

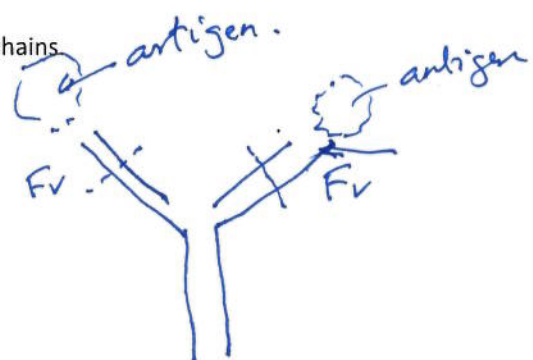
Lecture 10: Bonus Quiz

1. An antigen is (provide definition): ~~see~~ something recognized by immune system.

2. An example of an antigen is: bacteria, virus, fungi, pollen

3. An antibody contains 2 light chains and 2 heavy chains

4. Draw an antibody and indicate where the antigen binds.

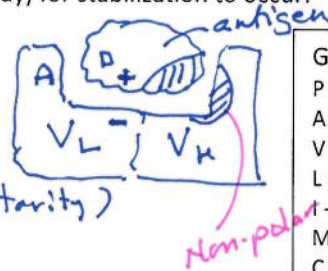


5. What is the name of a small fragment of an antibody that binds the antigen; indicate it on your diagram.

Fv

6. Which of the following interactions could be utilized to stabilize the bound antigen? Circle all that apply, and indicate what must be present on the antigen (and antibody) for stabilization to occur:

- a) hydrogen bonds *donors/acceptors*
- b) van der Waals *contact surfaces (shape complementarity)*
- c) hydrophobic effect *Non-polar groups*
- d) electrostatic attraction *charged groups*



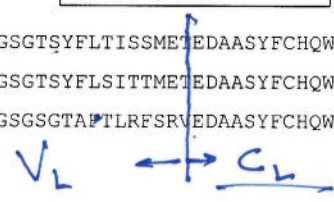
G - Glycine (Gly)
P - Proline (Pro)
A - Alanine (Ala)
V - Valine (Val)
L - Leucine (Leu)
I - Isoleucine (Ile)
M - Methionine (Met)
C - Cysteine (Cys)
F - Phenylalanine (Phe)
Y - Tyrosine (Tyr)
W - Tryptophan (Trp)
H - Histidine (His)
K - Lysine (Lys)
R - Arginine (Arg)
Q - Glutamine (Gln)
N - Asparagine (Asn)
E - Glutamic Acid (Glu)
D - Aspartic Acid (Asp)
S - Serine (Ser)

7. Antibodies were isolated that bind to: a) flu virus, b) E. coli bacteria, c) Salmonella bacteria. E. coli and Salmonella, although distinct species, are very similar to each other. The initial part of the amino acid sequence of the light chain from each antibody is shown below (using the one letter code).

1. I V L T Q S P A I M S A S P G E K V T L T C S A S S R L S S T Y L W Y Q Q K P G S S P T L W I Y S T S S L A S G V P A R F S G S G S G T S Y F L T I S S M E T E D A A S Y F C H Q W
2. W V L A Q S P A I M S A S P G Q K V T L T C S A S S R V S S T Y L W Y Q Q K P G S S P T L W I Y S T S S L A S G V P A R F S G S G S G T S Y F L S I T T M E T E D A A S Y F C H Q W
3. M T Q A A P S V P V T P G E S V S I S C R S S K S L L H S N G Y T Y L H W F L Q R P G Q S P Q L L I Y R V S N L A S G V P D R F S G S G S G T A P T L R F S R V E D A A S Y F C H Q W

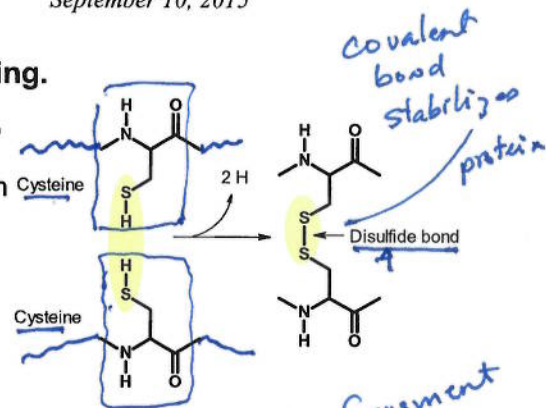
bacteria
flu

- Flu
- E.coli
- Salmonella



Lecture 9 - Antibody Structure & Protein-small Molecule Binding.

Disulfide bonds: These are covalent bonds between cysteine residues, they crosslink the otherwise linear polypeptide chains. They increase the stability of proteins and are often found on proteins that function outside of cells, such as antibodies.



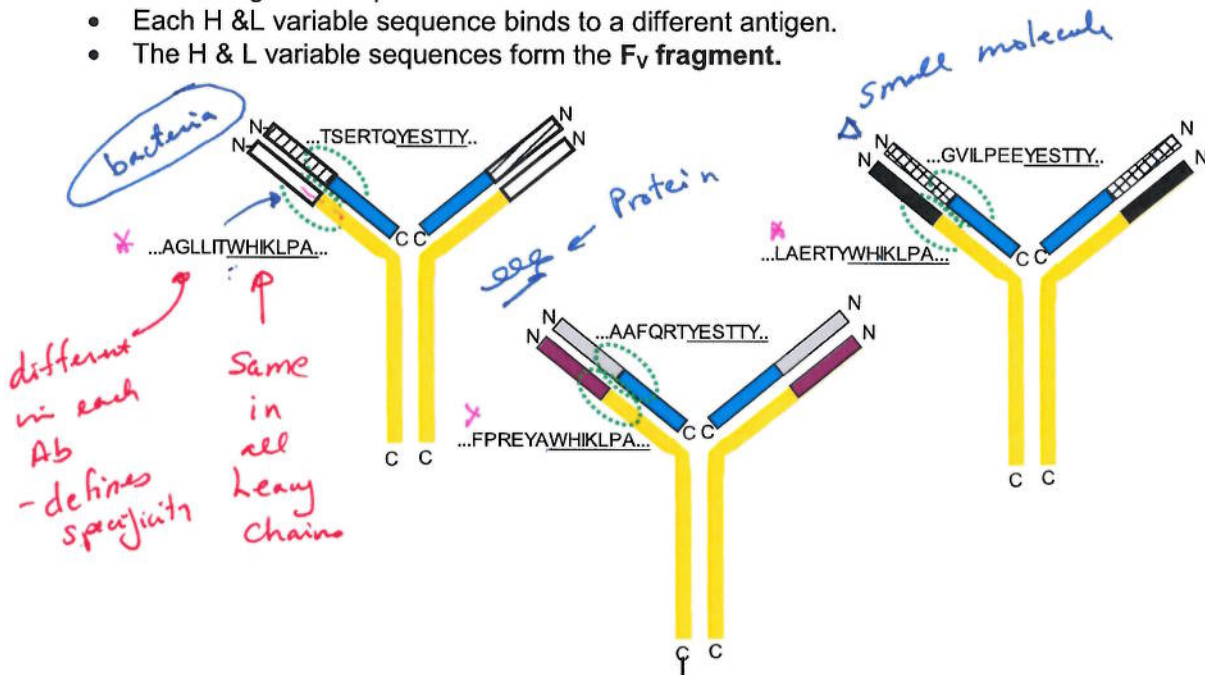
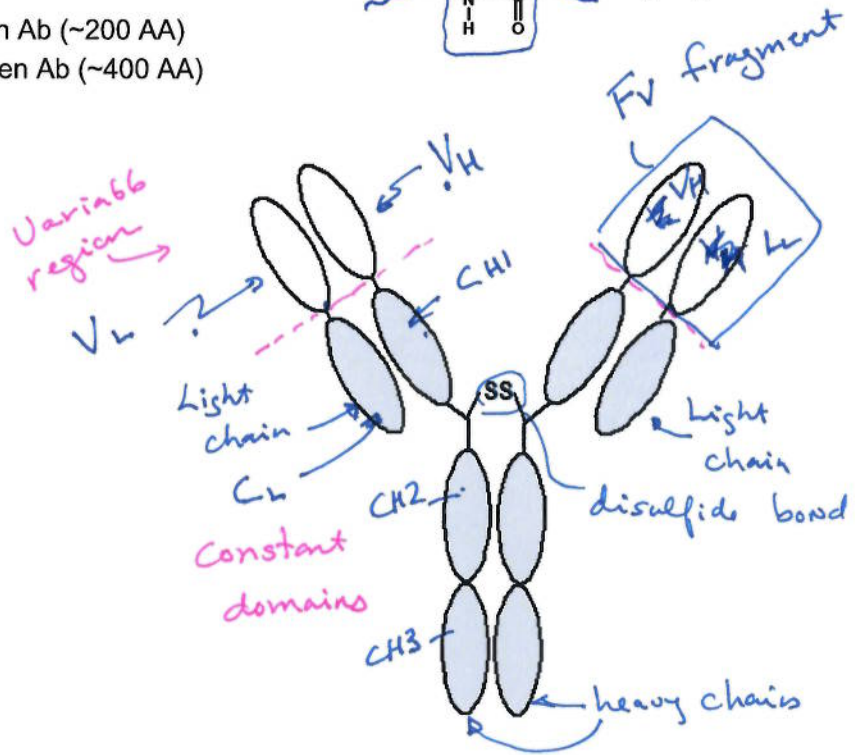
Antibody (Ab, Ig) Structure:

Quaternary structure:

- 2 Light + 2 heavy protein chains.
- Light chains are identical on any given Ab (~200 AA)
- Heavy chains are identical on any given Ab (~400 AA)
- Two binding sites/molecule
- Chains held together by disulfide bonds (and non-covalent forces).

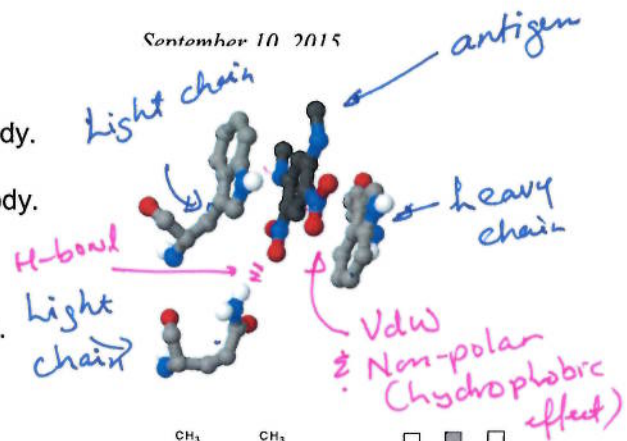
Primary Structure (Amino acid Sequence)

- The sequence of both chains can be divided into a variable and a constant region
- The sequence of the constant region is the same on all light chains and all heavy chains (but the constant sequences are different on light versus heavy)
- The variable sequence is different between antibodies that bind different things.
- There are about 10^9 different L+H variable sequences at any given time, generated by a fascinating random process.
- Each H & L variable sequence binds to a different antigen.
- The H & L variable sequences form the **F_V fragment**.

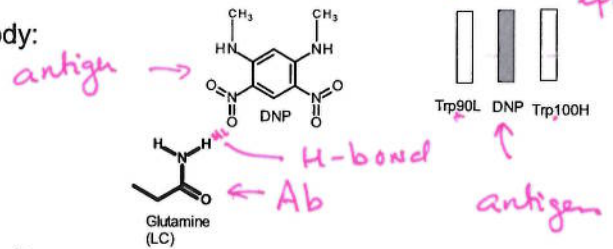


Antibody-Antigen Interactions.

- A specific complex forms between the antigen and the antibody.
- This complex is stabilized by complementary interactions between the antigen and amino acid residues from the antibody. One, or more, of the following interactions can stabilize the complex:
 - i) Hydrophobic effect – non-polar regions on antigens
 - ii) Hydrogen bonds – polar antigens with donors or acceptors.
 - iii) Van der Waals – shape complementarity
 - iv) Electrostatics – opposite charges attract!

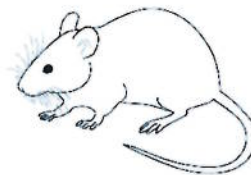
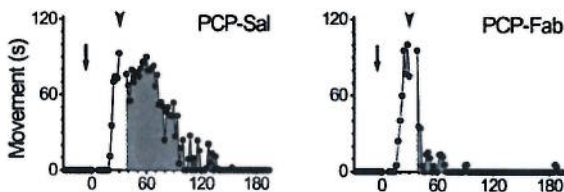


Example, the complex between dinitrophenyl and an antibody:



Applications of Antibodies:

A) Drug detoxification – antibodies bind drugs, preventing them from being toxic.



B) Treatment of Cancer

Trade Name	Used to Treat:	Approved in:
Rituxan	Non-Hodgkin lymphoma	1997
Herceptin	Breast cancer	1998
Mylotarg*	Acute myelogenous leukemia (AML)	2000
Zevalin*	Non-Hodgkin lymphoma	2002
Bexxar*	Non-Hodgkin lymphoma	2003
Erbixux	Colorectal, Head & neck cancers	2004, 2006
Avastin	Colorectal cancer	2004

Cancer cells eliminated by:

- i) Antibody carries drug to target cell.
- ii) Antibody on surface causes the immune system to destroy the target cell.