Exam Procedures:

STEP 1- NAME (*Print clearly*) _____ _____

(first) *(last)*

STEP 2 – Fill in your answer sheet, using a #2 scoring pencil, as follows:

- ☑ Your Student PID Number (excluding "A")
- ☑ Your last name and first name
- ☑ Course ID in "subject" …… **this is BMB 526 Exam #2**
- ☑ Date …… **11/25/13**
- ☑ Exam form in "period" …..**this is form A**
- ☑ By signing this coversheet for this exam, the student certifies that he/she has adhered to the policies of academic honesty in the performance of this exam.

_____

Signature

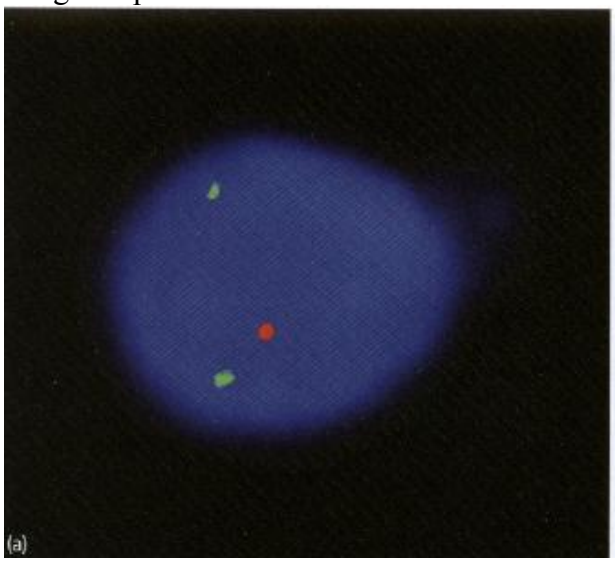
STEP 3 - Read these instructions:

- ☑ Make sure your exam has **34** questions.
- ☑ Read each question very carefully. Choose the single, best answer and mark this answer on your answer sheet. No points will be added for correct answers which appear on the exam page but not on the answer sheet.
- ☑ Cell phones must be off (not on vibrate) and stored with your bags/backpacks/other materials.
- ☑ The proctors have the authority/responsibility to assign any student a different seat at any time, without implication and without explanation, before or during the examination, as they deem necessary. Accomplish any relocation quietly and without discussion.
- ☑ We will not answer questions of clarification. However, if you think there is an error on your exam, summon an exam proctor.
- ☑ When you finish, place all exam materials (except the tear sheet) into the manila envelope. When you leave the exam room, please turn in your envelope to the proctors. Once you exit the auditorium, please leave the area. Hallway conversations disturb those still taking the exam.
- ☑ There will be answer keys to this exam posted on the course website by 5:00 p.m. the day of the exam. You may wish to copy your responses from your answer sheet onto the answer grid on the LAST page of this exam so that you can check your results. You can tear off the last page and take it with you.
- ☑ We will close the exam promptly at **9:10 a.m**. At the announcement of the examination end time, the examination and scantron and images (if provided as part of the examination) must immediately be placed into the manila envelope provided.

STEP 4 – Wait until instructed to proceed with the exam!

For Questions 1 and 2, the black-and-white images are shown on this page. You may wish to refer to the color versions of the same images (Plate X and Plate Y) found on the *SEPARATE SHEET*.

1) The image below shows Fluorescence in situ Hybridization (FISH) results on amniocytes using two probes:



green --- 22q-specific control probe

red --- 22q11.2-specific probe

Given that results on probing other chromosomes appear to be normal, this image would suggest that the fetus will most likely have:

A) Down syndrome
B) Edwards syndrome
C) Robertsonian syndrome
D) Shprintzen (Velocardiofacial) syndrome
E) Wolf-Hirschhorn syndrome

Plate X (Tobias6_F12.8(a)_p173)

2) In 25% of cells from several cultures derived from amniotic fluid, the following karyogram was obtained. There is an extra chromosome (shown on the lower right-hand corner), most likely representing an extra copy of chromosome 20. The remaining cells had a normal number of chromosomes. This situation is best described as:

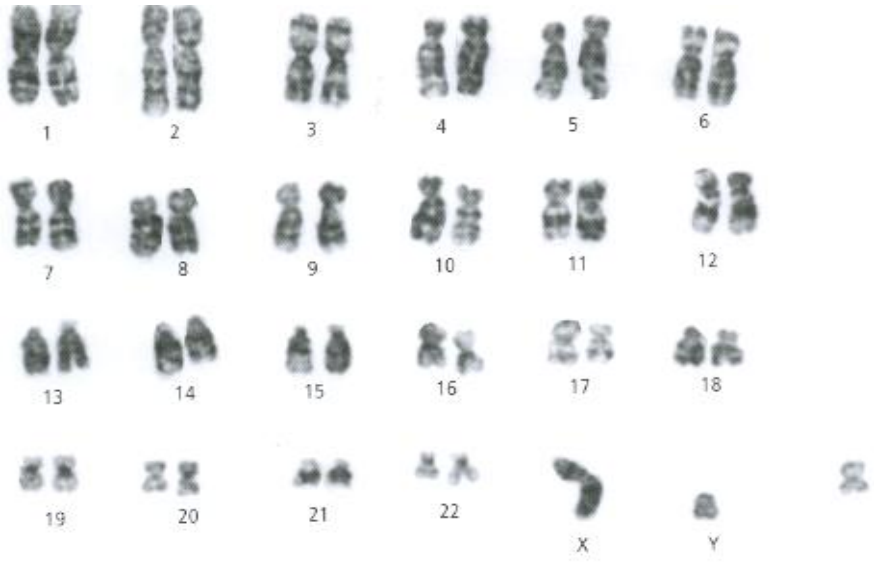
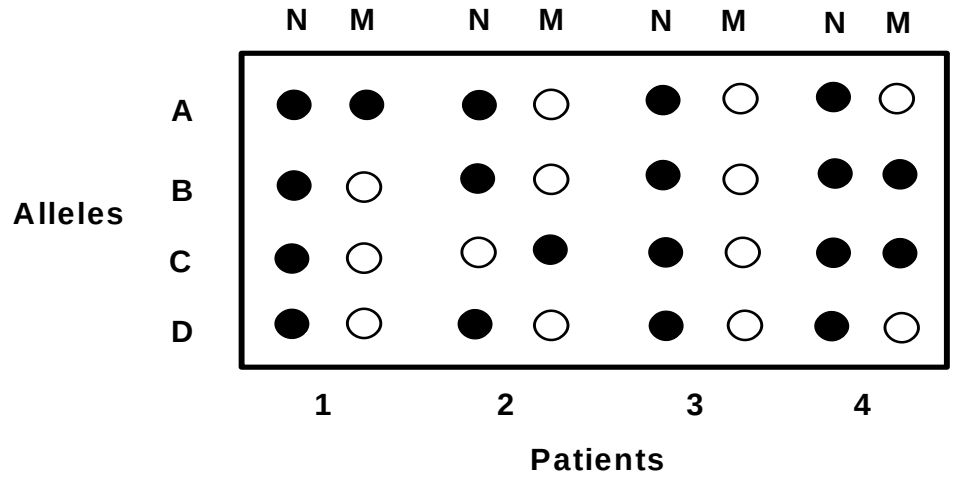


Plate Y
Tobias6_F12.7_p172

A. haploidy
B. monosomy
C. mosaicism
D. triploidy
E. balanced translocation

3) The data below show allele-specific oligonucleotide (ASO) probe results of testing patients for four mutant alleles in a gene whose inheritance pattern is X-linked recessive. All four patients are female. The letters N and M represent dot blotting using probes for the normal and mutant sequences, respectively. Which of the patients is/are likely to be most severely affected?

● hybridization ○ no hybridization



A) Patient 1
B) Patient 2 and probably patient 4
C) Patient 3
D) Patient 2 and probably patient 1
E) Patient 4

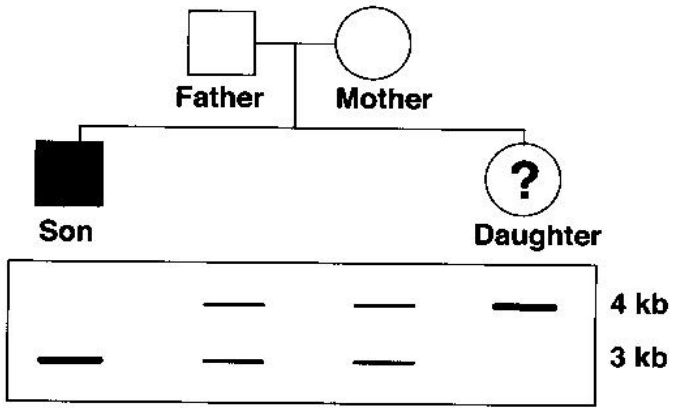
4) Using protein electrophoresis and Western blotting, 100 members of a population were studied to determine whether they carry genes for normal hemoglobin (HbA) or sickle hemoglobin (HbS). The following genotypes were observed:

Genotype	**Number of individuals**
HbA/HbA	88
HbA/HbS	10
HbS/HbS	2

What is the frequency of the HbS allele in this population?

A) 0.02
B) 0.04
C) 0.07
D) 0.10
E) 0.93

5) An Ashkenazi Jewish couple brings their 18-month-old son to you for evaluation of listlessness, poor head control, and a fixed gaze. You determine that he has Tay-Sachs disease, an autosomal recessive disorder. The couple also has a daughter. The family's pedigree is shown below, along with Southern blots of a restriction fragment length polymorphism very closely linked to the gene for hexoxaminidase A, which is defective in Tay-Sachs. Which of the following statements below is most accurate with respect to the daughter?



A) She has Tay-Sachs disease.
B) She has a 25% chance of having Tay-Sachs disease.
C) She is a carrier for Tay-Sachs disease.
D) She has a 50% chance of having Tay-Sachs disease.
E) She is homozygous normal.

6) Two patients with non-Hodgkin's lymphoma responded differently to therapy, suggesting that their lymphomas could be of different subtypes. Since the existing procedures for classifying the lymphomas could not confirm this possibility unambiguously, it was decided to compare the mRNA expression profiles of the cancer cells obtained from the two patients. Which of the following methods would you most likely use for determining the mRNA expression profiles?

A) genomic library construction
B) transcriptomics
C) Southern blot analysis
D) fluorescence *in situ* hybridization (FISH)
E) Western blot analysis

7) A 4-year-old male presents to his pediatrician. His mother expresses concern that the child has been regressing since the previous year. Upon examination, the patient has regressed in his milestones, specifically in motor and speech development. The patient was referred to a neuro-developmental specialist. Testing for Fragile X syndrome using STR (short tandem repeat) analysis of the FraX gene, for example, proved negative. Based on these findings and other symptoms, the specialist believes the patient has autism caused by a CNV (copy number variant). Given this hypothesis, a reasonable next test is:

A) Southern blotting for the autism gene
B) Polymerase Chain Reaction (PCR) using centromere-specific primers for chromosome 5
C) Chromosomal microarray (array CGH) analysis
D) Fluorescence *in situ* hybridization (FISH) analysis using probes specific to chromosome 7q11
E) Chromosome analysis using solid staining

8) The recognition sequence and cleavage pattern for the restriction enzyme *Bam*H I (from *baccillus amloliquifaciens*) is shown below. Although the enzyme cleaves both strands of a double-stranded DNA, *BamH* I is said, by convention, to make **one cut** in the double-stranded recognition sequence.

```
      ↓
5'-GGATCC-
   CCTAGG-5'
         ↑
```

Predict the number of cuts and the number of fragments produced if the DNA sequence shown below is presented as substrate for *BamH* I digestion.

```
5'-  GACGCGTCCTAGGTGACCGGATCCATGGAATTCGCGGCCACTGGTTAAC
3'-  CTGCGCAGGATCCACTGGCCTAGGTACCTTAAGCACCGGTGACCAATTG
```

	Number of cuts	**Number of fragments produced**
A)	0	1
B)	1	1
C)	1	2
D)	2	2
E)	2	3

9) A baby boy with several birth defects is found to have a duplication of the long arm of chromosome 10, and deletion of the short arm of chromosome 2. Which of the following pair of karyotypes best represent what a chromosome analysis of his parents is most likely to find?

Answer choice	Maternal	Paternal
A	46, XX	46, XY, t[2;10][2p24;10q25]
B	46, XX, t[2;10][2p24;10p25]	46, XY
C	46, XX, r(2)	46,XY, r(10)
D	45, XX, t[2;10]	46, XY
E	46, XX, i(10p)	46, XY, i(2q)

The next two questions (10-11) apply to the following scenario.
A 45 year old man has recently been diagnosed with Huntington disease; his family history is positive in that his mother developed HD at the age of 43, and his sister developed Huntington disease at age 44. Each has several children who have genetic testing, and some are found to carry the mutation.

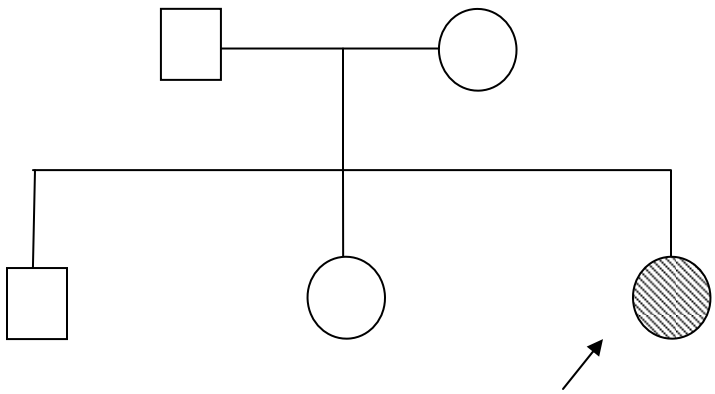
10) The man and his sister ask at what age the children would be expected to show symptoms? The most accurate response to this question is:

A. The man's children and sister's children will tend to develop HD much earlier than their parents
B. The man's children and sister's children will tend to develop HD much later than their parents
C. The man's children will tend to develop HD earlier than will the sister's children
D. The sister's children will tend to develop HD earlier than will the man's children
E. The man's children and sister's children will tend to develop HD at the same age as their parents

11) The man and his sister inform you that their brother died at age 30, but hadn't shown any symptoms of HD. You know from your reading that by age 30, only 25% of those with an HD trinucleotide repeat expansion have clinical manifestations of that disorder. Using Bayesian analysis, choose the best estimate of what the risk to the deceased man's offspring would be.

A. 1/10
B. 1/5
C. 3/7
D. 3/14
E. 1/2

12) What is the interpretation of the pedigree below?



A. An unrelated couple has one boy and two girls; the proband is a girl with a medical condition.
B. A brother and sister mating results in three children; the consultand is a girl with a medical condition.
C. An unrelated couple has one girl and two boys; the proband is a boy with a medical condition.
D. A brother and sister mating results in one boy and two girls; the consultand is a girl with a medical condition.
E. An unrelated couple has three children, with one of them stillborn.

13) You are a cardiologist seeing a young boy with pulmonic stenosis. This is his first visit to your office. His past medical records state that he had high calcium levels as an infant, but those have since resolved. When you walk into the room, he jumps up and greets you and asks for a hug. You notice that he has an interesting iris pattern and tends to drool because of his sagging lower lip. You suspect he likely has what condition?

A. Down syndrome
B. Trisomy 18
C. Williams syndrome
D. Klinefelter syndrome
E. Deletion 5p (5p-)

14) You are on a medical mission trip to the island of Comoros in the Indian Ocean. You are struck by the observation that many individuals on the island wear size 20 shoes, with many sharing the same last name. You discover that a few generations ago, a big-footed sailor washed up on shore. You are most suspicious that what you are observing is an example of:

A. Selective advantage
B. New mutation
C. Variable expressivity
D. Founder effect
E. Random mating

The next three questions (15-17) pertain to the same individual, the patient.

Your patient is a man with a slightly dilated aortic root who has a positive family history for similarly affected individuals. You want to know the cause, so you order the "dilated aortic root" panel of tests (a panel tests for mutations in several relevant genes at the same time).

15) You use a panel of tests specifically because dilated aortic root is a condition which shows:

A. Reduced penetrance
B. Allelic heterogeneity
C. Complex inheritance
D. Locus heterogeneity
E. Pleiotropy

16) The man is found to have a pathogenic (disease-causing) mutation. The lab report provides a brief description of this mutation stating that it's associated with a slower than usual progression of the disorder. The lab is able to make this statement because this mutation is known to be associated with:

A. Clinical heterogeneity
B. Reduced penetrance
C. Epistasis with another gene
D. Genotype-phenotype correlation
E. High frequency of de novo mutation

17) You do some more reading about the gene in which the mutation is found, and realize you also should have the man evaluated for spinal abnormalities, vision and hearing problems, and kidney disease. You do these evaluations because this condition is associated with which phenomenon?

A. Epistasis
B. Co-dominance
C. Reduced penetrance
D. Pleiotropy
E. Mosaicism

18) A woman delivers a stillborn male infant who is small and has numerous birth defects. The baby's karyotype is 92, XXYY. If the father's genotype at a particular locus is AB, and the mother's genotype at that same locus is CD, what infant genotype is most likely?

A. ABCD
B. ABCC
C. AABB
D. AACC
E. AACD

19) Which karyotype is most consistent with an individual having both a deletion from the short arm **and** a duplication of the long arm of the **same** chromosome?

A. 46, XY, del 22q/dup 22p
B. 46, X, i(Xq)
C. 46, XX, ring(15)
D. 46, XX, t(2;17)(p25;q11)
E. 45, XY, t(13;21)

20) If the carrier frequency of the autosomal recessive disorder phenylketonuria is 1/50, what is the disease frequency?

A. 1/50
B. 1/100
C. 1/2,500
D. 1/5,000
E. 1/10,000

21) Put the following relatives in the correct order in terms of degree of relationship [from closest to most distant].

1. half-sister
2. first cousin once removed
3. maternal great-uncle
4. brother

A. 1-4-2-3
B. 2-3-1-4
C. 3-2-4-1
D. 4-1-3-2

22) An individual with an extremely rare form of hearing loss is found to be a homozygote. Which situation would be the best explanation for this observation?

A. His mother and mother's father have the same autosomal recessive condition
B. His mother's mother is a first cousin of his mother's father
C. His father's grandparents are first cousins
D. His mother's father and father's mother are siblings
E. His father and father's mother have the same autosomal dominant condition

23) A woman with very curly hair registers with a matchmaking service, and has on her list of 250 ideal traits the requirement that her offspring have wavy hair. You know that degree of hair curl is a co-dominant trait. The man or men with which characteristic would make the best match?

A. Wavy hair
B. Wavy or curly hair
C. Straight hair
D. Straight or wavy hair
E. Curly or straight hair

24) Your patient is a 3-month-old boy with an X-linked metabolic disorder, ornithine transcarbamylase deficiency. His symptoms include seizures and lethargy. His family history is significant in that his mother's healthy older sister has an affected son, and his mother's younger sister is as severely affected as your patient, the infant boy. What BEST explains the phenotype in the mother's younger sister?

A. New mutation
B. Co-dominance
C. Skewed X-inactivation
D. Complex inheritance
E. Heteroplasmy

25) A man with a mitochondrial disorder caused by a mitochondrial mutation wants his wife to have prenatal testing to determine his child's chance of developing the same condition. You tell him his child's chance of having the same condition is closest to:

A. 100%
B. 50%
C. 25%
D. 0%
E. Cannot give a precise risk

26) A woman tells you that she thinks she has the same mitochondrial mutation as do other members of her family. A review of her history indicates that she has a history of seizures, but no evidence of eye problems (i.e., normal retina and normal vision exam). A muscle biopsy done in the past was abnormal. You are most suspicious she has which condition?

A. LHON
B. Myotonic dystrophy
C. MERRF
D. NARP
E. Fragile X

27) In which condition would you expect to see **anticipation**?

A. MELAS
B. Myotonic dystrophy
C. Prader-Willi syndrome
D. Angelman syndrome
E. Friedreich ataxia

28) You recently discovered that cooking ability has a heritability of 65%, whereas tidiness has a heritability of 70%. If a sloppy female chef marries a neat-freak who can't boil water without burning it, what is the **best** prediction of what traits you would see in their children?

A. Girls would be sloppy good cooks and boys would be neat but inept in the kitchen
B. Boys would be sloppy good cooks and girls would be neat but inept in the kitchen
C. Boys and girls would be sloppy good cooks
D. Boys and girls would be neat but inept in the kitchen
E. Boys and girls would be both neat and good cooks

29) What is the best test (or set of tests) to identify genes which predispose to the development of a complex disorder?

A. Sequence analysis
B. Chromosome analysis
C. Chromosomal microarray
D. Allele-specific oligonucleotide studies
E. Genome wide association studies

30) A 25 year old woman comes to her dermatologist concerned about a couple of suspicious skin lesions that turn out to be basal cell carcinomas. You do a more careful physical examination at her return visit, and notice a small bald spot on her scalp as well as a couple of pits on her hands. You now ask about her family history, and she tells you she has two brothers who have never had very much hair and have had several skin cancers beginning when they were teenagers. Her mother's father died in his 50's, after having had numerous surgeries for skin cancers. What is the most likely mode of inheritance for this condition?

A. Autosomal dominant
B. Autosomal recessive
C. Mitochondrial
D. X-linked
E. Multifactorial

The next two questions (31-32) apply to the scenario below.

Two women, who are sisters, are concerned about their family history and risks for their daughters to be carriers for Lesch-Nyhan syndrome, which is an X-linked disorder. The women have two brothers and a maternal first cousin who are affected with this disorder. Use Bayesian analysis where appropriate.

31) One of the sisters has three normal sons and one daughter. What is the chance that her daughter is a carrier?

A. 1/2
B. 1/4
C. 1/8
D. 1/9
E. 1/18

32) The other sister has one affected son and three daughters. What is each daughter's chance that she is a carrier?

A. 1/2
B. 1/4
C. 1/8
D. 1/9
E. 1/18

33) A woman with neonatal-onset diabetes, which is an imprinting disorder caused by uniparental disomy of chromosome 6, wants to know her chance of having affected children. The BEST estimate of this risk is

A. 0%
B. 50% for female offspring only
C. 50% for male offspring only
D. 50% for offspring of either sex
E. 100% for offspring of either sex

34) A child has the combination of behavioral problems and obesity. What observation would lead you to conclude that epigenetic modification is the MOST likely cause of this phenotype?

A. GWAS studies find a number of relevant SNPs
B. Chromosomal microarray studies find a small deletion
C. Sequencing studies of candidate genes identify two or more mutations
D. Sequencing and microarray studies are negative (normal)
E. There are similarly affected maternal and paternal relatives

END OF EXAMINATION - Tear off this sheet and save to check your answers.

- You may write in your answer to each question on this sheet. DO NOT make any other marks on this sheet. If there are any extraneous marks on this page it will be confiscated.
- Only the answer on the scantron is the official answer. **WE CANNOT USE THE ANSWERS ON THIS TEAR OFF SHEET TO DETERMINE YOUR GRADE.**

Please remember to:

- Write in the **letter of your form** in the area titled "Period" on the exam scantron.
- **Return your examination** in the envelope provided to a proctor **before leaving the exam room**.

BMB 526 FS 2013 Exam #2

FORM: A

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