7.013 Handout 5/16/02
Practice problems for closed book Final Exam
Final Exam Monday, May 20
1:30 PM - 4:30 PM Johnson

Bring a calculator and your ID to the Exam.

Review Session: Thursday May 16
10-250 7-9pm
Tutoring Session: Friday May 17
26-302 4-6pm

Tutors (HELPFUL PEOPLE)

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<th>Email</th>
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</tr>
</tbody>
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Monday 13  Tuesday 14  Wednesday 15  Thursday 16  Friday 17

Claudette’s office hour
12-1 pm
68-120d

Kevin’s office hour
4-5 pm
E17-524

Isaac’s 4:30-5:30
Kendall Sq. Au Bon Pain

Matt’s 7-8:30 pm student center coffee house

Luke ‘s 9pm Lobdell dining room

Claudette’s office hour
1-2 pm
68-120d

Sunny’s office hour
7-8 pm 26-310

Phil’s office hour
4-5 pm
26-310

Roberto’s office hour
4-6 pm
student center coffee house

Review Session 7-9pm
10-250

Tutoring Session 4-6 pm 26-302
Question 1

a) Indicate how an enzyme affects the activation energy ($E_a$), $K_{eq}$, and $\Delta G^\circ$ of a chemical reaction by circling the answer below.

i) $E_a$: Increase Decrease No effect

ii) $K_{eq}$: Increase Decrease No effect

iii) $\Delta G^\circ$: Increase Decrease No effect

For parts (b), (c), and (d), refer to the figure below, which shows GDP in the binding pocket of a G protein.

b) Circle the strongest interaction that exists between:

i) the side chain of Lys and the phosphate group of GDP
   van der Waals covalent hydrogen bond ionic

ii) the side chain of Glu and the ribose group of GDP
   van der Waals covalent hydrogen bond ionic

iii) the side chain of Tyr and the guanine base of GDP
   van der Waals covalent hydrogen bond ionic
Question 1, continued

c) You make mutations in the GDP-binding pocket of the G protein and examine their effects on the binding of GDP. Consider the size and the nature (e.g. charge, polarity, hydrophilicity, hydrophobicity) of the amino acid side chains and and give the most likely reason why each mutation has the stated effect. Consider each mutation independently.

   i) Arg is mutated to a Lys, resulting in a G protein that still binds GDP.

   ii) Asp is mutated to a Tyr, resulting in a G protein that cannot bind GDP.

Question 2

You are an immunologist who wants to make the big bucks. You decide to leave the world of science and get a job as a script-consultant on a new medical drama (ER-like) show. You test the writers with a few questions to see just how much they know.

a) Compare how macrophages and B cells recognize antigen.

b) Compare how macrophages and B cells present antigenic peptides (epitopes). They present epitopes exactly the same way on their MHC II molecules on the surface.

c) Macrophages and B cells present antigens to _______ ____-cells. (Fill in blanks.)

d) Name 2 components of the innate or nonspecific immune system.

   __________________________   __________________________

Below are short descriptions given to you by the writers of scenarios in the early episodes.

Scenario #1

One of the characters on the show is diagnosed with leukemia, a cancer of the blood system. She is very sick until her boyfriend bravely agrees to donate his bone marrow. The bone marrow transplant is successful and our character lives!

e) You tell the writers that the bone marrow transplant from the boyfriend is unlikely to be successful. Give the reason and the molecular basis for why.

Because of the different major histocompatibility molecules the marrow will be rejected.

Scenario #2

Many patients are coming into the emergency room with a disease caused by an unknown pathogen! A doctor studies this pathogen in order to create a vaccine against it.
**Question 2 continued**

f) He discovers that the infectious agent is an intracellular bacterium and its cell surface is coated with human-like proteins. Considering the mechanism of the pathogen, the doctor decides to generate a live-attenuated vaccine instead of a heat-killed vaccine.

i) What are the two advantages of using a live-attenuated vaccine vs. a heat killed vaccine in this case?

ii) What is a disadvantage of using a live-attenuated vaccine?

**Scenario #3**

The leading doctor gives birth to a baby boy. After some time, the child shows no acquired or specific immune response and is diagnosed with a rare disorder, Severe Combined Immune Deficiency (SCID), and as a result the boy must live in a germ-free environment.

Several causes of SCID have been described and are listed below.

g) For each cause, indicate which of the following branches of immune system are affected.

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<tr>
<td>DNA recombination deficiency</td>
<td></td>
</tr>
<tr>
<td>Absence of MHC class I molecules</td>
<td></td>
</tr>
<tr>
<td>Lack of MHC class II molecules</td>
<td></td>
</tr>
</tbody>
</table>

**Scenario #4**

Patients in the hospital are coming down with multiple infections. Lab results show that the sick are infected with a bacterium, *S. aureus*, that secretes “Protein A” which binds the constant region of antibodies.

h) What cell recognizes the constant region of secreted antibodies? 

i) Why might the effect of Protein A allow multiple (non *S. aureus*) infections?

j) What branch of the immune system does *S. aureus* evade using Protein A?

<table>
<thead>
<tr>
<th>Humoral</th>
<th>Cellular</th>
<th>Both</th>
</tr>
</thead>
</table>

k) Indicate the constant region of the antibody depicted below.

![Antibody Diagram]

**Question 3**

a) Indicate whether each of the following statements is true or false. If false, correct the statement or provide a brief explanation for why it is false.

i) DNA replication is initiated at promoter sequences in the DNA.

ii) RNA polymerase requires primers to initiate RNA synthesis.

iii) Okazaki fragments are the short fragments of DNA that are produced on the leading strand at the DNA replication fork.

iv) The 5’ to 3’ direction of DNA synthesis implies that deoxyribonucleotides are added to the 5’ OH group on the growing strand.

v) Transcription is terminated at stop codons in the mRNA.

b) Shown below is the DNA sequence of a gene from a virus that encodes a short viral peptide. Also shown is the sequence of the mRNA synthesized from this gene.

**Genomic DNA Sequence:**

```
5' - AGCTCATGTGCGAGTCCTGACGCTGACTAGG - 3'
3' - TCGAGTACACGCTCAGGACTGCGACTGATCC - 5'
```

**Mature mRNA Sequence (G* = G cap):**

```
5' - G* UCAUGUGCGAAGCUGACUAGGAAAAAAAAAAAAA... - 3'
```

i) In the genomic DNA sequence shown above, draw a box around each of the two exons in the gene.

ii) In the mRNA above, some nucleotides are present that are not coded for in the genomic DNA sequence. Name the two processes that have occurred to add these nucleotides to the mRNA.
Question 3 continued

iii) How many amino acids are in the viral peptide encoded by this gene?

iv) Is this virus more likely to replicate in prokaryotic or eukaryotic cells? Briefly explain your reasoning.

Question 4

A diagram of the *C. babel* gene *q* is shown below. The exons are drawn to scale, and the start and the two in-frame stop codons are indicated.

Gene *q* is expressed only in certain cells of *C. babel*:

- In nerve cells, no Q protein is found.
- In muscle cells, a Q protein of 50 amino acids (aa) is found.
- In skin cells, a Q protein of 100 aa is found.

a) In which cells of this worm would you find gene *q*? Circle all that apply:

- none of these
- nerve cells
- muscle cells
- skin cells

b) Draw the fully processed *q* mRNA found in muscle cells. Also indicate the 5' and 3' ends of the mRNA, the start and stop codons, and any features found in the mature mRNA.

c) You observe that in skin cells, the fully processed *q* mRNA is approximately the same length as that found in muscle cells. Draw the fully processed *q* mRNA found in skin cells. Also indicate the 5' and 3' ends of the mRNA, the start and stop codons, and any features found in the mature mRNA.
**Question 5**

You are studying a common genetic condition. The mutant allele differs from the wild-type allele by a single base-pair (bp) substitution. This substitution eliminates a \textit{NheI} restriction site that is present in the wild-type allele. (The mutant allele is not cut by \textit{NheI}.) A pedigree of a family exhibiting this condition is shown below:

You isolate DNA from four individuals in the pedigree. Using PCR techniques, you amplify a 1000 bp portion of their DNA which includes the site affected by the mutation. You digest the PCR products with \textit{NheI} and analyze the resulting DNA fragments on a gel:

<table>
<thead>
<tr>
<th>Individual:</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{NheI}</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1000 bp</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>600 bp</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>400 bp</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a) Based on these data, is this gene located on an autosome or the X-chromosome? Briefly justify your reasoning.

b) Based on these data, is the mutant phenotype dominant or recessive to wild-type and why?

c) If individuals 3 and 4 have a daughter, what is the probability that she will be affected? Justify your reasoning.
d) You sequence the region around the *Nhe*I site in the wild-type PCR product. You then sequence the corresponding region in the mutant PCR product and discover that not only did the mutation eliminate the *Nhe*I site in the mutant allele but it has created a new *Pvu*II restriction site. The recognition sites for the two enzymes are indicated below.

\[
\begin{align*}
NheI \text{ cuts at:} & \quad 5' \text{ GCTAGC} \quad 3' \\
& \quad 3' \text{ CGATCG} \quad 5' \\
PvuII \text{ cuts at:} & \quad 5' \text{ CAGCTG} \quad 3' \\
& \quad 3' \text{ GTCGAC} \quad 5'
\end{align*}
\]

A portion of one strand of the wild-type DNA sequence is shown below:

\[5'....GCTAGCTG...3'\]

What is the sequence of this same region in the mutant allele? Indicate the 5' and the 3' ends of the DNA sequence.

e) Individuals 1 and 2 have another child, 9, who is affected by the genetic condition.

\[1 \quad 2 \quad 5 \quad 6 \quad 9\]

You PCR amplify the 1000 bp region affected by the mutation from individuals 1, 2, and 9, digest the PCR products with *Nhe*I or *Pvu*II, and analyze the restriction fragments on a gel:

\[
\begin{array}{ccc}
\text{Individual:} & 1 & 2 & 9 \\
\text{NheI} & \text{PvuII} & \text{NheI} & \text{PvuII} & \text{NheI} & \text{PvuII} \\
1000 \text{ bp} & \blacksquare & \blacksquare & \blacksquare & \blacksquare & \blacksquare & \blacksquare \\
600 \text{ bp} & \blacksquare & \blacksquare & \blacksquare & \blacksquare & \blacksquare & \blacksquare \\
400 \text{ bp} & \blacksquare & \blacksquare & \blacksquare & \blacksquare & \blacksquare & \blacksquare
\end{array}
\]

What event occurred and how does this explain the data shown above?
Question 6

A) You infected mice with mouse mammary tumor virus (a retrovirus). After a period of time, most infected mice had developed breast tumors, whereas uninfected mice did not. You isolated cell lines from over 50 independent tumors. You demonstrated that all of these lines had virus integrations in the same chromosomal location. Can one conclude that the virus integrates into cellular DNA at only one site? Explain.

B) The ras oncogene is involved in a variety of human and animal cancers. DNA was isolated from a number of normal and cancerous tissues.

- Cellular DNA was digested with EcoRI.
- Digested DNA was separated by gel electrophoresis and transferred to a nitrocellulose membrane.
- The membrane was probed with the radioactive labelled cloned ras DNA and then the membrane was exposed to x-ray film.
- The resulting autoradiograph is shown below.

1) white blood cells from a healthy human
2) human lymphoma cells (cancerous)
3) human bladder carcinoma cells (cancerous)
4) human sarcoma cells (cancerous)
5) blood from a healthy mouse
6) mouse myeloma cells (cancerous)
**Question 6 continued**

a) How do you explain the presence of sequences complementary to the oncogene in the DNA from healthy human and mouse samples? Why don't they have cancer?

b) Why is the hybridizing band from sample 1 a different size than that from sample 5?

c) For each cancer examined above, based on the autoradiogram, choose the most likely mechanism of transformation and explain your choice:

1) point mutation within the gene
2) chromosomal rearrangement involving the gene
3) gene amplification
4) oncogenic retroviral insertion.

**Part C**

Erythropoietin (EPO), a protein growth factor secreted by the kidneys, is essential for the terminal differentiation of red blood cells (erythrocytes) in the bone marrow. EPO binds to a transmembrane EPO receptor found on erythroid precursor cells.

a) Is EPO an example of an **autocrine**, **paracrine** or **endocrine** signal?

b) The following homozygous mutations were made only in the hematopoietic stem cell lineage. How would these mutations affect (increase, decrease, or not change) the number of red blood cells formed, compared to the wild-type situation? Briefly explain your reasoning for each mutation. Consider each mutation independently.

i) A mutation in the EPO gene which resulted in the deletion of only the signal sequence of the EPO protein.

ii) A mutation in the EPO receptor gene that resulted in the deletion of only the transmembrane domain of the EPO receptor.

iii) A mutation in the EPO receptor gene that resulted in the deletion of only the cytoplasmic domain of the EPO receptor.
Question 7

a) Shown below is a schematic of the production of a heavy chain polypeptide for an antibody. At the top is the chromosomal arrangement found in an immature B cell, at the bottom is shown the heavy chain polypeptide.

i) Label the process indicated by each arrow. Choose the one best option for each from:

- protein processing
- transcription
- translation
- transduction
- DNA ligation
- DNA rearrangement
- RNA splicing
- RNA ligation

ii) Indicate on the diagram below where you would expect to find each of the following components:

- Promoter
- Transcription terminator
- start codon
- stop codon

iii) Indicate on the diagram below the variable and the constant region of the heavy chain polypeptide.

<table>
<thead>
<tr>
<th>V segments</th>
<th>D segments</th>
<th>J segments</th>
<th>constant segment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

= intron regions
Question 7 continued

b) Indicate whether each of the following statements is true or false. If false, correct the statement or provide a brief explanation for why it is false.

i) Memory cells are the basis for a strong secondary humoral immune response.

ii) T cells produce antibodies that bind antigen.

iii) Macrophages present antigenic peptides on MHC II proteins to B cells.

iv) Clonal expansion means that any B cells present at the time of exposure to an antigen will be stimulated to proliferate.

v) The two antigen binding sites formed by the variable regions in a single antibody molecule bind to two different antigenic determinants.

c) When a rabbit protein is injected into rabbits, no antibodies against this protein are generated. If, however, the same rabbit protein is injected into guinea pigs, the guinea pigs generate antibodies against the rabbit protein. Briefly (in one or two sentences) explain this observation.

d) The genomes contained in almost all of the somatic cells in an adult human are identical. Name one (diploid) cell type that is an exception to this and specify the process by which the genetic variation occurred.

e) Will siblings have the exact same antibody repertoire? What about identical twins? Briefly explain your reasoning.
Question 8

The following is a plot of an action potential measured at a single spot along an axon. Four points are highlighted along the curve, ❯, ⬠, ❥, ❦.

a) On the table below, identify which ion (Na⁺, K⁺, Ca²⁺, Cl⁻) is undergoing the greatest net flow across the membrane at the points indicated and state the direction that the ion is moving (into the cell or out of the cell).

<table>
<thead>
<tr>
<th>Point</th>
<th>Ion</th>
<th>Direction (in/out)</th>
</tr>
</thead>
<tbody>
<tr>
<td>❯</td>
<td></td>
<td></td>
</tr>
<tr>
<td>❥</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

b) The membrane potential is -70 mV at points ❯ and ❦, on the plot above. Which of the voltage-gated ion channels is closed at point ❯, but open at point ❦?

c) What dictates the closing of the voltage-gated channel that is open at point ❯?

d) There are at least three states in which the voltage-dependent Na⁺ channel exists. At ❥ on the above plot, the majority of voltage-dependent Na⁺ channels would be in which state? Circle the best answer.

Open	Closed	Inactivated
Two different pre-synaptic neurons, neuron 1 and neuron 2, synapse onto cell W as shown below. When neuron 1 is stimulated, the membrane of cell W is locally depolarized. When neuron 2 is stimulated, the membrane of cell W is locally depolarized to exactly the same extent as seen with neuron 1.

e) Circle the one correct statement below.

- If stimulated equally, neuron 1 is more likely to result in an action potential in cell W than neuron 2.
- If stimulated equally, neuron 2 is more likely to result in an action potential in cell W than neuron 1.
- If stimulated equally, neuron 1 and neuron 2 are equally as likely to result in an action potential in cell W.

f) If you were exposed to a toxin that irreversibly blocked voltage-gated Ca++ channels, indicate whether the following statements would be TRUE or FALSE.

<table>
<thead>
<tr>
<th>T</th>
<th>F</th>
<th>Secretory vesicles filled with neurotransmitters would stay in the nerve.</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>F</td>
<td>Your muscles would end up in a rigid contraction.</td>
</tr>
<tr>
<td>T</td>
<td>F</td>
<td>Secretory vesicles filled with neurotransmitters would fuse with the plasma membrane.</td>
</tr>
</tbody>
</table>
Solutions to Final Exam Practice problems:

Question 1:

a) i) $E_a$: Increase Decrease No effect
ii) $K_{eq}$: Increase Decrease No effect
iii) $\Delta G^{\circ'}$: Increase Decrease No effect

b) i) van der Waals covalent hydrogen bond ionic
ii) van der Waals covalent hydrogen bond ionic
iii) van der Waals covalent hydrogen bond ionic

c) i) Arg and Lys are both positively charged, thus the ionic interaction with the phosphate group is preserved. The side chains of both amino acids are also of similar size.

ii) Tyr is much larger than Asp. Although Tyr can form a hydrogen bond, GDP will no longer fit into the binding pocket. The Tyr side chain is also much more hydrophobic than the Asp side chain.

Question 2

You are an immunologist who wants to make the big bucks. You decide to leave the world of science and get a job as a script-consultant on a new medical drama (ER-like) show. You test the writers with a few questions to see just how much they know.

a) Compare how macrophages and B cells recognize antigen.
   - MØs nonspecifically engulf antigen.  
   - B cells take up antigens that their surface antibodies specifically bind.

b) Compare how macrophages and B cells present antigenic peptides (epitopes).
   - They present epitopes exactly the same way on their MHC II molecules on the surface.

c) Macrophages and B cells present antigens to helper $T$-cells. (Fill in blanks.)

d) Name 2 components of the innate or nonspecific immune system.
   - Skin, MØs, complement, mucus lining, mucocilliary ladder, lysozyme, sweat, etc.

Below are short descriptions given to you by the writers of scenarios in the early episodes.

Scenario #1

One of the characters on the show is diagnosed with leukemia, a cancer of the blood system. She is very sick until her boyfriend bravely agrees to donate his bone marrow. The bone marrow transplant is successful and our character lives!
e) You tell the writers that the bone marrow transplant from the boyfriend is unlikely to be successful. Give the reason and the molecular basis for why.

Because of the different major histocompatibility molecules the marrow will be rejected.

Scenario #2

Many patients are coming into the emergency room with a disease caused by an unknown pathogen! A doctor studies this pathogen in order to create a vaccine against it.

f) He discovers that the infectious agent is an intracellular bacterium and its cell surface is coated with human-like proteins. Considering the mechanism of the pathogen, the doctor decides to generate a live-attenuated vaccine instead of a heat-killed vaccine.

i) What are the two advantages of using a live-attenuated vaccine vs. a heat killed vaccine in this case?

*It’ll mimic the disease by invading cells, thus it will illicit both a humoral and cellular response.*

*Surface proteins will not be denatured by heat.*

ii) What is a disadvantage of using a live-attenuated vaccine?

Could acquire virulence factors, Need a “cold chain” (expensive refrigeration), it may make people sick.

Scenario #3

The leading doctor gives birth to a baby boy. After some time, the child shows no acquired or specific immune response and is diagnosed with a rare disorder, Severe Combined Immune Deficiency (SCID), and as a result the boy must live in a germ-free environment.

Several causes of SCID have been described and are listed below.

g) For each cause, indicate which of the following branches of immune system are affected.

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<td>Lack of MHC class II molecules</td>
<td>HUMORAL 3 points</td>
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Scenario #4

Patients in the hospital are coming down with multiple infections. Lab results show that the sick are infected with a bacterium, *S. aureus*, that secretes “Protein A” which binds the constant region of antibodies.
h) What cell recognizes the constant region of secreted antibodies? _______ MØ _______

i) Why might the effect of Protein A allow multiple (non S. aureus) infections?

Protein A sequesters all antibodies to all antigens by binding to the antibody. This will prevent macrophages from ridding the pathogen and will in fact precipitate out antibodies from the blood.

j) What branch of the immune system does S. aureus evade using Protein A?

   - Humoral
   - Cellular
   - Both

k) Indicate the constant region of the antibody depicted below.

---

**Question 3**

a)  
   i) FALSE. DNA replication is initiated at the origin of replication. RNA polymerases bind to promoter sequences to initiate transcription.

   ii) FALSE. RNA polymerase does not require primers to initiate RNA synthesis. DNA polymerase requires primers to initiate DNA replication.

   iii) FALSE. Okazaki fragments are made on the lagging strand at the replication fork.

   iv) FALSE. DNA synthesis occurs by addition of dNTPs to the 3' OH group of the nucleotide at the end of the growing strand.

   v) FALSE. Transcription terminates at the transcription termination sites in the DNA. Translation terminates at stop codons in the mRNA.

b)  
   genomic DNA sequence:
   
   5' -AGCTCATGTGCCAGCTCTGACGCTGACTAGG-3'
   3' -TCGAGTACACGCTCAGGACTGCGACTGATCC-5'

   mature mRNA sequence (G* = G cap):
   
   5' -G*UCAUGUGCAUGGACUGACUAGGAAAAAAAAAA....3'

   i) see DNA sequence above

   ii) 1) 5' capping  
         2) 3' polyadenylation
iii) There are four amino acids in this viral peptide:
\[ \text{NH}_3^+\text{-met-cys-glu-arg-COO}^- \]

iv) In eukaryotic cells because the RNA processing and splicing machinery is only present in eukaryotes.

**Question 4**

a) **none of these**

b) 

\[
5' \text{ cap} \quad \text{exon 1} \quad \text{exon 3} \quad \text{AAAAA}\ldots3' \\
\text{AUG} \quad \text{UAA}
\]

c) 

\[
5' \text{ cap} \quad \text{exon 1} \quad \text{exon 2} \quad \text{AAAAA}\ldots3' \\
\text{AUG} \quad \text{UGA}
\]

**Question 5**

a) An autosome, because individual 6, a male, has 2 alleles.

b) The mutant phenotype is recessive, because individuals 5 and 6 each have one copy of the mutant allele, m, and are both phenotypically normal.

c) 1/4. Since individuals 3 and 4 already have an affected child, then they must both be heterozygotes.

d) 5'...GCCAGCTG...3'

e) A mutation occurred which led to the production of a new mutant allele, m*. This mutant allele has a recessive phenotype and its PCR product is cut by neither *NheI* nor *PvuII*.

Individual 9 has the genotype *m/m*.

**Question 6**

A) One cannot conclude that the virus is able to integrate at only one site. However, one might propose that the virus can only cause cancer when it integrates into a certain chromosomal location or next to a specific gene. In fact, viruses can integrate many places throughout the genome. The reason you only observed integration events at one site is because you have examined only those events that cause tumors. Perhaps the integration of the virus next to a proto-oncogene can cause it to become oncogenic, possibly by activating expression of the oncogene in the wrong place or at the wrong time.

B) 

a) The sequences that are complementary to the probe in normal cell DNA correspond to the cellular proto-oncogene. The individuals from which the material came don't have cancer because they have not acquired the mutations necessary to turn the proto-oncogene into an oncogene.
b) Random sequence variation between mouse and human DNA alters the restriction map around the gene. The two species diverged from a common ancestor during the process of evolution, and DNA sequence variation has been accumulating since. Some of these variations occur in restriction enzyme sites.

c) - lane 2: a chromosomal rearrangement or a point mutation at one of EcoRI restriction sites are the most probable mechanisms because one copy of the gene has changed its location with respect to at least one of the flanking EcoR1 sites.

- lane 3: a point mutation within the coding sequence of the gene is the probable mechanism of transformation because there is no obvious change in the Southern blot--none of the restriction sites have been altered.

- lane 4: gene amplification has created many copies of the gene which probably are present in several tandem arrays in the sarcoma DNA.

- lane 6: retroviral transduction has brought an extra copy of the oncogene into the cell. Since the smaller fragment is still present in two copies per cell, there has probably not been any change in the "resident" proto-oncogenes.

C.

a) It is an example of endocrine signaling because the hormone erythropoietin is sent from the kidney via the blood to the bone marrow.

b) 

i) No effect on red blood cell (RBC) formation. If the EPO signal sequence was deleted, EPO would remain in the cytoplasm of the hematopoietic stem cell. EPO, however, is only made by kidney cells and thus the mutation should not affect RBC formation in the bone marrow.

ii) Red blood cell formation would decrease. Since the CFC-E cell is derived from the hematopoietic stem cell, a deletion of the transmembrane sequence would result in the secretion of the EPO-R outside of the CFC-E cells, and, as a result, it would not be able to signal the CFC-E cells to grow and differentiate to form erythrocytes.

iii) Red blood cell formation would decrease. If the EPO-R receptor lacked its phosphorylation site, it cannot be activated. After binding EPO, the activated EPO-R could not signal the CFC-E cell to differentiate into erythrocytes.
**Question 7**

a) 

- V segments
- D segments
- J segments
- constant segment
- promoter
- DNA rearrangement
- transcription terminator
- ATG
- Transcription
- stop codon
- AUG
- RNA splicing
- stop codon
- Translation
- variable region
- constant region

*note: you can position the promoter and the transcription terminator by looking at the mRNA

b) 

i) True.

ii) False. B cells produce antibodies that bind antigen.

iii) False. Macrophages present antigen to T helper cells. Only T cells can recognize peptides in MHCII complexes on macrophages and B cells.

iv) False. Clonal expansion means that only the B cells which express antibodies that recognize a particular foreign antigen will proliferate when exposed to that particular antigen.

v) False. The two antigen binding sites of an antibody molecule bind to identical antigenic determinants.

c) The rabbit protein is recognized as foreign (non-self) by the guinea pig.

d) B cells, by gene rearrangement of Ab genes (VDJ rearrangement). Also, T cells (by rearrangement of T cell receptor genes).

e) Neither siblings nor identical twins will produce the same antibodies, because the DNA rearrangement process that produces the antibody repertoire is a random event in each B cell.
Question 8

The following is a plot of an action potential measured at a single spot along an axon. Four points are highlighted along the curve, ↕, ↘, ♥, ↗.

![Graph of an action potential](image)

a) On the table below, identify which ion (Na\(^+\), K\(^+\), Ca\(^{++}\), Cl\(^-\)) is undergoing the greatest net flow across the membrane at the points indicated and state the direction that the ion is moving (into the cell or out of the cell).

<table>
<thead>
<tr>
<th>Point</th>
<th>Ion</th>
<th>Direction (in/out)</th>
</tr>
</thead>
<tbody>
<tr>
<td>↘</td>
<td>Na(^+)</td>
<td>in</td>
</tr>
<tr>
<td>♥</td>
<td>K(^+)</td>
<td>out</td>
</tr>
</tbody>
</table>

b) The membrane potential is -70 mV at points ↙ and ↗, on the plot above. Which of the voltage-gated ion channels is closed at point ↙, but open at point ↗?

voltage-gated K\(^+\) channel

c) What dictates the closing of the voltage-gated channel that is open at point ↘?

TIME

d) There are at least three states in which the voltage-dependent Na\(^+\) channel exists. At ♥ on the above plot, the majority of voltage-dependent Na\(^+\) channels would be in which state? Circle the best answer.

Open  Closed  Inactivated
Question 8 continued

Two different pre-synaptic neurons, neuron 1 and neuron 2, synapse onto cell W as shown below. When neuron 1 is stimulated, the membrane of cell W is locally depolarized. When neuron 2 is stimulated, the membrane of cell W is locally depolarized to exactly the same extent as seen with neuron 1.

![Diagram of neurons synapsing onto cell W](image)

e) Circle the one correct statement below.

- If stimulated equally, neuron 1 is more likely to result in an action potential in cell W than neuron 2.
- If stimulated equally, neuron 2 is more likely to result in an action potential in cell W than neuron 1.
- If stimulated equally, neuron 1 and neuron 2 are equally as likely to result in an action potential in cell W.

f) If you were exposed to a toxin that irreversibly blocked voltage-gated Ca\(^{++}\) channels, indicate whether the following statements would be TRUE or FALSE.

<table>
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<tr>
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<tr>
<td>2</td>
<td>T</td>
<td>F</td>
</tr>
<tr>
<td>3</td>
<td>T</td>
<td>F</td>
</tr>
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STRUCTURES OF AMINO ACIDS at pH 7.0

ALANINE (ala)

ARGININE (arg)

ASPARAGINE (asn)

ASPARTIC ACID (asp)

CYSTEINE (cys)

GLUTAMIC ACID (glu)

GLUTAMINE (gln)

GLYCINE (gly)

HISTIDINE (his)

ISOLEUCINE (ile)

LEUCINE (leu)

LYSINE (lys)

METHIONINE (met)

PHENYLALANINE (phe)

PROLINE (pro)

SERINE (ser)

THREONINE (thr)

TRYPTOPHAN (trp)

TYROSINE (tyr)

VALINE (val)
Formulas and Equations:

**Thermodynamics**

For the reaction:

\[ A + B \xrightleftharpoons[K_{eq}]{\text{}} C + D \]

\[ \Delta G = \Delta G^{\circ'} + R T \ln \left( \frac{[C][D]}{[A][B]} \right) \]

\[ K_{eq} = \frac{[C][D]}{[A][B]} \]

where:

- if \( T = 25 \) °C then \( RT = 0.59 \) kcal/mol
- if \( T = 37 \) °C then \( RT = 0.61 \) kcal/mol

**Enzyme Kinetics**

For the enzyme catalyzed reaction:

\[ S + E \xrightarrow[k_1]{k_2} ES \xrightarrow[k_3]{k_1} E + P \]

where: \( S \) = substrate; \( E \) = enzyme; and \( P \) = product

the reaction velocity is given by

\[ V = \frac{V_{max} [S]}{K_M + [S]} \]

where:

\[ K_M = \frac{k_2 + k_3}{k_1} \]

and:

\[ V_{max} = k_3 [E]_{total} \]

**The Genetic Code:**

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<th>G</th>
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<tr>
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<td>val (V)</td>
<td>GGG</td>
<td>ala (A)</td>
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