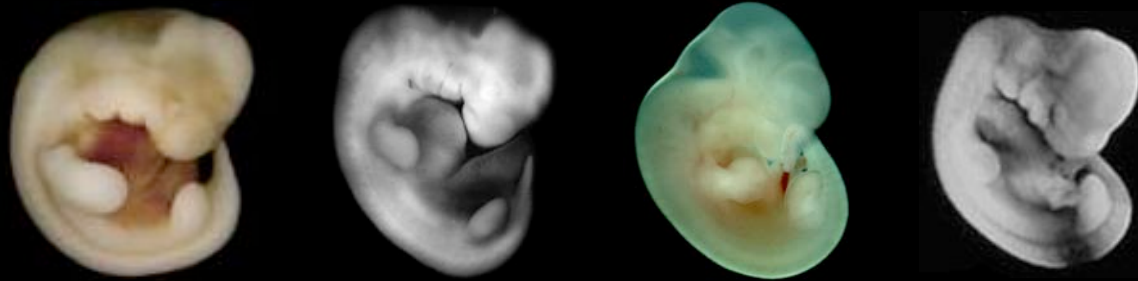
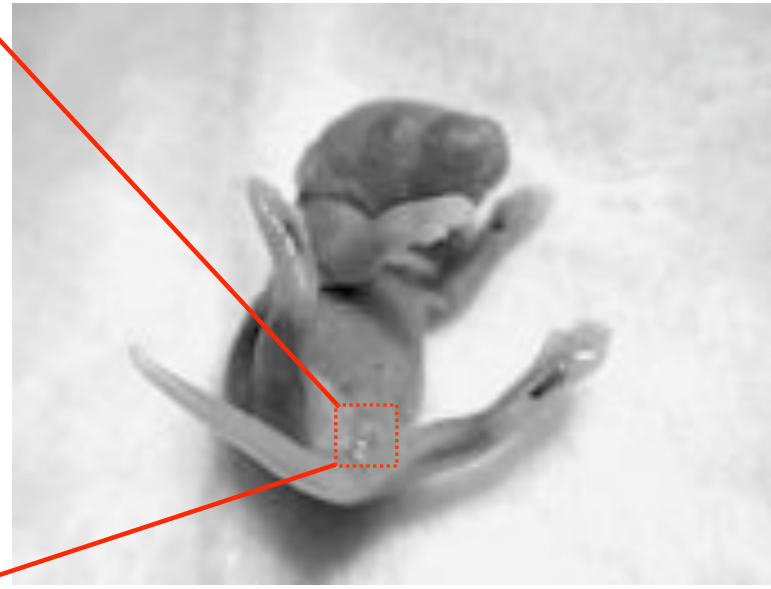


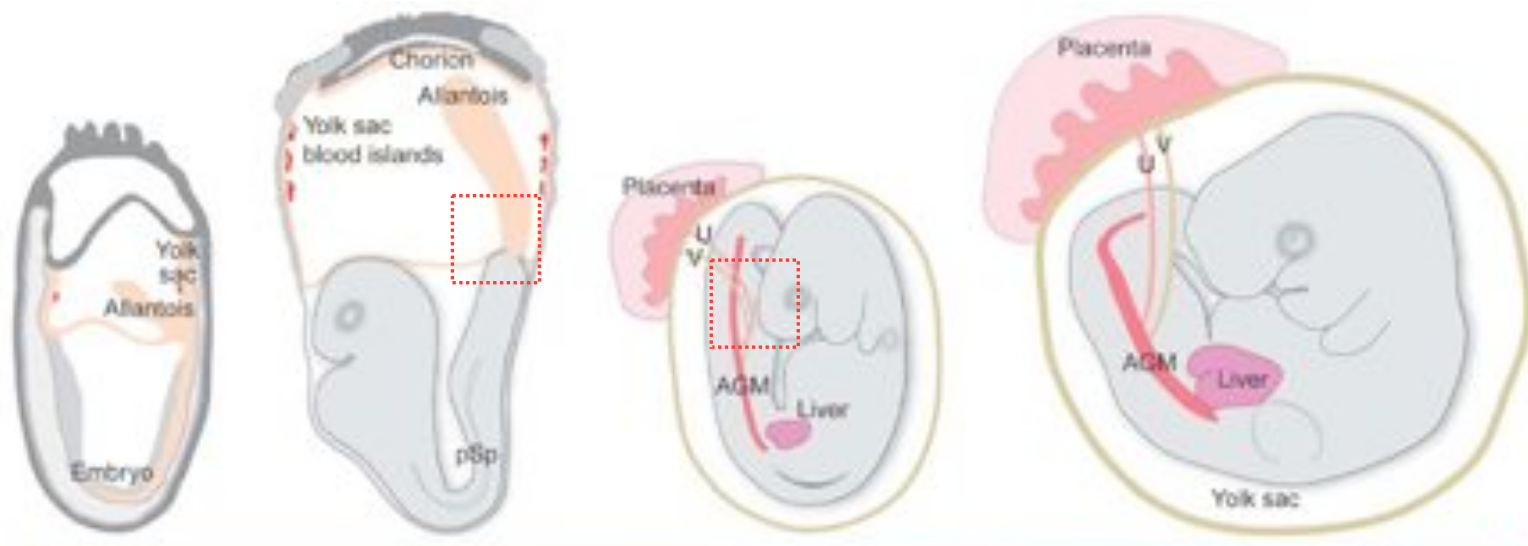
Vertebrate Anogenital Development



Ashley W. Seifert
Department of Biology

Murine External Genital Development



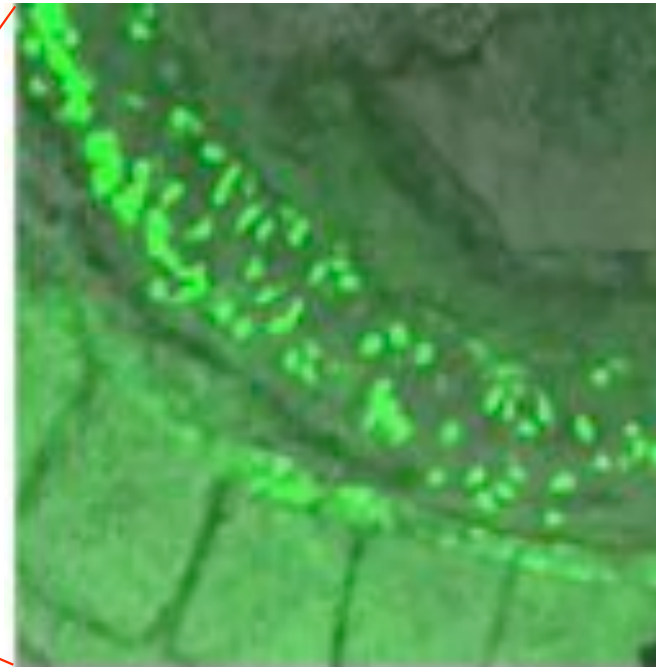
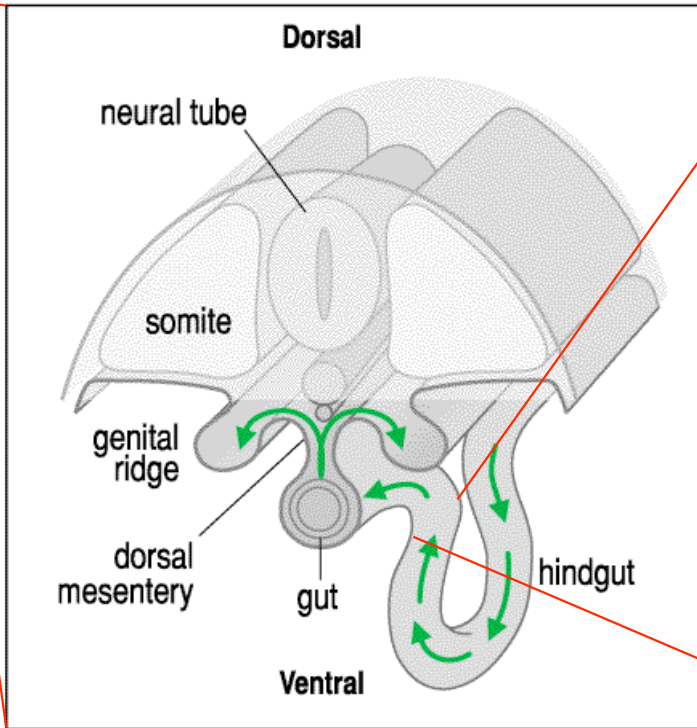
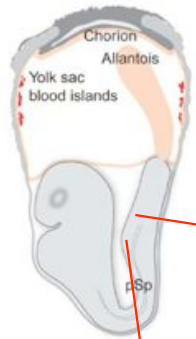


E7.5

E8.5

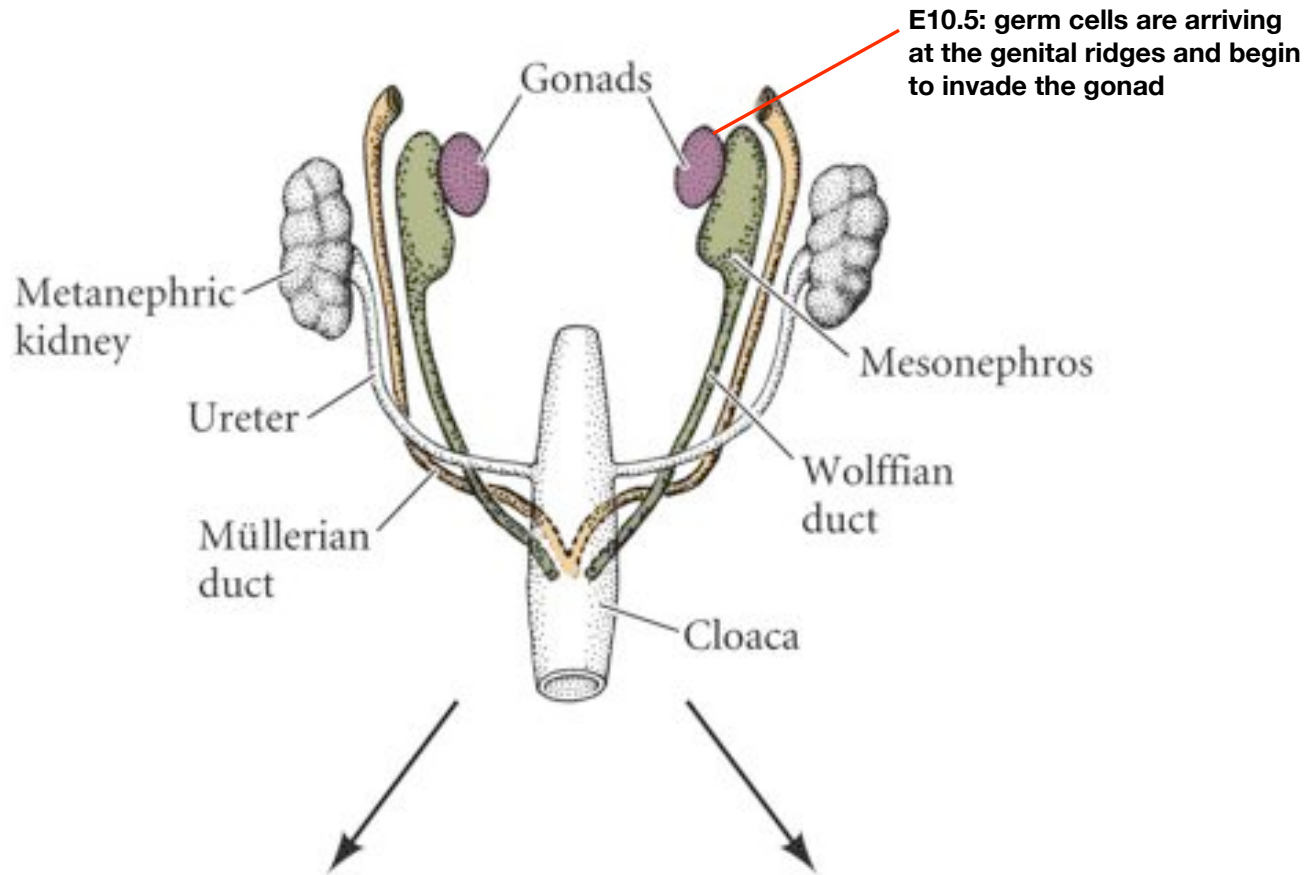
E9.5

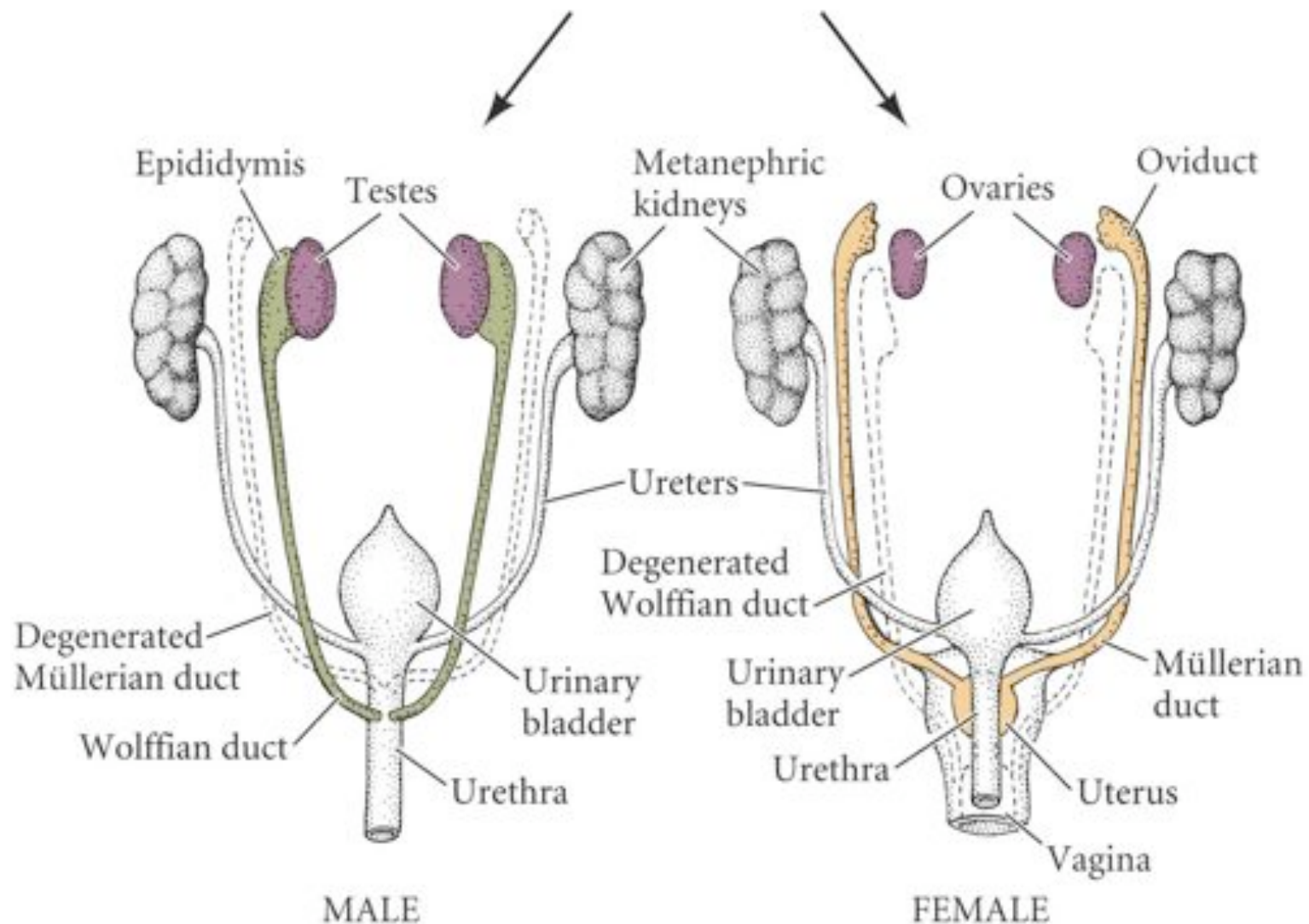
E10.5





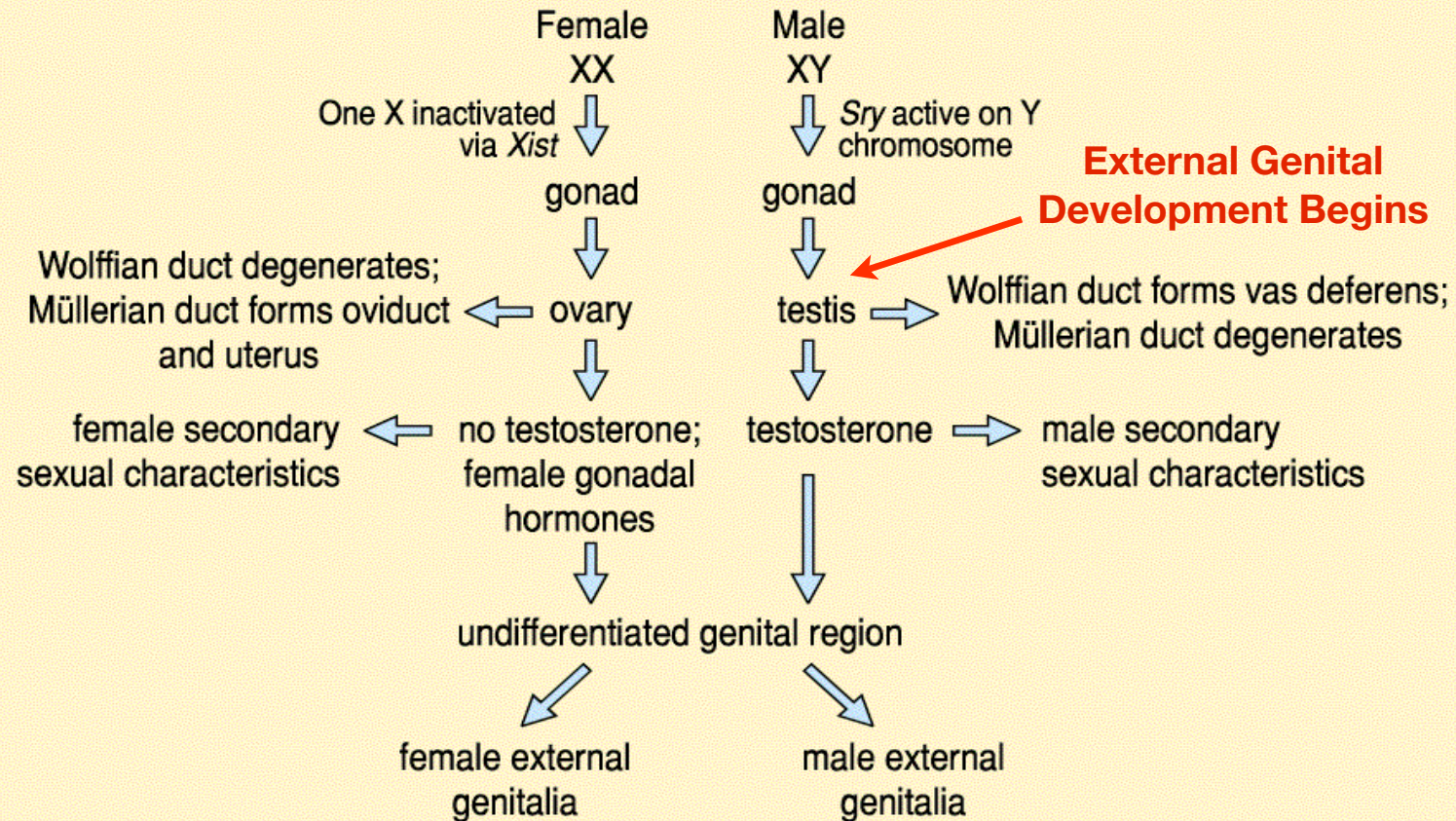
SEXUALLY INDIFFERENT



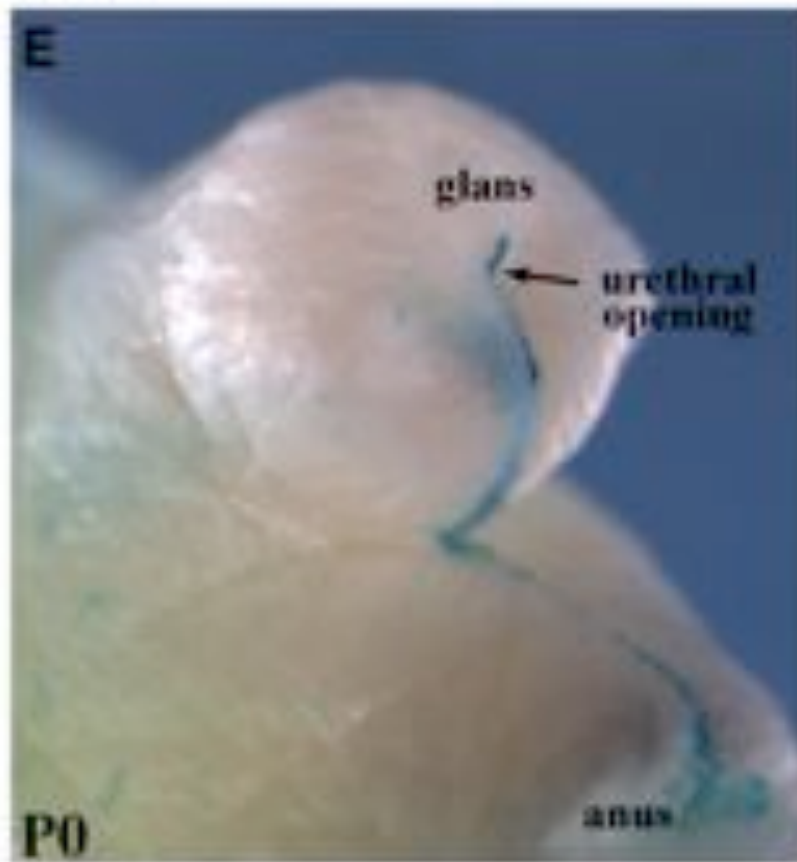


Summary: determination of sexual phenotype

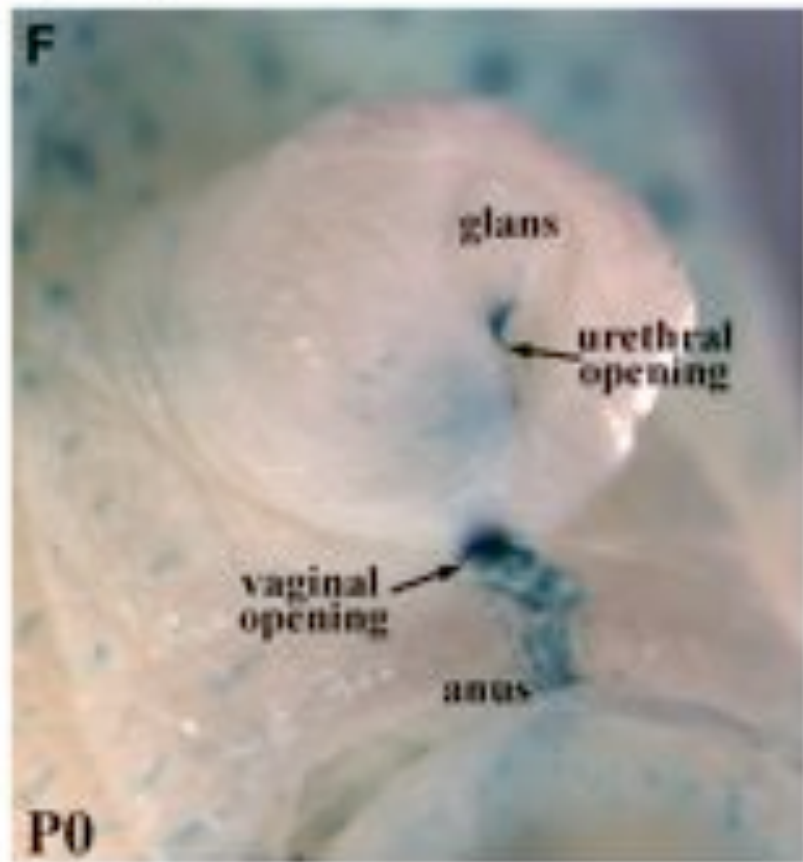
Mammals



Male

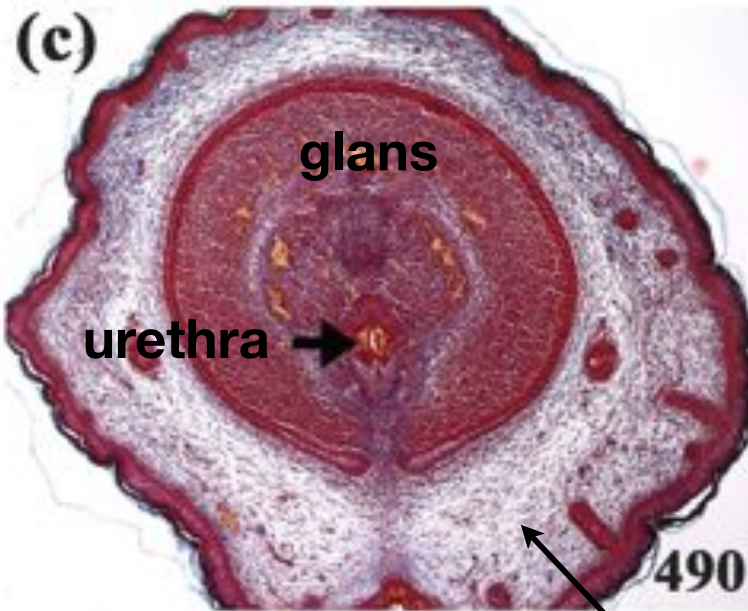


Female



Male

Female

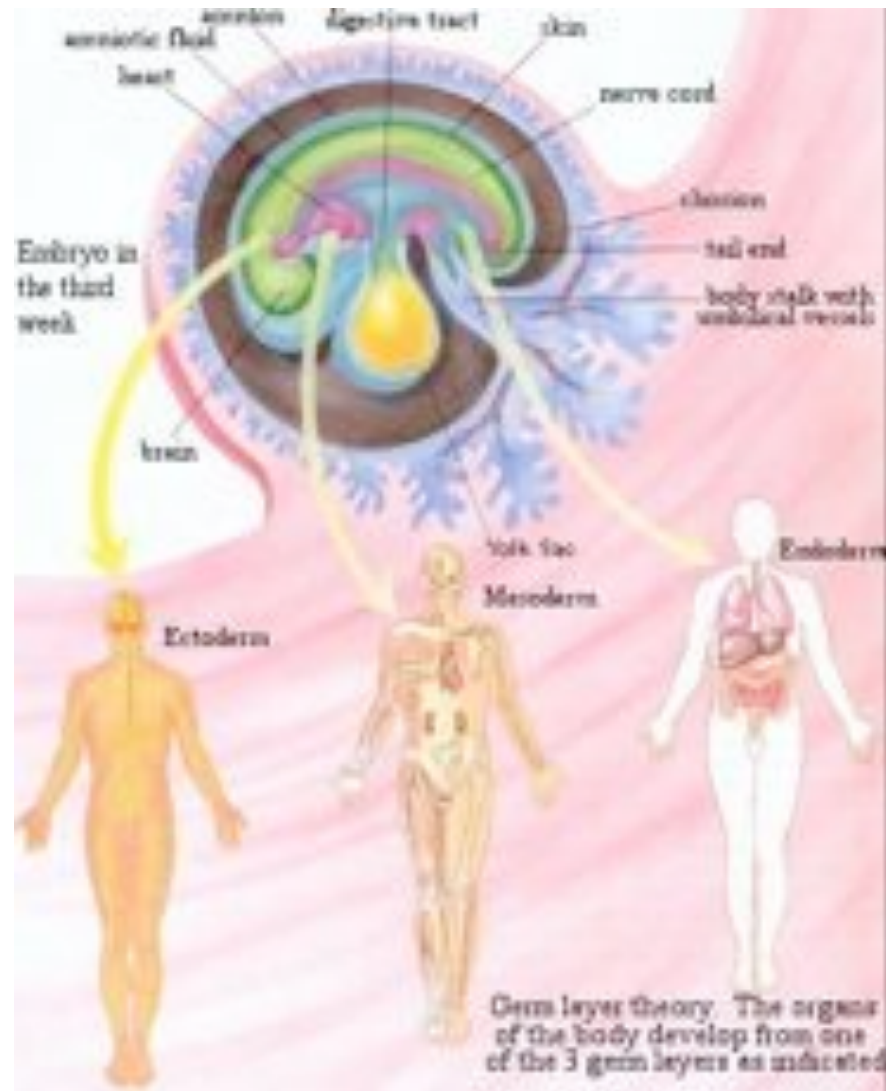


prepuce

Modified from: Perriton (2003) Dissertation

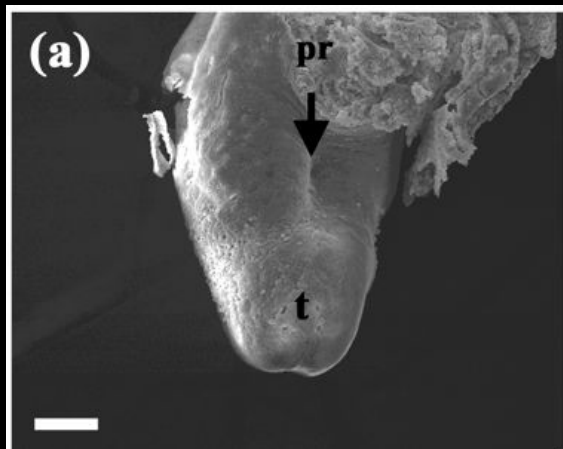
Ectoderm
preputial
glands, skin

Mesoderm
erectile tissue,
connective
tissue, smooth
muscle,
cartilage, bone

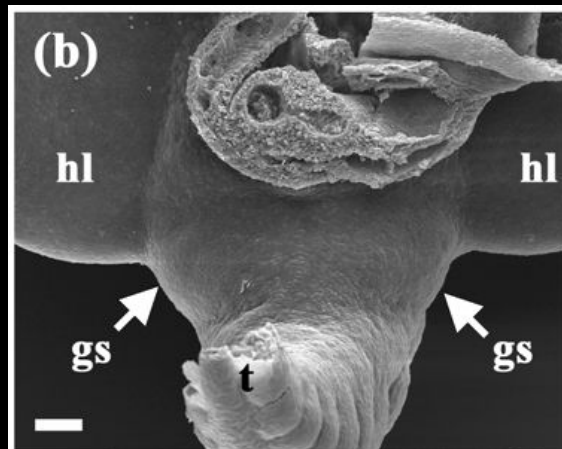


Endoderm
urethra

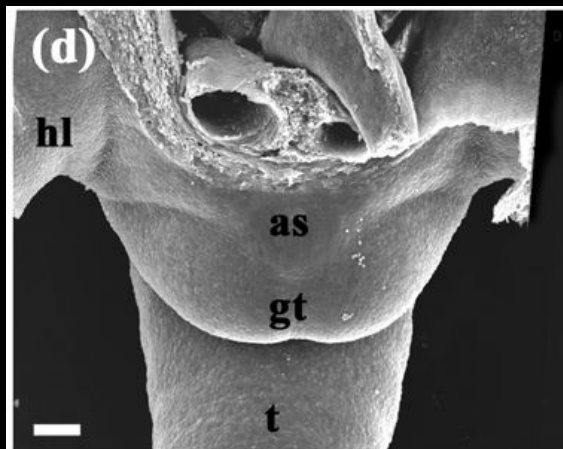
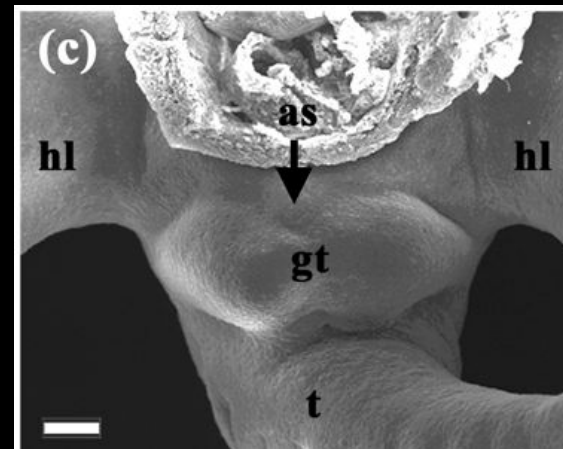
E9.5



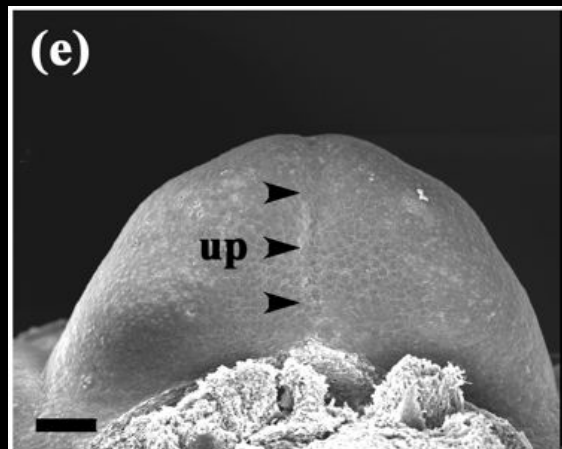
E10.75



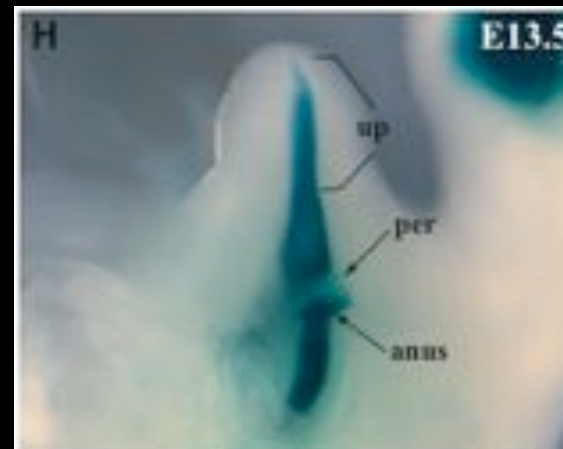
E11.5



E12.0



E12.5



E13.5





cloacal membrane

urogenital sinus

genital tubercle

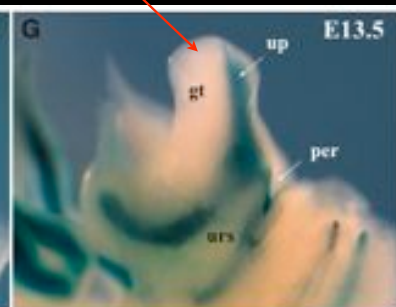
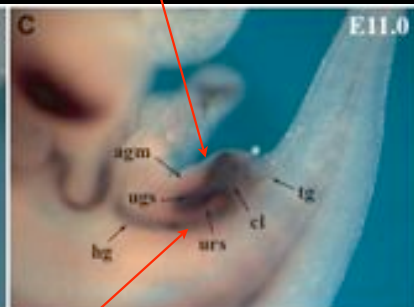
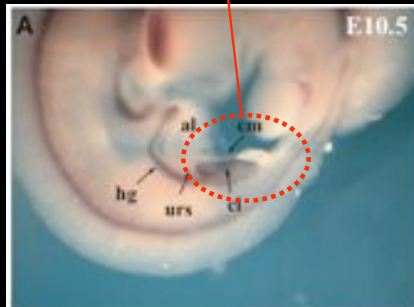
Mouse

E10.5

E11.0

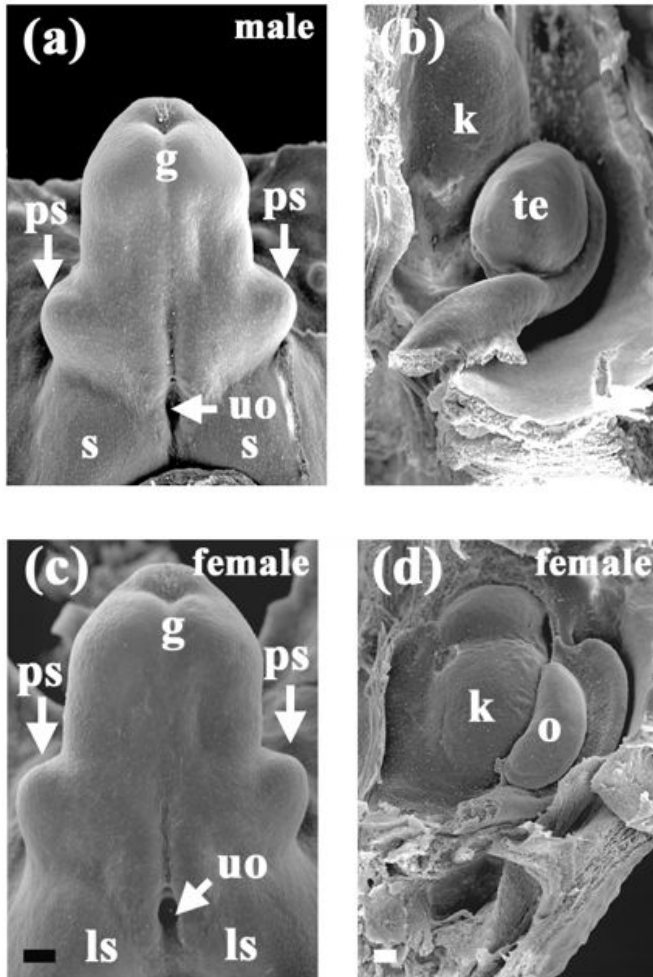
E12.5

E13.5



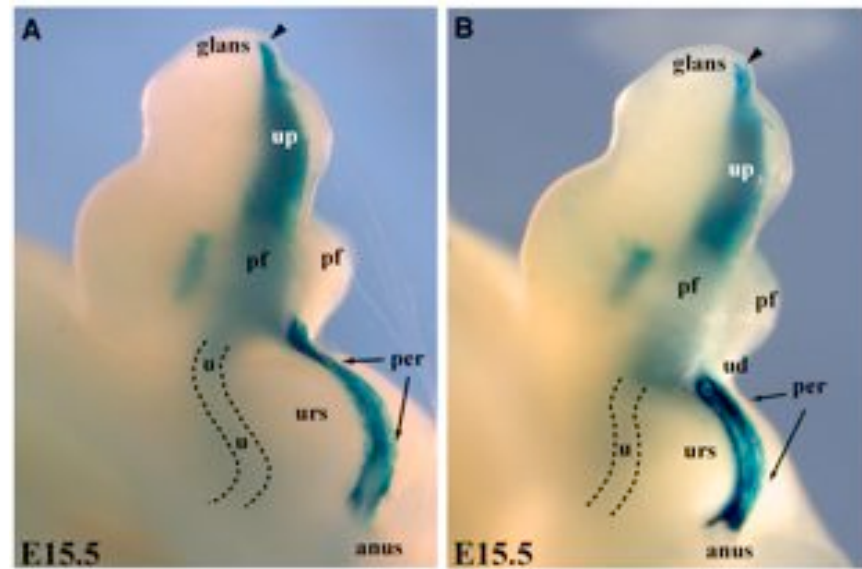
hindgut

E14.5 Sexual Differentiation



Modified from: Perriton (2003) Dissertation

E15.5

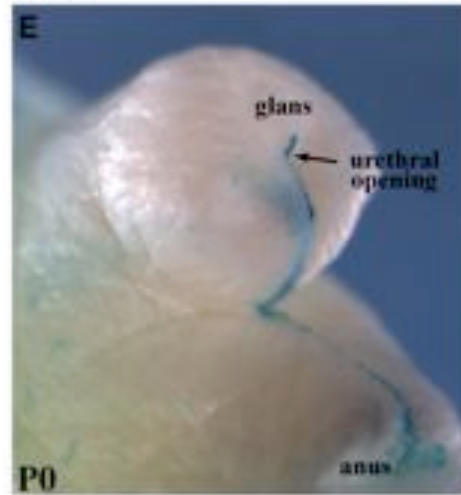
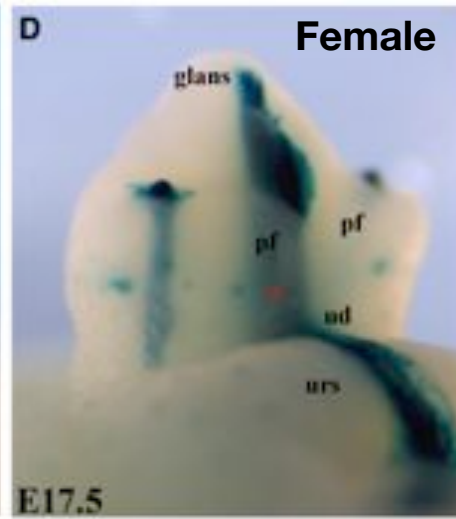
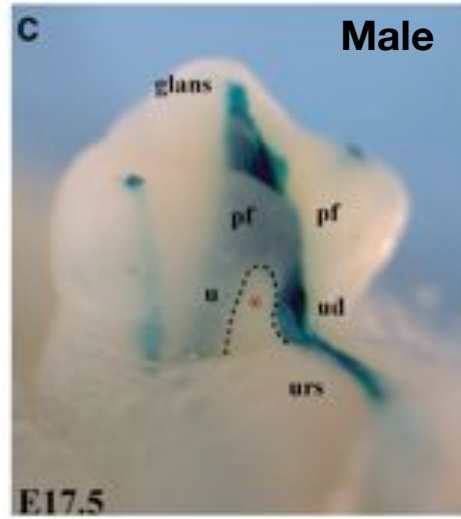


Male

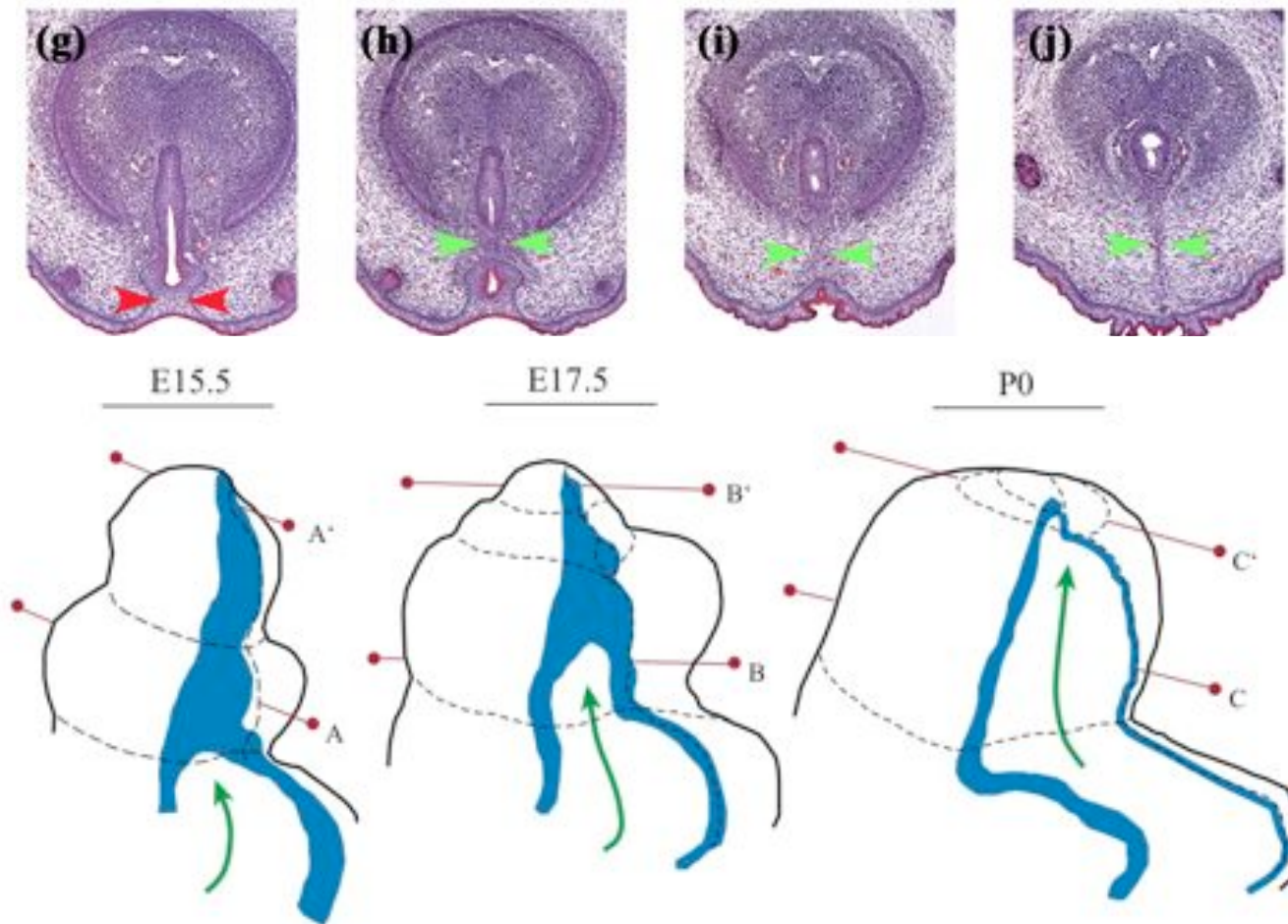
Female

Hormonal Regulation

Seifert et al. 2008 Dev. Biol



Androgen signaling drives masculinization



Sexual Maturation of the External Genitalia

Human St. 22 (E52) = ~mouse E14.5



♂



+ Testosterone



ADULT

♀

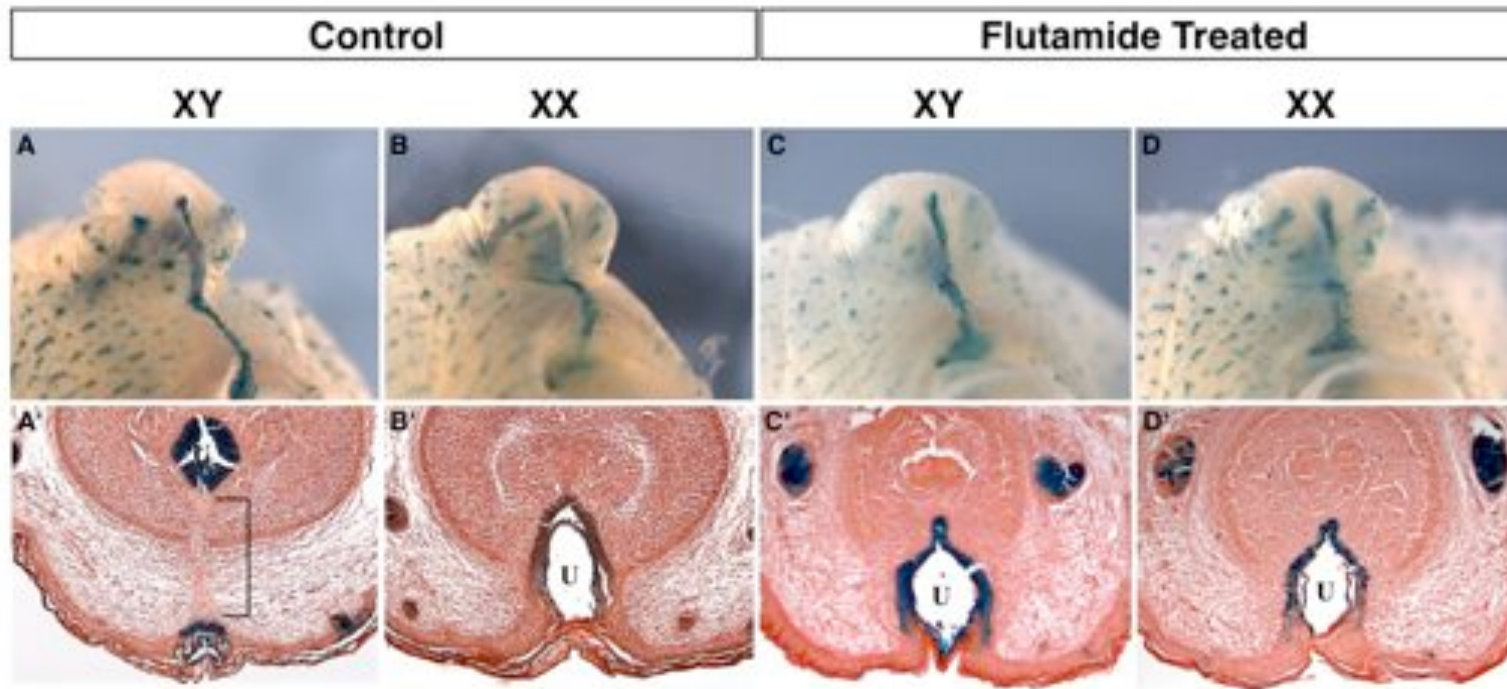


ADULT

O'Rahilly and Müller 1987. The Carnegie Collection

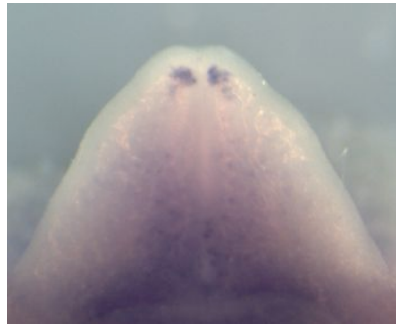
SEM images courtesy of Kathy Sulik

Androgen signaling drives masculinization



From morphology to molecules...

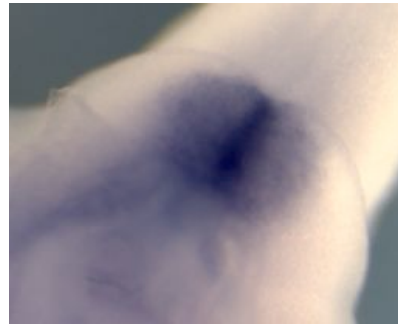




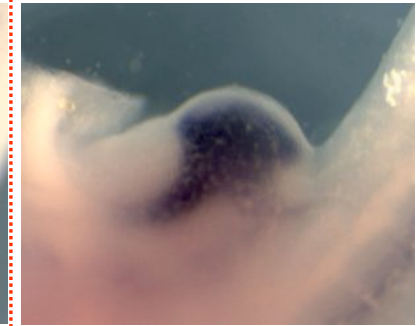
C1qA



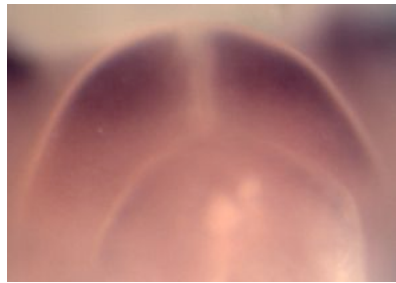
Eya1



Msx2



Shh



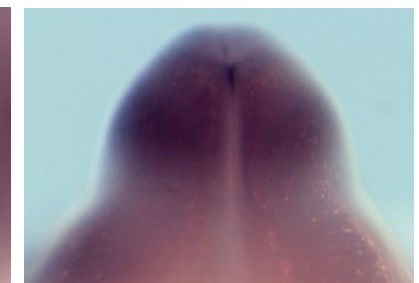
Twist



En-1



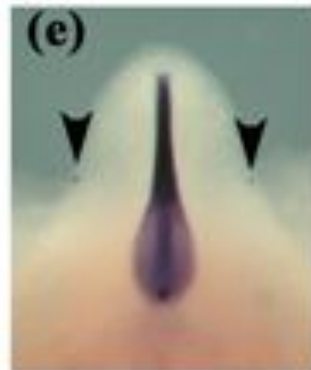
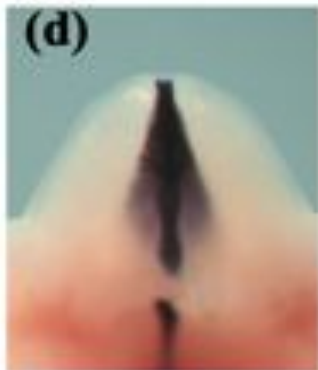
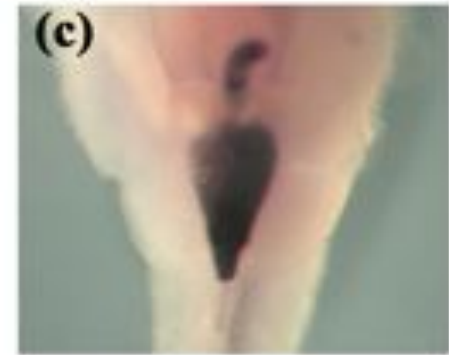
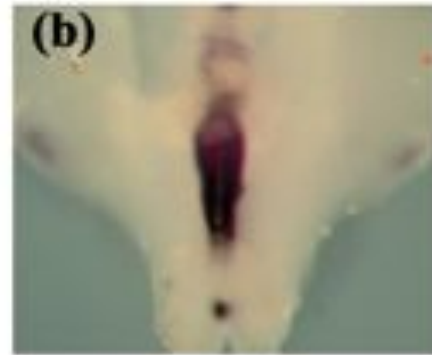
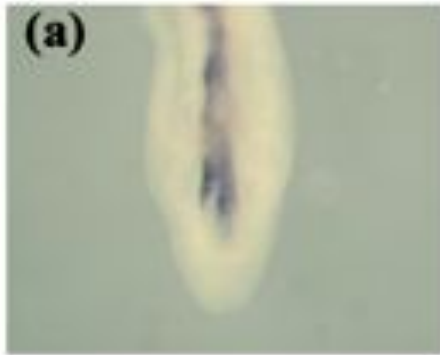
Fgf8



Wnt5a

Sonic hedgehog expression

Ventral



Modified from: Perriton (2003) Dissertation



Wildtype mouse

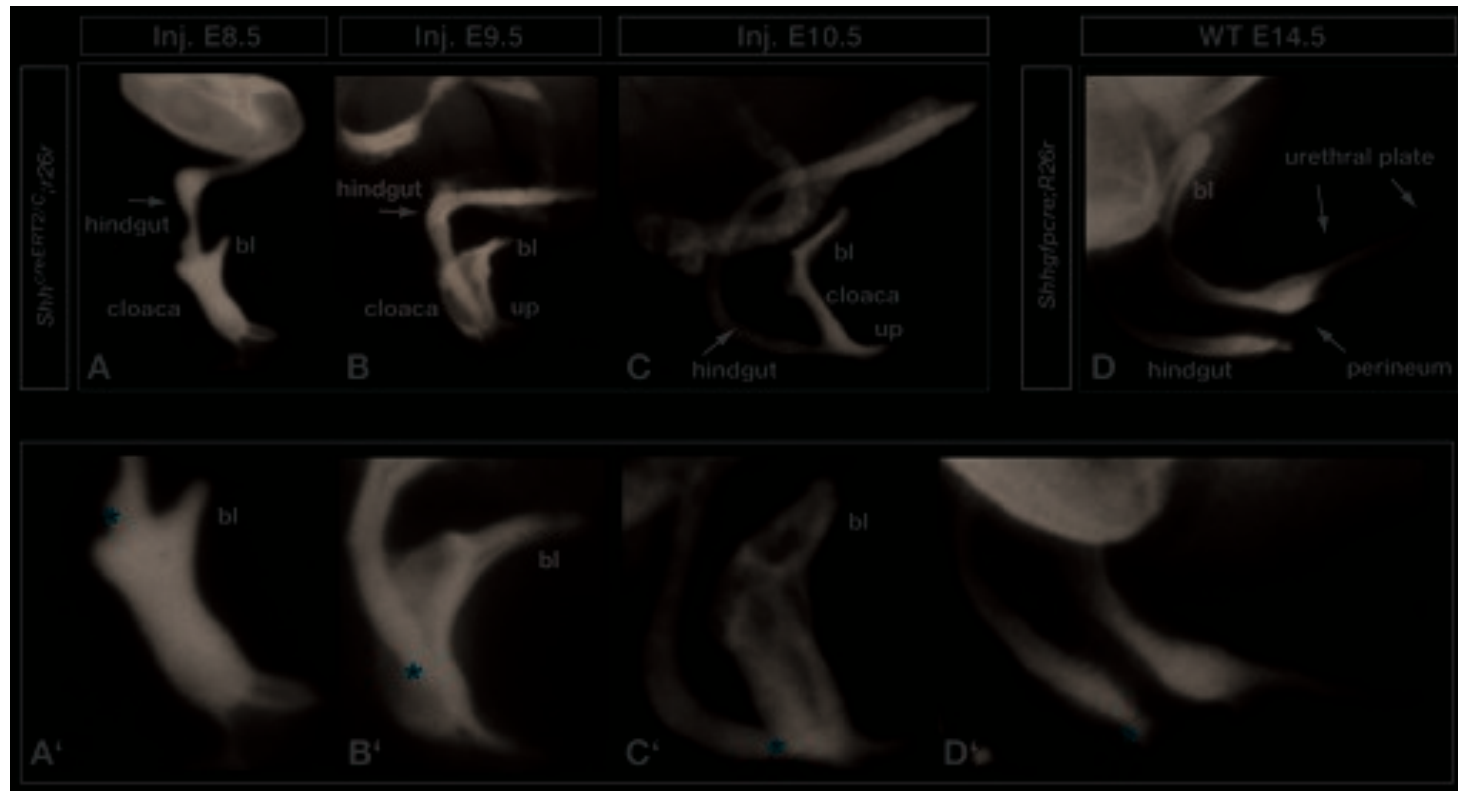


Mouse null for *Sonic hedgehog*

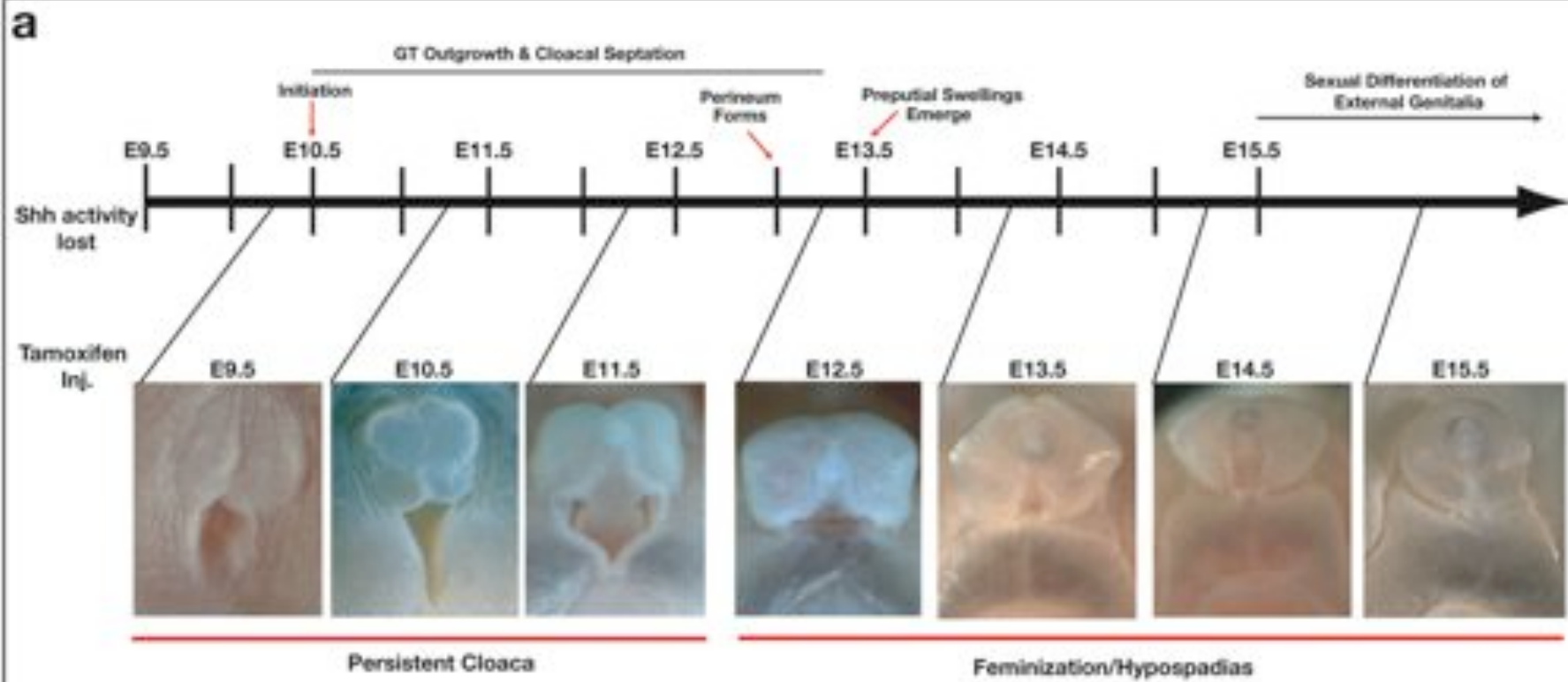


Shh removed at various time points

Wildtype



Seifert et al. (2009) Development



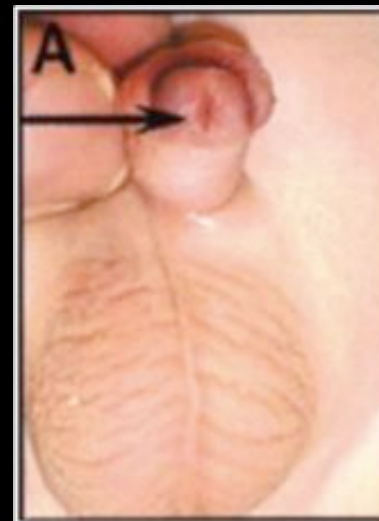
Abnormal Development: Research = Prevention

Some congenital malformations
affect multiple organ systems
and are infrequent

1:5000 up to 1:30,000

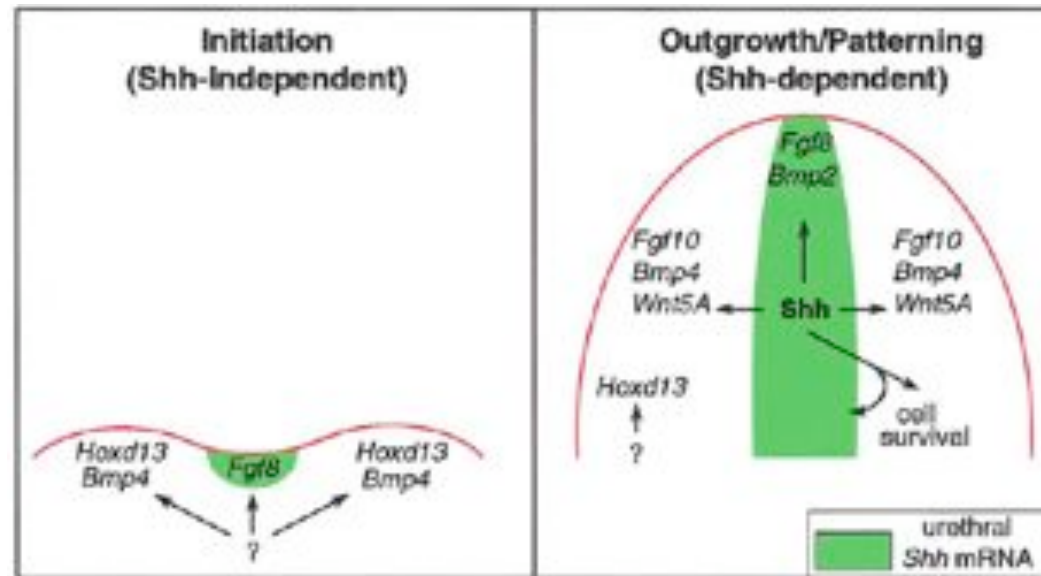
Hypospadias

1:250 live births

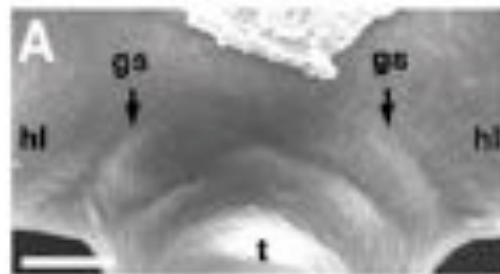


Del Campo et al. 1999 AMHG
Courtesy of Sarah Bowdoin M.D.
Baskin et al. 2001

Can investigate genetic networks during genital development

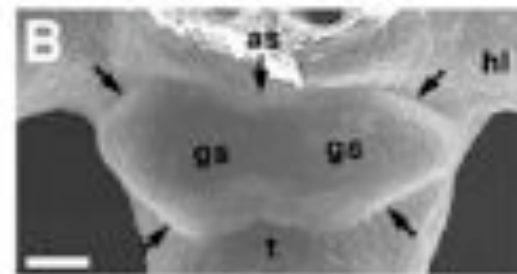


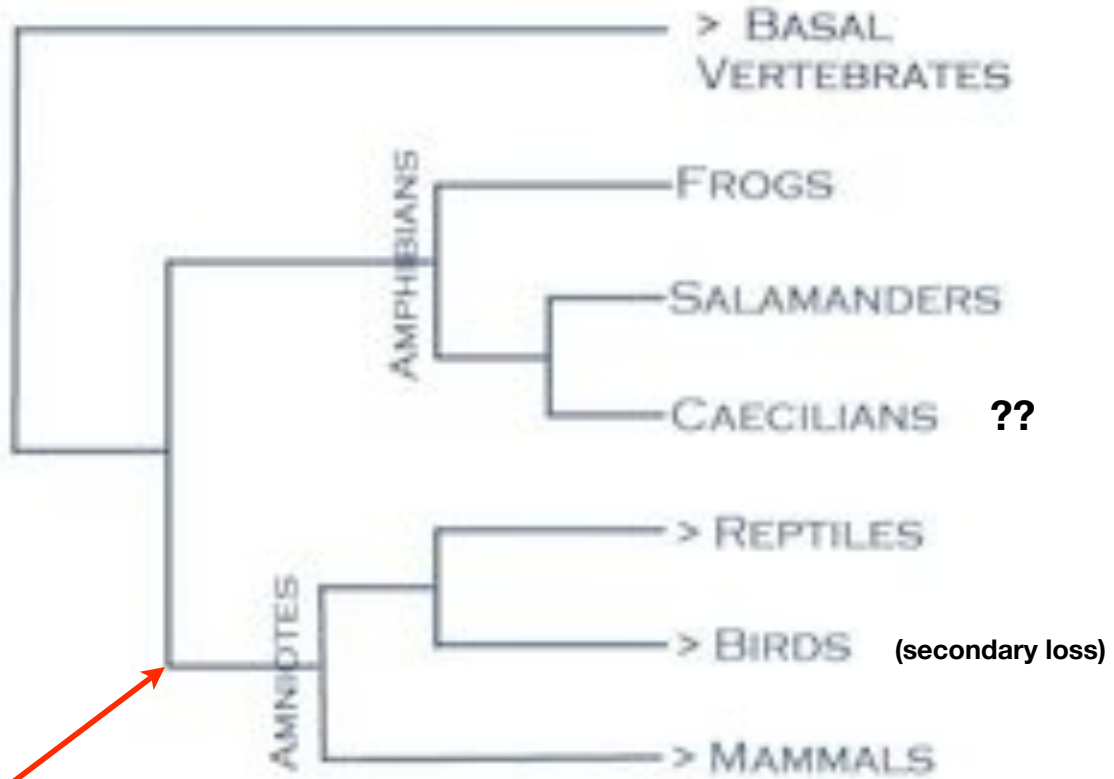
Shh -/-



E11.5

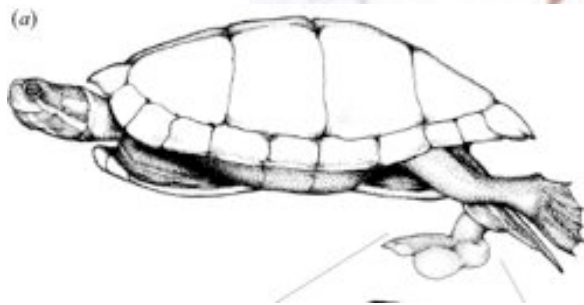
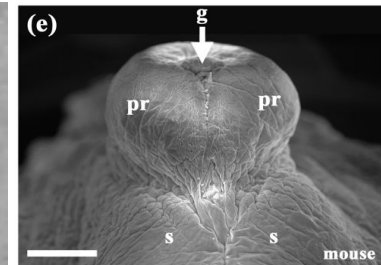
WT





external genitalia

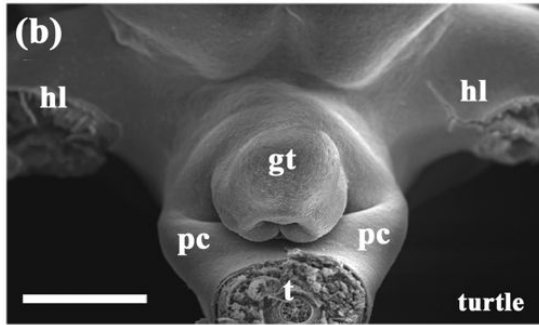
Phenotypic Diversity in Morphological Structures





**Classic model systems have no external genitalia
and undivided cloaca**

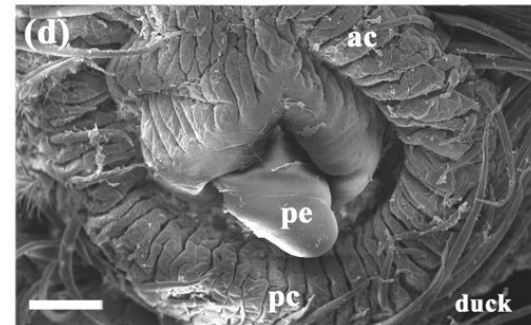
Photos: Michelle Leung (chick)



turtle

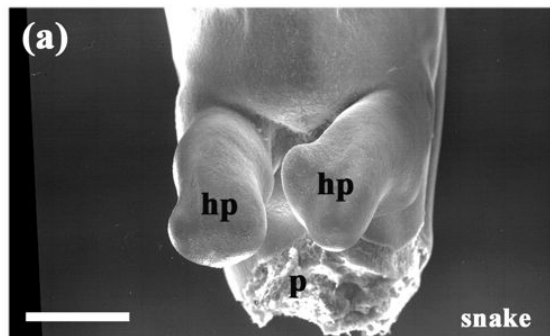


alligator

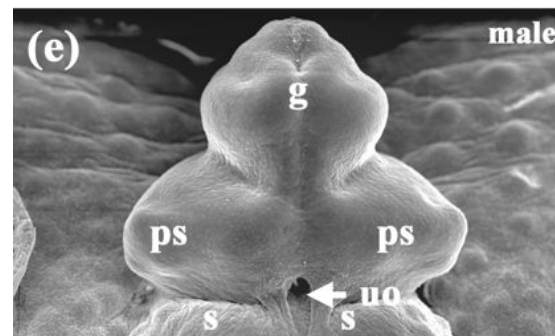


duck

snake

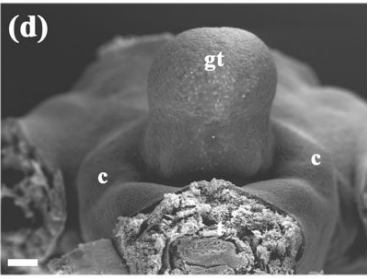
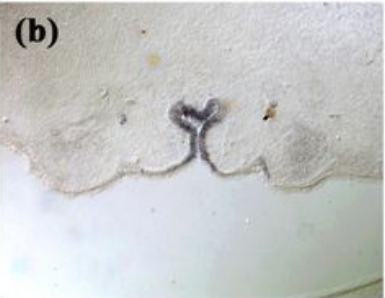


mouse

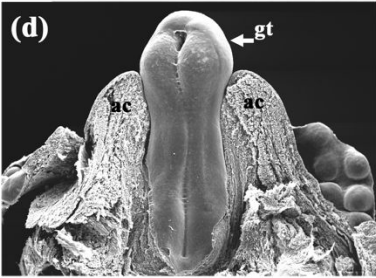


Comparison of *Shh* expression in vertebrate genitalia

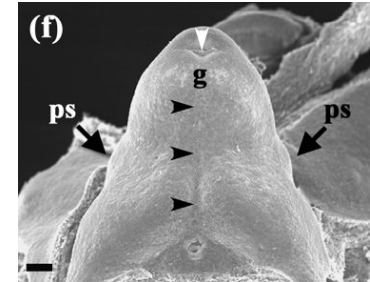
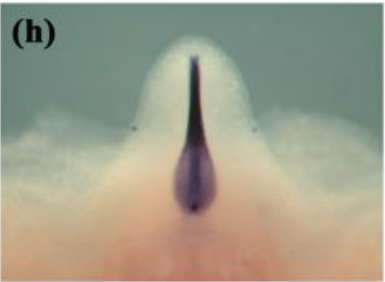
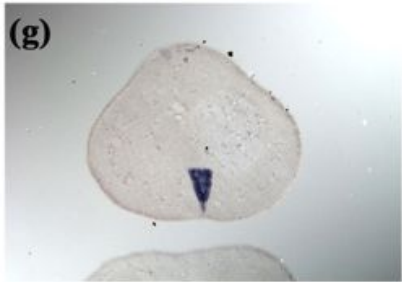
turtle



duck



mouse



Modified from: Perriton (2003) Dissertation