

# **Biomanufacturing Pathways**

# Biomanufacturing in Puget Sound

- Reasons Shoreline is adding a Biomanufacturing Certificate
  - To provide training to enable students to get jobs in this growing industry.
  - To meet industry demand for qualified entry level job candidates
- Current Biomanufacturing companies in our region
  - Bristol-Myers, Squibb (Juno/Celgene)
  - AGC Biologics (a CRO)
  - Just-Evotec
  - SeaGen (Seattle Genetics)
  - Lyell Pharmaceuticals
  - Sound Biologics
  - Partner Therapeutics
  - Lumen Bioscience (spirulina)

# Biomanufacturing in Puget Sound

- Projection of Work Force need and job forecast
  - Demand for biotechnology workforce and biotechnicians is growing at an exceptional rate in Washington state and nationally.
  - According to the U.S. Bureau of Labor Statistics, the profession will grow nationally by 7% over the next 10-years and in Washington state at 2% per year for the next decade (BLS 2020; WA State Demand 2020).
  - In 2018, the immunotherapy and cell-therapy sectors were valued at over \$1.07 billion and are projected to grow at an annual rate of over 36% in which by 2025 the sector is estimated to be valued at about \$12 billion.
  - In Fall 2020, Merck and Seattle Genetics finalized a \$1.4 billion deal to more-than-double its biomanufacturing footprint in the Puget Sound region (Campbell, 2020).
  - These numbers demonstrate continued high demand for biotechnology/biomanufacturing technicians.

# What is Biomanufacturing?

**Biomanufacturing** uses cells (bacteria, fungi, plant, mammal) to produce proteins used in therapeutics, diagnostics, and industrial applications.

The cells may be naturally occurring or derived through genetic engineering.

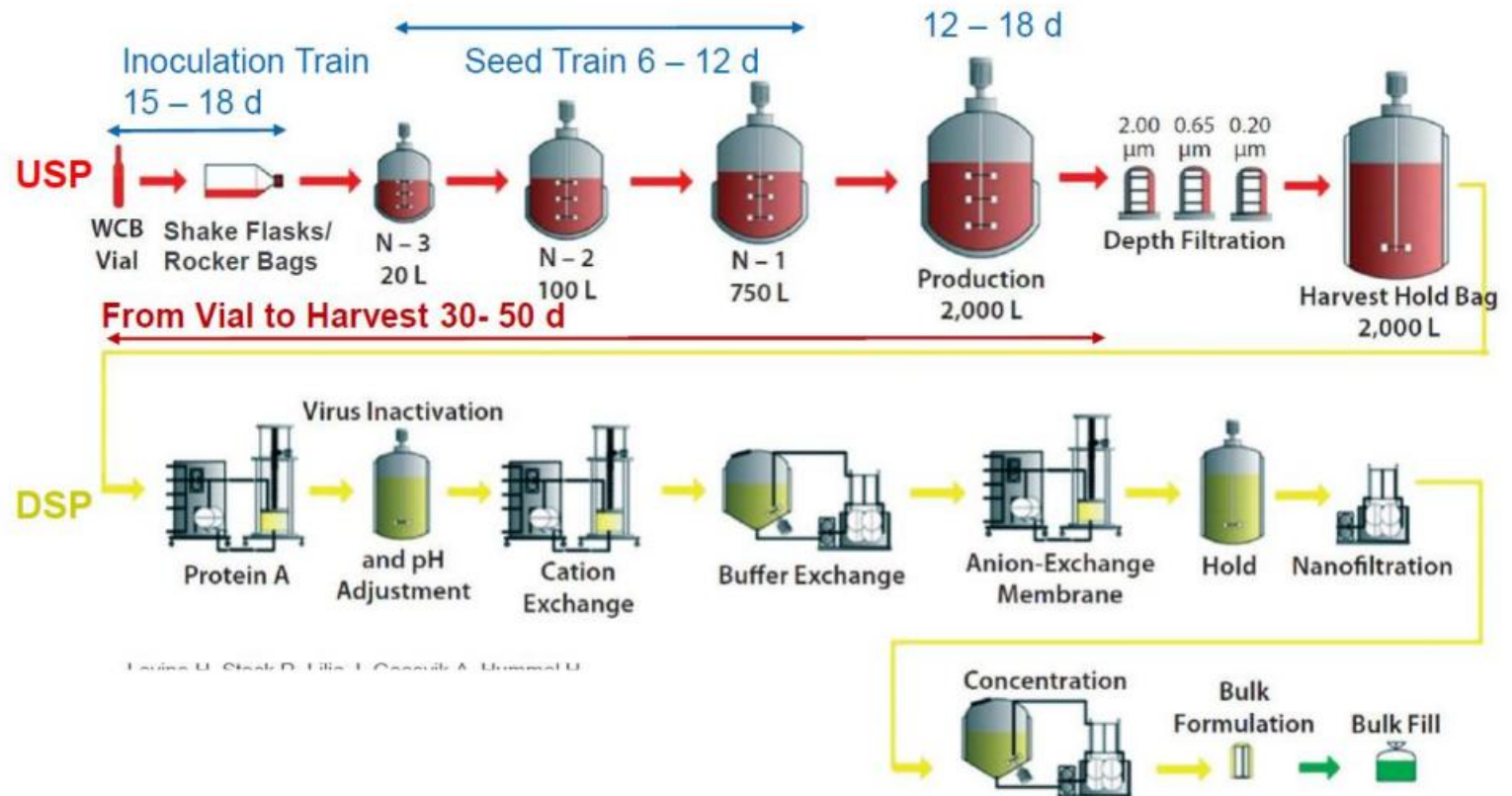
Cells act as the factories for the production of the desired proteins. Cells are nurtured and grown, then harvested and eliminated to obtain the target.



# Research, Development and Biomanufacturing

- Once a potential drug candidate is identified, it has be scaled up for use, first for testing and hopefully later as a marketable product
- Requires expertise in biomanufacturing techniques and federal regulations, and the use of specialized equipment (\$\$\$)
- Can be done 'in-house' by profitable Biopharma companies
  - or –
- Can be sent to Contract Biomanufacturers who can begin with transformed/transfected cell lines (or even just the DNA sequence), and return a protein in purified form for the originators to use in testing

# Biomanufacturing Process Diagram



Levine, HL. et al. Single-Use Technology and Modular Construction. Enabling Biopharmaceutical Facilities of the Future. Bioprocess Int. 11(4), p40-45, (2013).

**USP** = Upstream process

**DSP** = Downstream process

# Biomanufacturing Products

Biopharmaceuticals include:

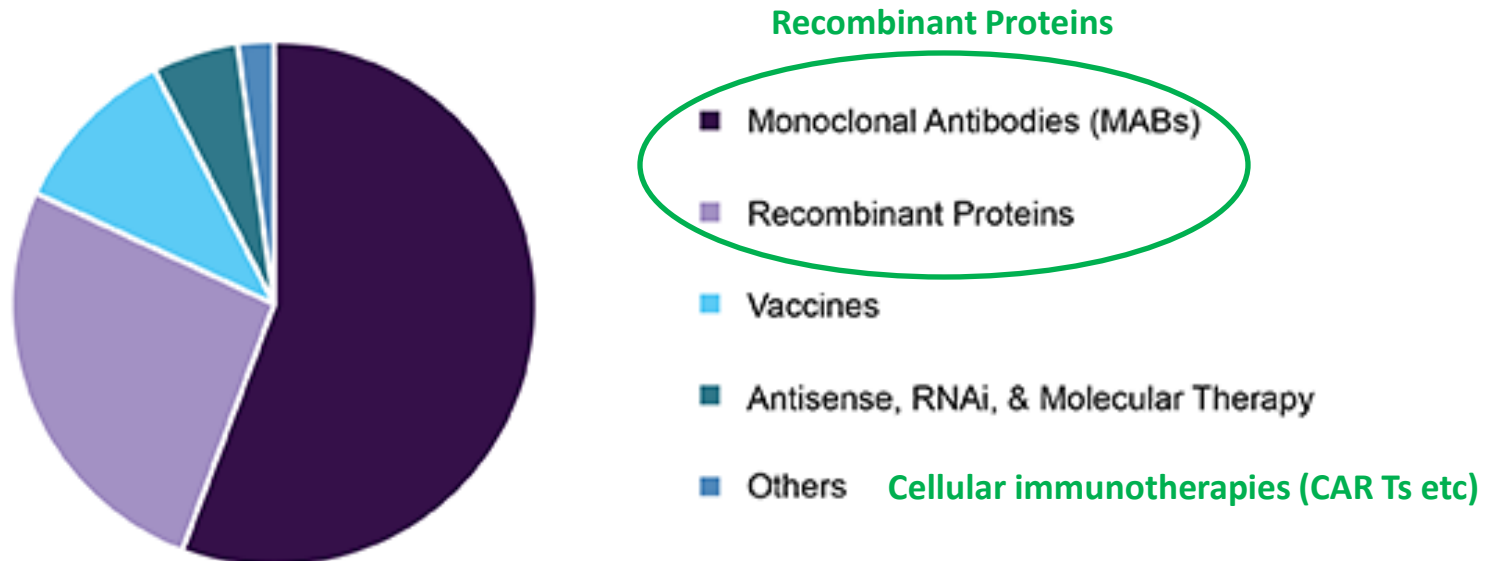
- Hormones
- Growth Factors
- Blood Proteins
- Clotting Factors
- Enzymes
- Antibodies
- DNA and RNA
- Stem cells
- Cellular Immunotherapeutics (CAR T cells etc)

Applications of Biopharmaceuticals in Health and Medicine:

- Therapeutic proteins for treatment of disease
- Vaccines to prevent disease
- Protein or DNA-based diagnostics
- Regenerative medicine technology
- Gene Therapy

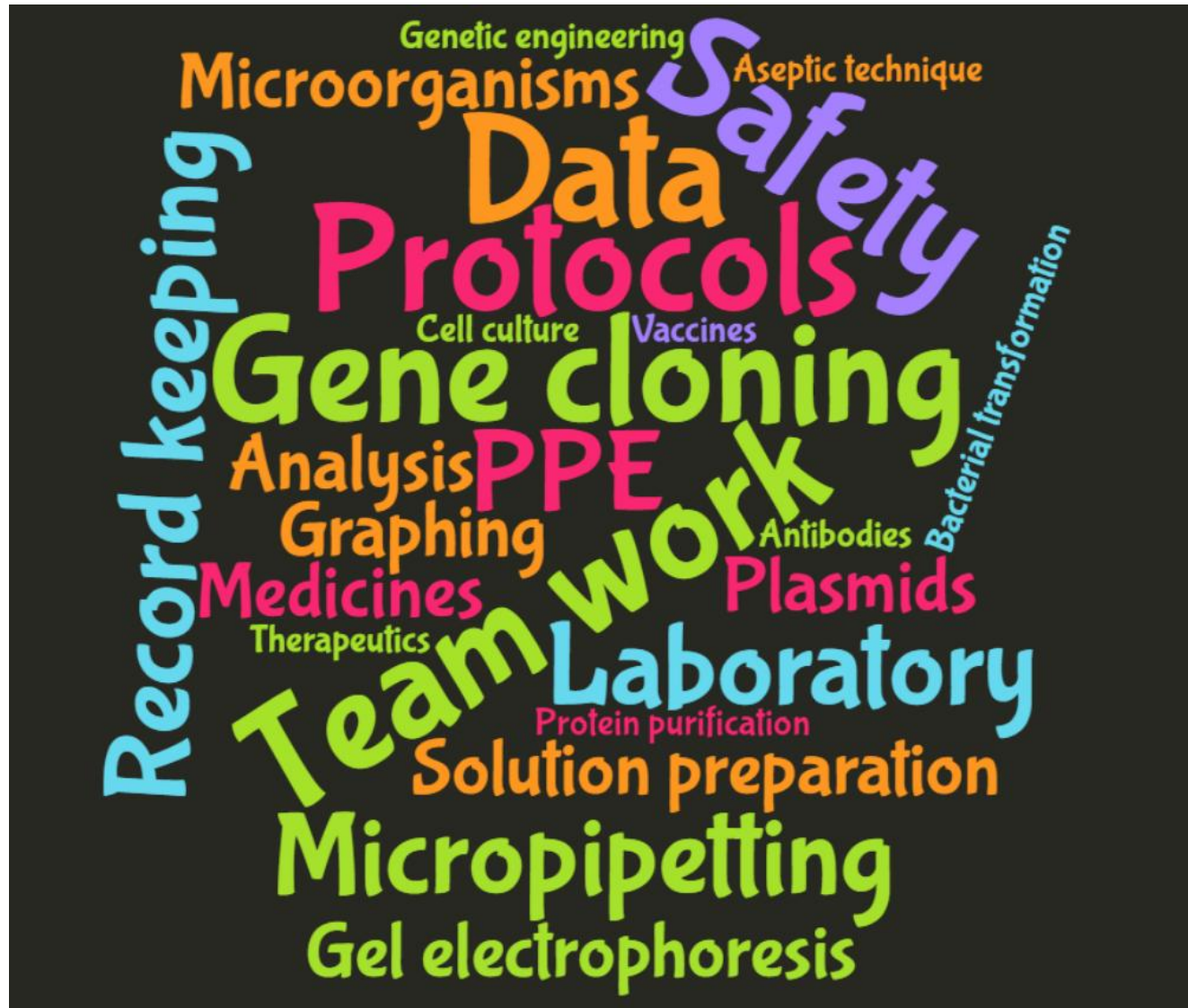
# Biomanufacturing Products

Global biopharmaceuticals contract manufacturing market share, by biologics, 2017 (%)





# Common Concepts between HS Biotech and Biomanufacturing



# These Biomanufacturing concepts may not currently be a part of most HS Biotech classes

- Standard Operating Procedures (SOP) – detailed and regulated processes to ensure repeatability and consistency in product
- Good Manufacturing Practices (GMP) - ensures therapeutics for use in patients MUST be of the same quality and purity in EVERY batch
- FDA Regulatory Role in drug development
- Quality Control – verifies safety and veracity of product
- Quality Assurance – verifies all processes have been followed

# High School Connections

## Career connections and pathways

- What type of education background is needed to work in biomanufacturing?

Biomanufacturing programs prepare students for positions in pharmaceutical manufacturing, bioprocessing (which generally refers to the processing of agricultural commodities into products), media preparation, bioenergy production (e.g. ethanol and biodiesel), and the food processing industry.

Courses may include:

- Chemistry
- Biology
- Laboratory math
- English
- Introduction to computer science
- Internships
- Depending on the emphasis of the program, extensive training in industrial plant operations including electrical, mechanical, and process control technologies.

Source = InnovATEBIO

# High School Connections

- Career connections and pathways
  - Where can students get training in Biomanufacturing?
    - There are currently 22 Community College locations that offer degrees or certificates in biomanufacturing.
    - Shoreline CC would be number 23.

Locations of programs offering degrees and(or) certificates for this topic



Source = InnovATEBIO

# High School Connections

- Under Review
  - Possible Articulation with Shoreline if high school students complete biomanufacturing courses at SCC.

# Biomanufacturing Training Programs at Shoreline Community College

## 10-week Fundamentals of Biomanufacturing Certificate

**Pilot group Fall 2021**

**No prior experience required, leave prepared for entry-level positions – 8 credits**

**Current industry partners BMS & SeaGen**

**Aseptic Techniques, Regulatory Affairs, QA/QC, Bioreactors & Cleanroom Dynamics**

**Planning Guide:**

**[https://catalog.shoreline.edu/preview\\_program.php?catoid=6&poid=1684&returnto=672](https://catalog.shoreline.edu/preview_program.php?catoid=6&poid=1684&returnto=672)**

**For more information: [biomanufacturing@shoreline.edu](mailto:biomanufacturing@shoreline.edu)**

## High School Biomanufacturing Internship Program

**Year-long program for high school students**

**No prior experience required, leave prepared for entry-level positions**

**Earn 9 college credits through Shoreline Community College**

**2022 – structure changing to include participation from other company sponsors & mentors**



# Funding

- Current Source – Career Connect Intermediary (WA State)
- Goals – Outline of Biomanufacturing Kit Curriculum
  - Purchase of equipment and supplies
  - Payment of Teacher collaborators
- Time Period – Ends at end of May, 2021
- Continue work with – Shoreline Community College BioHub/Immunotherapy (NSF)
- End Product – Biomanufacturing Kit

# Biomanufacturing Kit Planning

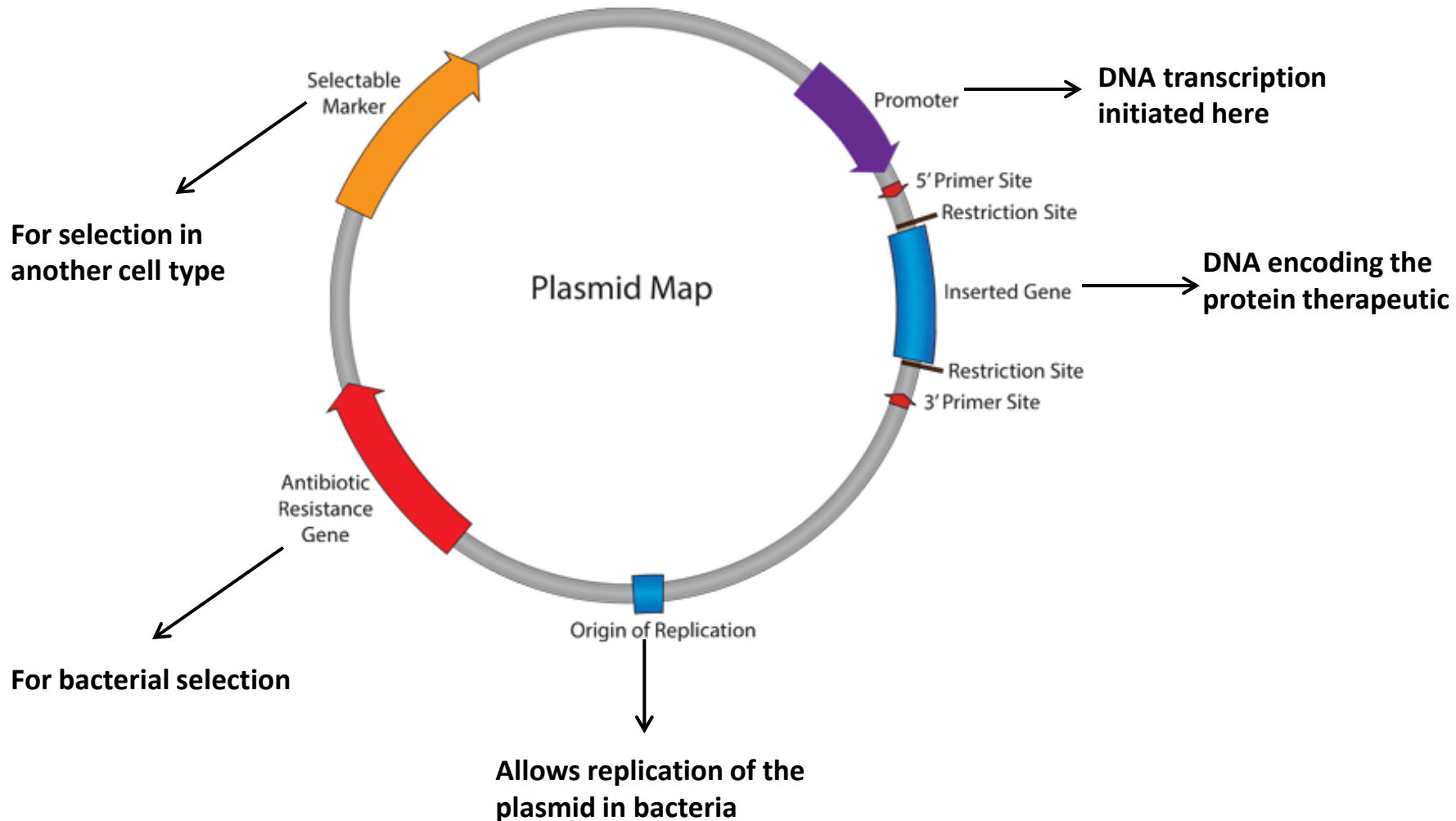
- What do teachers really need in terms of curriculum?
- How long would this lesson set be?
- What skills and concepts can it incorporate that are already taking place?
  - Build off of ABE labs 1-5 (production/purification of RFP)?
  - Build off BioRad GFP lab (production/purification of GFP)?
- What new Biomanufacturing skills and concepts can be added?
- Create a compelling 'scenario' – vaccines? Other?
- Lab activities must be things that can be done in a high school classroom/lab.
- Make sure the kit curriculum supports the current Biotech curriculum.
- Make sure the kit curriculum and activities reflect the industry standards.
  - Biotechnology Research and Development Pathway Standards
  - National Health Science Foundation Standards



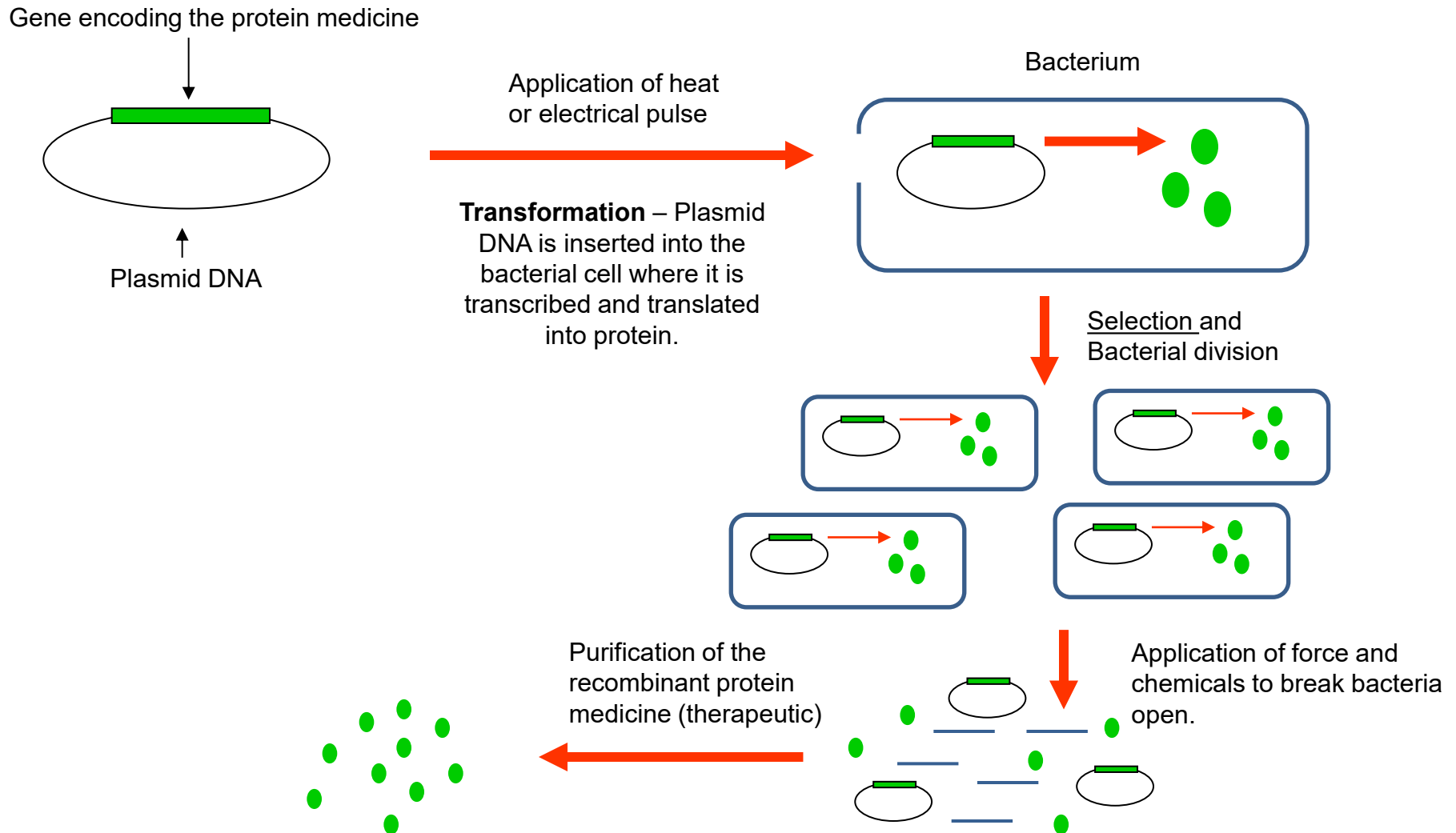
# STOP HERE

- I think the rest of the slides are important for another time.

# Plasmid Selection

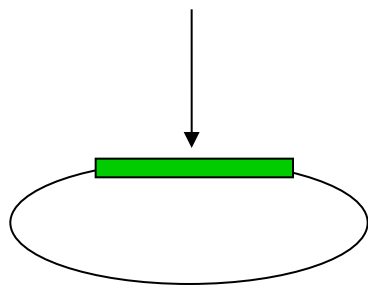


# Some Recombinant Proteins Can be Produced in Bacterial Cells



# Other Recombinant Proteins must be Produced in Mammalian Cells

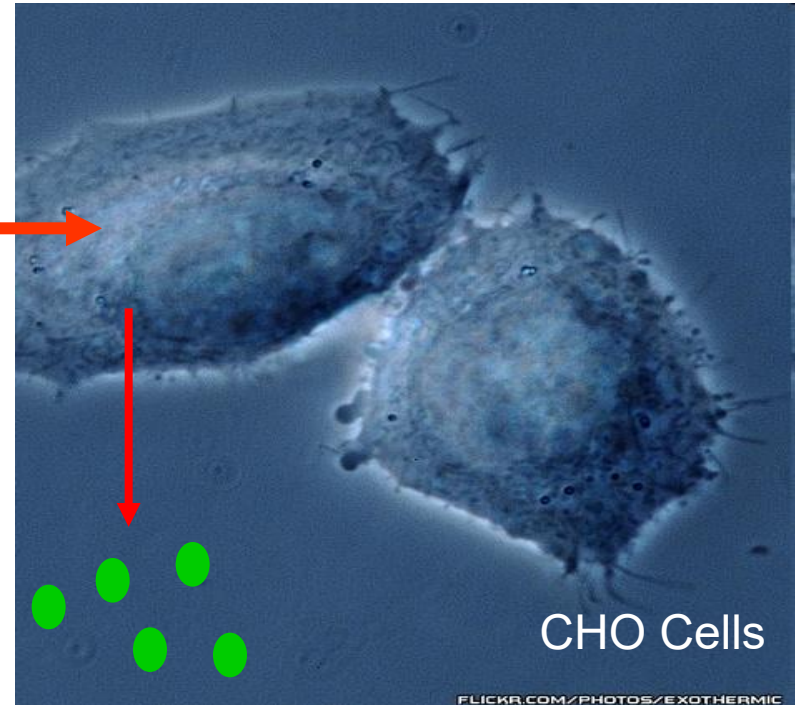
Gene encoding the protein medicine



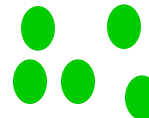
Plasmid DNA

**Transfection** – Plasmid DNA is inserted into cell and enters the nucleus where it can be transcribed and translated into protein.

The cell makes and secretes the recombinant protein medicine into the liquid the cell is growing in.

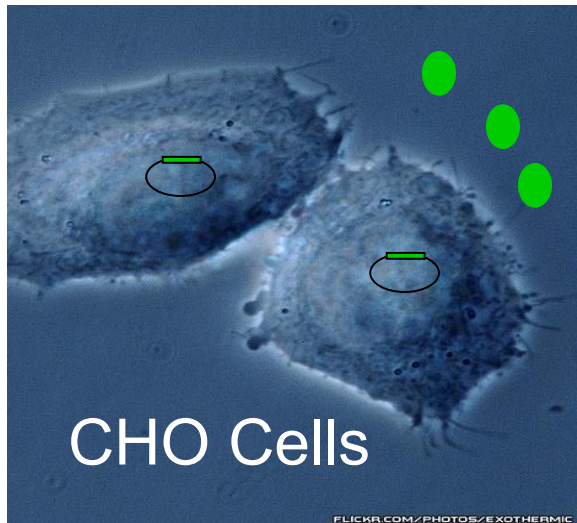
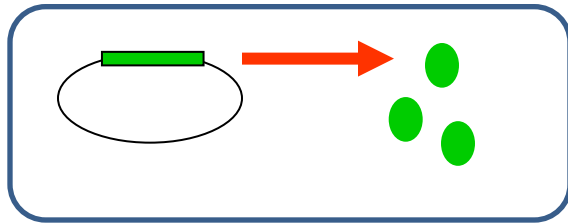


Purification of the protein medicine (therapeutic)

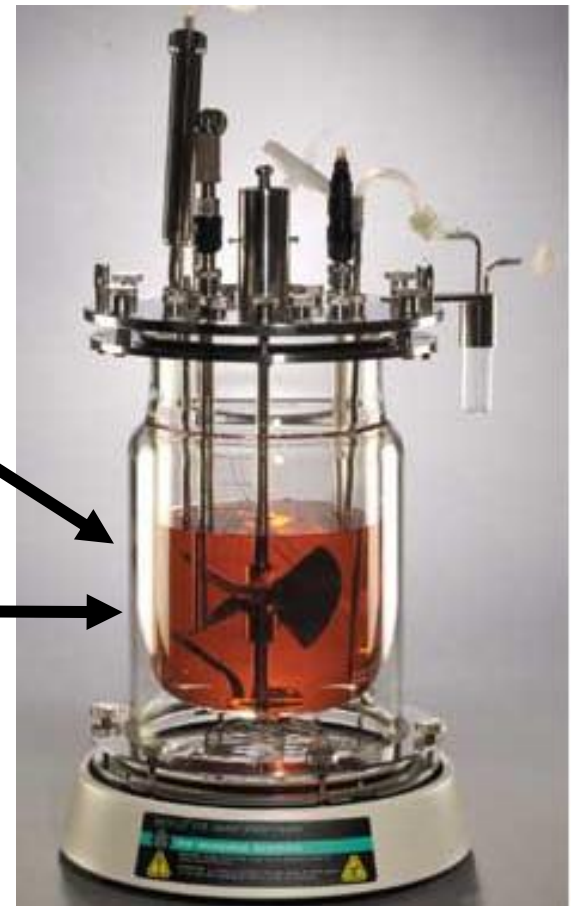


# The Cells Serve as Protein Factories

Bacterium

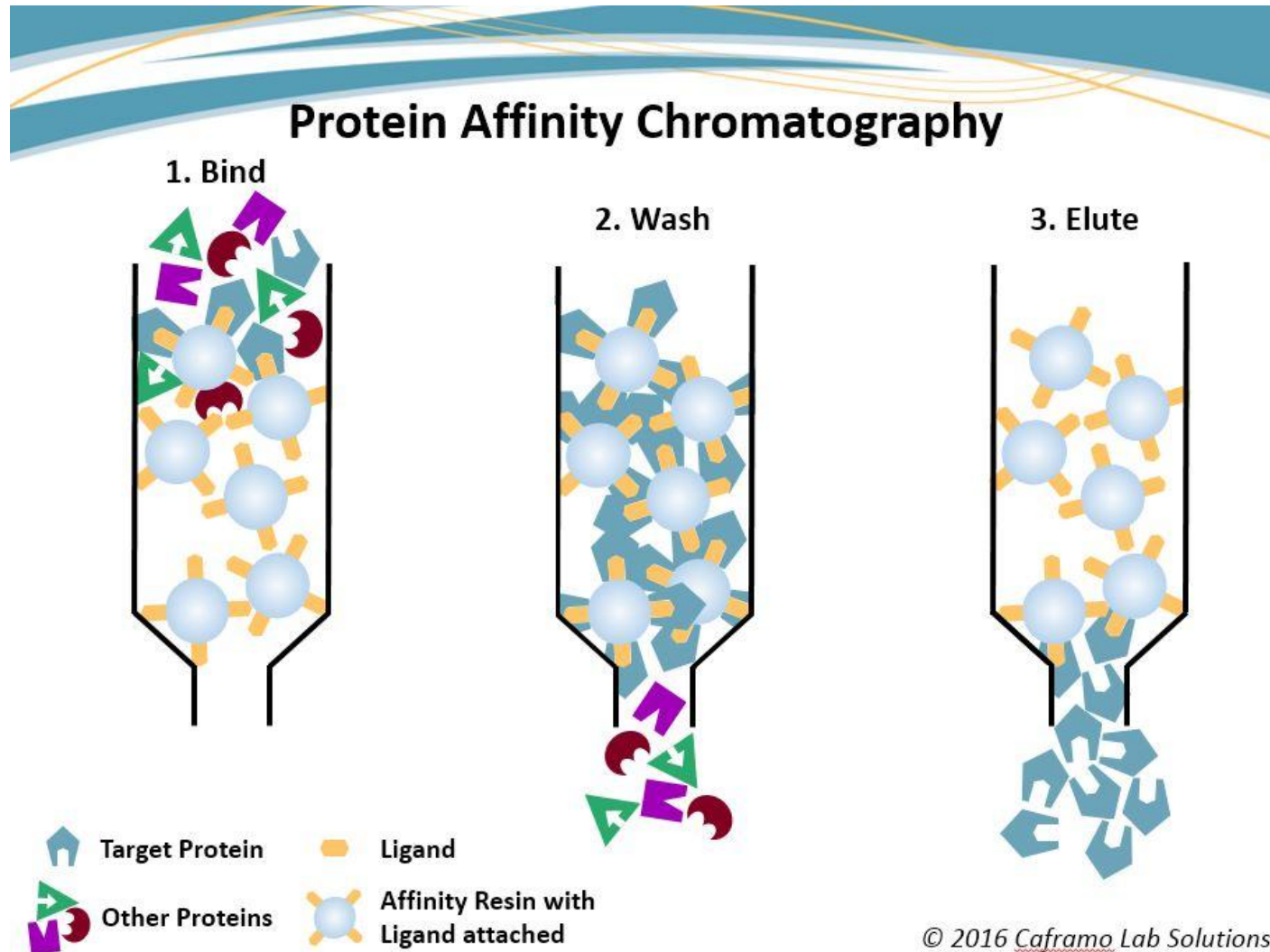


Fermenter (Bacteria/Yeast)



Bioreactor (Mammalian cells)

# Different Types of Resin Can be used to Purify Proteins with Different Biochemical Characteristics.



A **ligand** is a protein the target protein will bind to.

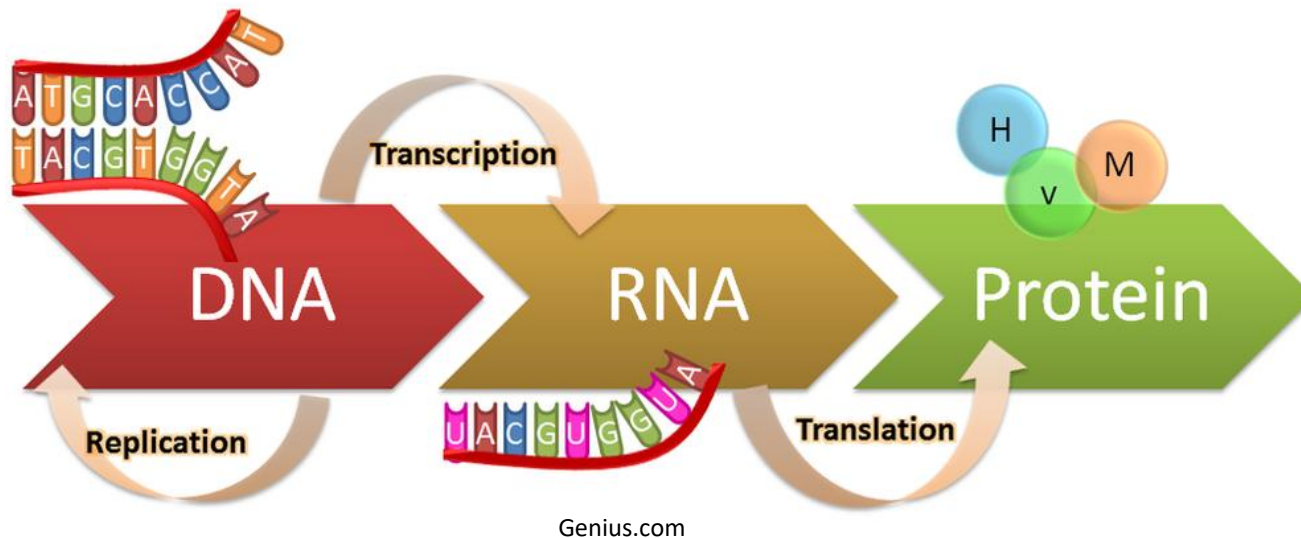
# Biomanufacturing a Quality Product



- Recombinant protein therapeutics that are being tested in clinical trials or sold for use in patients **MUST** be of the same quality and purity in **EVERY** batch.
- The system that ensures quality in all manufactured goods is called **Good Manufacturing Practice** or **GMP**.
- Good manufacturing practices are the practices required in order to conform to the guidelines recommended by agencies that control the authorization and licensing of the manufacture and sale of food and beverages, cosmetics, pharmaceutical products, dietary supplements, and medical devices.
- **GMP** covers all aspects of production from the starting materials, premises, and equipment to the training and personal hygiene of staff. Detailed written procedures are essential for each process that could affect the quality of the finished product. There must be systems to provide documented proof that correct procedures are consistently followed at each step in the manufacturing process - every time a product is made.

# Recombinant Protein Drugs Must Be Produced in Cells

- Biotech drugs/therapies are often proteins.
- Proteins are encoded by genes (DNA).
- Proteins must be produced in cells.

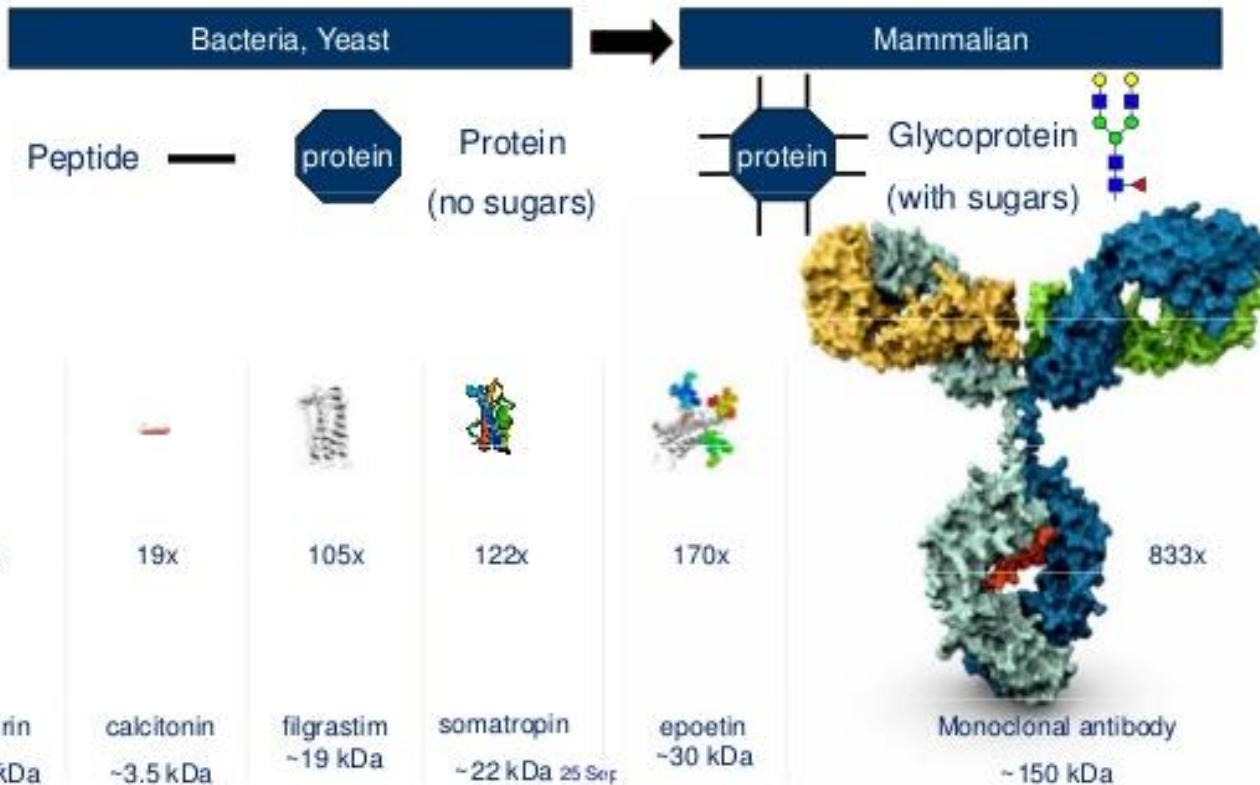


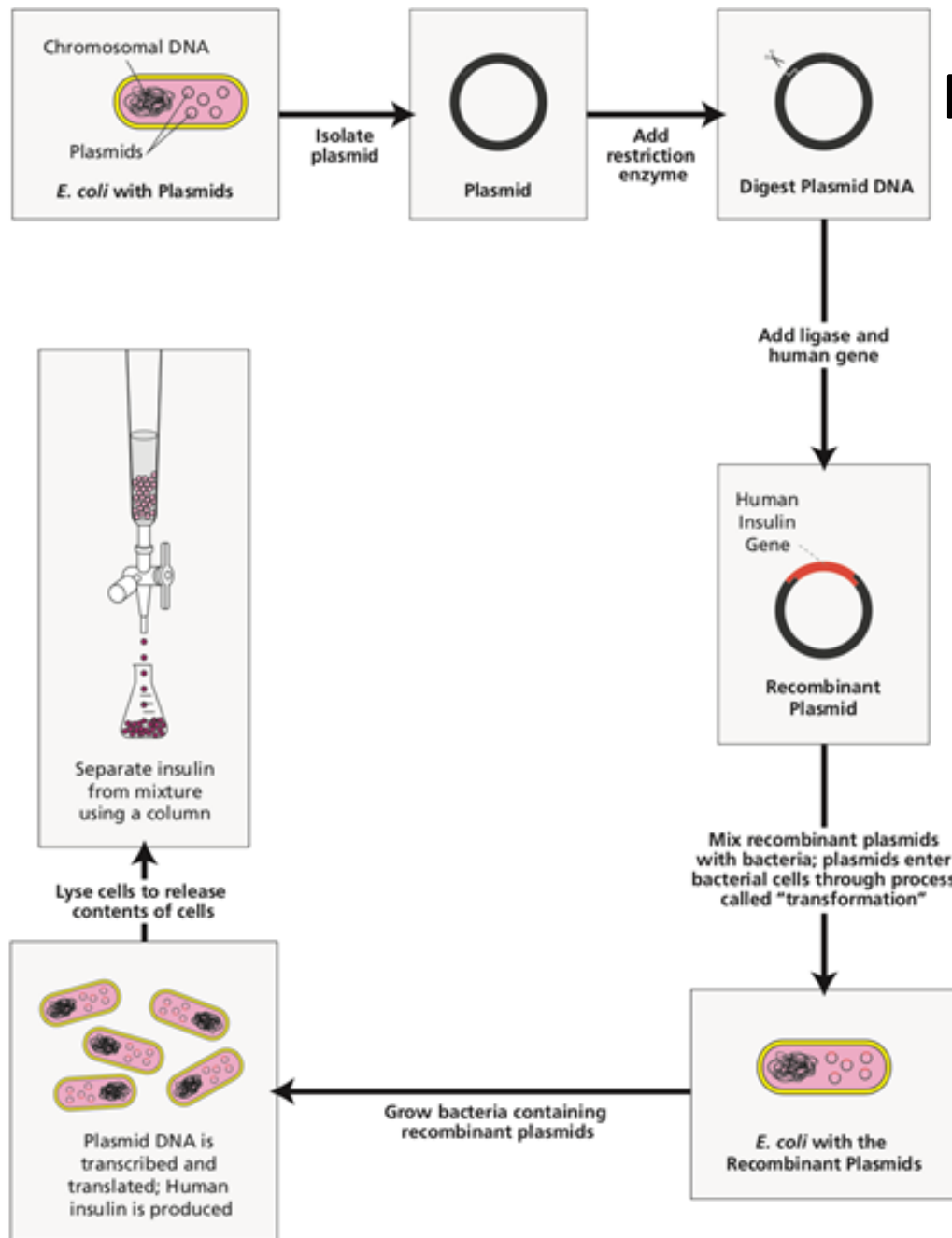
The central dogma



# Biotechnology vs. Pharmaceutical Drugs

***Biologics are more complex than small molecules...***

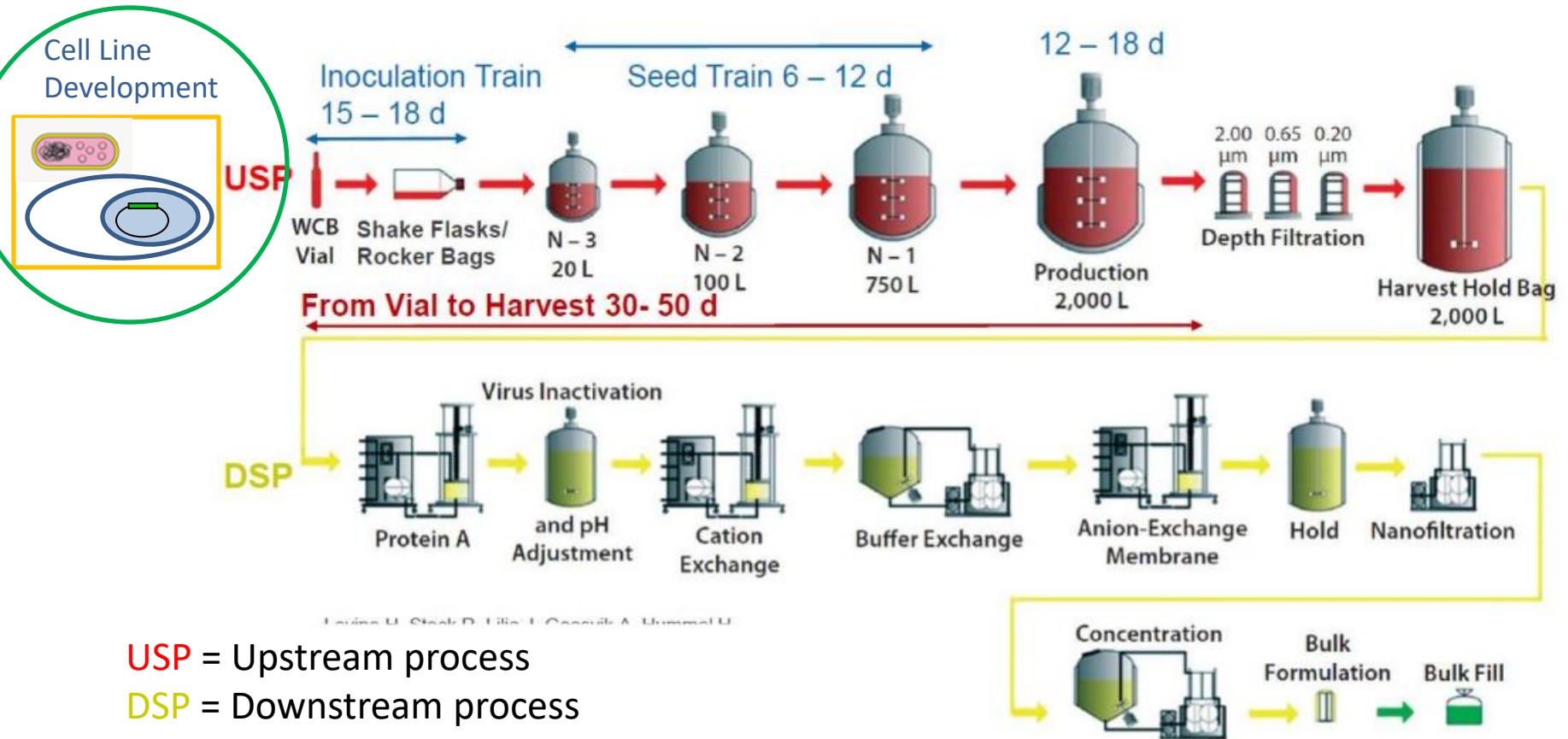




# Recombinant Insulin – One of the First Recombinant Protein Therapeutics

The plasmid is used to deliver foreign/different DNA into the cell – sort of like delivering a message containing instructions for how to build a protein.

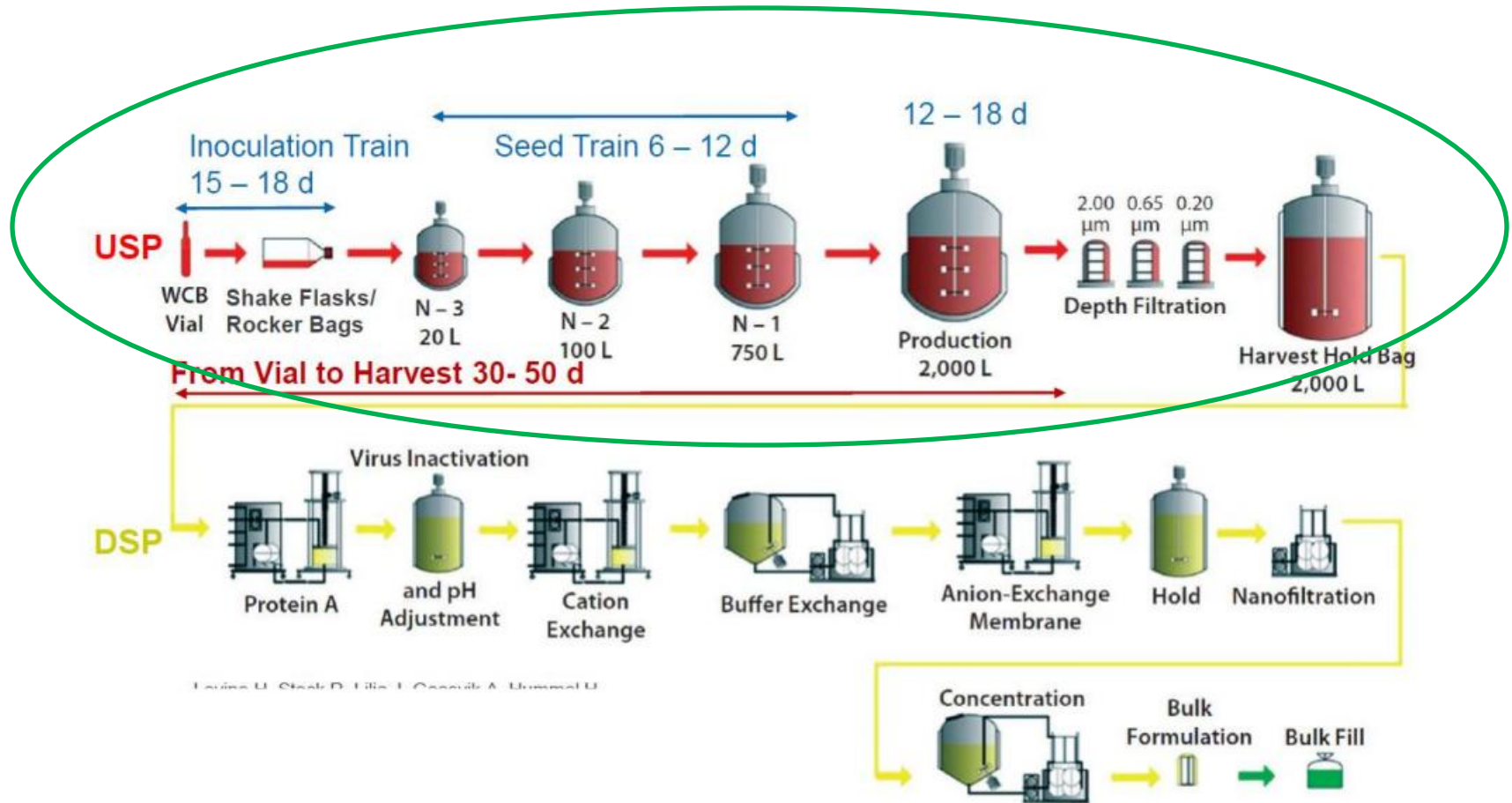
# Cell Line Development



Levine, HL. et al. Single-Use Technology and Modular Construction. Enabling Biopharmaceutical Facilities of the Future. Bioprocess Int. 11(4), p40-45, (2013).

All of the parts of these processes must be established for the production of each recombinant protein therapeutic. The act of establishing these processes is called Process Development.

# Upstream Process



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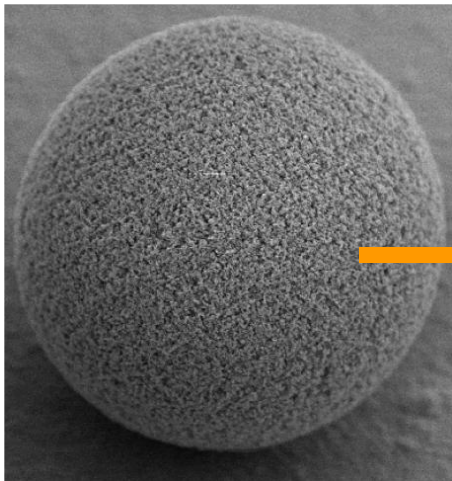
**DSP** = Downstream process



# Columns are Tools for Separating Proteins.



↑  
Resin bead



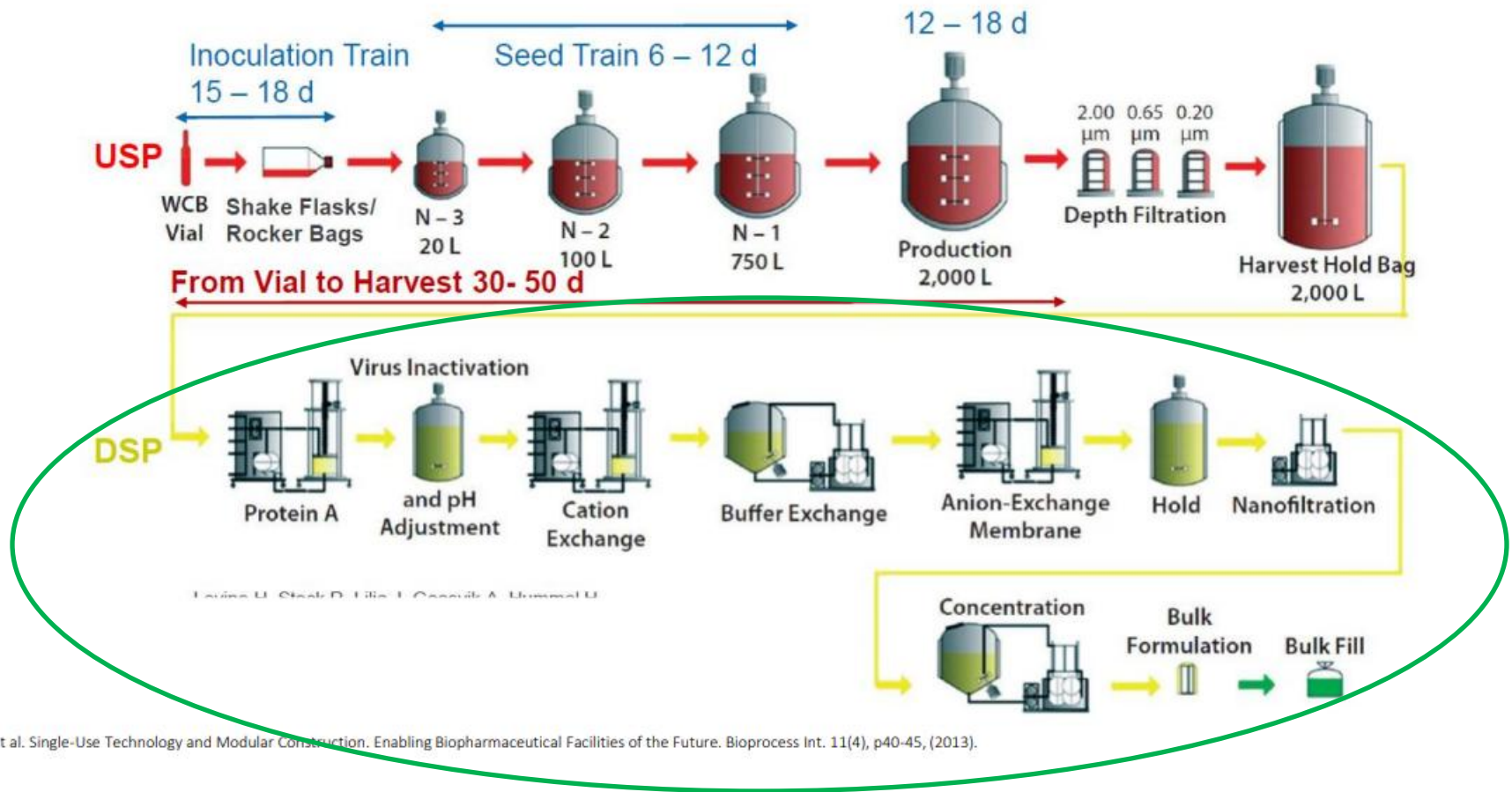
# Bioreactors Can Be Very Large

The bioreactor shown here can contain 2,000 liters of cells.

2,000 liters of cell media can contain billions of cells.



# Downstream Process



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# The Recombinant Protein Must Be Purified Away From Everything Else in the Cell Growth Mixture.



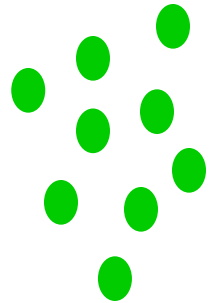
Cells or cell debris

Nutrients

Waste Products

Other Cellular Proteins

Recombinant Protein



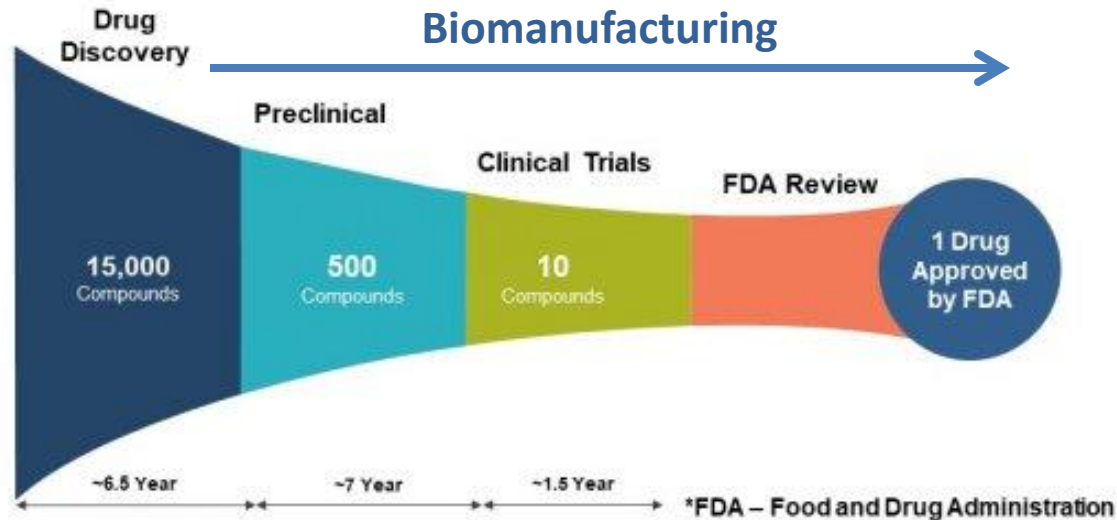
Purification of a Recombinant Protein Involves Understanding What is Unique about the Recombinant Protein.



# Biomanufacturing is Part of the Drug Discovery Process

Not every recombinant protein therapeutic candidate makes it through what is called the 'drug development'.

Out of thousands of candidates, maybe 1 or 2 recombinant protein therapeutics will make it through the entire process and become FDA approved.



# Formulation

Occurs after purification the quality and purity of the protein is determined.

The protein may also need to be concentrated.

Different chemical substances, including the active drug/therapeutic, are combined to produce a final medicinal product.



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# Bulk Fill

If the therapeutic meets specifications, it can be dispensed into vials or bottles.

This process is called 'bulk fill'.



# Relationship of GMP, QA and QC

