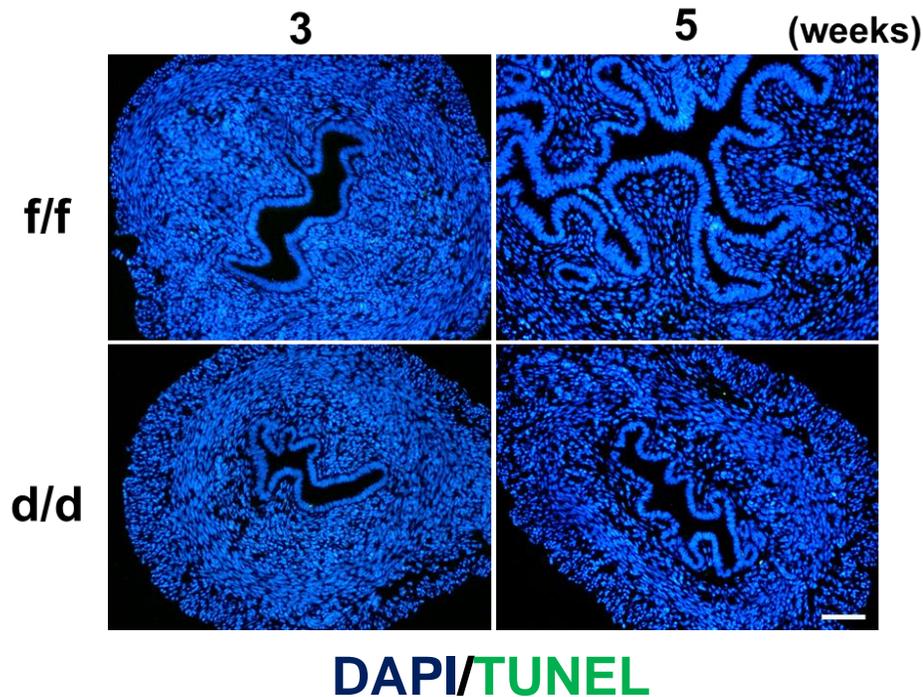


At PND 28, PR was exclusively localized not only in the epithelium but also in the stroma.

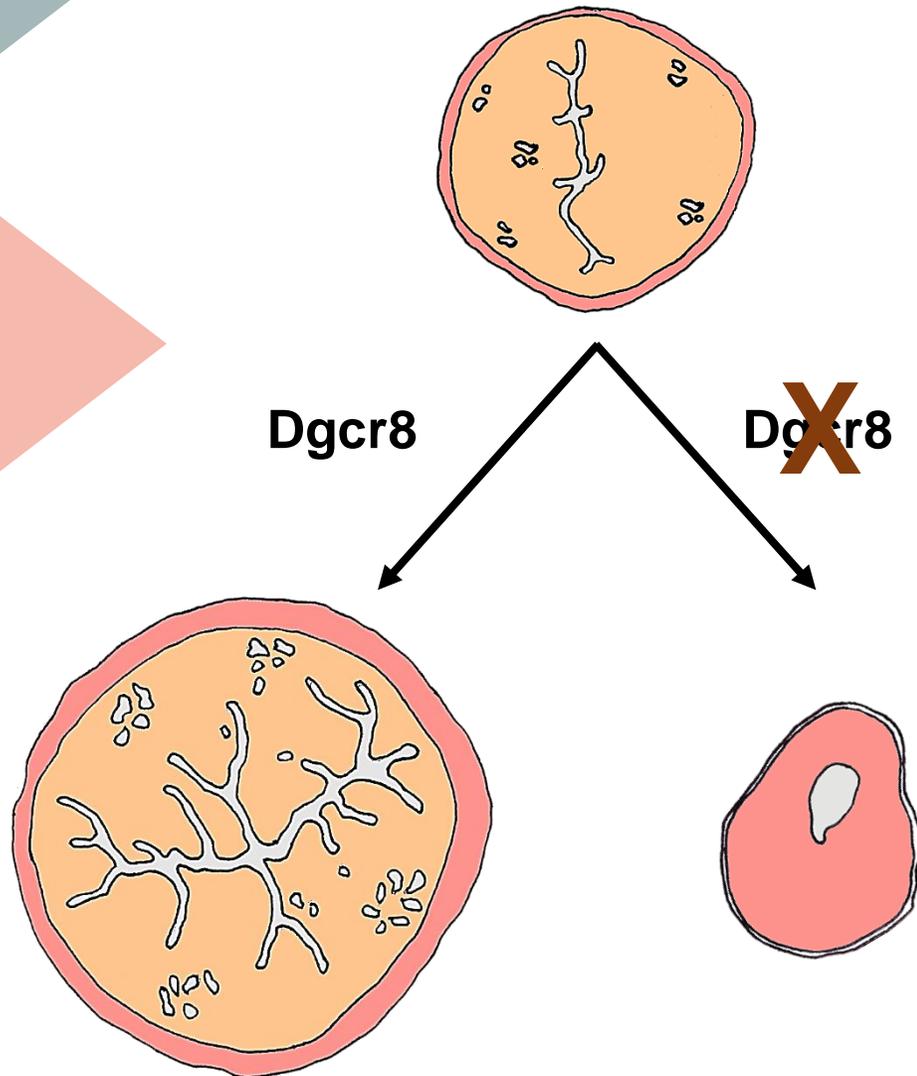
Disturbed hormone responses in stromal cells cause aberrantly reduced cell proliferation in *Dgcr8*^{d/d} mice



Severe atrophy in stromal cell compartment in the uteri of *Dgcr8*^{d/d} mice is not associated with facilitated apoptosis



Conclusion



- $Dgcr8^{d/d}$ mice are **infertile** due to acyclicity.
- $Dgcr8^{d/d}$ mice have multiple uterine abnormalities such as reduced number of **glands** and severe **stromal atrophy**.
- Uterine stromal cells aberrantly respond to ovarian steroid hormones leading to **no stromal proliferation**.
- Deficiency of canonical microRNAs leads to recruitment of **acute inflammatory** cells reactive to semen
- ***Dgcr8-dependent miRNAs plays critical roles in uterine development and physiology***

ACKNOWLEDGEMENT



Lab of Molecular Developmental Genetics

Professor. Haengseok Song

Hye-Ryun Kim, Ph.D

Jung-Ah Yoon, M.S.

Seung Chul Yang

Mira Park



Thank you

for your attention !

