Exam 5 Outline

Topics Covered

 - Sex Determination

 - Saga of the Germ Line

 - Post Embryonic Development

**Sex Determination**

I. Chromosomal Sex Determination

 i. Mammals: XX = female, XY = male

 ii. Avians: ZZ = male, ZW = female

 iii. Flies: XX = female, X = male

 iv. Bees, Ants: 2n = female, 1n = male

II. Mammalian Sex Determination Overview

 i. Primary and Secondary Sex Determination happen at different times

 1) For example: In humans, primary Determination happens during embryonic development. Secondary Determination happens during adolescent puberty.

 2) Because they occur at different times, there is more room for mistakes

 ii. Primary Sex Determination

 1) Bipotential "indifferent" primordia

 2) Occurs in intermediate mesoderm near the mesonephros

 3) The default gender is female. Need the SRY gene, which is found on the Y chromosome, to become male.

 iii. Secondary Sex Determination

 1) Development of genitalia, mammaries, size, voice, musculature, and hair.

 2) Induced by paracrine and endocrine signals from gonads.

 3) Since female is default, absence of gonad produces female phenotype

III. Differentiation of Gonads

 i. Bipotential gonads start as genital ridge epithelium in intermediate mesoderm.

 1) Mullerian duct develops parallel to Wolffian duct in both gender since gender is not specified at this point

 ii. Germline stem lines come from elsewhere to populate genital ridge.

 2) Sex determination of gonad is determined by the arriving germline cells

 iii. Differentiation of Gonads in males

 1) After germline cells arrive, the epithelial cells in the genital ridge become Sertoli cells.

 - Sertoli cells provide survival and differeniational factors to male germline stem cells.

 2) Mesenchyme cells become Leydig cells

 3) Germ cells will become spermatogonia

 4 Ductal Fates

 - Sertoli AMF degenerates Mullerian duct

 - Leydig testosterone provides survival factor to Wolffian duct

 - Testis cords will become seminiferous tubules

 - Rete testis canals join testes cords to the vas deferens and then epididymous.

 - Survival of Wolffian duct and degeneration of Mullerian duct = male development

 iv. Differentiation of Female Gonad

 1) Epithelium of genital ridge becomes granulosa cells

 2) Mesenchyme becomes thecal cells

 3) Germ cells will become meiotic oogonia

 4) These cells together form the follicles

 5) Ductal Fates

 - No AMF from Sertoli cells allow Mullerian duct to survive, causing oviduct, uterus, cervix, and upper vagina to develop

 - Lack of testosterone degenerates Wolffian duct

 - Survival of Mullerian duct and degeneration of Wolffian duct = female development

IV. Secondary Sex Determination

 i. Starts at puberty.

 1) Sexual development usually match gonadal sex determination

 2) The dominant influence is gonadal steroid hormones

 3) 0.4-1.7% of population develop mixed traits call pseudohermaphroditism

 4) In males, testosterone needs to be converted to dihydrotestosterone for 2ndary determination to occur

 - People who don't do this are often raised as female until testosterone overwhelms them.

 5) Mutation in testosterone receptor

 - Female development during puberty but Mullerian duct still degenerates.

V. Sex Determination in Brain

 i. Unlike most tissues, sex determination occurs before gonadal determination

 1) Have over 50 genes that are already sexually established before the gonads, including SRY gene

 2) Gonadal hormones refine an already present sex

 ii. Testosterone must be converted to Estradoil (an estrogen) via aromatase in order to masculinize brain.

VI. Environmental Sex Determinants

 i. The gender of some reptiles are affected by environmental temperature

 1) They can be heavily affected by global warming

 ii. Increased environmental estrogen can have even bigger influence, leading to crash in male populations

 1) Human source of environmental estrogen: Atrazine weed killer, Estrogen/Progesterone birth control, Estrogenic plastics

 iii. Chemical contaminants can cause testosterone to change to estrogen via aromatase, devastating certain animal populations

**The Saga of the Germ Line**

I. Two step processes

 i. Specification

 1) Primordial gem cells (PGCs) are determined in a specific part of the embryo

 ii. Migration

 1) PGCs migrate to gonad and become progenitors for sperm and egg

**Specification**

II. Two Methods of Germ Cell Determination

 i. Autonomous Specification

 1) Determinants lie in the egg cytoplasm

 - Zone where the determinants are found is called Germ Plasm

 2) Organisms that use this method includes: Nematodes, flies, frogs

 ii. Conditional Soecification

 1) Signal for determination comes from surrounding cells

 2) Majority of sexually reproducing organisms use this method, including mammals

II. Germ Cell Determination in *C. elegans*

 i. The germ line precursor is the P4 cell, part of the P-lineage "founder" cell. P4 is the original P1 cell that has divided 4 times.

 1) P-granules enter the P4 cell instructs it to be the germ line precursor.

 2) The content of the P-granules blocks transcription and therefore blocks all differentiation.

III. Germ Cell Determination in *Drosophilia*

 i. PGCs cells form as a group of cells call the "pole cells" at the posterior end of the egg during cellularization.

 ii. They migrate into the posterior region during the ninth nuclear division and become surrounded by the **pole plasm**.

 1) Pole plasm is a collection of mitochondria, fibrils, and **polar granules**.

 - Polar granules causes no translation, no transcription, and stabilizes germline

 2) One component of pole plasm is mRNA of the **germ cell-less (gcl) gene***.*

 - This gene appears to be crucial for pole cell production. Knocking out this gene will cause no germ cells to be produce.

IV. Germ Determination in Frogs

 i. Uses cytoplasmic determinants. Vegetal region of fertilized frog egg contain similar materials as *Drosopholia* pole plasm.

 1) Cells that take up the granule containing these materials are the primordial germ cell precursors and will migrate to the gonad.

 - These material include **Nonos** proteins. Nonos is also found in fly pole plasm and stops meiosis and transcription in germ cells.

V. Conditional Specification in Mammals

 i. PGC in mammals arise from epiblast cells. These cells are no different from other epiblast cells.

 ii. The specification occurs and completes during gastrulation.

 iii. WNT3 and NODAL from surrounding endoderm make them competent to respond to BMP4 signals.

 iv. Epiblast cells that received the highest concentration of BMP4 signals from surrounding extraembryonic ectoderm will become PGCs.

 v. Repress differentiation by repressing gene expression.

 1) Specification occurs outside embryo forming cells. Once gene expression is shut down, the PGC can migrate back into embryo without responding to signals that would cause them to differentiate.

**Migration**

VI. Germ Cell Migration in *Drosophila*

 i. Pole cells attach to the endoderm and rides it as it moves to the posterior midgut during gastrulation.

 ii. Gut endoderm expresses repellent molecules, causing the germ cells to migrate through the blind end of the midgut and into the visceral mesoderm.

 iii. Protein of the *wunen* gene splits the PGCs split into two groups and guide them during their migration via chemorepulsion.

 iv. Proteins in gonads attract PGC cells into it. This is called chemoattraction.

 v. E-cadherin MET forms epithelium around PGCs.

 vi. Mesoderm and PGCs continue to divide during larval stage and differentiate at metamorphosis.

 - Anterior PGCs in the gonad become the germ line stem cells during larval-pupal transition in metamorphosis.

 - PGCs attach to top stromal cap in ovaries and attach to hub cells in testes.

VII. Germ Cell Migration Zebrafish

 i. Zebrafish develops rapidly, it takes 24 hours to go from one cell to an embryo.

 ii. Zebrafish uses germ plasm for PGC specificaion.

 iii. Migration of PGC clusters into the developing gonad follows the signal Sdf-1 using the receptor CXCR4.

VIII. Germ Cell Migration Frogs

 i. Germ plasm collects at the vegetal pole of the zygote. During cleavage, it rises up and eventually becomes associated with the endodermal cells of the floor of the blastocoel.

 ii. Become concentrated in the posterior region of the larval gut and then migrate through the dorsal side of the gut.

 1) The first migrate along the dorsal mesentery and along the abdominal wall and into the genital ridge.

 iii. Uses Sdf signals and its receptor CXCR4.

IX. Germ Migration Mice

 i. PGC starts in the extraembroynic epiblast in the endoderm.

 ii. They start by migrating into the allantosis and then into the hindgut endoderm.

 iii. During the 9th day, they migrate out of the dorsal end of the hindgut, through the dorsal mesentary, and into the genital ridge by day 12.

 iv. They continuously divide during journey and receive signals from somatic cells along the way to guide them to their destination.

 1) They follow fibronectin trails. They also use Sdf-1 signaling to guide them.

X. Germ Cell Migration: Birds and Reptiles

 i. Germs cells derived from epiblast cells that migrated from the area pullucida to the hypoblast in the anterior border of the area pullucida.

 1) This region is called the **germinal crescent** and the PGCs divide there.

 ii. They migrate to gonads by means of the bloodstream when extraembryonic vessels from.

 iii. They are carried to the area of the developing hindgut and exit there to the mesentary and eventually into the genital ridges.

 - Sdf-1 signal is what drives them out of the blood stream.

**Post-Embryonic Development**

I. Two types of Development

 i. Direct Development: Child is a miniature size adult. Old cells are still reconstructed to new ones.

 ii. Indirect Development or Metamorphosis: Hormonally activated

**Metamorphosis**

II. Involves development of a larval and an adult stage that are specialized in different functions.

 i. Larval stage usually specialized for growth and dispersion.

 ii. Adults specialized for reproduction

III. Two Major types of Larvae

 i. Primary: little to no similarity to adult (sea urchin)

 ii. Secondary: add and subtract parts from similar form

IV. Metamorphosis: Sea Urchin

 i. Larval stage is a primary larval, no trace of adult morphology.

 ii. Larval feeds and once the adult rudiment forms, they start to find a suitable place to start metamorphosis.

 iii. Adult rudiment will grow and form the adult structures. All of larval structures will eventually die off.

V. Metamorphosis: Amphibians

 i. Primary signals for metamorphosis are the thyroid hormone T3 and T4

 ii. Four Major Morphological Processes

 1) Growth of new structure

 2) Cell death of old existing structures

 3) Remodeling of existing structures

 4) Biochemical Respecification

 - Shift in the genes expressed and the physiological functions they control

 iii. Binocular Vision

 1) Eyes of tadpoles are on the side and they do not have binocular vision like the adult frog, who has eyes in the front of the head.

 - Eyes migrate dorsal and rostrally.

 2) New neurons differentiate to form contralateral and ipsilateral tract so they fuse their vision

 3) Bilateral vision allows the adult frog to focus on a target, which is essential to being a good hunter

 iv. Cell Death of Existing Structure

 1) Apoptosis

 - Thryroid signal T3 induces tail and gills to commit apoptosis

 - Occurs in gut due to ECM loss

 2) Phagocytosis

 - Macrophage finishes off the tail cells

 - Destroys larval red blood cell so new ones with adult hemoglobins can replace them

 v. Remodeling of Existing Structure

 1) Head region

 - As metamorphosis goes on, bones in cartilage grows out.

 - New signals tell neural crest cells that to the face during embryonic development to now activate.

 - Neural crest cells start to form facial bone and as they do, the shift the eyes up to the front.

 2) Limbs

 - Tadpoles have limb fields and all the necessarily structures to start limb development but they are not activated until metamorphosis.

 vi. Biochemical Respecification

 1) Tadpoles do not need to convert ammonia to urea because they can just dump it into the water.

 2) Frogs live on land and water so they can't do this. T3 causes shift in TF expressions that upregulate the genes necessary to change ammonia to urea.

VI. Actions of Thyroxine (T4) and Tri-iodothyronine (T3)

 i. Thyroid receptors are found in nucleus where they are bond to inactive receptors.

 ii. Different cells react different to thyroid, which is why thyroid can cause all these different changes.

 iii. Thyroid have an iodine chain and how a cell takes off the iodine from the chain determines the effect it will have

 - Cells that make high levels of deiodinase II will only take one iodine to turn the T4 into a T3. T3 is high active.

 - Cells that high high levels of deiodinase III will take off 2 iodines to turn T4 into T2, which is barely active. These requires higher concentration of T4 to become as active as those with deiodinase II.

 iv. When thyroid enters a cell, it binds to the receptor in the nucleus, activating the TF for that specific gene.

 - What gene you have your thyroid receptor on will determine your function

 v. The amount of deiodinase II that a certain cell type have is important

 - Limb buds have lots of deoidonase II because it is advantageous to form the limbs as soon as possible.

 - Tail have low amounts and commit apotosis at a slower rate. Advantageous because they want to make sure the limbs are fully form before you lose the swimming abilities of the tail.

 vi. Organization of tissue before T4 arrival is important

 - Head and body have basal stem cells but tail does not. Both tail and skin of head and body commit apotosis with thyroid hormones but only the skin regrow.

VII. Amphibian Alternatives to Metamorphosis

 i. Some amphibian species have evolved alternatives to metamorphosis, these are called **Heterochrnoy**

- **Neoteny**: Normal gonadal maturity but the adult retains the form of the juvenile form

 - Example is the Mexican axolotl. However, artificially adding T4 will cause it to metamorphose into an adult form not seen in nature.

 - **Progenesis:** Accelerated gonadal maturity and retains juvenile form

 - **Direct Development**: No larval form. Adult is a larger form of the juvenile

 - Example is the Puerto Rican frog. Large eggs allow for a frog to hatch from it, not a tadpole

VIII. Metamorphosis: Insects

 i. Larva eat a lot to store food for the non-feeding pupal stage

 ii. Have larval cells that will apotose and rudiments of imaginal adult cells

 - Larval cells will apotose in the pupa and imaginal disc will form wings, legs, antennae, eye, head, thorax, and genitalia

 - Imaginal cell cluster will replace larval organs with adult ones

 iii. All adult structures are partially developed before metamorphosis occurs

 iv. Leg Imaginal Disc

 - Before formation of pupa, epidermis cells form a hollow tube that coils

 - After formation of pupa, the coil grows out and form the limbs

 - Fig 15.13. The center of the disc secrets Wingless (which Wnt) and Decapentaplegic (which is TGF-B). Knock out Wingless will cause a wingless adult. Over 15 stuctures will be lost if Decapentaplegic is knocked out.

 v. Metamorphosis of insect is also controlled by hormones

 - *juvenile-hormone* causes larval molting and increases the size of the larva

 - *20-hydroxyecdysone* overwhelms above hormone to start metamorphosis

**Regeneration**

IX. Restore missing tissue and occurs in some form in all species

 i. Stem cell-mediated regeneration

 ii. Epimorphosis: surrounding cells re-differentiate to replace damaged ones

 1) New TF are made and chromotin is re-methylated. Chromotin is what locks a cell to its current cell type so that its daughter cells will also be the same type

 2) All cancer is re-differentiated cell type. Heart disease involves this too

 3) Telomeres may also be lengthen during the re-differentiating process

 iii. Morphallaxis: adult cell repatterning

 1) Hydra: a fully differentiated cell can bud off and revert back to embryonic cell and form a whole new organism

 iv. Compensatory regeneration: adult cell division

 1) Can't dedifferentiate but all five cell types can produce more of themselves

 2) Oval cells: progenitor cells of liver cells and serves as a backup

**Aging**

I. Life span vs. Senescence

 i. Life span is how long you live. Senescence is the decline of your strength. You can have a longer life span but start senescence earlier than someone else

 ii. Things that can effect these processes are mutations, environmental factors, and random epigenetic changes

II. Humans have extended the average age of death but have not really extend life

III. Epigenetic Alterations

 i. Fig. 15.36(1) Twins have little differential DNA methylation patterns as infants but as they grow older the differences increases dramatically. Reasons for changes is due to enviromental factors such as lifestyle.

IV. Fig. 15.37 Reproductive capacity can vary greatly