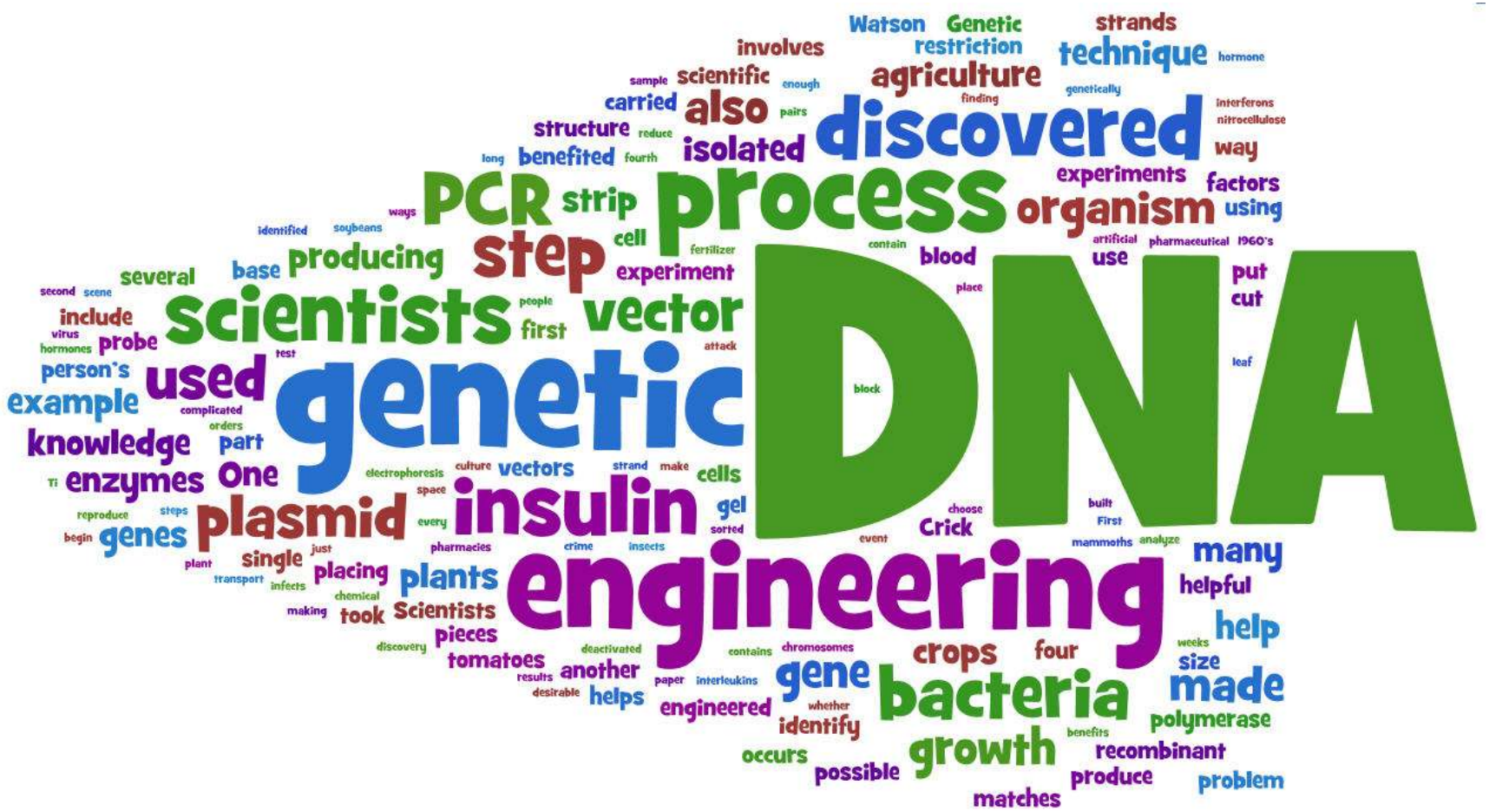
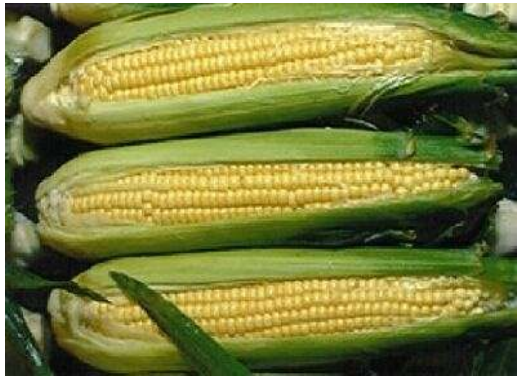
History of Genetic Engineering



Genetic Engineering

- **Manipulating an organism's genome to**
  - **alter microbes, plants, and animals for our benefit**
  - **correct genetic defects in humans**

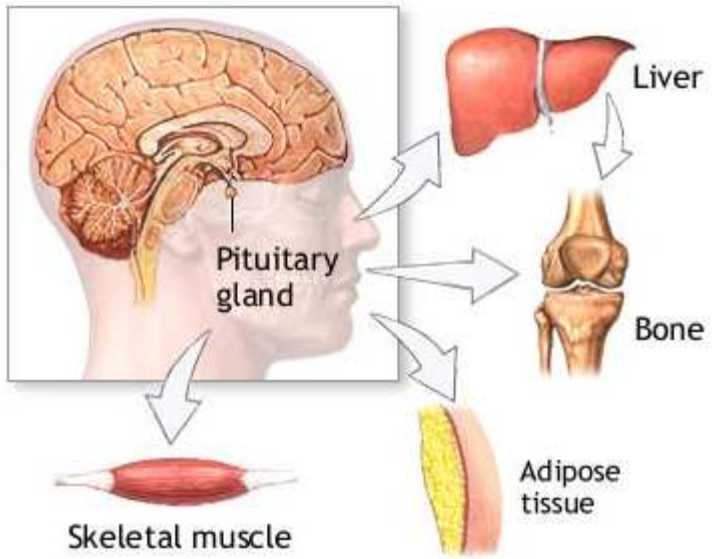
Genetically modified plants

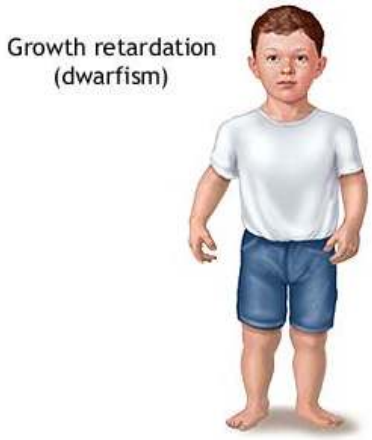


Use of recombinant plasmids in agriculture

- **plants with genetically desirable traits**
  - **herbicide or pesticide resistant corn & soybean**
    - **Decreases chemical insecticide use**
    - **Increases production**
  - **Cold and salinity tolerance**
  - **Instect resistance brinjal**

The luciferase gene from a firefly is transformed into tobacco plant using the Ti plasmid. Watering the plant with a solution of luciferin (the substrate for firefly luciferase) results in the generation of light by all plant tissues.





- **Insulin**
  - Hormone required to properly process sugars and fats
  - Treat diabetes
  - Now easily produced by bacteria

- **Growth hormone deficiency**
  - Faulty pituitary and regulation
  - Had to rely on cadaver source
  - Now easily produced by bacteria

Farm Animals and "Pharm" Animals

- **Trangenic plants and animals have genes from other organisms.**
- These transgenic sheep carry a gene for **a human blood protein**
  - This protein may help in the treatment of cystic fibrosis

Transgenic animals

History of genetic engineering

1917 Karl Ereky coined the term ‘Biotechnology’

1940 A Jost coins the term “Genetic Engineering”

1970 First restriction endonuclease isolated

Werner Arber

Hamilton O Smith

Daniel Nathans

The Nobel Prize in Medicine 1978 was jointly awarded to Werner Arber, Daniel Nathans and Hamilton O Smith for the discovery of restriction enzymes and their application to problems of molecular genetics in 1970

Recombinant DNA technology was developed by

Stanley N. Cohen , who received the Nobel Prize in Medicine in 1986 for his work on discoveries of growth factors.

Herbert Boyer , who constructed the first recombinant DNA using bacterial DNA and plasmids.

in 1973

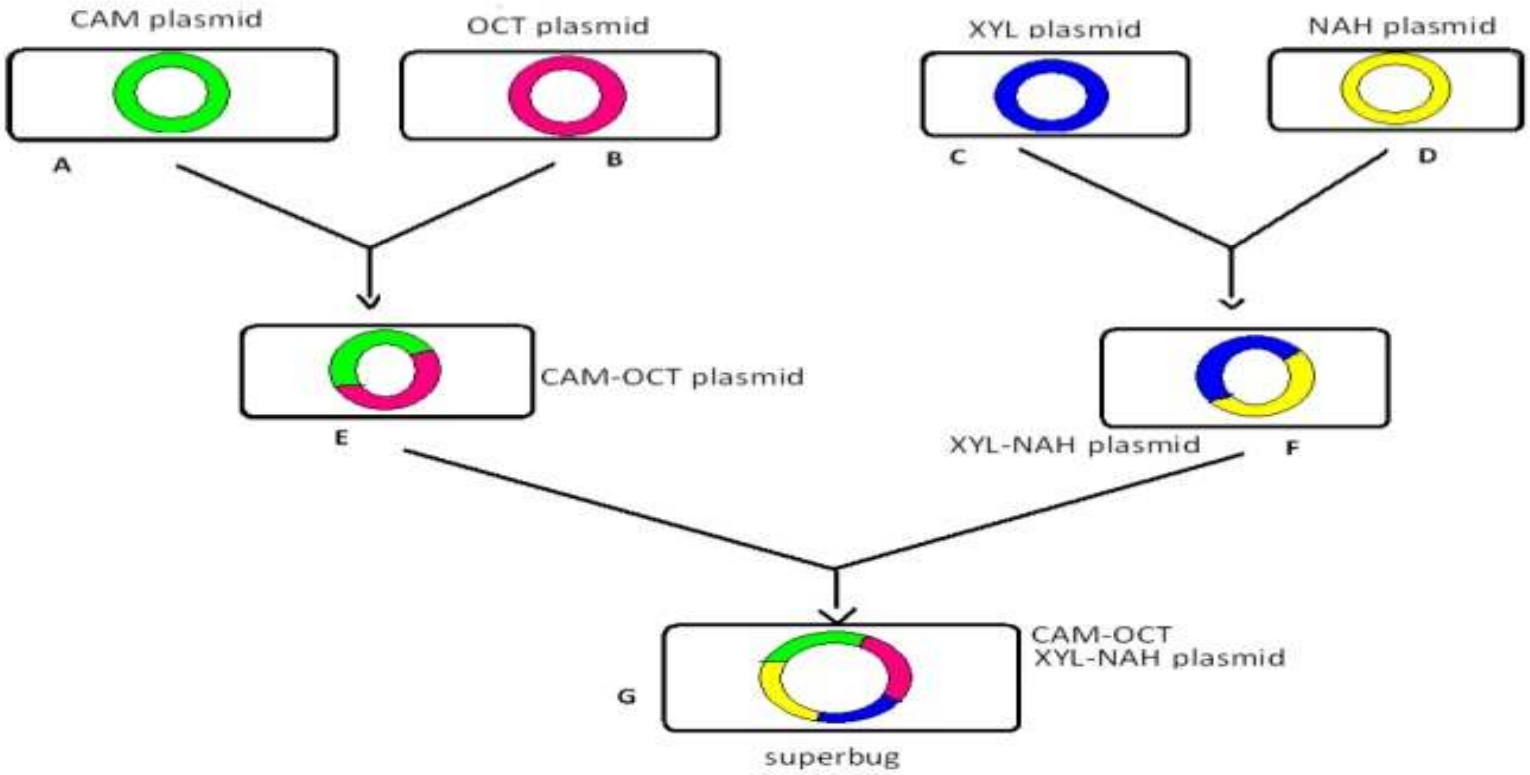
1978 Genentech produced Human insulin in *E.coli*

1980 US Supreme court declared genetically modified micro-organisms can be patented (Anand Chakrabarty)

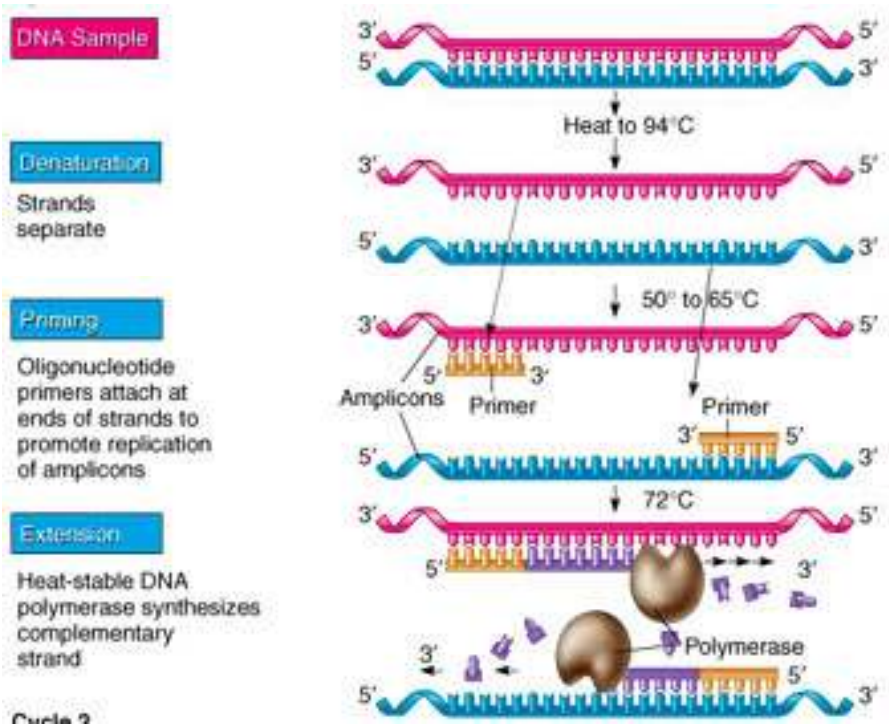
1982 First commercial automated DNA synthesized and sold (Kangas *et. al.*)

- **Prof. Ananda Mohan Chakraborty** et al. (1980) developed and patented a "**superbug**" that degraded petroleum (camphor, octane, xylene, and naphthalene) by plasmid transfers.

Construction of superbug



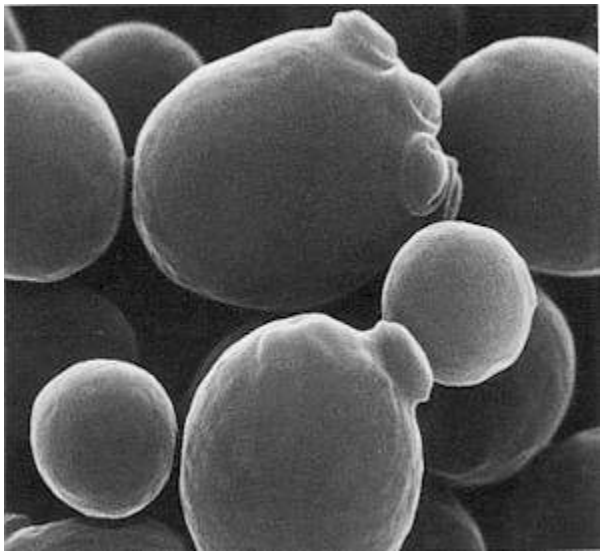
1988 **Kary B Mullis** publishes Amplification of DNA by Polymerase Chain Reaction (PCR)



Nobel Prize Winner in 1993 (chemistry)

1996 *S. cerevisiae* genome sequenced

2000 *Arabidopsis* genome sequenced



2000 Vitamin A rich golden rice developed

Transgenic Rice

- Genetically modify plants to produce beta-carotene
- Beta Carotene is converted to vitamin A in humans
- Vitamin A deficiency leads to poor vision and high susceptibility to disease

~70% of children <5 years old in SE Asia suffer from vit. A deficiency

Required to make vitamin A

Ingo Potrykus

geranylgeranyl-PP

↓ *phytoene synthase*

phyoene+ 2 pyrophosphate

↓ *crt1*

zeta-carotene

↓ *crt1*

lycopene

lycopene cyclase ↙ ↘

alpha-carotene beta-carotene

psy **(phytoene synthase) from daffodil (*Narcissus pseudonarcissus*)**

crtI **(carotene desaturase) from the soil bacterium *Erwinia uredovora***

2001 Human genome sequenced

2002 Complete human gene microarrays commercially available

Medicine

The Nobel Prize in Physiology or Medicine 2006

"for their discovery of RNA interference - gene silencing by double-stranded RNA"

Photo: L. Cicero/Stanford

Andrew Z. Fire

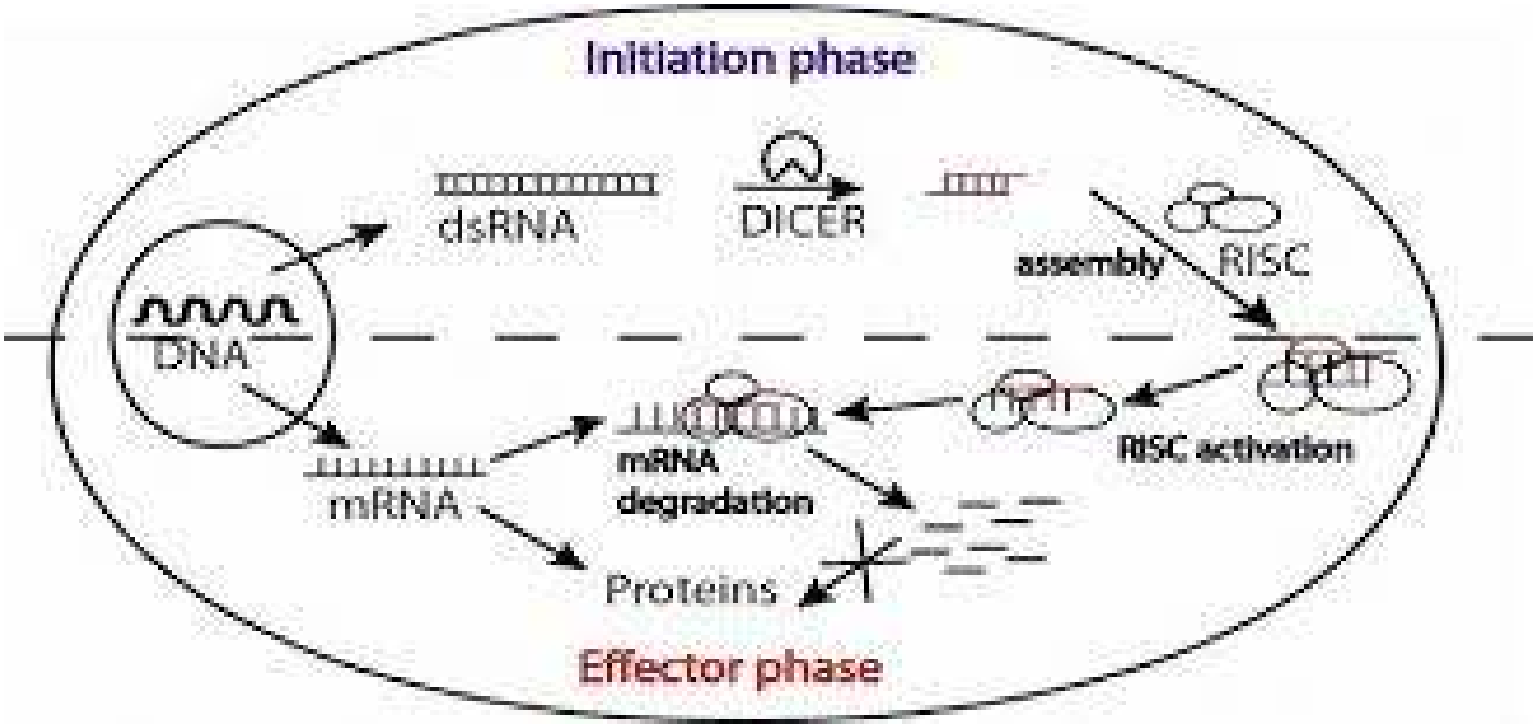
1/2 of the prize

Photo: R. Carlin/UMMAS

Craig C. Mello

1/2 of the prize

RNA Interference (RNAi)



Step 1 the trigger RNA (either dsRNA or miRNA primary transcript) is processed into an short, interfering RNA **(siRNA)** by the RNase II enzymes **Dicer and Drosha.**

Step 2 The siRNA is unwound during **RISC (RNA-induced silencing complex)** assembly and the single-stranded RNA hybridizes with mRNA target. Gene silencing is a result of nucleolytic degradation of the targeted mRNA by the RNase enzyme **Argonaute** (Slicer).

Applications of RNAi

Cotton seeds are rich in dietary protein

but naturally contain the toxic terpenoid product gossypol

RNAi has reduced levels of delta-cadinene synthase, a key enzyme in gossypol production,

Gossypol is itself important in preventing damage from plant pests

Gossypol free cotton seeds

Nicotine free tobacco,
decaffeinated coffee,
nutrient fortified and hypoallergenic crops