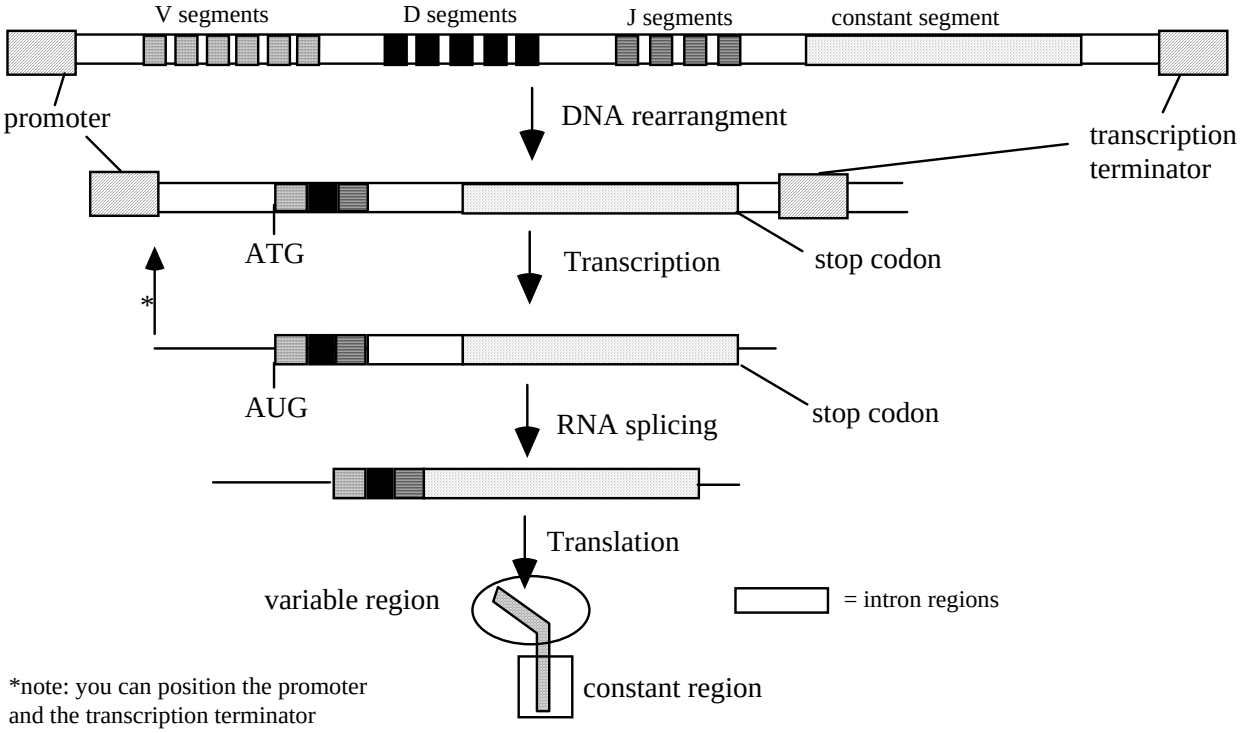
Recitation Section 20 Answer Key
April 25-26, 2005

Immunology

A. Antibody production

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.



1. Label the process indicated by <u>each</u> arrow. Choose the one best option for each from:
   protein processing
   transcription
   translation
   transduction
   DNA ligation
   DNA rearrangement
   RNA splicing
   RNA ligation

2. Indicate on the diagram below where you would expect to find each of the following components:
   promoter
   Transcription terminator
   start codon
   stop codon

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

An activated B cell undergoes cell division and produces many daughter cells. Some daughter cells will function as B cells, some will function as plasma cells and other will become memory cells.

4. Assume that an activated B cell undergos somatic mutation and produces two different B cells each with a slightly altered version of the antibody. This event occurs early in the immune response (*i.e.* when antigen was present in the organism). Mutation A makes the antibody-antigen interaction stronger, mutation B makes the antibody-antigen interaction much weaker.

   i) Would you expect memory cells derived from the original activated B cell? __*Yes*__
   ii) Would you expect memory cells derived from the daughter B cell with mutation A (antibody-antigen interaction stronger)? __*Yes*__
   iii) Would you expect memory cells derived from the daughter B cell with mutation B (antibody-antigen interaction much weaker)? __*No*__

Explain your answers.

With antigen still present, any B cell that binds antigen and internalizes it will present antigenic peptides to T_H cells and thus be able to be activated. The better the antibody is at binding antigen, the more likely activation of that B cell will occur. Therefore you should see memory B cells derived from the original B cell, and from the daughters carrying mutation A. Because the daughter cells carrying mutation B do not bind antibody as well, they are less likely to be activated and they may not be represented in the memory cell population.

B. Immunology and Immunizations

The varicella zoster virus (VZV) is the infectious agent that results in chickenpox, a common childhood illness that causes itchy red spots on the skin. Contracting VZV as a child is relatively benign, but can present serious health issues when contracted as an adult.

1. How does a VZV infected cell signal the immune system? How are the infected cells specifically eliminated from the body?

Once a body cell is infected, peptides specific to VZV are presented on class I MHC molecules on the surface of the infected cell. Some cytotoxic T cells will recognize the MHC I/ VZV peptide complex as non-self, become activated and destroy the VZV-infected cells.

2. Over the course of a lifetime, the average person is exposed to VZV many times, yet usually only displays symptoms once. What is the immune system mechanism that results in lifetime resistance?

Once infected with VZV, the individual mounts a full immune response and eventually clears the virus. Part of the immune response is the generation of memory B and T cells. Upon re-exposure to VZV, the immune system is primed with cells proven effective against VZV. The secondary immune response is faster and more effective and eliminates the virus before symptoms of VZV occur.

As of September 1999 any child entering kindergarten must have had chickenpox or received a new vaccine against VZV.

3. Present an argument in support of this vaccination campaign.

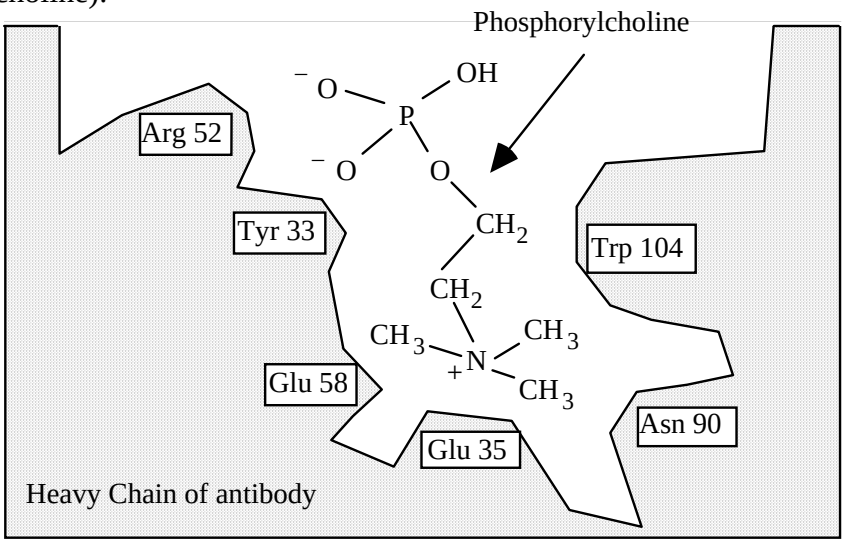
An argument for vaccination is to reduce pain and discomfort in young children, and ensure that no one enters adulthood susceptible to the disease.

4. Present an argument opposed to this vaccination campaign.

An argument against vaccination is driven by the concern that the vaccine may not provide lifetime immunity against VZV. It is not clear that whether the lifetime immunity of individuals is due to contracting the disease, or whether subsequent exposure to the VZV virus (from siblings, classmates, etc.) acts as an immune system booster. If all children receive the vaccine, then after several years there will be no secondary exposures and thus no boost to the immune system. The fear is then that these children reach adulthood they may be exposed to VZV (not every country will vaccinate all their children) and no longer have immunity. The consequences of contracting VZV as an adult are unpleasant at best and life-threatening in some cases.

C. Immunology and Central Dogma

Shown below is a diagram of the interaction of an antibody molecule with an antigen (phosphorylcholine).



1. Indicate the strongest type of interaction that occurs between the amino acids listed and the Phosphorylcholine molecule.

Phosphorylcholine and Arg 52	*ionic*
Phosphorylcholine and Tyr 33	*hydrogen*
Phosphorylcholine and Glu 35	*ionic*
Phosphorylcholine and Trp 104	*van der Waals or hydrophobic*

2. Each of the following mutations alters the binding of the antigen to the antibody. Explain in terms of the change in interactions why the binding of the Phosphorylcholine to the antibody has remained the same, been made stronger, or been made weaker.

	mutation in antibody	binding of antibody to phosphorylcholine
1	Trp 104 -----> Leu 104	same
2	Arg 52 -----> Lys 52	stronger
3	Glu 35 -----> Gln 35	weaker
4	Tyr 33 -----> Phe 33	weaker

1: Both trp and leu have non-polar side chains, so the hydrophobic and van der Waals forces have not change.
2: Both arg and lys have positively charged side chains so the ionic bond remains intact. However, the three dimensional shape of the mutant antibody somehow allows better binding of the antigen.
3: A charged amino acid has been changed to a polar amino acid, therefore the ionic bond is replaced with a weaker hydrogen bond.
4: Tyr can form a hydrogen bond, but phe can not, therefore the antibody-antigen interaction is weaker.

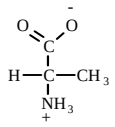
3. Can any of these mutations be due to a single base pair substitution?
If so, give one possibility.

*Trp ---> Leu, U**G**G ---> U**U**G*
*Glu ---> Gln, **G**AA ---> **C**AA OR **G**AG ---> **C**AG*
*Arg ---> Lys, A**G**A ---> A**A**A OR A**G**G ---> A**A**G*
*Tyr ---> Phe, U**A**U ---> U**U**U OR U**A**C ---> U**U**C*

The Genetic Code

	U	C	A	G	
U	UUU **phe**	UCU **ser**	UAU **tyr**	UGU **cys**	U
	UUC **phe**	UCC **ser**	UAC **tyr**	UGC **cys**	C
	UUA **leu**	UCA **ser**	**UAA STOP**	**UGA STOP**	A
	UUG **leu**	UCG **ser**	**UAG STOP**	UGG **trp**	G
C	CUU **leu**	CCU **pro**	CAU **his**	CGU **arg**	U
	CUC **leu**	CCC **pro**	CAC **his**	CGC **arg**	C
	CUA **leu**	CCA **pro**	CAA **gln**	CGA **arg**	A
	CUG **leu**	CCG **pro**	CAG **gln**	CGG **arg**	G
A	AUU **ile**	ACU **thr**	AAU **asn**	AGU **ser**	U
	AUC **ile**	ACC **thr**	AAC **asn**	AGC **ser**	C
	AUA **ile**	ACA **thr**	AAA **lys**	AGA **arg**	A
	AUG met	ACG **thr**	AAG **lys**	AGG **arg**	G
G	GUU **val**	GCU **ala**	GAU **asp**	GGU **gly**	U
	GUC **val**	GCC **ala**	GAC **asp**	GGC **gly**	C
	GUA **val**	GCA **ala**	GAA **glu**	GGA **gly**	A
	GUG **val**	GCG **ala**	GAG **glu**	GGG **gly**	G

STRUCTURES OF AMINO ACIDS
at pH 7.0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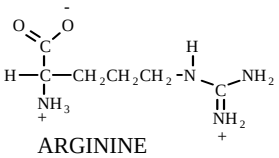
(ala)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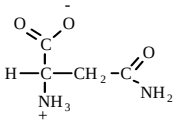
(arg)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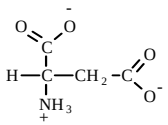
(asN)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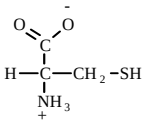
(asp)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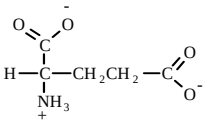
(cys)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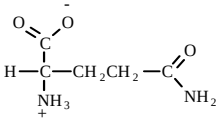
(glu)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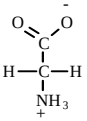
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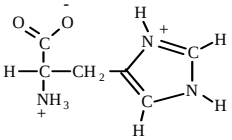
(gly)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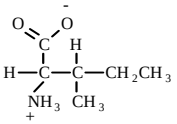
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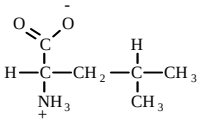
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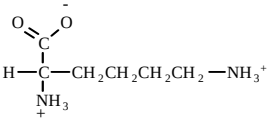
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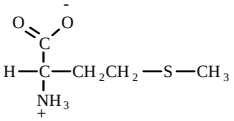
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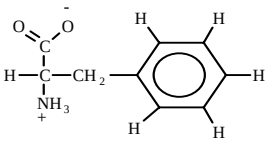
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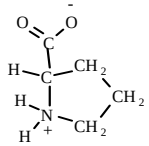
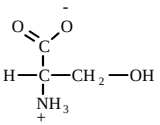
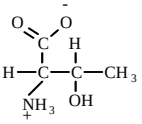

PROLINE
(pro)


SERINE
(ser)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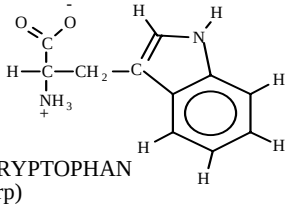
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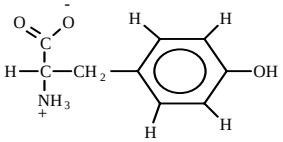
(trp)


TYROSINE
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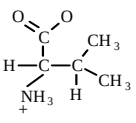
VALINE
(val)