



What is Biotechnology ?

- Biotechnology is the culmination of over 8,000 years of human experience using living organisms and the process of fermentation to make useful products for mankind.



Biotechnology...

- First defined in 1917 by Karl Ereky ...
“All lines of work by which products are produced from raw materials with the aid of living things.”



...useful products such as

- BEER
- WINE
- CHEESE
- BREAD

And, oh yea, biopharmaceutical drugs



What is Biotechnology...

“ A combination of advances in our understanding of molecular and cell biology and human genetics, and how the human immune system fights disease.”



How Does Biotechnology work ?

“MAGIC!”

“No ... And it isn't voodoo either.”

“OK, so what is it?”



DNA

All living things are made up of cells that are programmed by the same basic genetic material...DNA.





Genetic Material

The nucleotides of each DNA unit pair up into strands that twist together...

You guessed it, the world famous **DOUBLE HELIX**...and while every cell in an individual organism has the same DNA units...



The different segments of DNA coding tell individual cells how to differentiate (or what to do) or what to produce (proteins, enzymes,... that kind of stuff).





Okay, So How Does It Work?

- Biotechnologists (the folks in the white coats) use recombinant DNA technology to transplant and/or combine genetic information from one organism to another.

Yes, this is genetic engineering. And it works because all living things are made up of the same type of genetic material.



What Are Biologics?

Biological therapeutic products...

Biologics generally encompass any protein, virus, vaccine, blood product, or gene transfer product.





Therapeutic Proteins

- Proteins that are produced in biological organisms or in recombinant DNA technology.
- These proteins include monoclonal antibodies, cytokines and growth factors.



Biologics vs. Small Molecule Drugs

- Small molecule therapeutics compromise most traditional pharmaceutical drugs.
- Developed via chemical synthesis.
- Taken orally.
- Absorbed through the intestine walls into the bloodstream.
- Usually designed to block targets.



Biologics vs. Small Molecule Drugs

- Biologics are very fragile molecules that easily degrade in the digestive system.
- Injected into bloodstream.
- Designed to interact with molecules outside the cell.
- Typically more difficult and costly to manufacture.



OK, So Why Biologics ?

- Protein therapeutics can more effectively interact with a large number of target receptors; small molecule drugs do not.
- This interaction is more effective in triggering the desired biological response (in layman's terms, the biologics are more effective at “turning on the switch” to bring about the desired result).

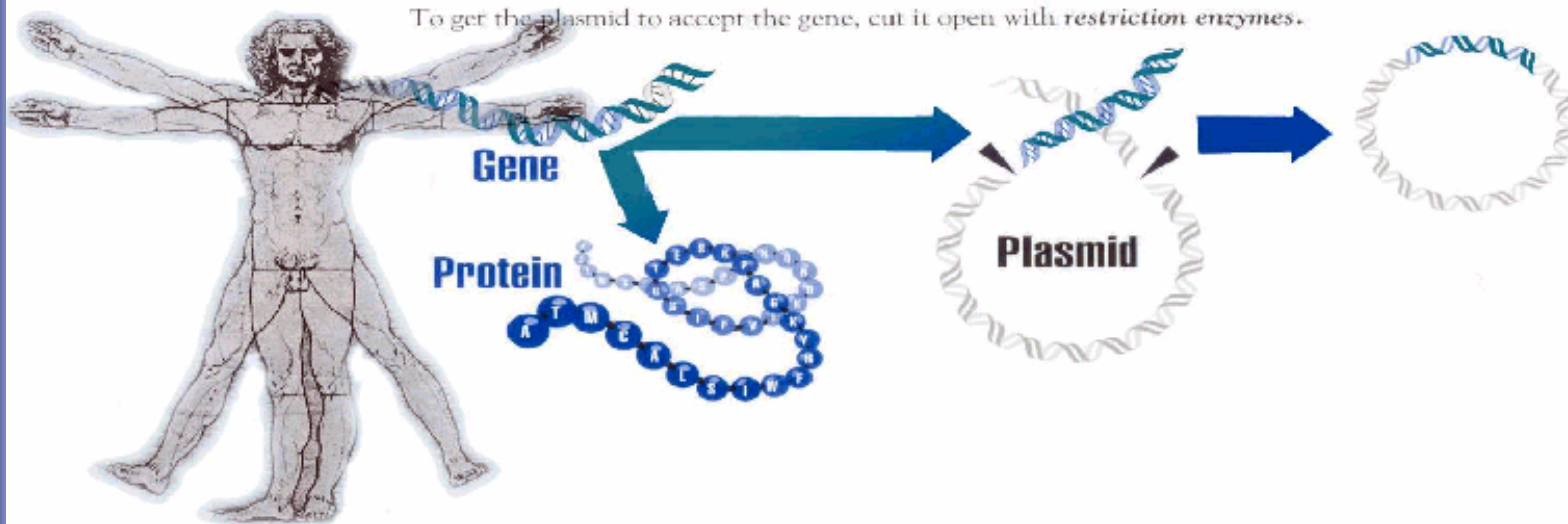
Biotech Basics - Recombinant DNA

Recombinant DNA

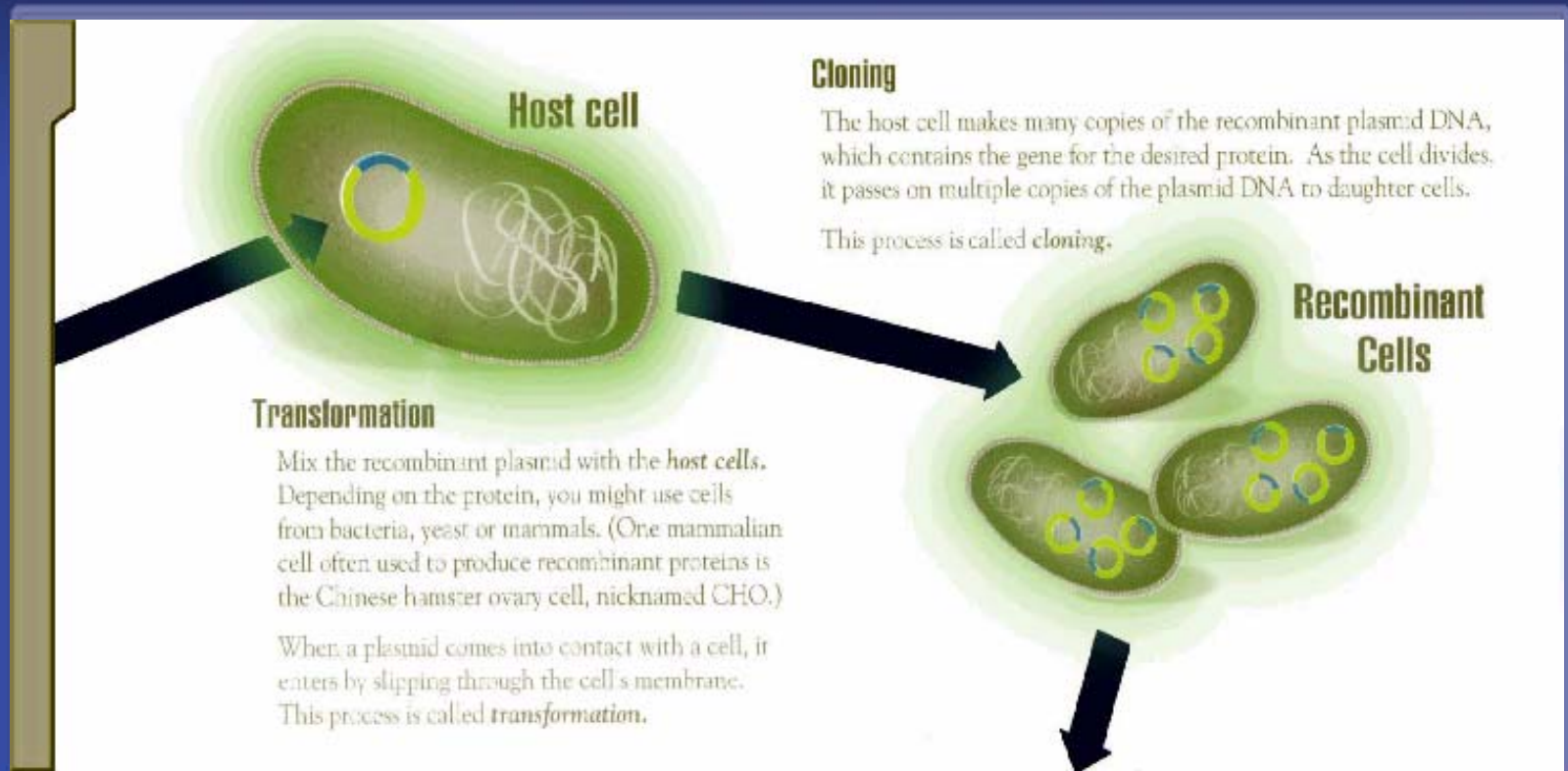
A *gene*[®] is one small piece of all the *DNA* in the nucleus of living cells. It contains genetic instructions used to direct a cell to make a particular *protein*.

To make a protein pharmaceutical by genetic engineering, isolate the gene for the desired protein from human cells and insert it into a "DNA transporter" called a *plasmid*.

To get the plasmid to accept the gene, cut it open with *restriction enzymes*.



Biotech Basics - Transformation



Biotech Basics

Development & Testing

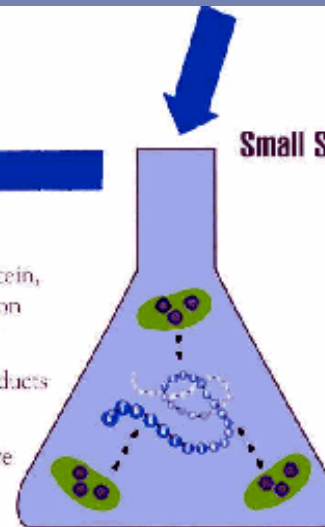
Assay Development & Animal Testing

After the cells have had time to grow and produce the desired protein, harvest the protein from the cell or the growth media, depending on whether the protein is intracellular or secreted from the cell.

Purify the recombinant protein away from the cellular protein products and/or growth media using a variety of separation techniques.

Develop and use several **biological and chemical assays** to measure the activity of the recombinant protein and to confirm that it is identical to the desired protein from the human source.

Test the protein in animals to make sure it has the desired action and is not toxic.

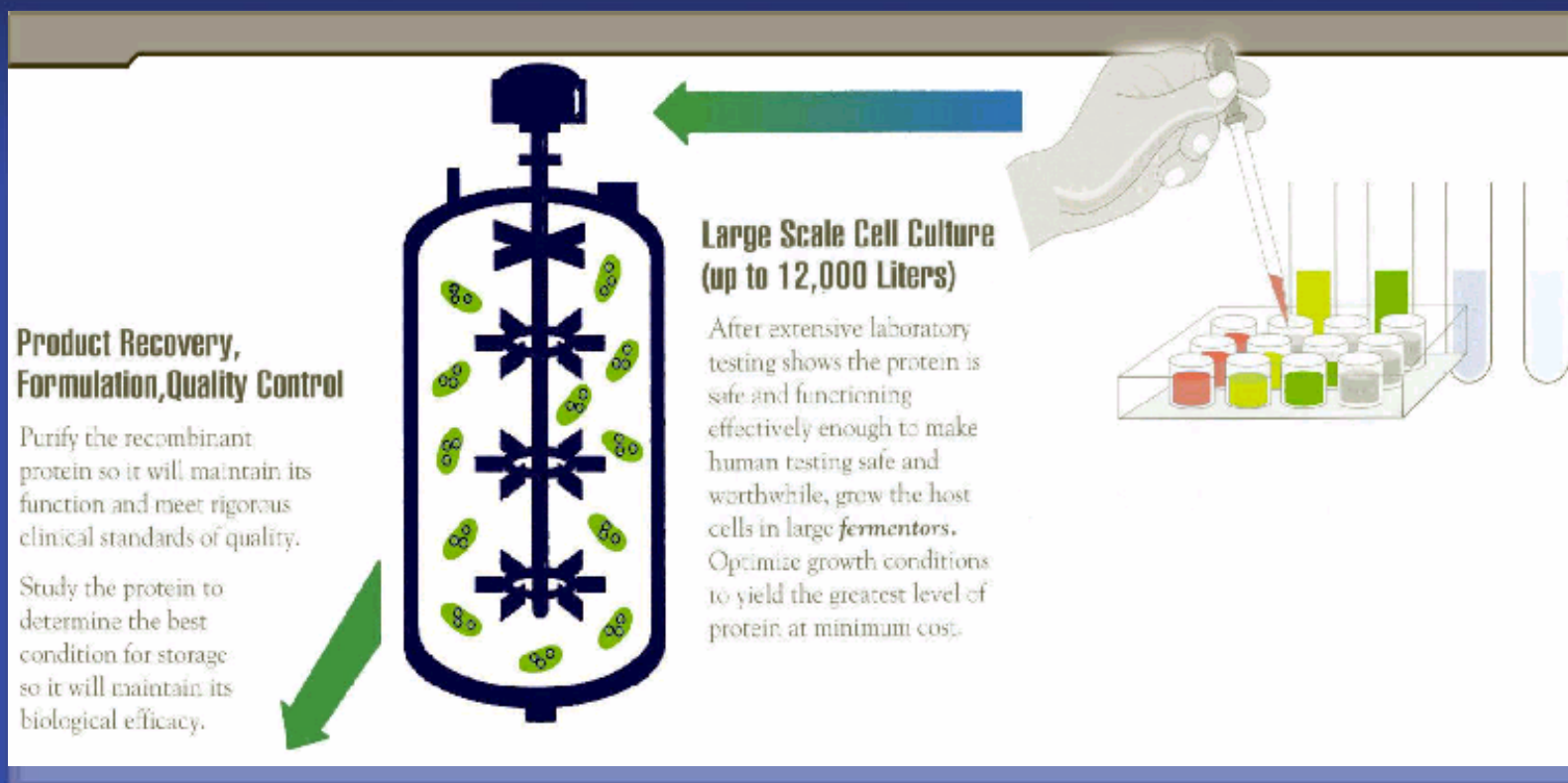


Small Scale Cell Culture (1 Liter)

Grow the host cells in flasks containing a nutritious growth medium.

Using the genetic instructions provided by the plasmid, the dividing cells make the recombinant protein along with the host cells' normal cellular proteins.

Biotech Basics - Recovery





The Basic Process Elements

- Bioanalysis
- Fermentation
- Separation
- Purification
- Filling



Bioanalysis

Nearly every process conducted in a biopharm company requires analytical methods to “back it up.”





Analytical Methods

- Back up regulatory submissions.
- Support preclinical and clinical studies.
- Monitor environmental conditions during manufacturing.
- Monitor quality of the manufacturing process.



Fermentation

The process by which living cells obtain energy through the breakdown of glucose and other molecules.

(That 8,000 year old process, remember?)





Cell Culture

Cells taken from living organisms
and grown under controlled
conditions.





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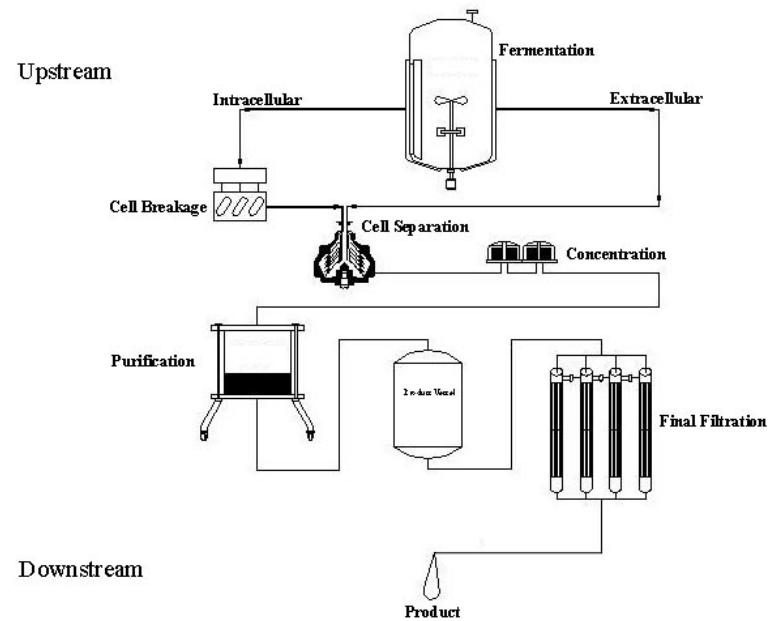




Fermentation is part of what is known as “upstream processing,” literally engineering and growing the cell line to be used.



Biotech Process Steps





Fermentation or Cell Culture...

- Fermentation refers to the large scale cultivation of microorganisms.
- Cell culture is a specific kind of fermentation that applies similar techniques for growing cells from plants and animals.



Bioreactor vs. Fermentor

- Bioreactors are used to cultivate animal cells.
- Fermentors are used to cultivate microbes.





Once fermentation is complete, the desired product must be recovered, separated out, and purified.





Recovery: the separation of crude product from microbial mass and other solids and liquid medium, to prepare it for purification.





Product recovery usually
requires cell disruption.





Cell Disruption

- Nonmechanical
 - Freezing
 - Detergents
 - Enzymes
- High pressure
 - Centrifugation
- Homogenization
- Mechanical grinding





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Separation

- Extraction & Precipitation
- Filtration
 - Microfiltration
 - Ultrafiltration





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Purification

- Chromatography
 - Gel filtration
 - Ion exchange
 - Hydrophobic interaction (HIC)
 - Affinity



IsoPak Group and Slurry Transfer Skid

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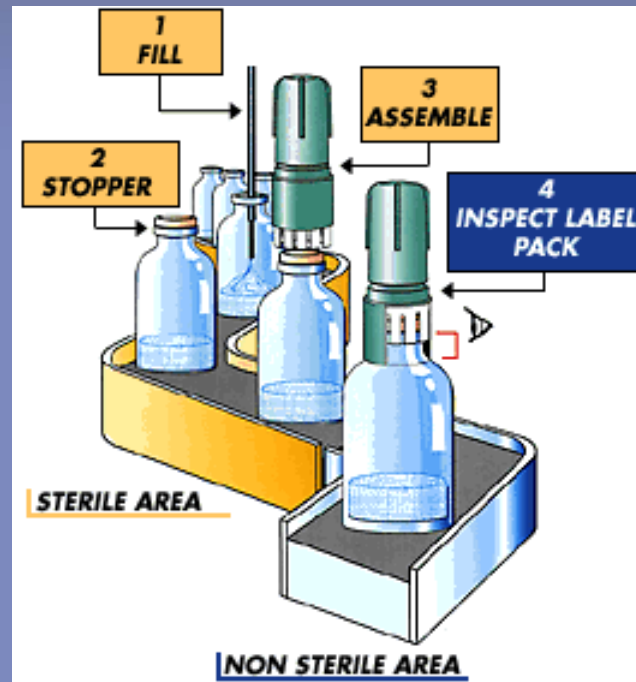
Filling

- Filling is the process of putting the drug product into a sterile container.



Two General Categories of Filling

- Bulk
- Final



Bulk Filling

Bulk filling is defined as the placement of larger quantities (5L – 100L) of product into containers for shipment/storage.



Final Filling

- Final filling is defined as the placement of the sterile drug product into its final container/closure system. These include:
 - Vials
 - Ampules
 - Syringes
 - Dental Cartridges





Biotechnology has a language all its own.....

Absorption: Removing a particular antibody or antigen from a sample (from serum, for example) by adding the corresponding antigen or antibody.

Adsorption: Nonspecific adherence of substances in solution or suspension to cells or other particulate matter.

Adventitious Agents: Acquired, sporadic, accidental contaminants.

Aerobe: An aerobic organism is one that grows in the presence of oxygen. A strict aerobe grows only under such a condition.

Aggregate: A clustered mass of individual cells – solid, fluffy or palletized – that can clog the pores of filters or other fermentation apparatus.

Amino Acids: A class of 20 hydrocarbon molecules that combine to form proteins in living things.

Anaerobe: An anaerobic organism grows in the presence of air or oxygen. Some anaerobic organisms are killed by brief exposure to oxygen, whereas oxygen may just retard or stop the growth of others.



And in closing, from the the immortal words of Frank James (famous wine cooler manufacturer):

“We thank you for your support.....”

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