SNS COLLEGE OF ENGINEERING

(AN AUTONOMOUS INSTITUTION)

COIMBATORE-107

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19GET277 / Biology For Engineers

IV YEAR / VII SEMESTER

UNIT-V: BIOLOGY AND ITS INDUSTRIAL APPLICATION

BIO PHARMING

Presentation Outline

- What is biopharming?
- History
- Strategies for Biopharming
- Why use plants?
- Industrial importance
- Risks and Concerns
- Current and evolving regulation
- What are the risks and concerns?
- Current challenges
- Future directions

What is biopharming?

- The use of agricultural plants for the *production of useful molecules* for non food, feed or fiber applications. (also called molecular farming, pharming, or biopharming)

- Biopharming is different because the plants are *genetically engineered* (GE) to produce the molecules we want them to.(Plant or animal)

- Biopharming started about 20 years ago with the promise to produce therapuetic molecules for a fraction of their current costs
- Some therapeutic molecules are very expensive to produce (e.g. glucerobrosidase enzyme)

How will biopharming do that?

Biopharming aims to replace very expensive bioreactors (upstream process) by the pharmaceutical industry used for producing therapeutic molecules

- These 'expensive' molecules can now be expressed in
plants through the insertion of the genes that express the proteins

- Biopharming may also be cheaper in the process of extracting (downstream process) the desired molecules

History

- 1990 – Human serum albumin produced in genetically engineered tobacco and potato plants
- In development
  - Recombinant subunit vaccines against Norwalk and rabies viruses
  - Recombinant monoclonal antibodies against tooth decay-causing bacteria

Plant Products

1. Plant-derived pharmaceuticals (non-GE)

   Over 120 pharmaceutical products currently in use are derived from plants. Mainly from tropical forest species (e.g. Taxol from Yew trees)

2. Plant-made pharmaceuticals (PMPs) and industrial products (PMIP) (GE)

Industrial products

- proteins
- enzymes
- modified starches
- fats
- oils
- waxes
- plastics

Pharmaceuticals

- recombinant human proteins
- therapeutic proteins and pharmaceutical intermediates
- antibodies (plantibodies)
- Vaccines

Neutraceuticals

Why biopharming?

Heralded by biotech industry and associated scientists as:

- Moneymaker (get some of those pharma $)
- Overcoming public resistance to GM crops
  - Belief that resistance is due to 'no consumer benefit' of 'first-generation' GM crops
  - Belief that 'cheaper' drug production will be seen as consumer benefit

Strategies for Biopharming

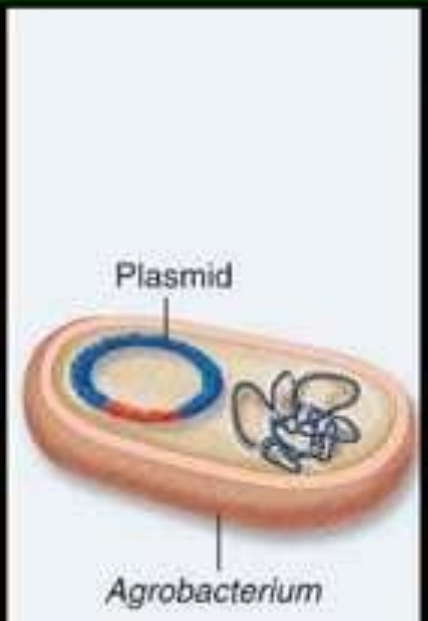
1. Plant gene expression strategies

- Transient transformation
  - adv. – quick and easy production
  - disadv. – small amount of product, processing problems

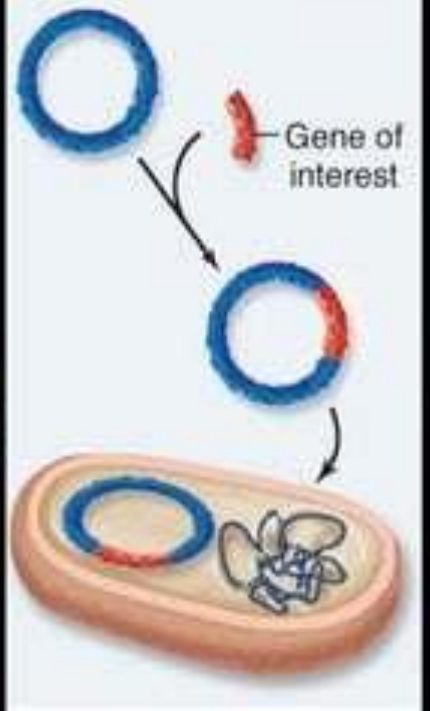
- Stable transformation
  - adv. – use for producing large quantities of protein, stability and storage
  - disadv – gene flow - outcrossing w/native species

- Chloroplast transformation
  - adv. – reduce gene flow through pollen
  - disadv. – protein not stable for long periods of time therefore complications extraction/processing times

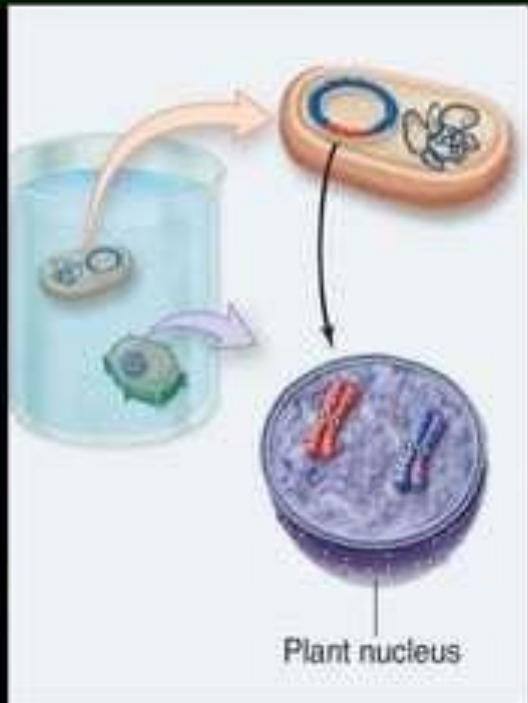
Agrobacterium mediated gene transformation



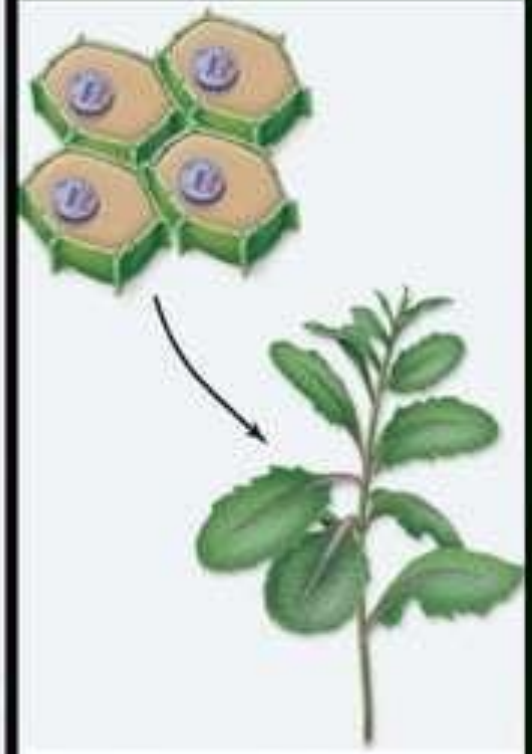
1. Plasmid is removed and cut open with restriction endonuclease.



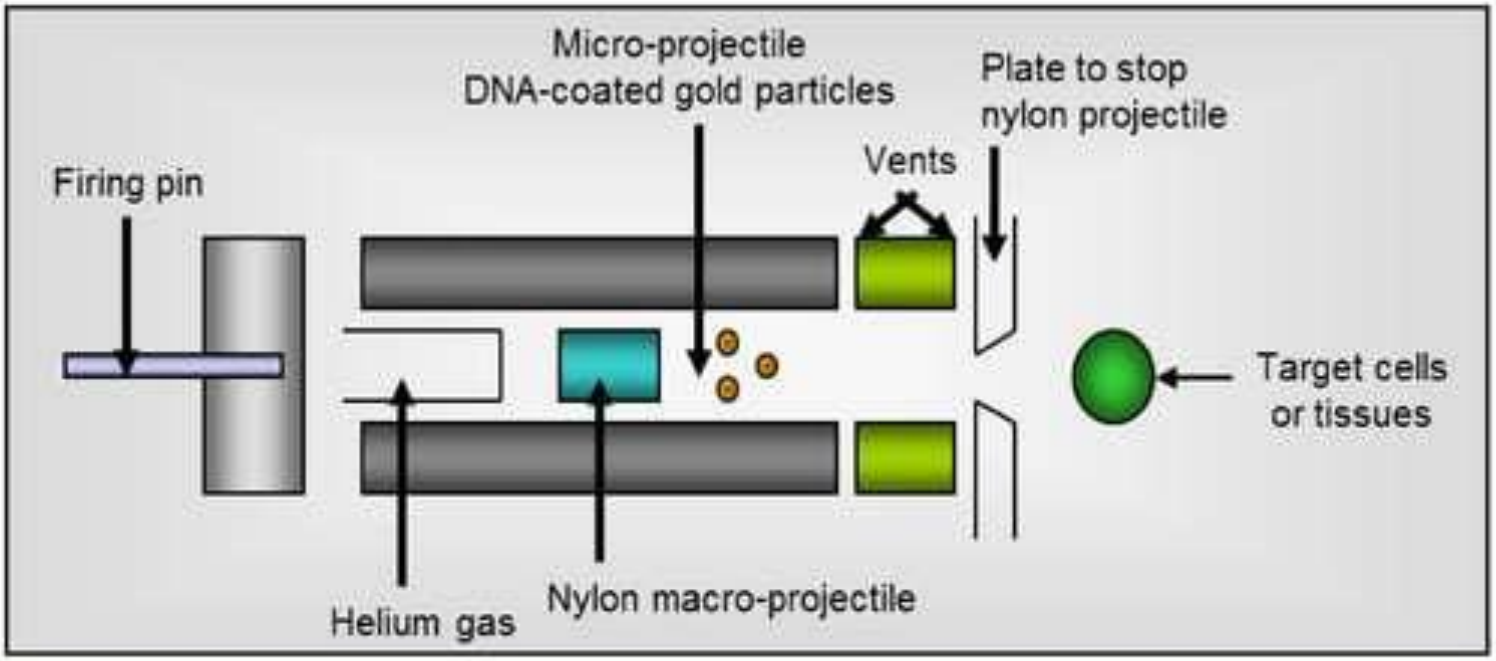
2. A gene of interest is isolated from the DNA of another organism and inserted into the plasmid. The plasmid is put back into the *Agrobacterium*.

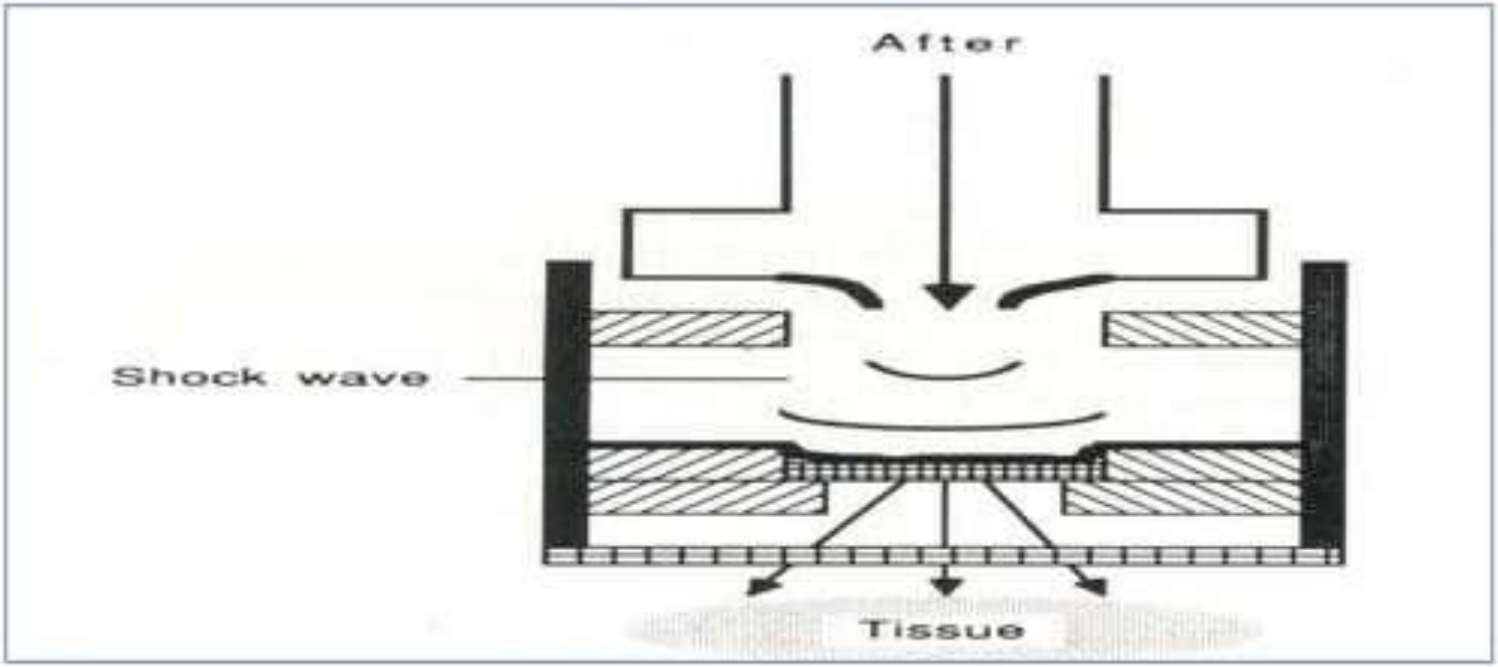


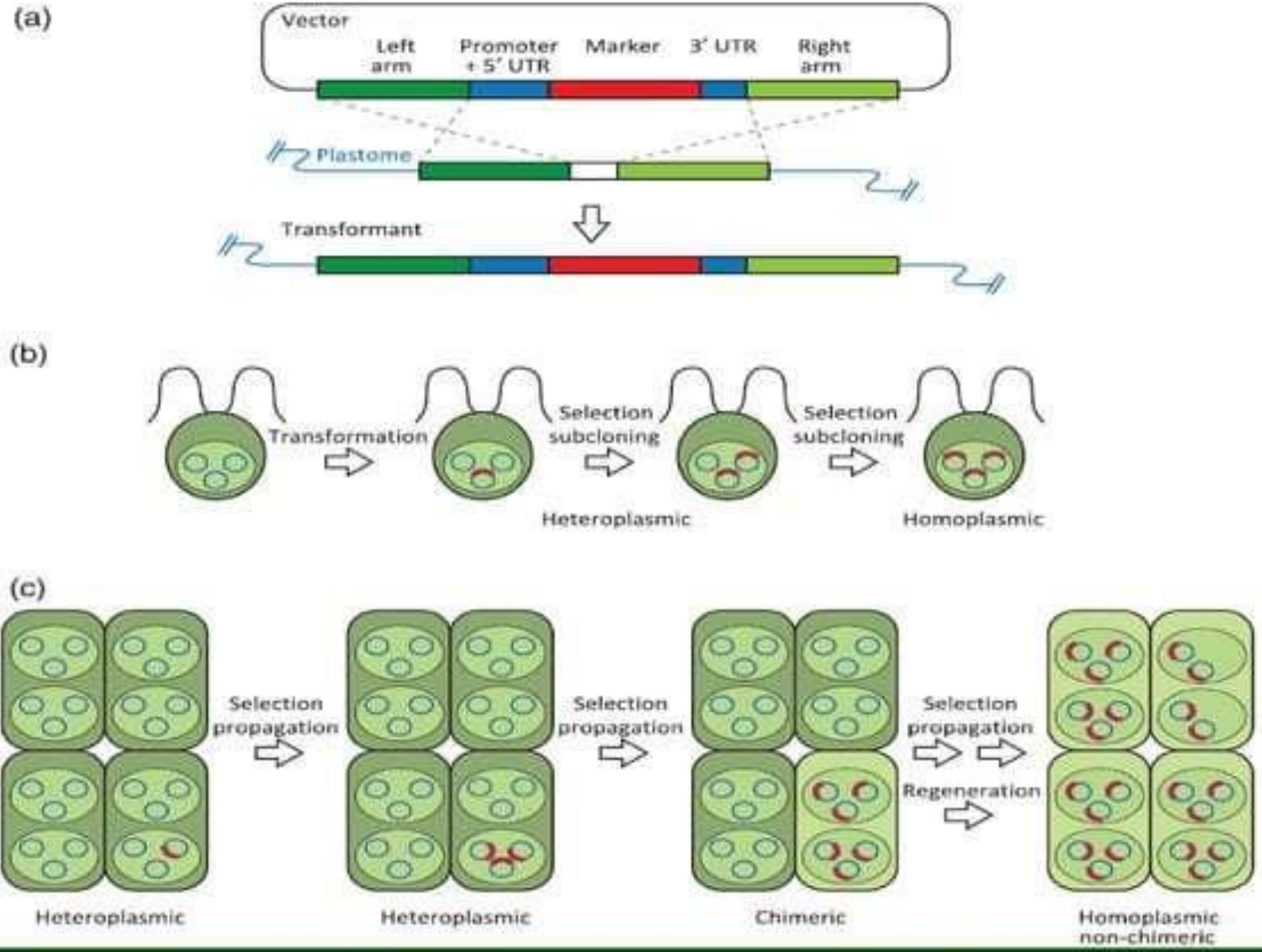
. When used to infect plant cells, *Agrobacterium* duplicates part of the plasmid and transfers the new gene into a chromosome of the plant cell.



4. The plant cell divides, and each daughter cell receives the new gene. These cultured cells can be used to grow a new plant with the introduced gene.


Micro-projectile
DNA-coated gold particles
Plate to stop
nylon projectile
Vents
Firing pin
Target cells
or tissues
Helium gas
Nylon macro-projectile


After
Shock wave
Tissue



Anil Day[1] and Michel Goldschmidt-Clermont

Strategies for Biopharming

1. Plant gene expression strategies
2. Location of transgene expression

Protein quantity and preservation

- Whole plant
  - adv. - an obtain large amts of protein
  - disadv. - problems w/preservation
  - examples - tobacco, alfalfa, duckweed
- Target specific tissues (e.g. seed, root)
  - adv. - high amts of protein in seed/root, long-term storage capability.
  - examples: soy, corn, rice, barley

Strategies for Biopharming

1. Plant gene expression system
2. Location of trans-gene expression
3. Selection of plant species and characteristics

    - Mode of reproduction – self/outcrossing
    - Yield, harvest, production, processing

Why use plants?

Advantages

Cost reduction

- scalability (e.g. Enbrel®)
- low/no inputs
- low capital cost

Stability

- storage

Safety

- eukaroytic production system
- free of animal viruses (e.g. BSE)

Disadvantages

Environment contamination

- gene flow
- wildlife exposure

Food supply contamination

- mistaken/intentional mixing w/human food

Health safety concerns

- Variable, case-specific

Industrial products on the market

Avidin by Sigma

- transgenic corn
- traditionally isolated from chicken egg whites
- used in medical diagnostics

GUS (β-glycuronidase) by Sigma

- transgenic corn
- traditionally isolated from bacterial sources (*E.Coli*)
- used as visual marker in research labs

Trypsin by Sigma

- transgenic corn
- traditionally isolated from bovine pancreas
- variety of applications, including biopharmaceutical processing
- first large scale transgenic plant product
- Worldwide market = US$280 million in 2014 (Promo pharma

Industrial products close to market

Product	Company or companies	Use
Trypsin[a]	ProdiGene	Pharmaceutical intermediate
GUS	ProdiGene	Diagnostic reagent
Avidin[a]	ProdiGene	Immunological reagent
Aprotinin[a]	ProdiGene, Large Scale Biology	Reduce SIR and bleeding, promote wound closure, mammalian cell culture
Collagen[a]	ProdiGene, Medicago, Meristem Therapeutics	Gel caps, skin sealant, scar treatment (see text)
Lipase[a]	Meristem Therapeutics	Exocrine pancreatic insufficiency, steatorrhea, cystic fibrosis
Lactoferrin[a]	Ventria, Meristem Therapeutics	Natural defense protein against infections, iron repository
Lysozyme[a]	Ventria	Anti-viral, anti-bacterial, anti-fungal
Brazzein	ProdiGene	Natural protein sweetener
TGEV edible vaccine	ProdiGene	TGEV vaccine in swine
α-Caries MAb	Planet Biotechnology	Prevention of dental caries
α-Herpes MAb	Epicyte Pharmaceutical	Prevention of herpes transmission

[a] Currently obtained from animal sources