GENETICS: PART I

Course Syllabus:

1. Genetic Transmissions
2. Cell Cycle and Mitosis
3. Meiosis
4. Mendel inheritance and Linkage and mapping
5. Extensions of Mendels'

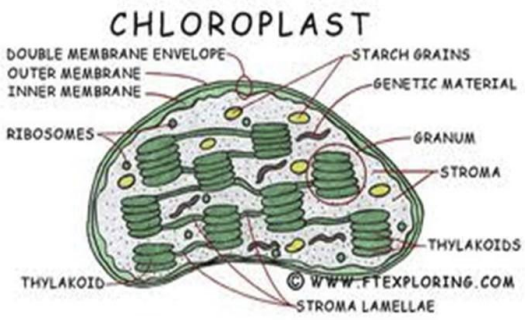
Lecture 1: GENETICS TRANSMISSION

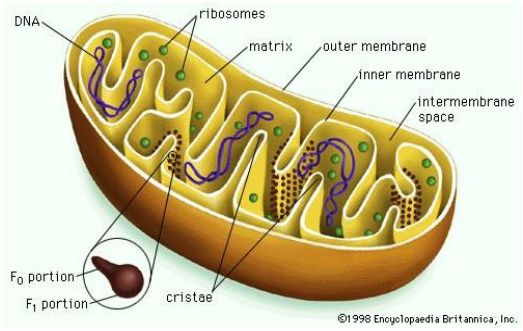
Genetics

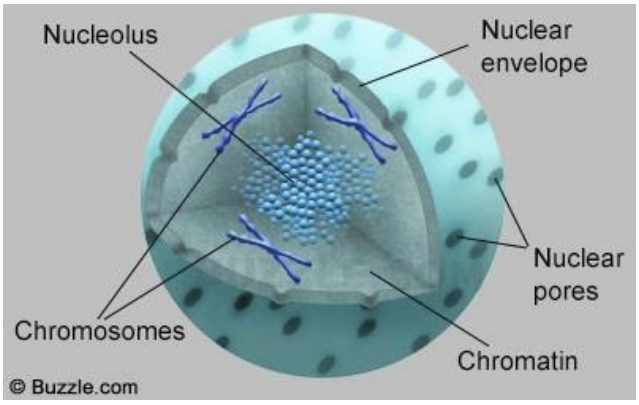
It is the science that seeks to understand, explain and ultimately exploit the phenomenon of heredity (i.e. transmission of biological characteristics, its mechanism and its variation).

Genetic material

The genetic material of a cell can be a gene, a part of a gene, a group of genes, a DNA molecule, a fragment of DNA, a group of DNA molecules, or the entire genome of an organism or even RNA in certain viruses. They are found in the nucleus, cytoplasm, mitochondria and plastids (for algae and plant), which play a fundamental role in determining the structure and nature of cell substances, and capable of self-propagating and variation.







Heredity - the passing on of characteristics from parents to offspring.

Genetic transmission (genetic transfer, GT) is almost synonymous with heredity, which study of how genetic information from genes are transmitted from cell to cell and generation to generation (from parent to offspring), how they recombine and segregate, with the goal of explaining the numerical proportions of the progeny in cross.

There are two types of genetic transmission:

1. **Vertical gene transmission** (VGT) is the transmission of genes from one generation of species (the parental or ancestor generation) to the next generation of the same species (offspring) via sexual or asexual reproduction (figure below).

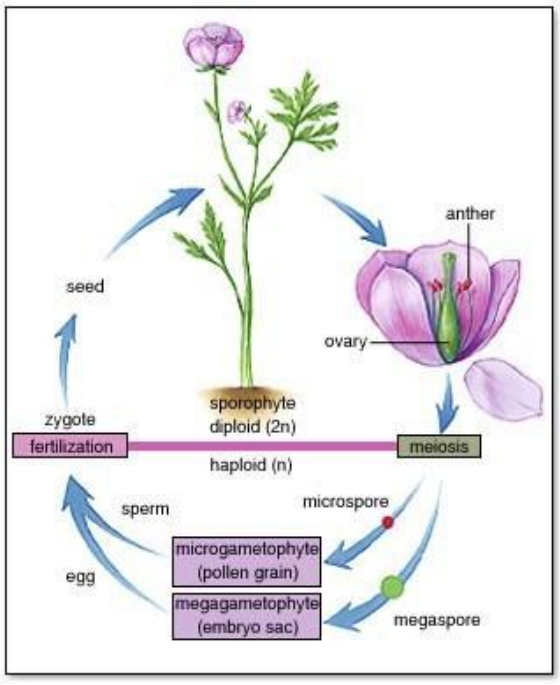
DNA encodes all the information necessary to make an organism.

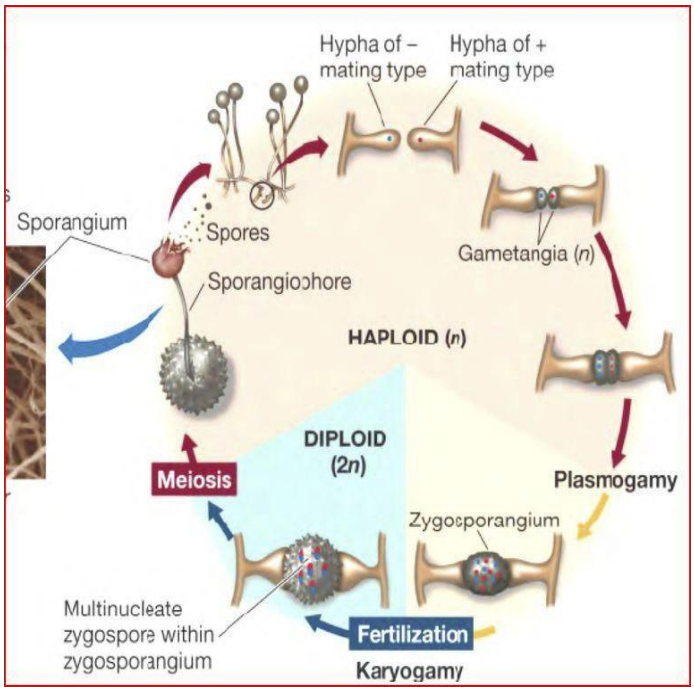
DNA → RNA → Protein

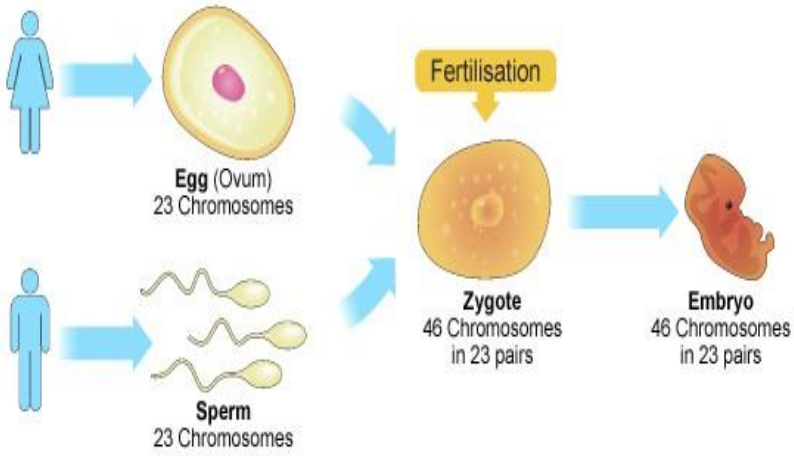
Every organism's DNA is made of the same basic parts, arranged in different orders.

There are two ways for vertical gene transfer:

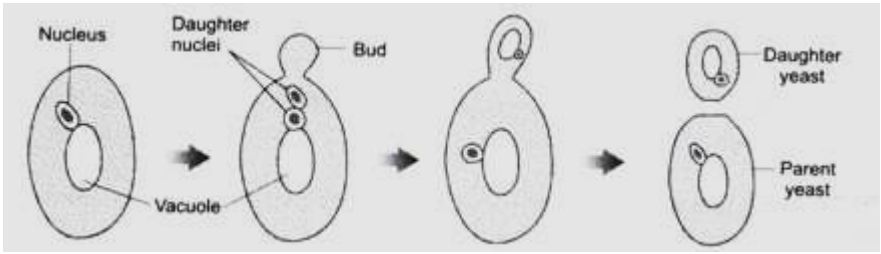
Sexual reproduction is a biological process by which organisms create descendants that have a combination of genetic material contributed from two (usually) different members of the species using meiosis. Sexually reproducing organisms have different sets of genes (2 or more) for every character (trait) called alleles. Offspring inherit one allele for each trait from each parent, thereby ensuring that offspring have a combination of the parents' genes. Most animals (including humans) and plants reproduce sexually. Some microorganisms also do it.



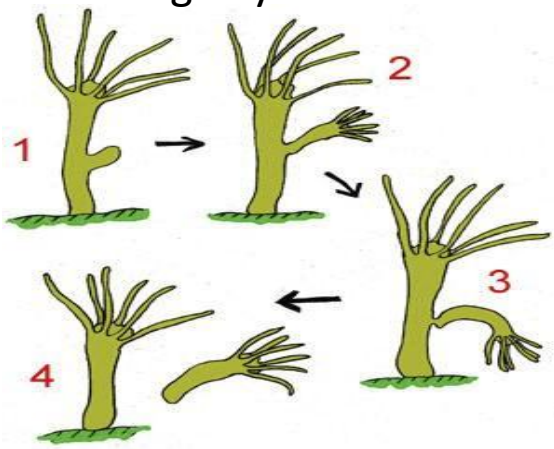




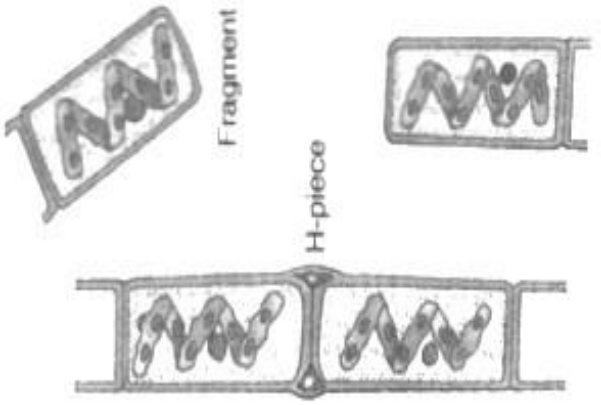
Asexually reproducing organisms creates descendants that have a copy of the same genetic material using mitosis. Bacteria and *Euglina* divide asexually via binary fission; Hydras (invertebrates of the order *Hydroidea*) and yeasts are able to reproduce by budding. Other ways of asexual reproduction include fragmentation (as *Spirogyra*) and spore formation (as in Fungi).



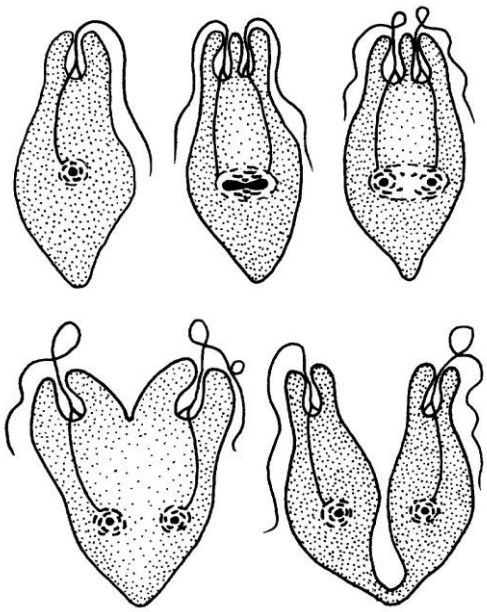
Budding in yeast



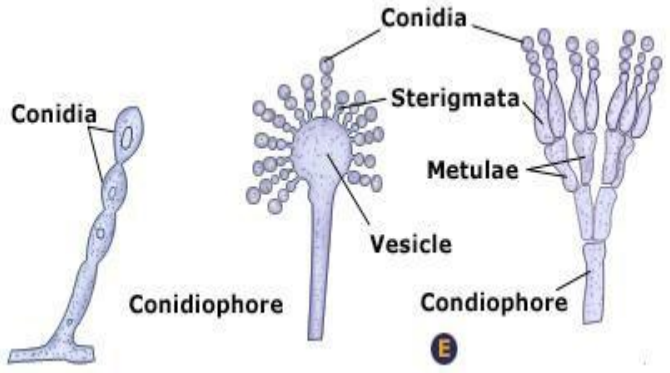
Budding in Hydra



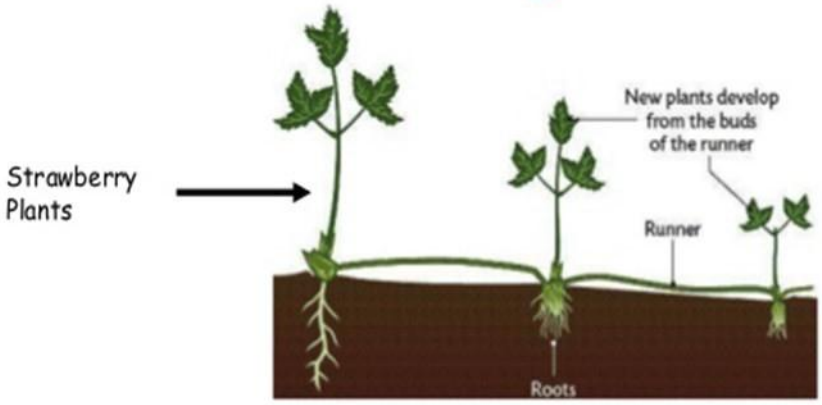
Fragmentation in *Spirogyra*



Binary fusion in *Euglina*



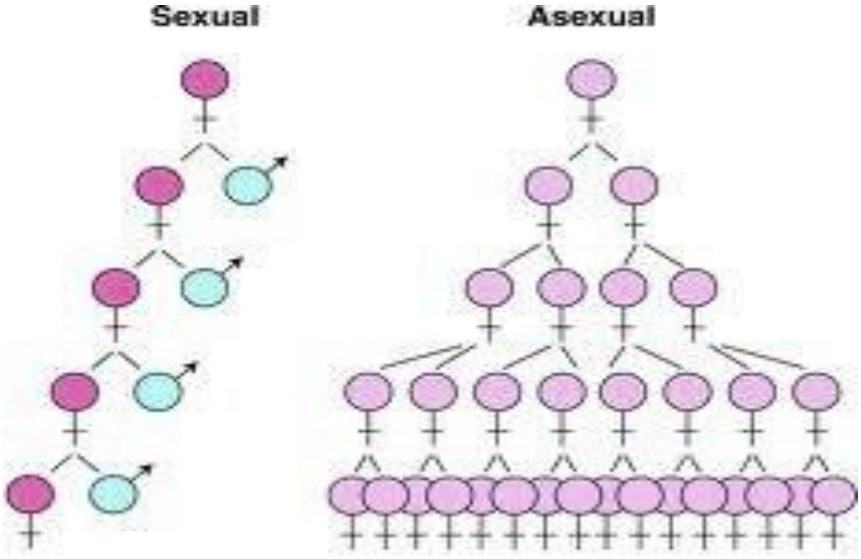
Spore formation in Fungi



Growth and development

Growth and development in Human

Both these mechanisms (sexual and asexual rep.) involve duplication of DNA, which then gets passed to offspring. RNA is a key component in the duplication of DNA.

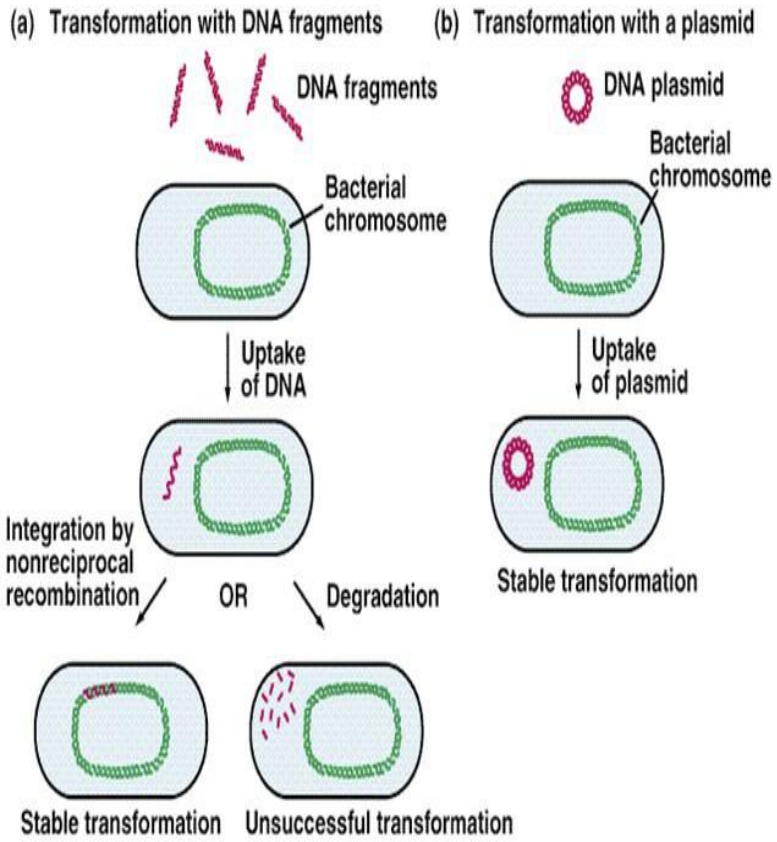


Milinski M. 2006.
Annu. Rev. Ecol. Evol. Syst. 37:159–86

2. **Horizontal gene transmission** (**HGT**) refers to the transfer of genes between organisms, from one species to another species, in a manner other than traditional reproduction. It is also termed lateral gene transfer.
   HGT has been shown to be an important mechanism that drives evolution of many organisms due to the incorporation of genetic material from an organism to another one without being the offspring of that organism.

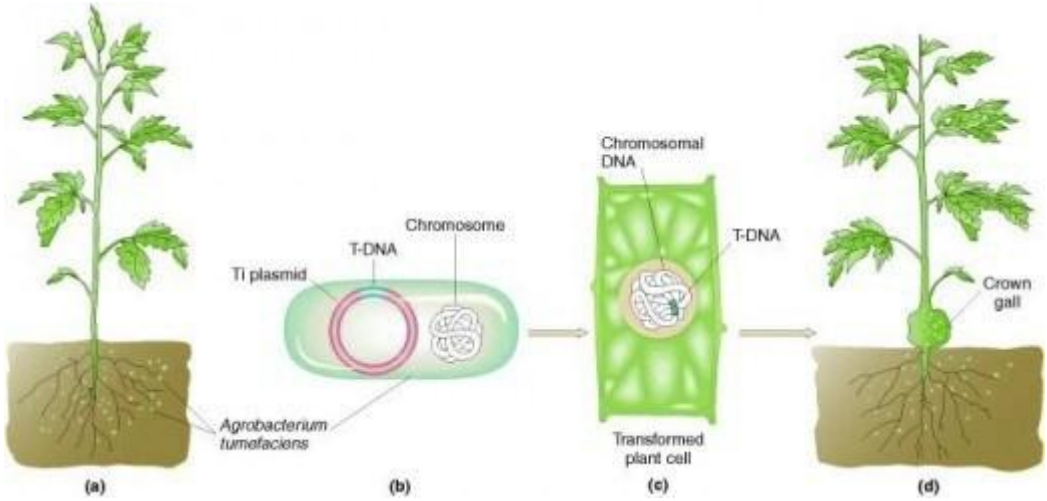
There are three main mechanisms for horizontal gene transfer:

a. **Transformation,** the genetic alteration of a cell resulting from the introduction, uptake and expression of foreign genetic material in form of fragment (DNA or RNA) or plastids either naturally or artificially (figure below).



Application:

Natural transformation of plants happen by either *Agrobacterium tumefaciens* or *A. rhizogenus* to insert the T-DNA of their plasmid to the infected plants.

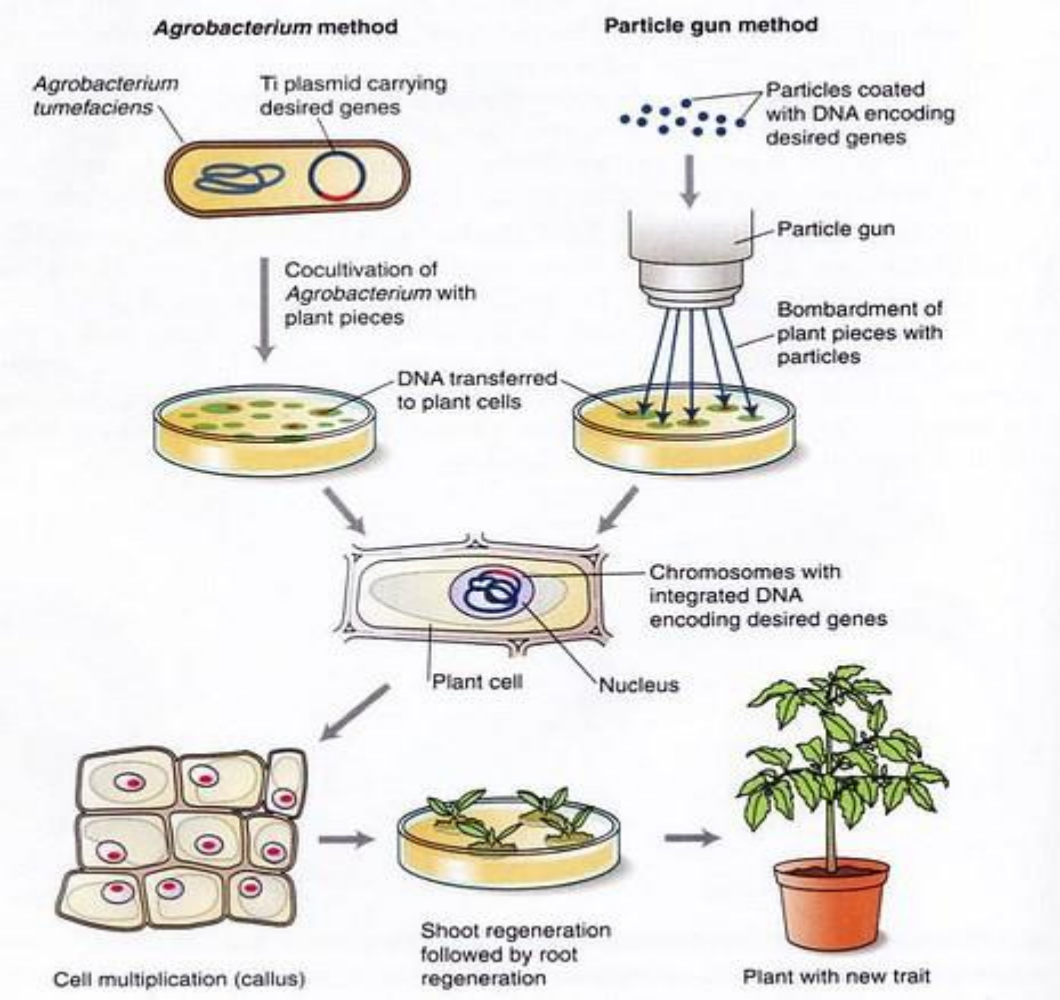


Artificial transformation happens in laboratories to insert novel genes into microorganisms, plant, animal, stem cell, insect, … for research experiments or for industrial or medical applications through molecular biology and biotechnology. Artificial transformation of tomato, potato, canola, … with *Agrobacterium tumefaciens* or by gene gun (biolistic) are used for fungal or salt tolerance.

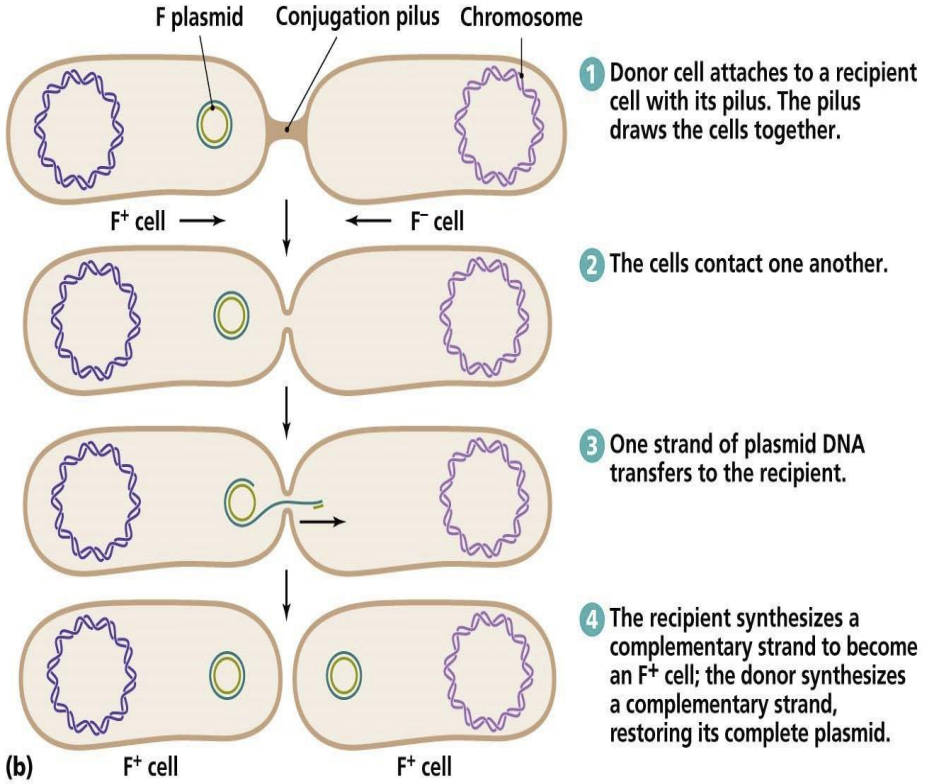
Artificial transformation of some medicinal plants with *Agrobacterium rhizogenes* or by gene gun (biolistic) is performed to increasing important metabolites in the ameliorated root system.

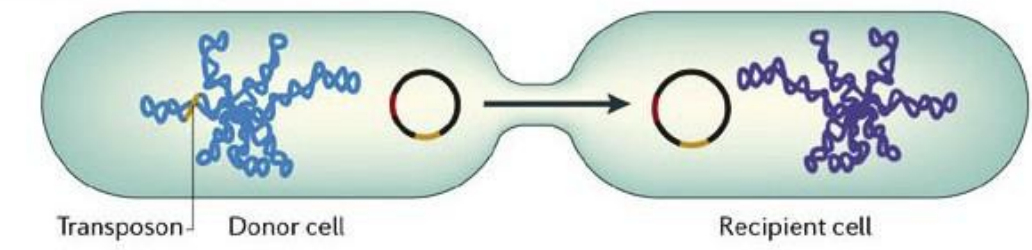
At The New York Times.com (Tues. 4 Nov. 2014)

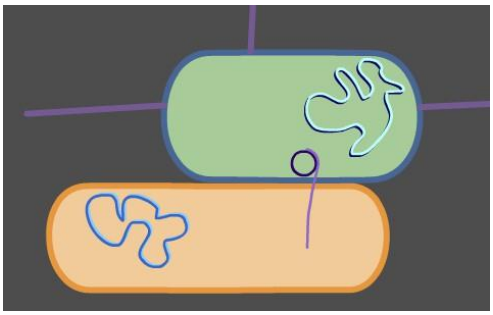
Biotech potato tubers were developed by the J. R. Simplot Company, an initial supplier of frozen French fries to McDonald's since the 1960s has been approved for commercial planting, by the Department of Agriculture of USA on Friday. They were genetically engineered to reduce the amounts of a potentially harmful ingredient (acrylamide) in French fries and potato chips, which is suspected of causing cancer in people, when the potato is fried.



b. Conjugation, a process in which a cell transfers genetic material to another cell by cell-to-cell contact or by a bridge-like connection between two cells (figures below). During conjugation the donor cell provides a conjugative or mobilizable genetic element that is most often a plasmid . Most conjugative plasmids have systems ensuring that the recipient cell does not already contain a similar element. This process is common in bacteria.

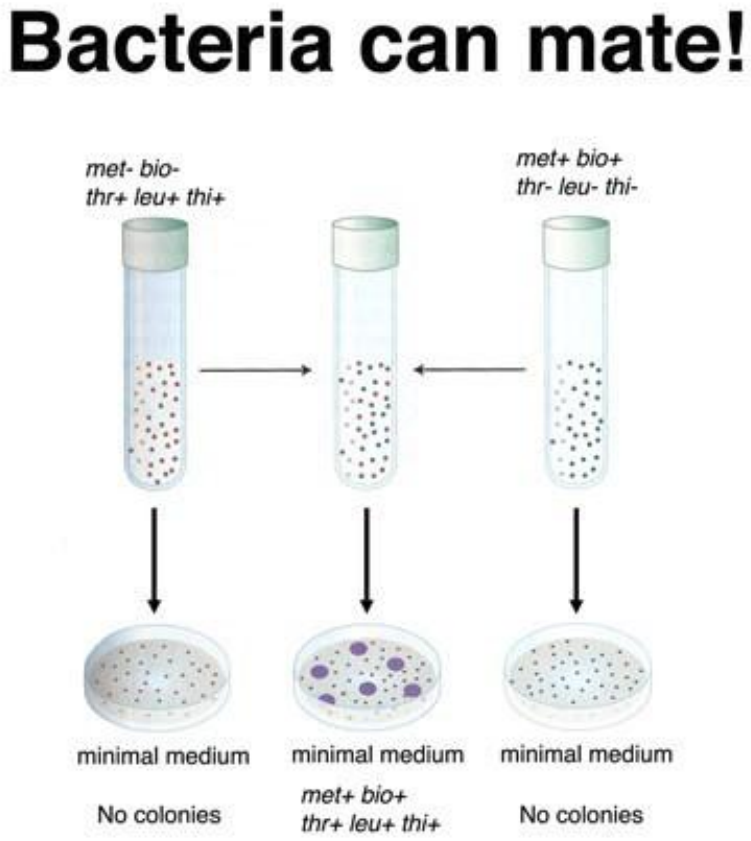






Application:

The genetic information transferred is often beneficial to the recipient. Benefits may include antibiotic resistance, xenobiotic tolerance or the ability to use new metabolites (figure below).

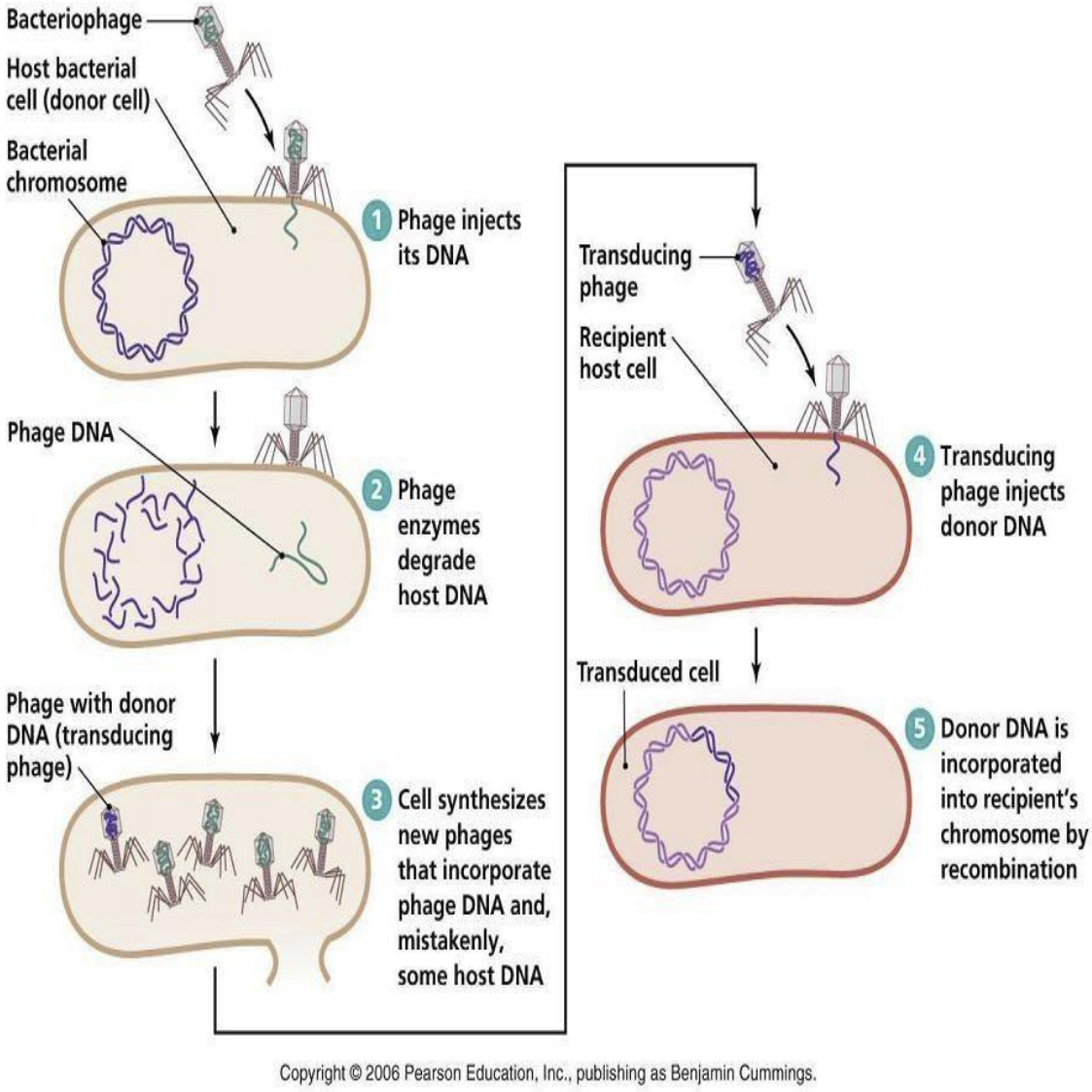


DNA from one bacterium is transferred to another bacterium. The recipient bacterial strain subsequently develops phenotypic characteristics of the donor strain with its own ones.

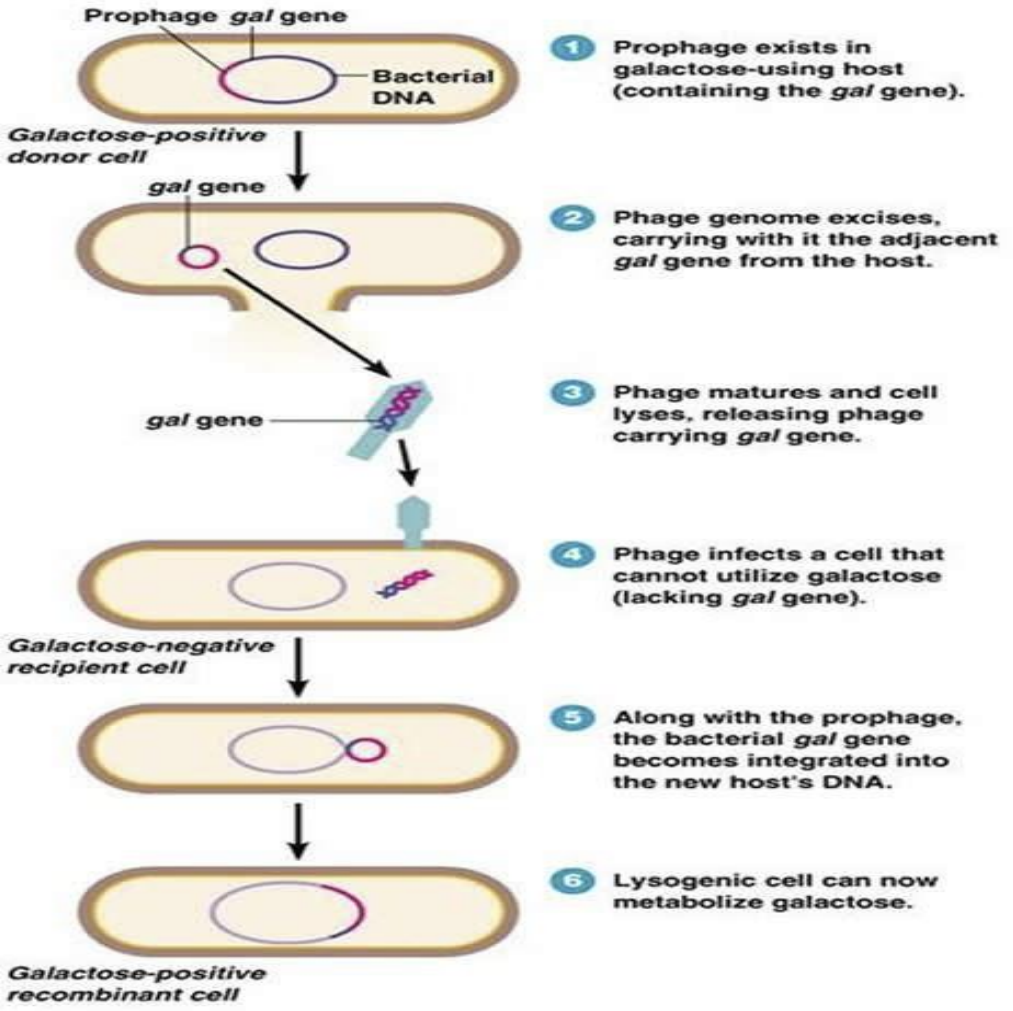
At Healthline news.com (Frid. 18 Oct. 2013)

Though the human body contains trillions of bacteria and (usually) remains healthy, many bacteria continue to evolve to outsmart (resist) current antibiotic medications. Tom Frieden, director of the U.S. Centers for Disease and Control and Prevention (CDC), warns that we're buying time on the biological clock and that current medications soon will not be able to cure people of life-threatening infections.

c. Transduction is a method in which bacterial DNA is moved from one bacterium to another by a virus. When the process whereby foreign DNA is introduced into another cell by bacteriophage is called **Generalized transduction (natural)**, while the process used a viral vector (prophage) is known as **Specialized transduction (artificial)**. Transduction does not require physical contact between the cell donating the DNA and the cell receiving the DNA (which occurs in conjugation). Phages also inject their DNA into host DNA so it's copied and passed on (figure below).



Generalized transduction



Specialized transduction

Application:

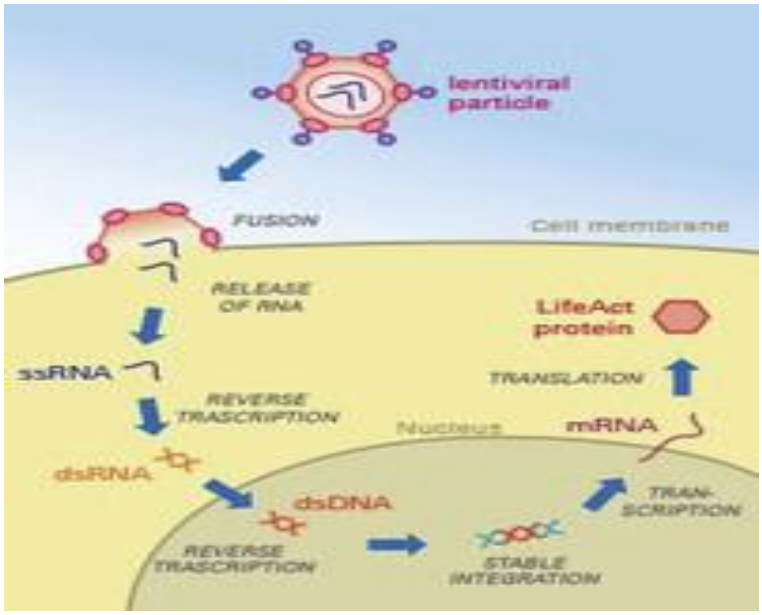
Transduction is a common tool used by molecular biologists to stably introduce a foreign gene into a host cell's genome. Transduction is especially important because it explains:

- mechanism by which **antibiotic drugs become ineffective** due to the transfer of antibiotic-resistance genes between bacteria, which is becoming a medical challenge to deal with. This is the most critical reason that antibiotics must not be consumed and administered to patients without appropriate prescription from a medical physician.

- the **evolution** of bacteria that can degrade novel compounds such as human-created pesticides, and in the evolution, maintenance, and transmission of virulence.

Example:

Fusion of a lentiviral vector with the cell membrane of mammalian cells, here rLV-LifeAct.



Recombinant lentiviral vectors have been shown to be powerful tools for stable gene transfer to both dividing and non-dividing cells in vitro and in vivo as they integrate into the host genome. They have a broad host cell range that also includes cell types such as neurons, lymphocytes, and macrophages. Moreover, lentiviral vectors have also proven to be effective in transducing brain, liver, muscle, and retina in vivo without toxicity or immune responses. The ibidi LifeAct-Lentiviral Vectors mediate efficient transduction, integration, and long-term expression of LifeAct into these cell types.

At Reuters.com (Wed. 26 Nov. 2014)

The Western world's first gene therapy drug (Glybera) from Dutch biotech firm UniQure and its unlisted Italian marketing partner Chiesi is set to go on sale in Germany. It fights an ultra-rare genetic disease called lipoprotein lipase deficiency (LPLD) that clogs the blood with fat. The drug consists of a harmless modified virus that carries a corrective gene into the body's cells.

NOTE: Most thinking in genetics has focused upon vertical transfer, but there is a growing awareness that horizontal gene transfer is a highly significant phenomenon and among single-celled organisms perhaps the dominant form of genetic transfer.

Animation:

Gene gun

https://www.youtube.com/watch?v=I2Z5j1eSO1Q

Artificial transformation

https://www.youtube.com/watch?v=L7qnY_GqytM

conjugation

https://www.youtube.com/watch?v=EtxkcSGU698

generalized transduction

https://www.youtube.com/watch?v=C44ymgwgA-o