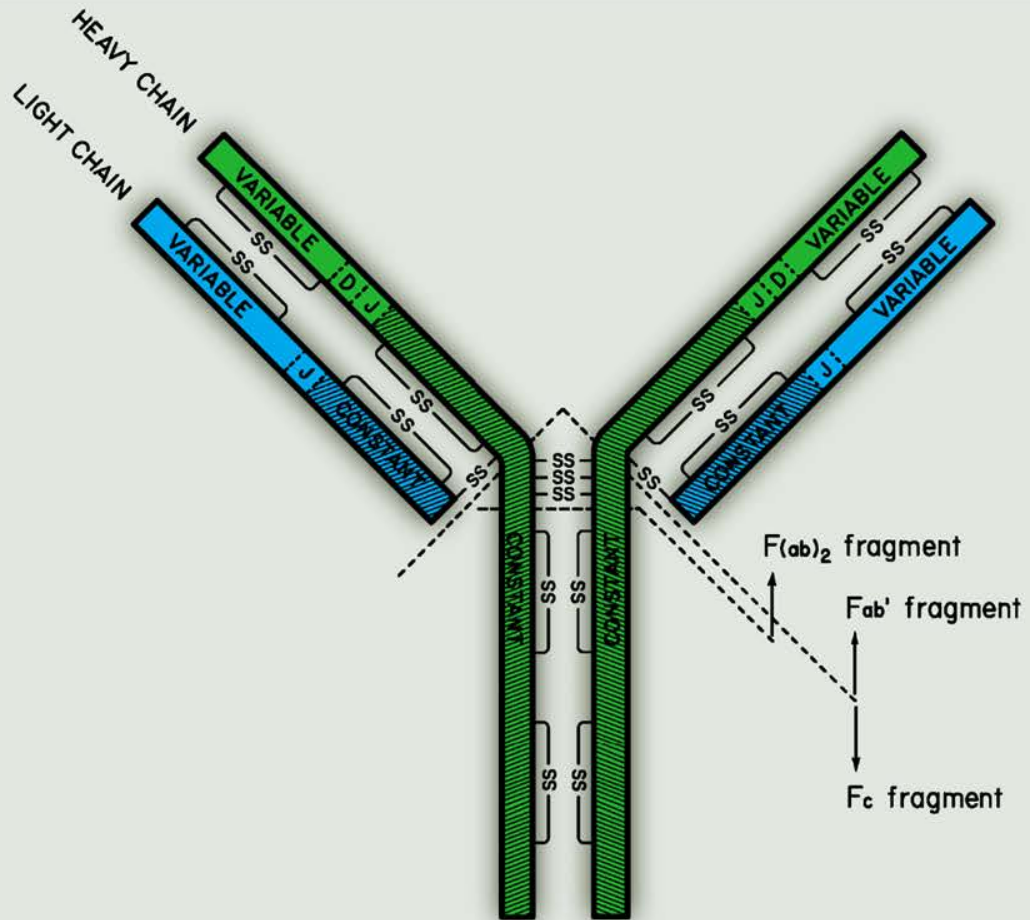


Immunoglobulin

FIGURE 1 OF THE '415 PATENT

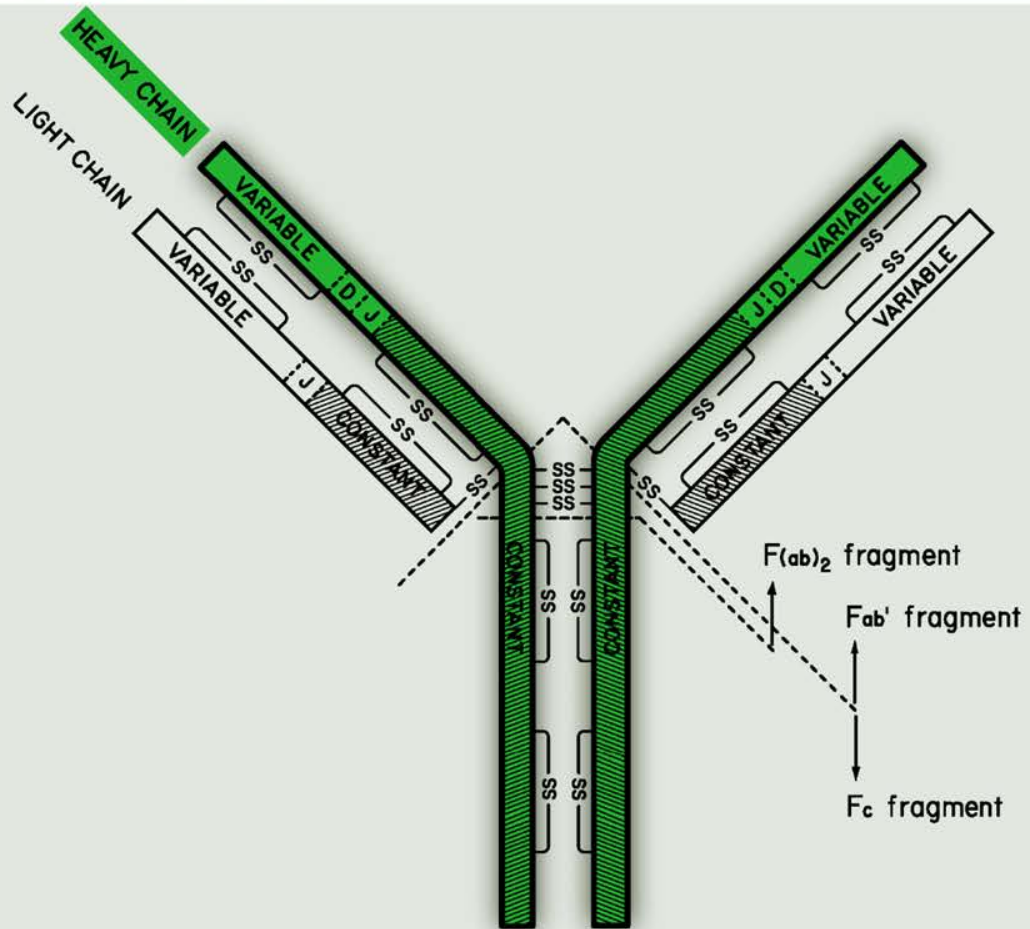
- A tetrameric molecule



Immunoglobulin

FIGURE 1 OF THE '415 PATENT

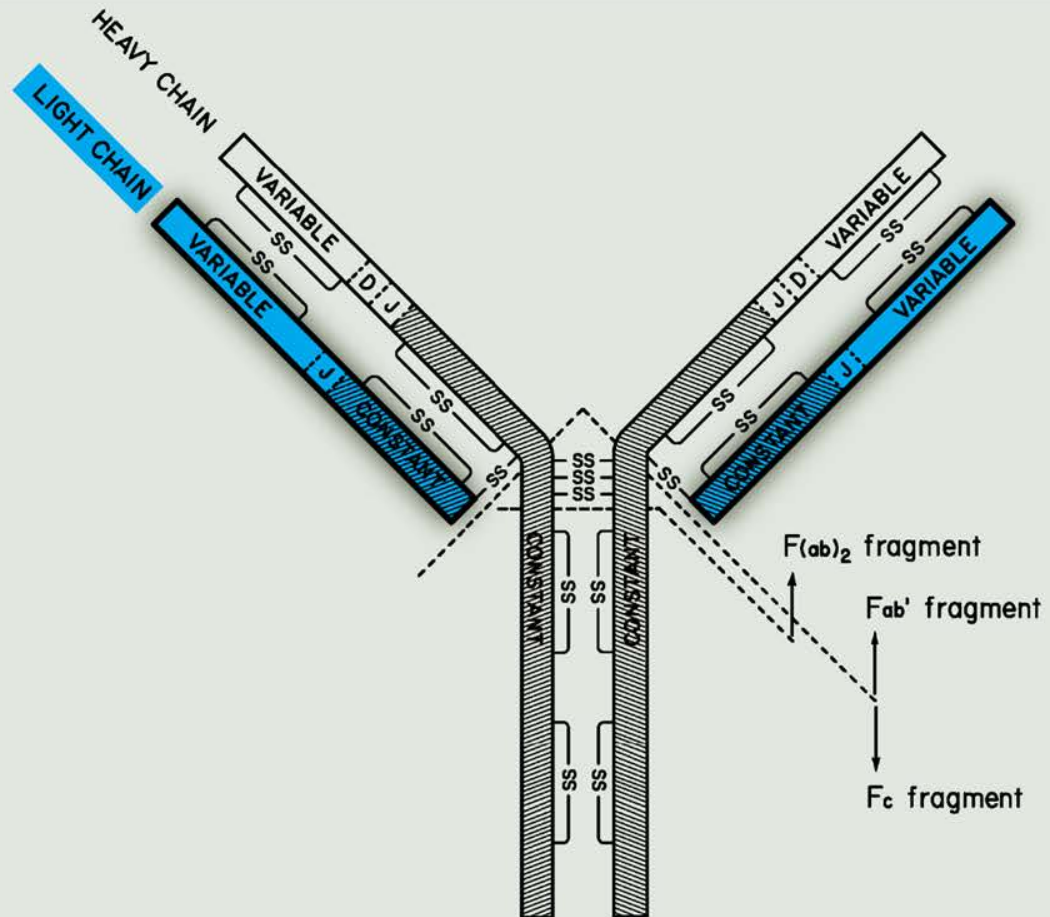
- A tetrameric molecule
- consisting of two relatively long polypeptide chains called **heavy chains**



Immunoglobulin

FIGURE 1 OF THE '415 PATENT

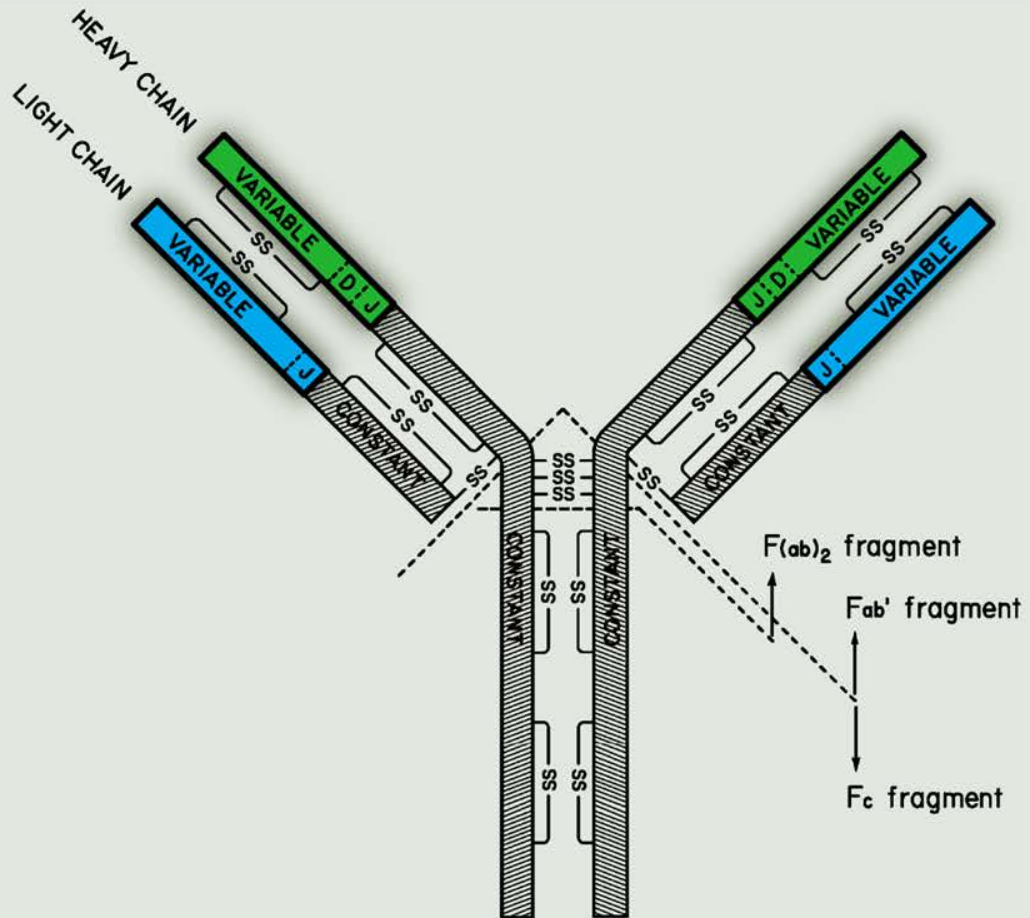
- A tetrameric molecule
- consisting of two relatively long polypeptide chains called **heavy chains**
- and two shorter polypeptide chains called **light chains**



Structures of an Immunoglobulin

FIGURE 1 OF THE '415 PATENT

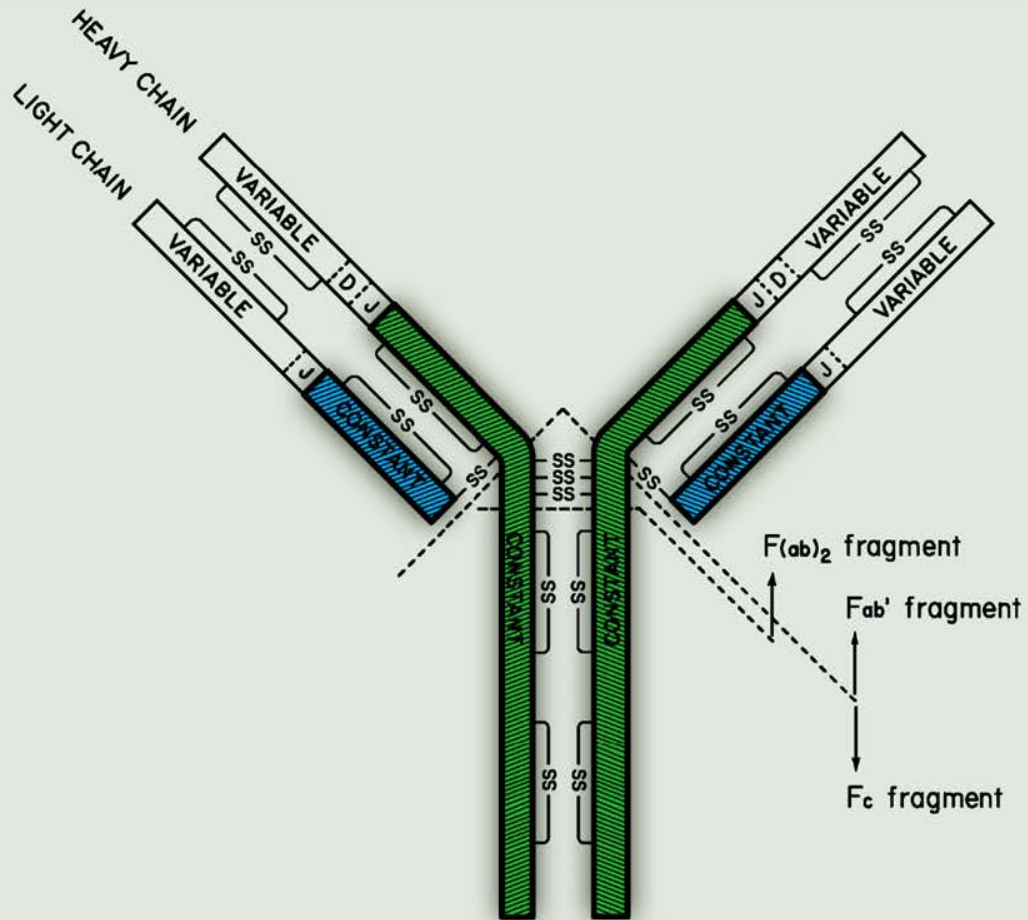
Variable Regions



Structures of an Immunoglobulin

FIGURE 1 OF THE '415 PATENT

Constant Regions

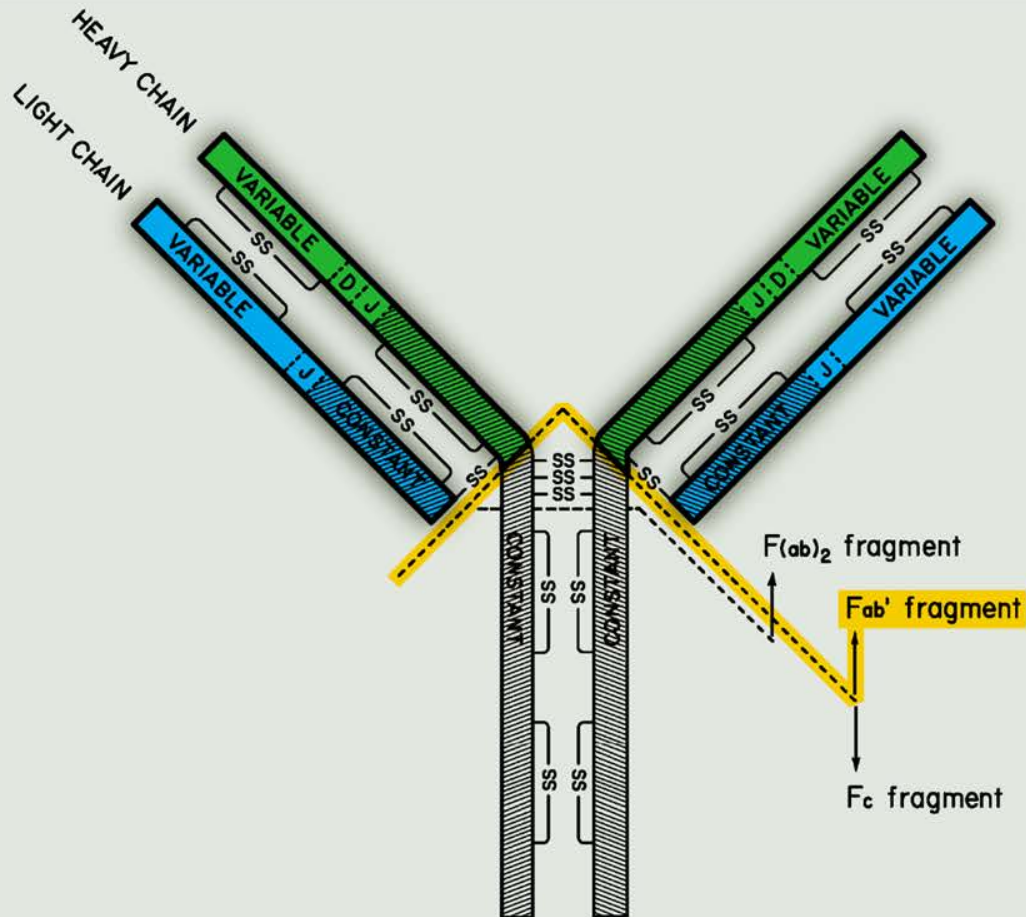


Structures of an Immunoglobulin

FIGURE 1 OF THE '415 PATENT

Fab Regions:

— Fab'

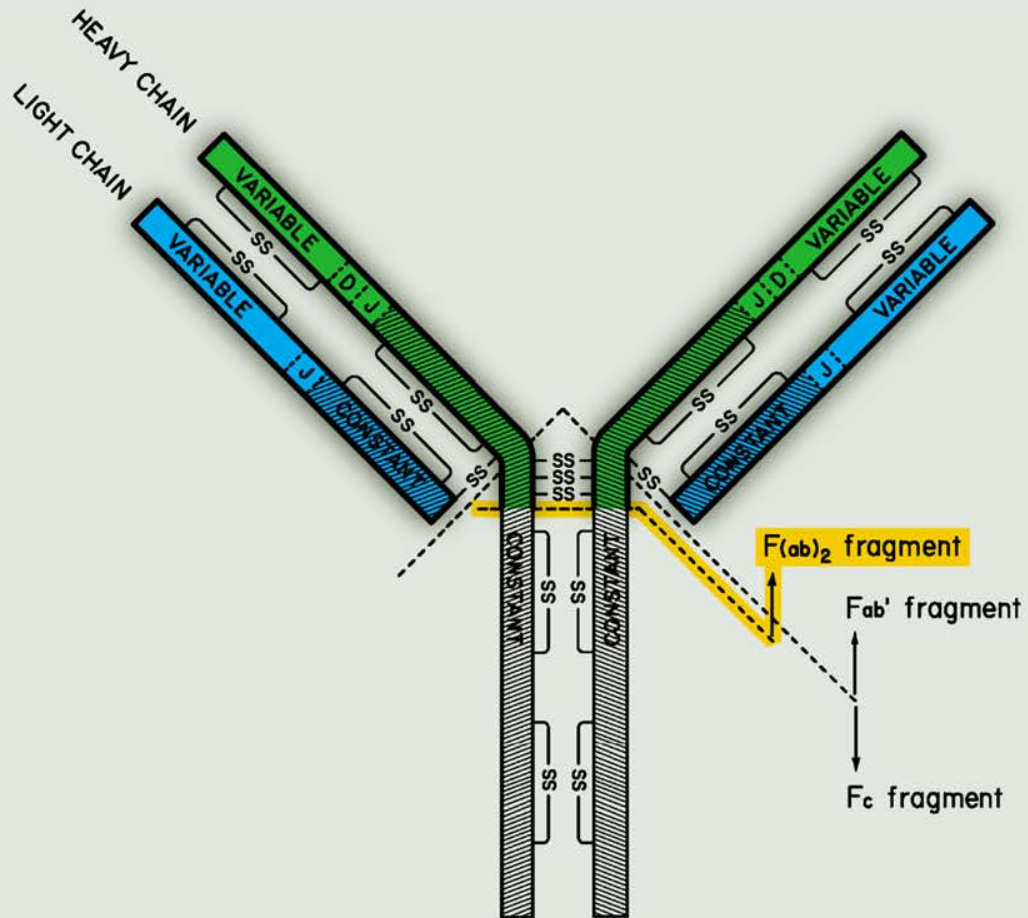


Structures of an Immunoglobulin

FIGURE 1 OF THE '415 PATENT

Fab Regions:

— $F(ab)_2$

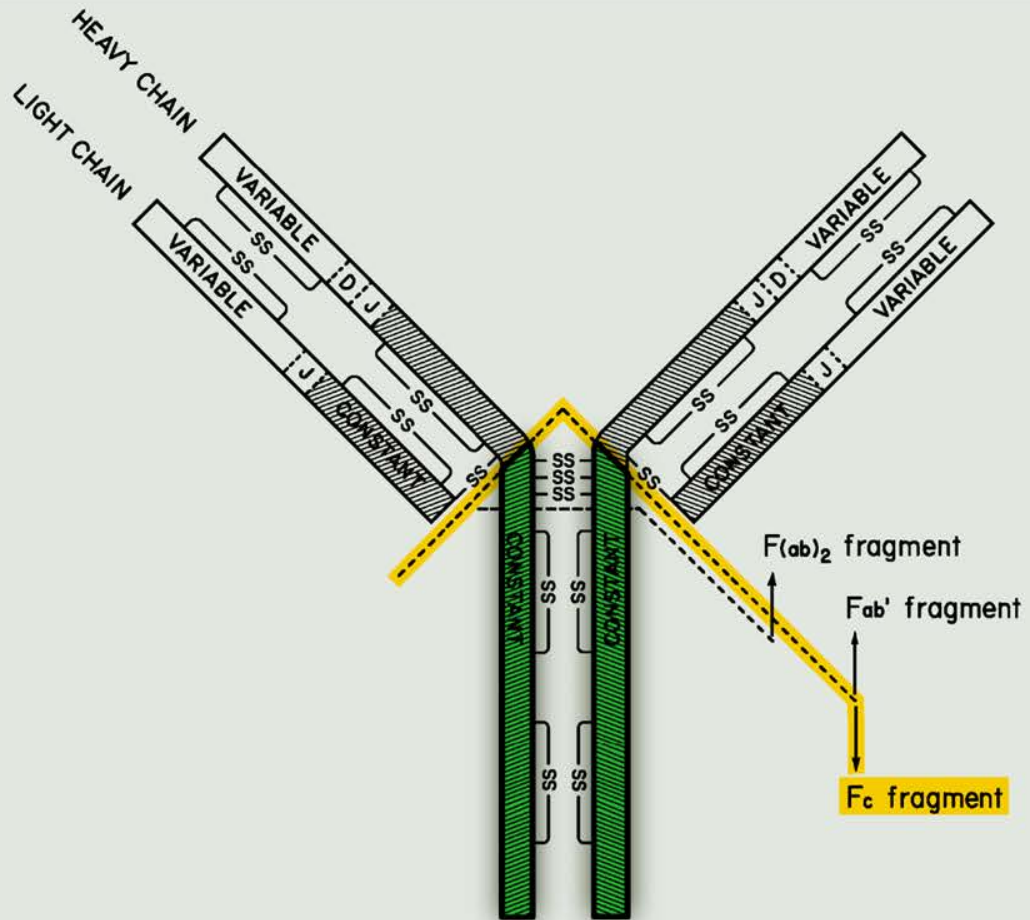


Structures of an Immunoglobulin

FIGURE 1 OF THE '415 PATENT

Fab Regions:

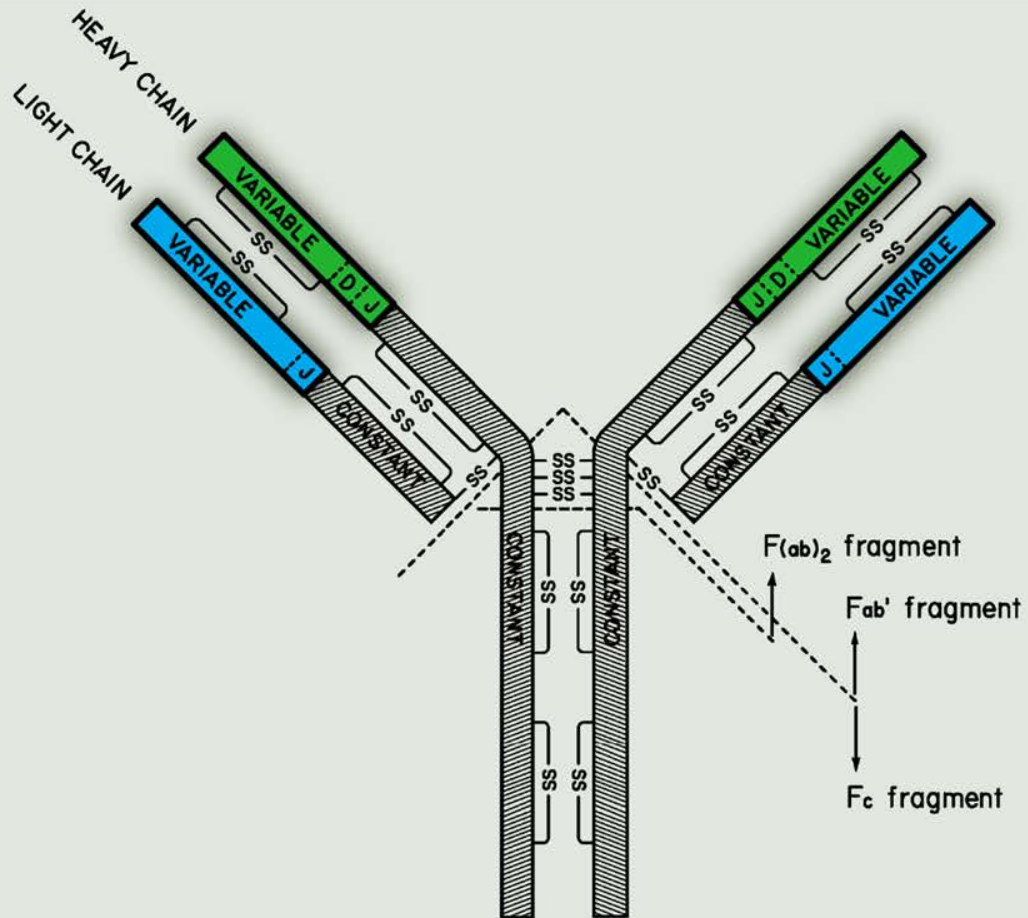
– F_c



Variable Domain of the Immunoglobulin

The part of the immunoglobulin that runs from the N-terminal (the top of the Y) to the constant region

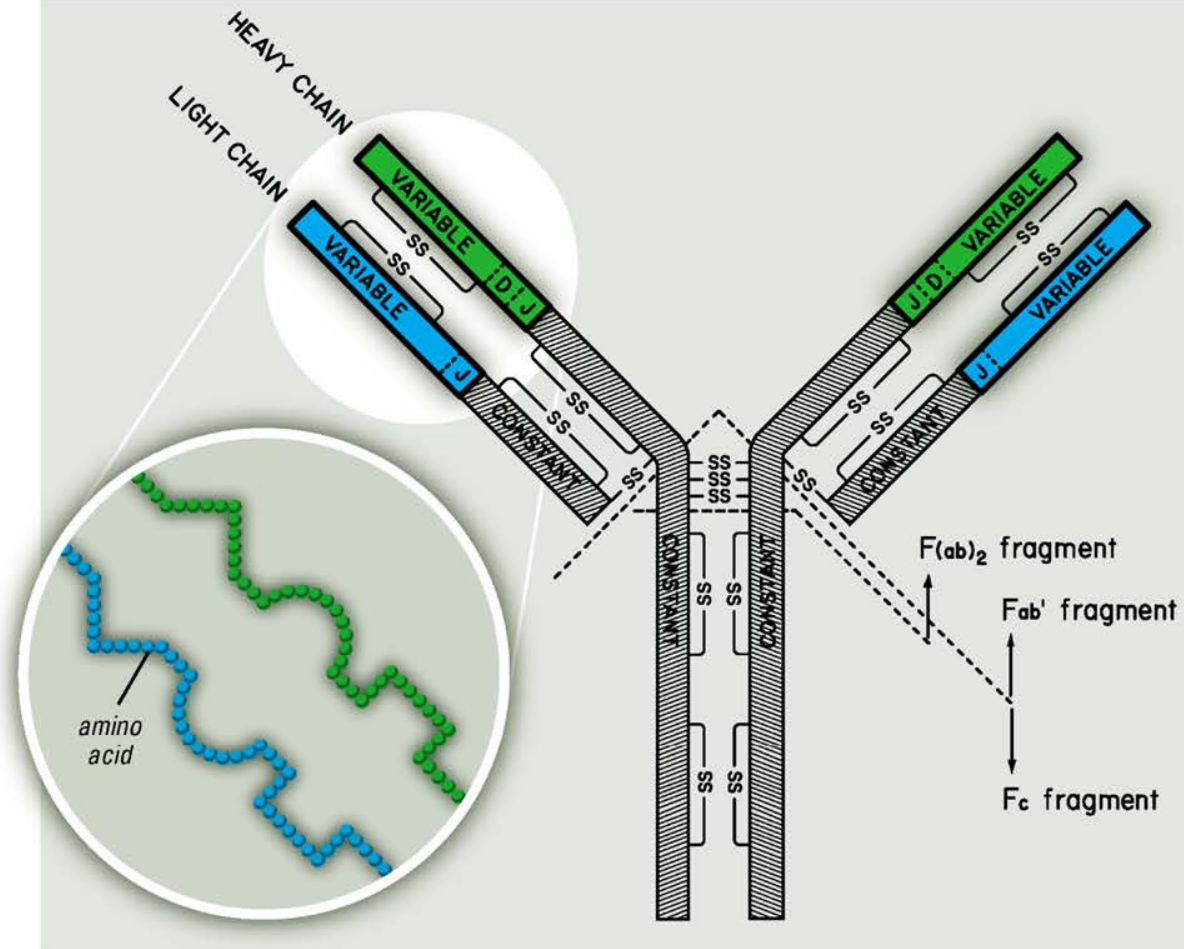
FIGURE 1 OF THE '415 PATENT



Variable Domain of the Immunoglobulin

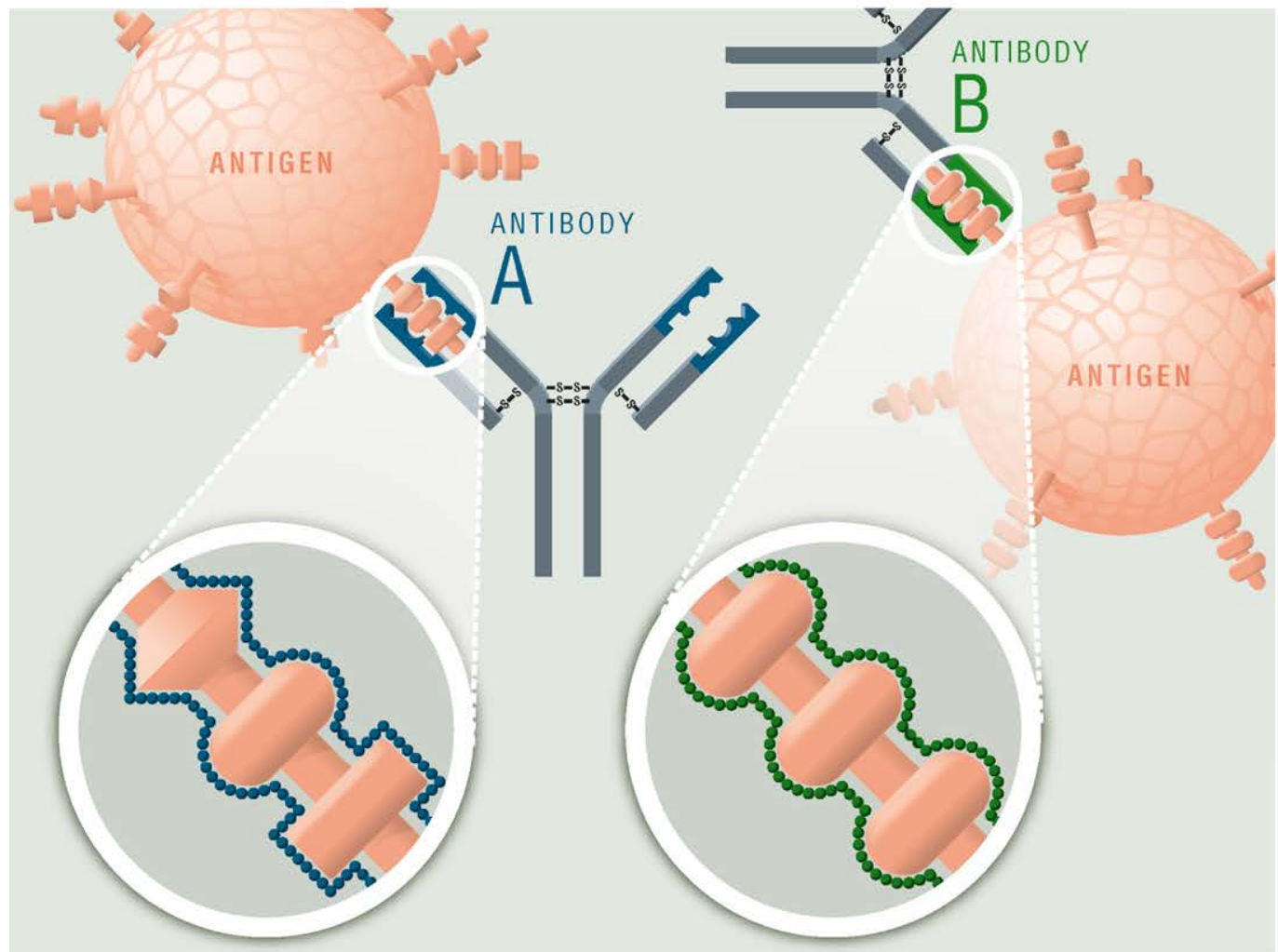
MODIFIED FIGURE 1 OF THE '415 PATENT

The part of the immunoglobulin that runs from the N-terminal (the top of the Y) to the constant region **and is elicited by a single antigen.**



Antigen/Antibody Complexes

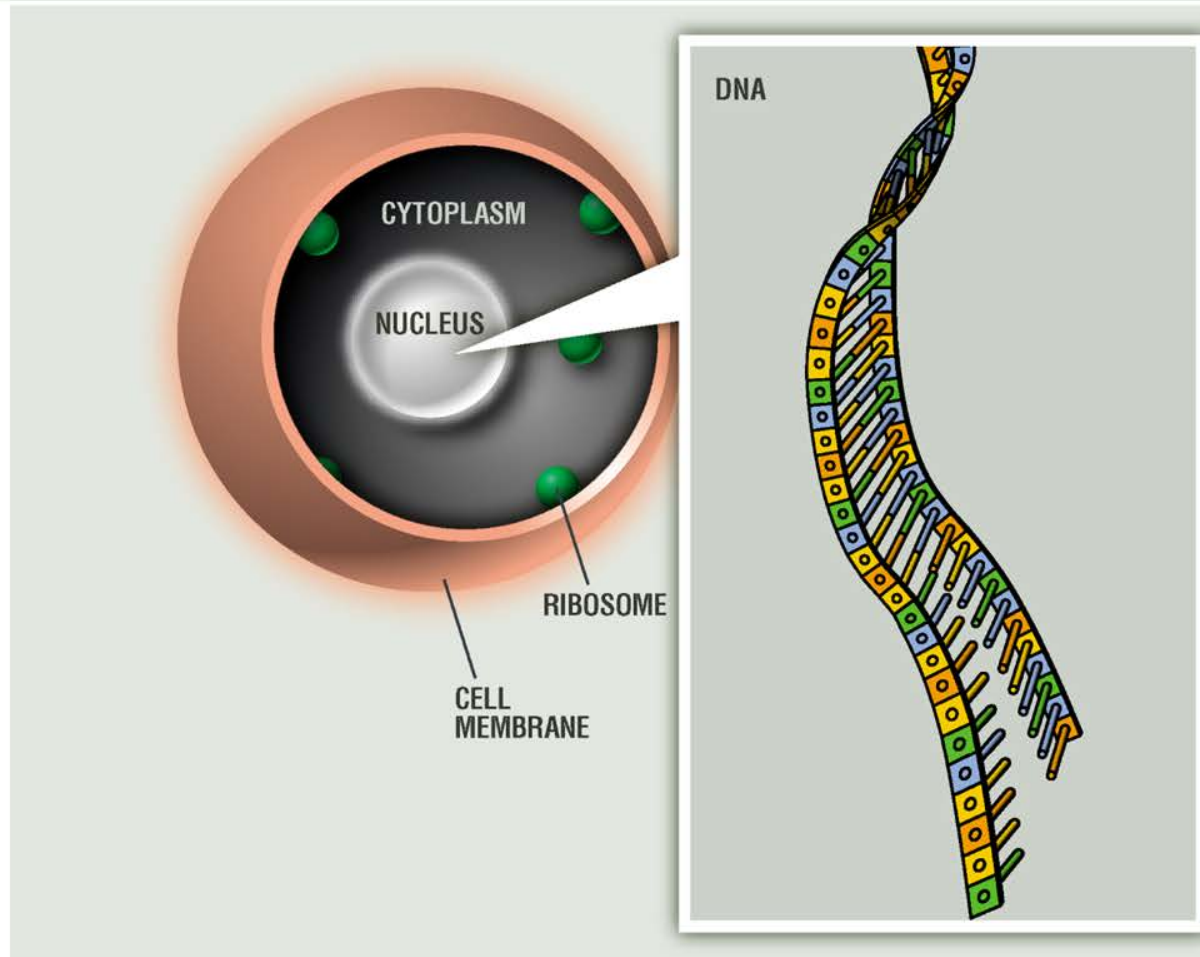
Different amino acid sequences within the variable regions of an immunoglobulin cause the immunoglobulin to selectively bind with different target antigens.



Transcription and Translation

TRANSCRIPTION

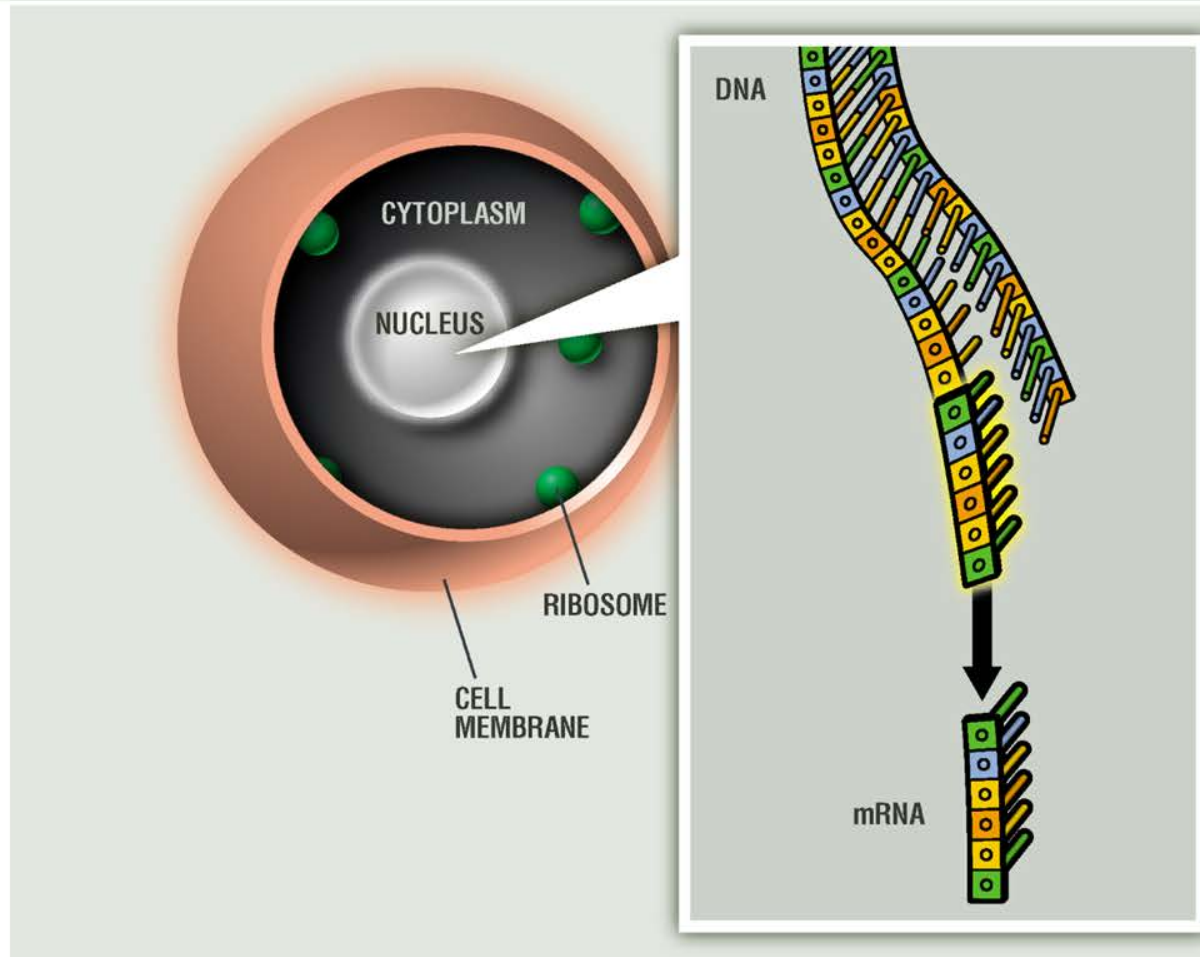
In the nucleus, the DNA coding sequence acts as a template for the formation of messenger ribonucleic acid or mRNA.



Transcription and Translation

TRANSCRIPTION

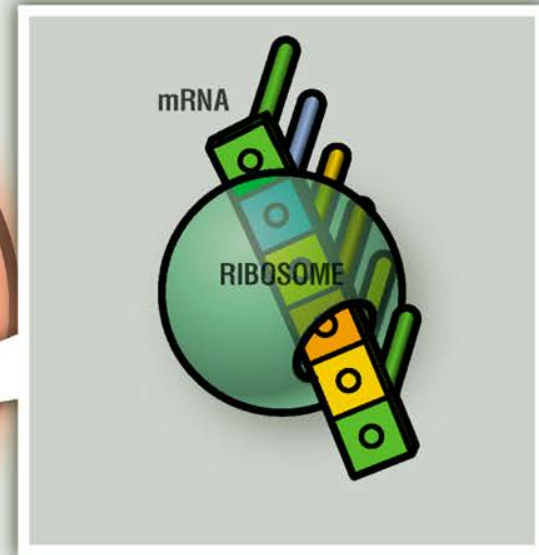
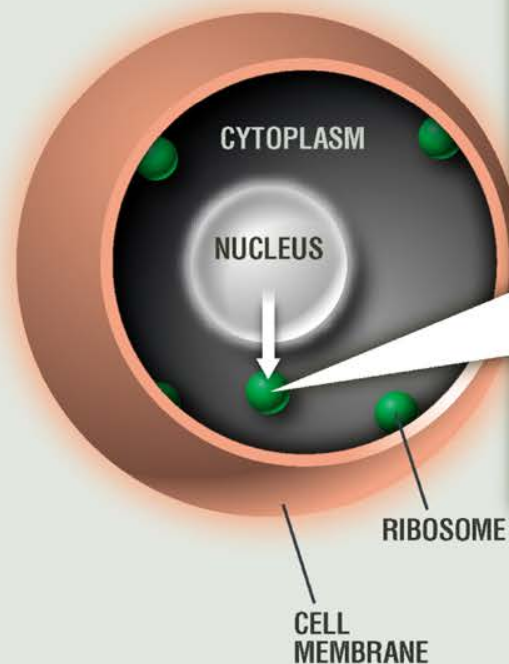
In the nucleus, the DNA coding sequence acts as a template for the formation of messenger ribonucleic acid or mRNA.



Transcription and Translation

TRANSLATION

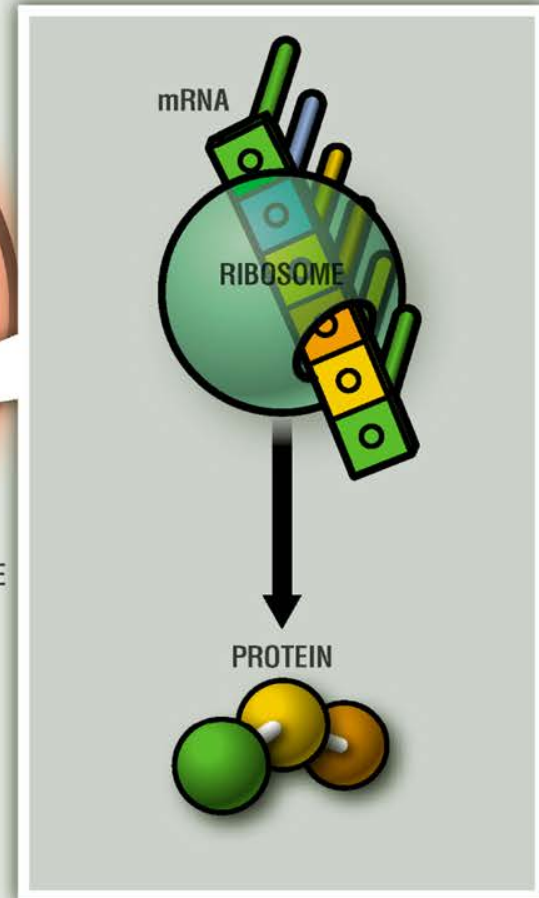
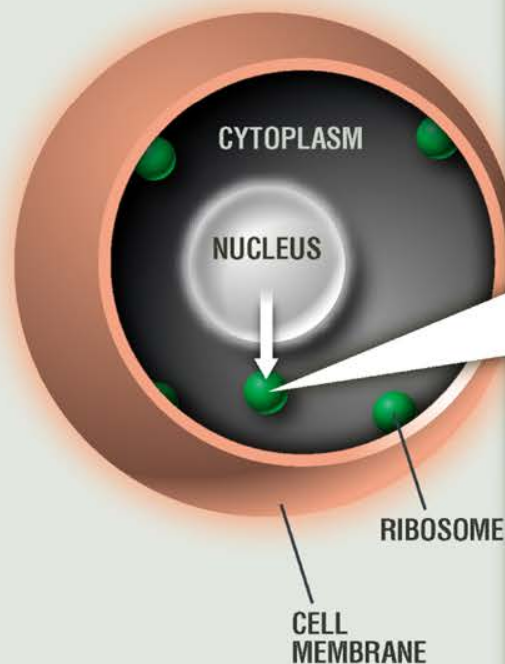
The mRNA leaves the cell nucleus and enters the cytoplasm where it attaches to the ribosomes.



Transcription and Translation

TRANSLATION

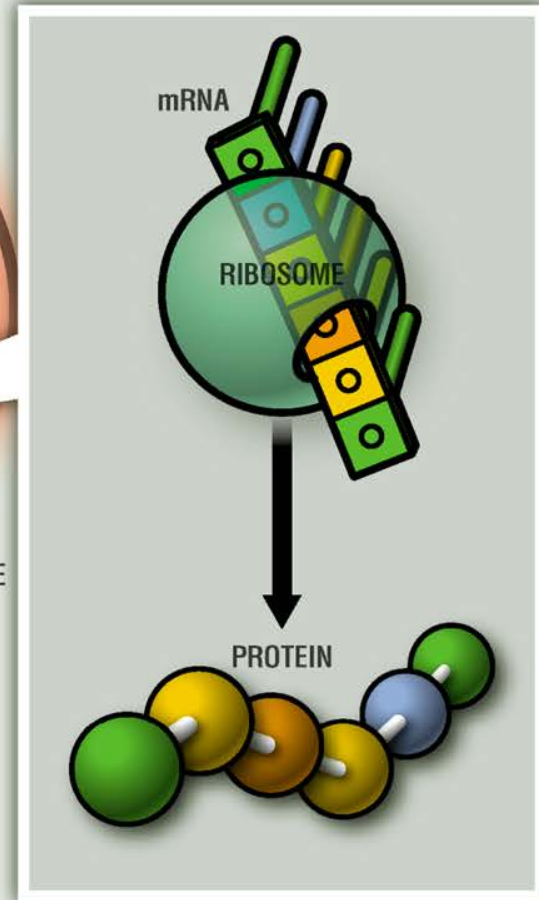
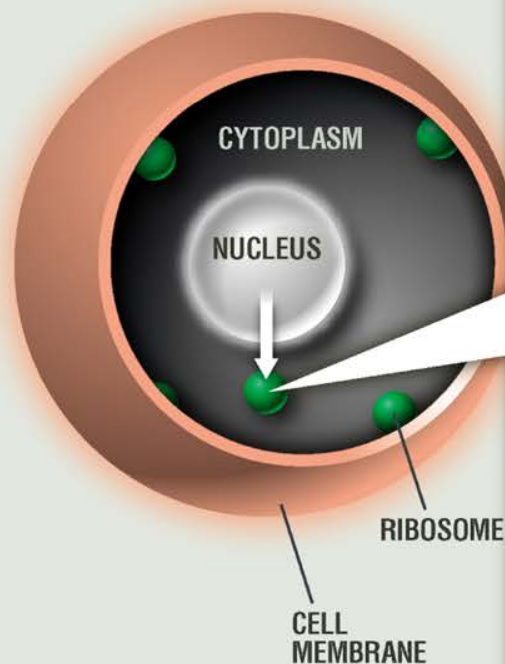
The mRNA leaves the cell nucleus and enters the cytoplasm where it attaches to the ribosomes. The ribosomes produce the protein by following the sequence of nucleotide bases in the mRNA.



Transcription and Translation

TRANSLATION

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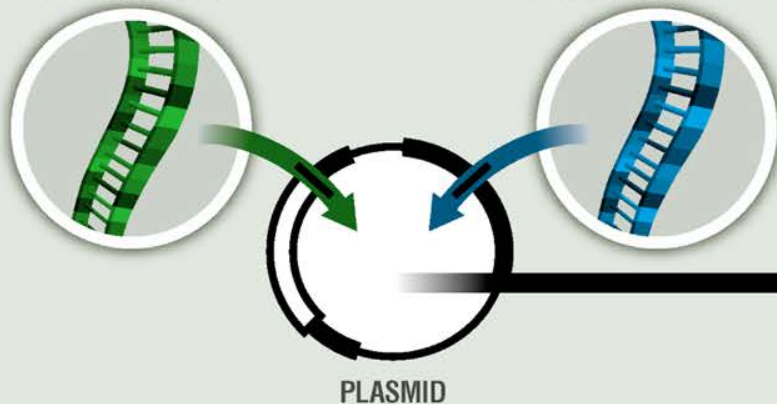


The '415 Patent Specification Describes Combining Separate Heavy and Light Chains OUTSIDE the Host Cell

DNA ENCODING TO PRODUCE SEPARATE HEAVY AND LIGHT CHAINS

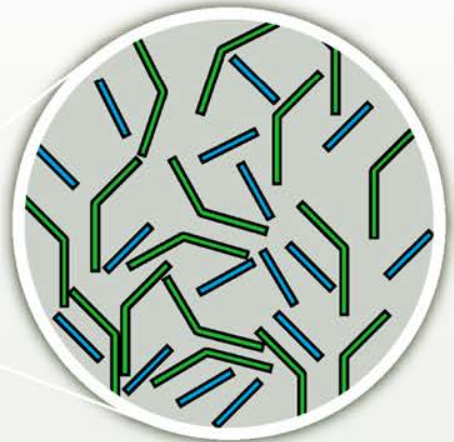
DNA CODING SEQUENCE FOR **HEAVY CHAIN**

DNA CODING SEQUENCE FOR **LIGHT CHAIN**



TRANSFORMED HOST CELL

HOST CELL



“[T]he gene coding for the light chain and that coding for the heavy chain... may be **inserted into separate expression plasmids**, or together in the same plasmid, so long as each is under suitable promoter and translation control.”

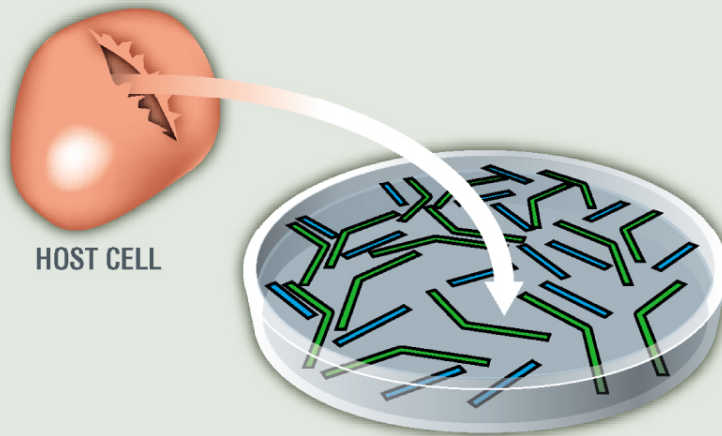
Col. 12, ll. 17–22 (emphasis added)

“The ability of the method of the invention to produce **heavy** and **light** chains or portions thereof, **in isolation from each other....**”

Col. 12, ll. 58–60 (emphasis added)

The '415 Patent Specification Describes Combining Separate Heavy and Light Chains OUTSIDE the Host Cell

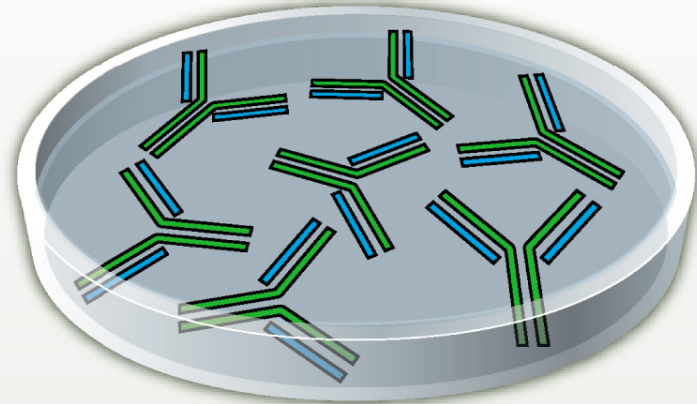
LYSIS OF HOST CELL TO OBTAIN SEPARATE HEAVY AND LIGHT CHAINS



“The resulting product may be **obtained by lysis**, if necessary, **of the host cell** and recovery of the product by appropriate purifications from other proteins.”

Col. 4, ll. 29–32 (emphasis added)

HEAVY AND LIGHT CHAINS ASSEMBLED OUTSIDE THE CELL

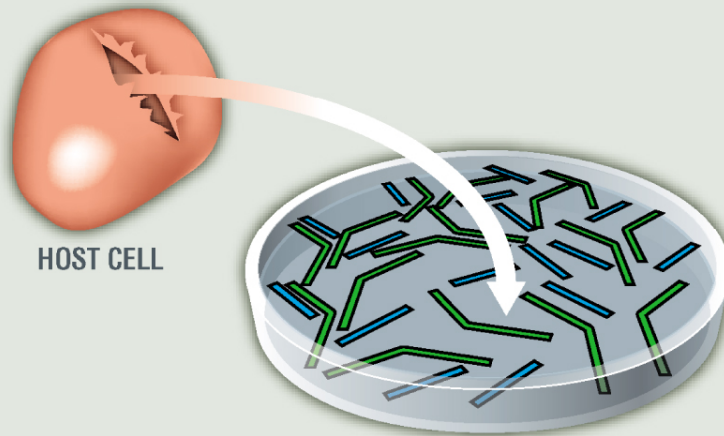


“When heavy and light chain are coexpressed in the same host cell, the isolation procedure is designed so as to recover reconstituted antibody. **This can be accomplished in vitro as described below,...**”

Col. 12, ll. 50–53 (emphasis added)

The '415 Patent Specification Describes Combining Separate Heavy and Light Chains OUTSIDE the Host Cell

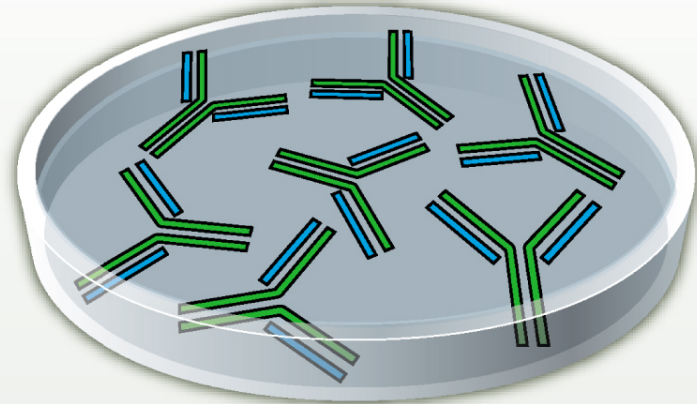
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HEAVY AND LIGHT CHAINS ASSEMBLED OUTSIDE THE CELL

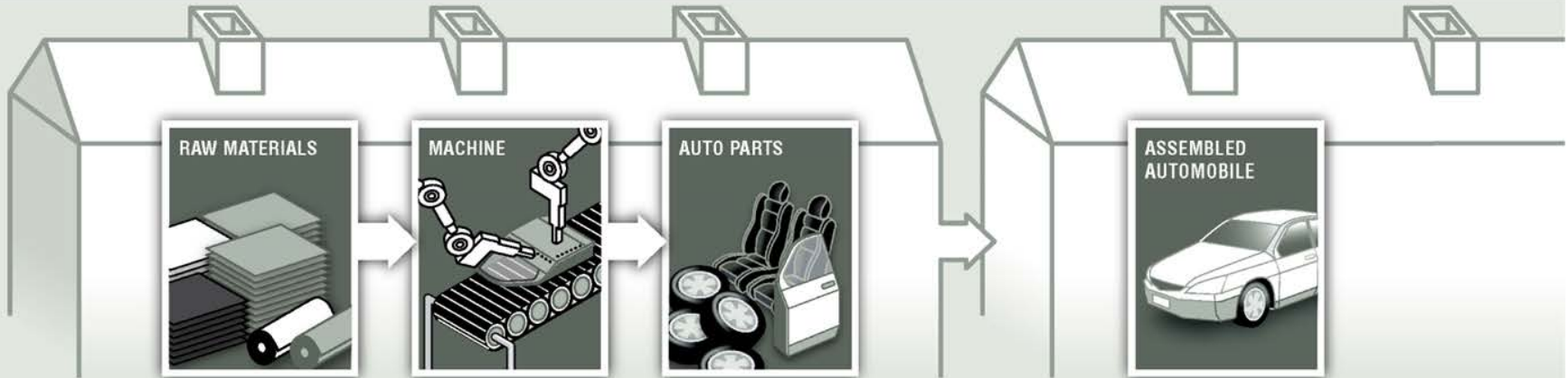


“When heavy and light chain are coexpressed in the same host cell, the isolation procedure is designed so as to recover reconstituted antibody. **This can be accomplished in vitro as described below, or might be possible in vivo in a microorganism** which secretes the IgG chains out of the reducing environment of the cytoplasm.”

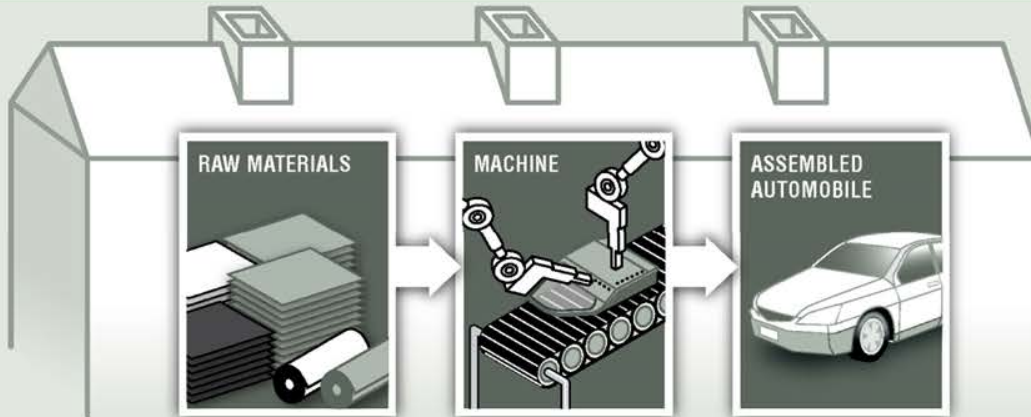
Col. 12, ll. 50–55 (emphasis added)

An Analogy to Illustrate the Parties' Constructions

MEDIMMUNE'S CONSTRUCTION



DEFENDANTS' CONSTRUCTION



The '415 Patent Does NOT Describe Assembly of Chains INSIDE the Single Host Cell

| | | | | | | | | | |
|---------|---------|---------|---------|---------|---------|---------|---------|---------|---------|
| Col. 1 | Col. 2 | Col. 3 | Col. 4 | Col. 5 | Col. 6 | Col. 7 | Col. 8 | Col. 9 | Col. 10 |
| Col. 11 | Col. 12 | Col. 13 | Col. 14 | Col. 15 | Col. 16 | Col. 17 | Col. 18 | Col. 19 | Col. 20 |
| Col. 21 | Col. 22 | Col. 23 | Col. 24 | Col. 25 | Col. 26 | Col. 27 | Col. 28 | Col. 29 | Col. 30 |

The '415 Patent Does NOT Describe Assembly of Chains INSIDE the Single Host Cell

Recovery of reconstituted antibody “can be accomplished **in vitro** as described below, or might be possible **in vivo** in a microorganism which secretes the IgG chains out of the reducing environment of the cytoplasm.”

A “Mere Wish or Plan” Is NOT An Invention

Col.
1

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Recovery of reconstituted antibody “can be accomplished **in vitro** as described below, **or might be possible in vivo** in a microorganism which secretes the IgG chains out of the reducing environment of the cytoplasm.”

Col.
11

Col.
12

A “mere wish or plan” for *in vivo* assembly of the heavy and light chains does not demonstrate that the inventors had possession of this invention.

Regents of Univ. of Cal. v. Eli Lilly & Co., 119 F. 3d 1559, 1566 (Fed. Cir. 1997)

Col.
21

Col.
22

Col.
23