Name:_____KEY_____ Student Number: _____

BIO380HF—HUMAN DEVELOMENT
First Midterm Test—October 7, 2009
Professor Danton H. O'Day
Test Length: 1.5h; 100 Marks Total
Answer all questions giving the best or most appropriate answer in each case. No aids allowed.

KEY

PART I. TUTORIAL QUESTIONS (30 marks total)

I.A. MULTIPLE CHOICE—Underline the best answer (1 mark each; 5 marks total & 2 bonus marks)

1. Which of the following is first observed in *Drosophila* development, right after fertilization?
a) A multicellular embryo
b) A large multinucleate cell
c) A larva with a clearly defined axis
d) An embryo with a group of cells at its periphery and pole cells at its posterior
e) Pole cell formation

2. What is the identity of the molecule that initiates polar granule formation in Drosophila?
a) Oskar protein
b) Vas protein
c) PAR-1 protein
d) Oskar mRNA
e) Tudor protein

3. A *Drosophila* mutant with a defect in the *vas* gene would be predicted to:
a) Fail to localize Vas at the posterior of the embryo
b) Fail to localize Oskar at the posterior of the embryo
c) Fail to localize Tudor at the posterior of the embryo
d) Both a) and c) are correct
e) All of the above are correct

4. Which of the following is true regarding the hormones that function during the menstrual cycle?
a) GnRH from the pituitary gland stimulates the secretion of FSH and LH by the hypothalamus
b) Progesterone is secreted by the corpus luteum during the proliferative phase
c) An ovulatory surge of FSH and LH occurs at the end of the proliferative phase
d) Both a) and c) are correct
e) All of the above are correct

5. An effect of a knockout experiment might not be seen due to:
a) Gene redundancy
b) Compensation
c) Improper screening techniques
d) All of the above
e) A) and b) only

Name:_____KEY_____ Student Number: _____

I.B. SHORT ANSWER. Answer in point form or sentences. Where appropriate, your answer must be clearly written, organized and progress in a logical sequence (25 marks total).

1. Define the Following Terms (2 marks each; 10 marks total)

Rescue experiment	Introduce the missing component of the embryo to try to return the function after a cutting experiment
Reverse genetic approach	start with known gene and mutate it to infer its function
Chimera	embryo composed of cells from two different sources, so that it contains populations of genetically distinct cells
Dominant negative receptor	growth factor receptor engineered to lack the intracellular signalling domain
Electroporation	method of introducing donor DNA into cells by subjecting them to an electric current

2. What is the difference between a malformation and a deformation? Give an example for each (4 marks).

-malformation: abnormality in a structure due to a direct effect of a mutation and/or teratogen on the development of that structure (1)
-malformation ex: spina bifida (neural tube defect) (1)
deformation: abnormality in a structure due to a secondary effect of malformation of another structure (1)
-deformation ex: clubbed feet due to oligohydramnious (1)

3. For any **two** of the six model organisms discussed during tutorial, give its common and scientific name and provide a specific example of how this organism is a useful model in researching developmental biology. (3 marks).

a) What are the full common and scientific names of the organism? (0.5 mark each)
Fruitfly – *Drosophila melanogaster;* Nematode worm – *Caenorhabditis elegans;* Zebrafish – *Danio rerio*
South African clawed toad – *Xenopus laevis* or *Xenopus tropicalis;* Chick – *Gallus gallus domesticus*
Mouse – *Mus musculus*

b) Provide a specific example of how this organism was a useful model for researching developmental biology? (1 mark each)

- Any of the examples on pages 135-142

4. You are a developmental biologist and you want to understand the function of a newly discovered gene that you know nothing about. What 2 experimental embryology techniques could you use? Describe the basic principle of each and information it will provide you with (8 marks).

- Immunohystochemistry and/or in situ hybridization – localization of gene products in the embryo (4)
- transgenic techniques (knock-out/overexpression/ectopic expression) – possible function of the gene (4)

PART II. LECTURE QUESTIONS (70 marks total)

II. A. MULTIPLE CHOICE—<u>Underline</u> the best answer (1 mark each; 15 marks total & 2 bonus marks)

1. A teratoma:
a. is a malignant tumor
b. is formed from primordial germ cells
c. contains differentiated cells.
<u>d. all of the above</u>
e. none of the above

2. Human male germ cells arise in the:
a. placenta prior to gastrulation
<u>b. epiblast prior to gastrulation</u>
c. neurogenital ridges prior to gastrulation
d. testicles prior to gastrulation
e. none of the above

3. The routes the germ cells follow is lined with:
a. fibronectin
b. extracellular matrix
c. laminin
d. extracellular proteins
<u>e. all of the above</u>

4. Teratomas can contain:
a. skin
b. hair
c. teeth
<u>d. all of the above</u>
e. only skin and hair

5. Mutants in the human DAZ gene lead to:
a. the absence of gonads
b. the absence of genital ridges
c. the absence of sperm
d. all of the above
e. none of the above

6. The secondary follicle
a. is surrounded by several layers of follicle cells
b. contains some follicular fluid
c. contains a secondary oocyte
d. all of the above
e. a and b are correct

7. The tertiary follicle
a. is surrounded by a single layer of follicle cells
b. contains no follicular fluid
c. contains a tertiary oocyte
d. contains a secondary oocyte
e. contains a primary oocyte

8. Which of the following are not part of the mature male genitalia
a. Urethra
b. Bartholomew's gland
c. Vasa efferentia
d. Cowper's gland
e. Bulbourethral gland

9. Which of the following statements about the human ejaculate are not true:
a. It contains as many as 250×10^7 sperm
b. It has a volume of 20mL
c. A count of 5 million sperm/mL is sufficient for male fertility
d. Semen has a pH of 8.7
e. All of the above
f. All of the above except b

10. Which of the following statements about alkaline phosphatase is not true?
a. It removes phosphate groups from molecules
b. It works at a pH above 7.0
c. It is a marker for primordial germ cells
d. It is a marker for both primordial germ cells and semen
e. It is an enzyme

11. Which of the following statements about acid phosphatase is not true?
a. It removes phosphate groups from molecules
b. It works at a pH below 7.0
c. It is a marker for primordial germ cells
d. It is a marker for semen
e. It is an enzyme

12. Which of the following statements about integrin is true?
a. It is found in the extracellular matrix
b. It binds to fibronectin
c. It is a marker of primordial germ cells
d. It lines the pathways primordial germ cells follow
e. It is an enzyme

13. Which of the following statements about the primary oocyte is not true?
a. It is locked in diplotene
b. It has started meiosis I
c. It has not started meiosis I
d. It has not started meiosis II
e. It has not released a polar body

14. Which of the following statements about meiotic non-disjunction is true?
a. It is considered to be a result of the "maternal age effect"
b. It is not related to the "paternal age effect"
c. It can be due to non-disjunction during mitosis
d. It does not involve the spindle apparatus
e. All of the above are correct

15. Which of the following statements about Turner syndrome is true?
a. It is due to the lack of an X or Y chromosome
b. It leads to a female phenotype
c. It occurs in 1 in 2500 females
d. It leads to cognitive defects
e. All of the above are true

16. Which of the following statements about annulate lamellae is not true?
a. It is adjacent to the germinal vesicle of the developing egg
b. It is found in the cytoplasm of the developing egg
c. It likely contributes to the forming pronuclei
d. It is derived from the developing pronuclei
e. It consists of parallel stacks of nuclear envelope-like membranes

17. Which of the following statements about the axoneme is not true?
a. It has a central doublet of microtubules
b. It is surrounded by a cell membrane
c. It is able to undergo microtubular sliding
d. It possesses dynein which converts cAMP into ATP
e. It is surrounded by dense fibres

Name:_____KEY_____ Student Number: _____

II. B. Fill in the blanks (1 Mark each; Total = 10).

1. List three important functions of Sertoli Cells:

a. ___provide nutrients_____

b. ___ provide support/synchronize spermatogenesis _____

c. ___ provide critical proteins/take up residual body by phagocytosis/hormones? other?_____

2. List the two cellular layers that surround the ovulated ovum:

a. ___corona radiata_____

b. ___cumulus oophorus_____

3. Two components added to semen by the prostate gland are__ions; citric acid_____and acid phosphatase___

4 One component added to the male ejaculate by seminal vesicles is_____Fructose_____

5. Sperm movement from the vagina into the uterus is slowed by: cervical mucous_____

6. After exiting the uterus sperm movement is assisted by: cilia lining fallopian tubes_____

C. SHORT ANSWER. Answer in point form or sentences. Where appropriate, your answer must be clearly written, organized and progress in a logical sequence. (15 Marks total)

1. Give the full names for the following acronyms (5 marks).

Acronym	Full Name
SDF-1	Stromal Derived Growth Factor-1
GFP	Green Fluorescent Protein
TGFβ	Transforming Growth Factor Beta
DSCR1	Down Syndrome Critical Region 1 protein
NFATc	Nuclear Factor of Activated T Cells

Name:_____KEY_____ Student Number: _____

2. Using diagrams and point form, explain the nucleoprotein changes that occur in the human sperm and their significance. (10 marks)

Why the changes are significant (5 marks)

-Each species of animal has a species-specific sperm morphology which often involves the shape, size and density of the nucleus.

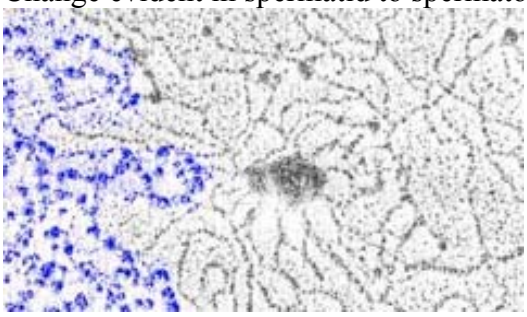
-The change in nuclear morphology is referred to as nuclear morphogenesis.

-In humans spermatogenesis, nuclear morphogenesis involves a number of changes:

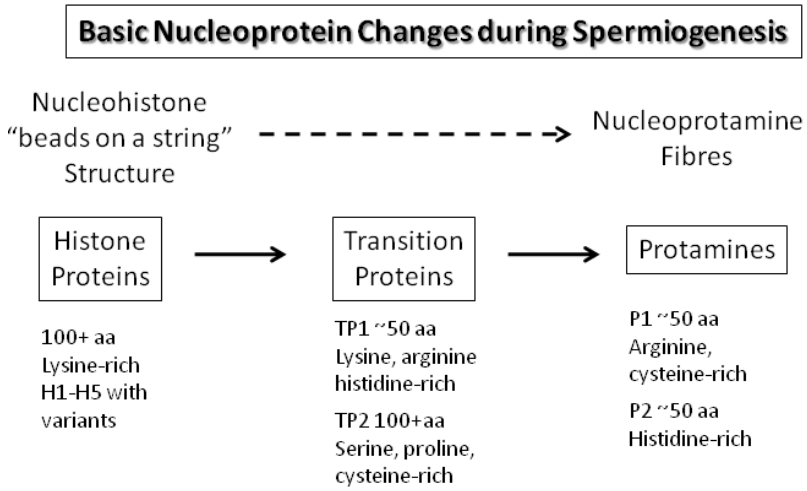
- The Nucleus changes shape and density giving it a specific morphology
- Chromatin is repackaged to protect it from environment (esp. chemicals)
- Histone & DNA constitute chromatin of somatic cells; nucleosomal organization
- Sperm specific protamine proteins appear during spermiogenesis; non-nucleosomal organization allows tighter DNA packing

- In the early stages of spermatogenesis, somatic cells package their DNA with somatic histones (basic proteins) that results in the formation of nucleosomes which are seen throughout the nucleus. This gives chromatin the appearance of "beads on a string" (like a pearl necklace). During spermiogenesis, the somatic histones are replaced with protamines which don't form nucleosomes and so allow a tighter packing of the DNA.

Change evident in spermatid to spermatozoan nucleus:



Comments on the specific events shown in the following figure should be included—give extra marks for a complete figure (5 marks): some indication about the size changes and types of amino acids that characterize the types of basic proteins but don't need full accounting.

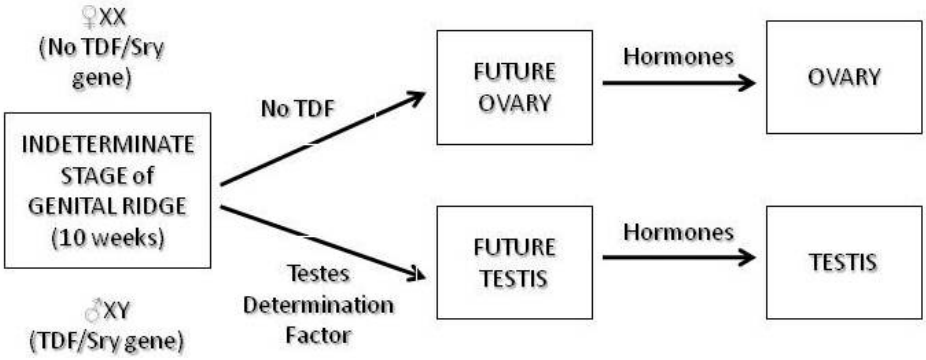


Name:_____KEY_____ Student Number: _____

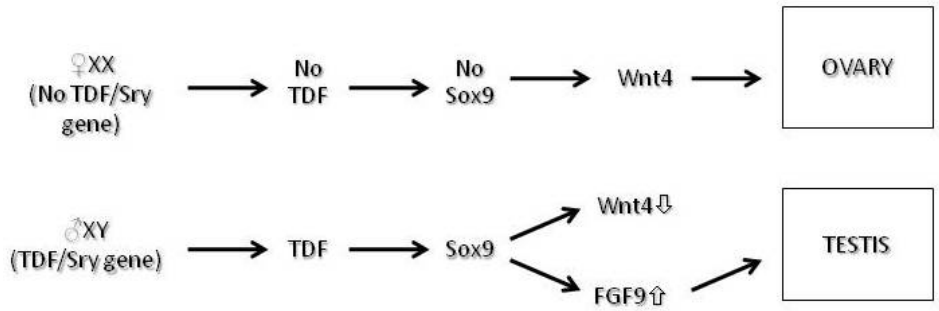
II. C. ESSAY QUESTIONS. Answer the following questions in essay format using the space provided. Use diagrams as needed to clarify your answers.

1. Explain the role of TDF in human embryonic development. Also include the alternative name for TDF. (15 marks)

First part (6 marks)
-The determination of sex begins at fertilization (Males XY, females XX).
-At the "Indeterminate Stage" of sexual development (~10 Weeks in above figure) the genital ridge is bipotential. It can develop either into male or female genitalia.
-TDR/Sry gene on the Y chromosome that is not present on the X chromosome leads to the production of testis determination factor (TDF).
-TDF causes each genital ridge to develop into a testis.
-In the absence of TDF, the genital ridge develops into an ovary. TDF has also been called Sry (Sex determining Region of the Y chromosome).
This diagram is not needed since it is just the same info as above.



Part 2. (6 marks)
As summarized in the following figure, the presence of TDF induces the expression of the transcription factor Sox9 which in turn leads to an increased expression of Fibroblast Growth Factor 9 (FGF9) and the downregulation of Wnt4 expression. These events are part of the signaling pathways that underlie the development of the testis. In contrast, the lack of Sox9 expression in female embryos allows expression of the secreted protein Wnt4 leading to ovary development.



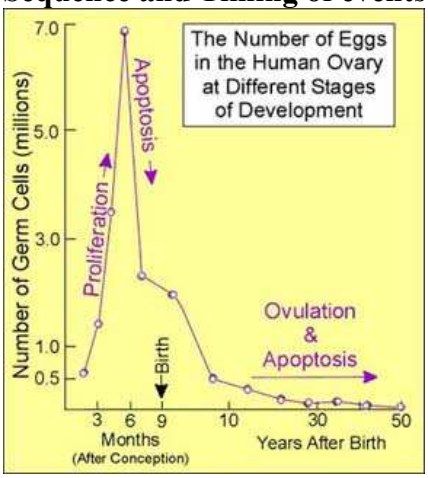
Need to include what TDF/Sry (DNA binding protein), Sox 9 (Transcription factor),Wnt4 (signaling protein) and FGF9 actually are/what they do (covered above).

3 marks for completeness, clarity and organization

Name:_____KEY_____ Student Number: _____

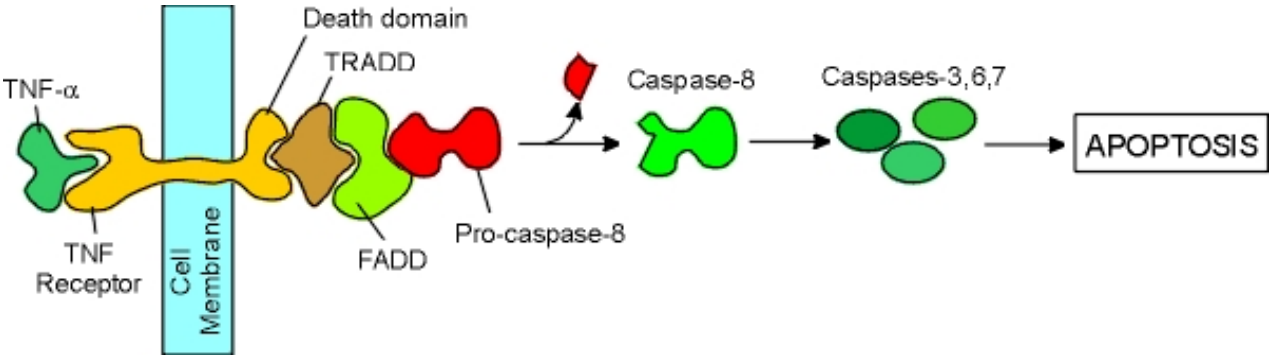
2. The number of eggs in the ovary changes over time. Draw a graph showing the changes that occur in the ovary from fetal development to post-menopause. Then detail the role and sequence of signaling events of the extrinsic pathway of apoptosis in reducing egg cell numbers in the ovary. Note: do not discuss the morphological events of apoptosis. (15 marks).

Sequence and Timing of events (6 marks)



- Increases to ~7 million by 6 months in utero
- Then # decreases due to apoptosis
- Only ~2 million at birth
- ~0.5 million at puberty
- Continual decline until menopause: ovulation and death.

Extrinsic pathway details (6 marks)



Surface receptors can be activated by specific ligands that bind to "death receptors" (i.e., "Extrinsic Pathway"). Death receptors are members of the tumour necrosis factor (TNF)/nerve growth factor (NGF) receptor superfamily. They make up a subfamily characterized by the intracellular death domain (DD). The binding of TNF-α to its receptor (TNF-receptor or TNFR) makes the receptors intracellular death domain available for binding to TRADD (TNFR-associated death domain). TRADD is an adaptor that in turn directs the binding of FADD (Fas-associated death domain) another adaptor that mediates the binding of pro-caspase-8 to this multiprotein complex. This leads to the proteolytic processing of the inactive pro-caspase-8 into the active caspase-8 enzyme. Caspase-8 is an initiator caspase that in turn proteolytically activates several other caspases. The activated caspases-3,6 and 7 are effector caspases that proteolytically digest a number of target proteins ultimately leading to apoptosis.

3 marks for completeness, clarity and organization