Genetic disorder in Human beings

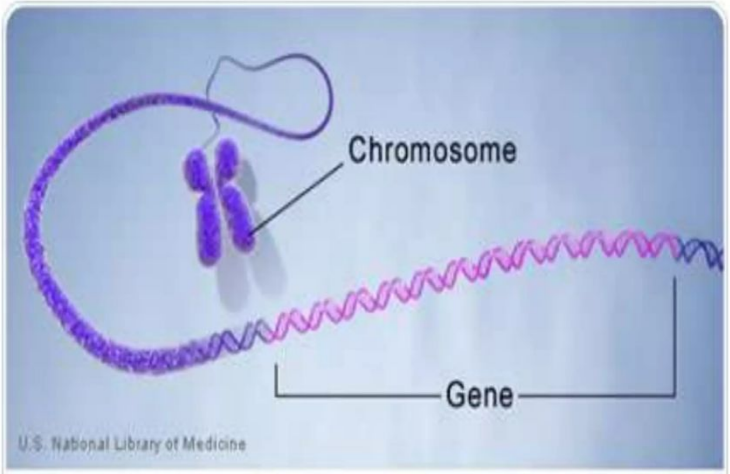
UNIT-V

Topics:

- Genetic disorder in Human beings (Down's, Turner's, Klinefelter's)
- Transposons in bacteria
- Ac-Ds elements in maize and P elements in Drosophila
- Transposons in humans

What are Genetic Disorders?

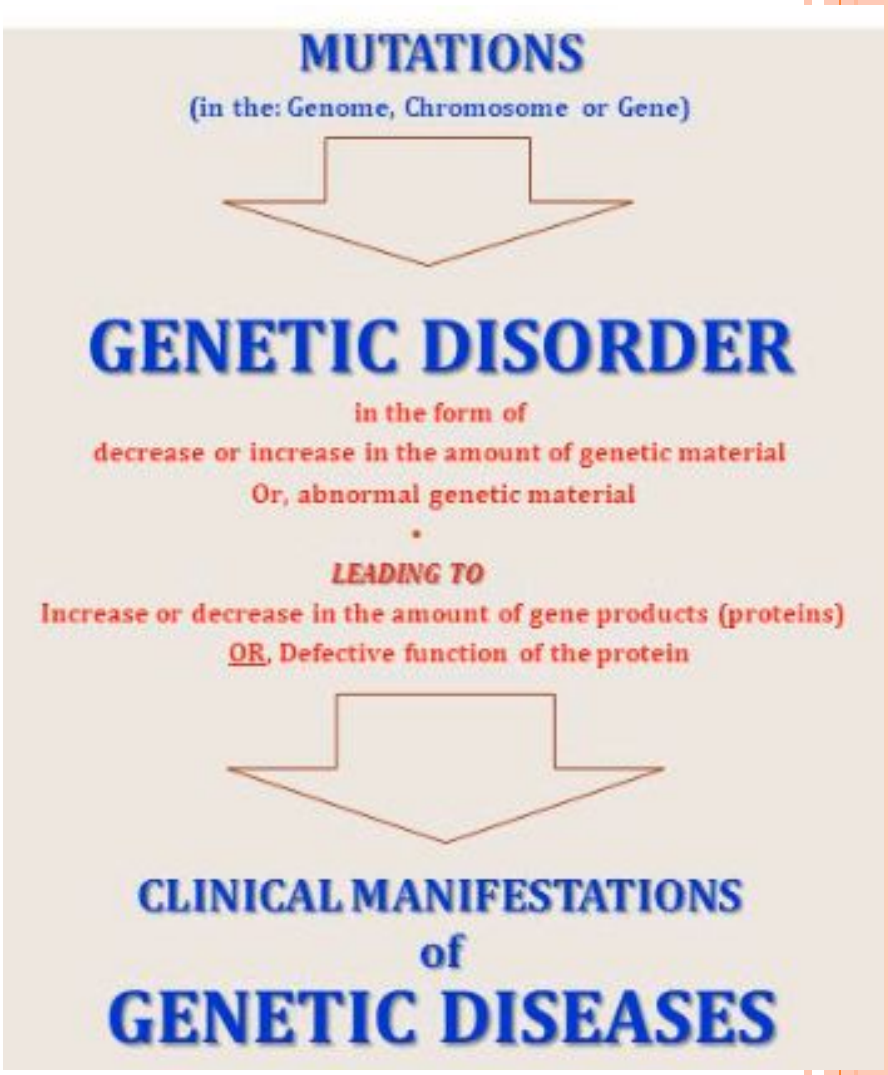
- **Genetic disorder-** an abnormal condition that a person inherits through genes or chromosomes
- Genetic disorders are caused by **mutations**
- The mutation may occur when sex cells form or may be passed down from parent to offspring



Genes are made up of DNA. Each chromosome contains many genes.

Genetic disorder in Human beings

- A genetic disorder is a disease caused in whole or in part by a change in the DNA sequence away from the normal sequence
- Genetic disorders occur when a mutation affects your genes or chromosomes. Some disorders cause symptoms at birth, while others develop over time.

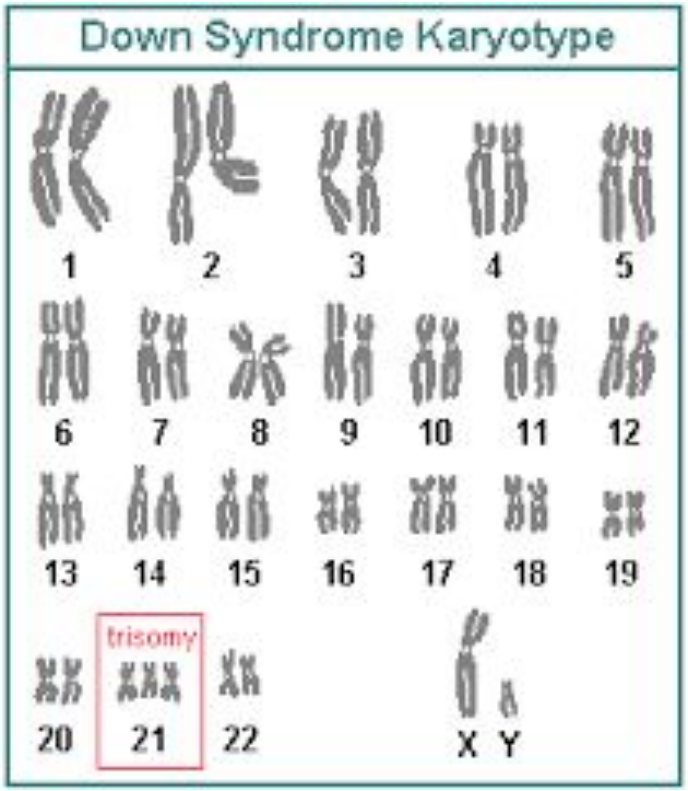


Three types of genetic disorders:

- **Single-gene disorders**, where a mutation affects one gene.
  - Sickle cell anemia is an example

- **Chromosomal disorders**, where chromosomes (or parts of chromosomes) are missing or changed. Chromosomes are the structures that hold our genes.
  - Down's, Turner's, Klinefelter's syndrome is a chromosomal disorder.

- **Complex disorders**, where there are mutations in two or more genes. Often your lifestyle and environment also play a role.
  - Colon cancer is an example.


Down Syndrome Karyotype
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trisomy
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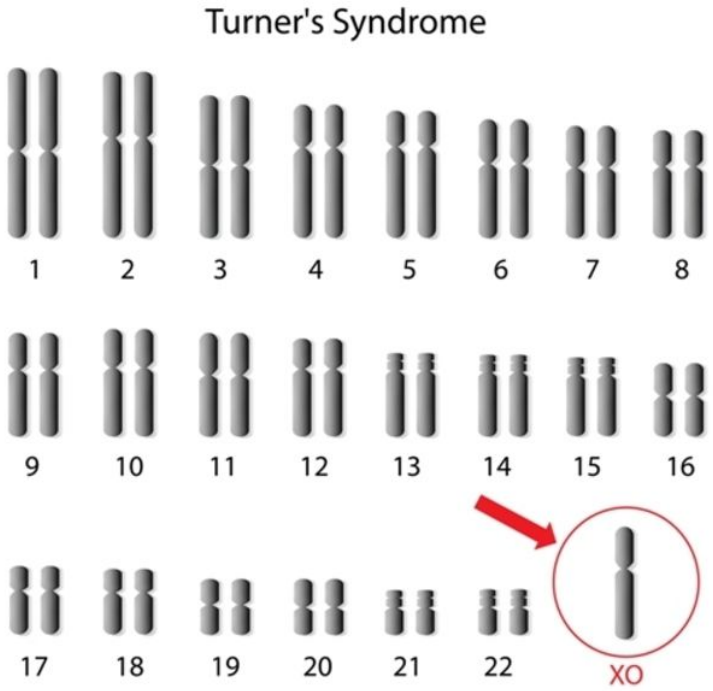
X Y


Turner's Syndrome
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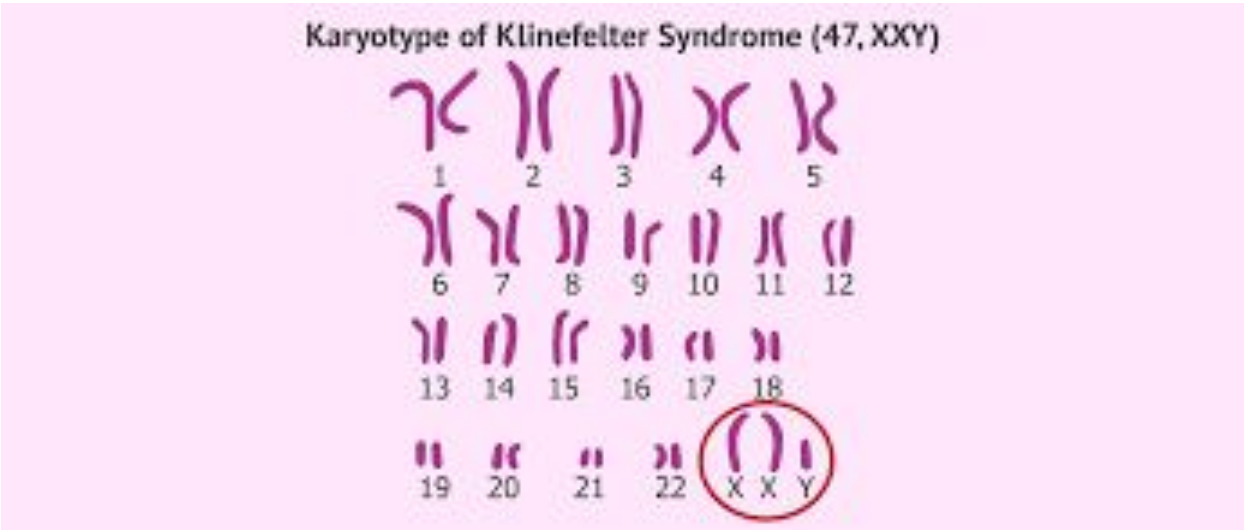
Karyotype of Klinefelter Syndrome (47, XXY)
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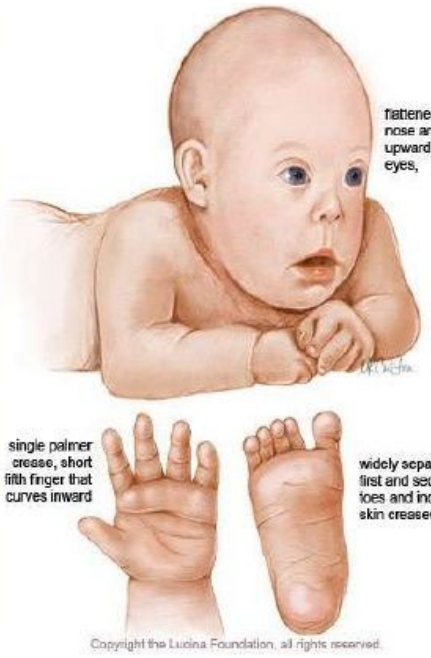
Down's syndrome: Trisomy 21

- Down's syndrome is a genetic disorder caused when abnormal cell division results in extra genetic material from chromosome 21.

• Symptoms of Down Syndrome

- Down syndrome is often easily recognized by features including a
  - round face and upturned eyes, and a short, stocky build.
  - Low muscle tone (hypotonia) at birth



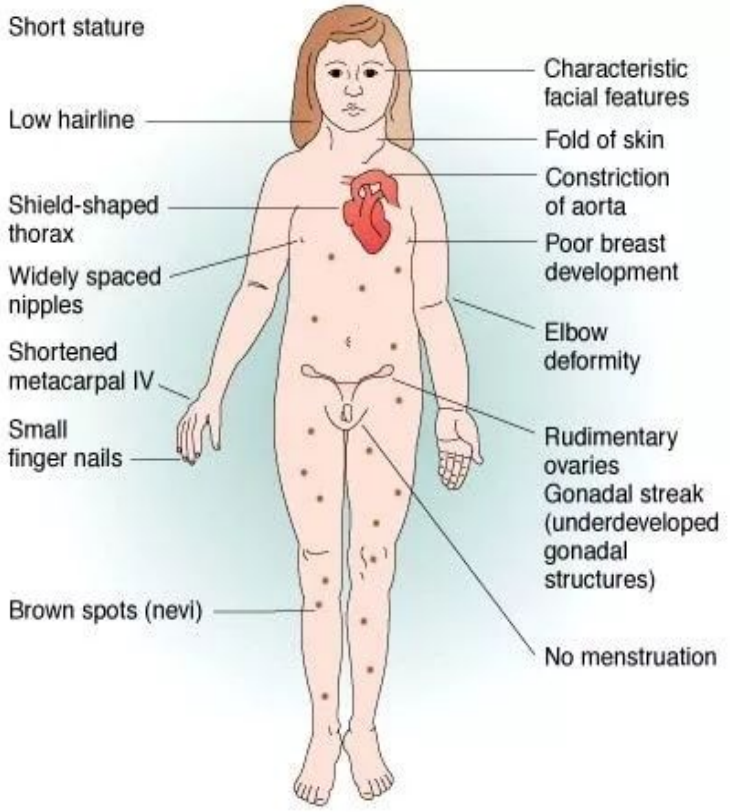
- Decreased muscle tone at birth
- Excess skin at the nape of the neck
- Flattened nose
- Upward slanting eyes
- Small ears
- Small mouth
- Wide, short hands with short fingers
- Separated joints between the bones of the skull
- Single crease in the palm of the hand
- White spots on the colored part of the eye

Turner syndrome: 45,X, or 45,X0

- Turner syndrome (TS), also known as 45,X, or 45,X0, is a genetic disorder in which a female is partially or completely missing an X chromosome.
- Turner's syndrome is a random genetic **disorder that affects females**. The main characteristics include **short stature** and i**nfertility**.
- Turner syndrome, also referred to as congenital ovarian hypoplasia syndrome

symptoms of Turner's syndrome

- Features of Turner syndrome may include a
- short neck with a webbed appearance,
- low hairline at the back of the neck,
- low-set ears, hands and feet that are swollen at birth
- soft nails that turn upward.
- Stature. Girls with Turner syndrome
- grow more slowly than other children.



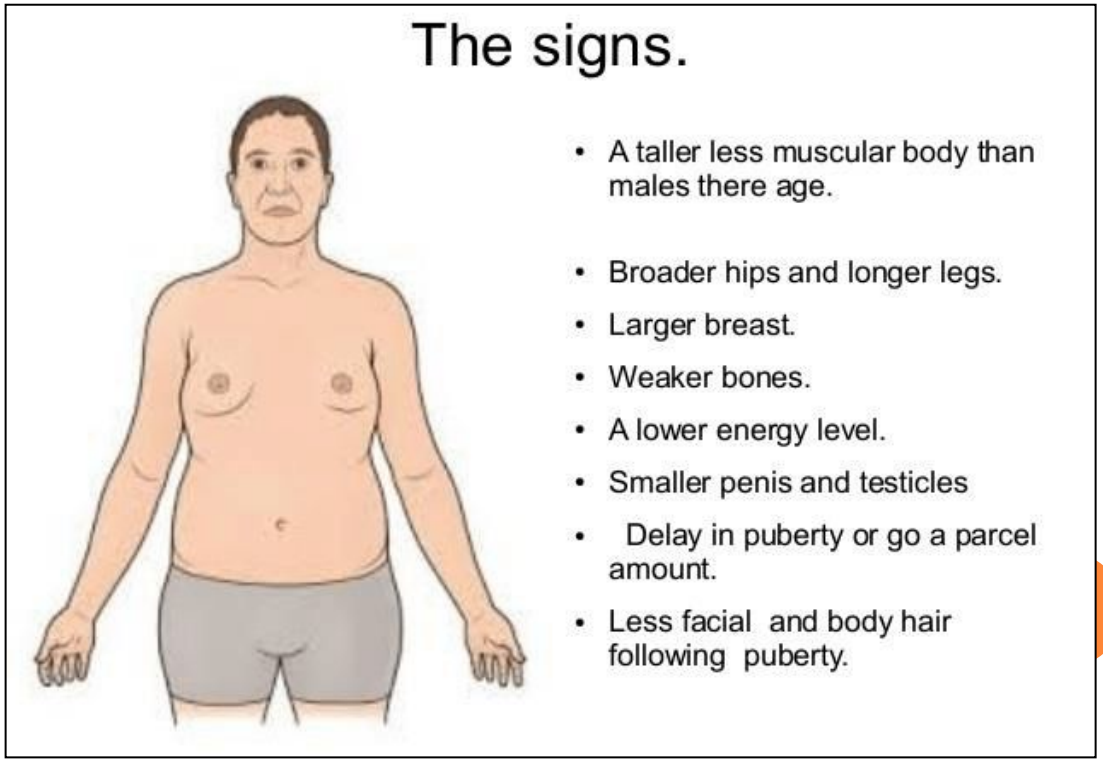
Turner's syndrome	Down's syndrome
• It affects only females.	• It affects both males and females.
• It is a condition of monosomy where females contain only one X chromosome.	• It is a condition of trisomy where there is an extra chromosome at 21st pair.

Klinefelter syndrome : XXY Syndrome

- Klinefelter syndrome is a chromosomal condition in **boys and men** that can affect physical and intellectual development.
- Klinefelter syndrome (KS), also known as **47,XXY,** is an aneuploid genetic condition where a male has an additional copy of the X chromosome.

Common symptoms:

- Breast enlargement in men,
- Delayed puberty,
- Flaccid muscles,
- Infertility,
- Low-set ears,
- Small penis
- Osteoporosis,
- Reduced sex drive,

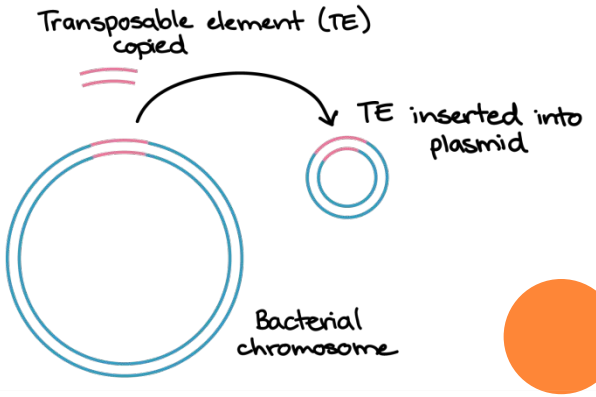


Transposons in bacteria

- Transposons are repeating DNA sequences with the ***ability to migrate from one site in the genome to another*** (transpose).
- **In bacteria**, ***transposons can jump from chromosomal DNA to plasmid DNA and back, that cause the transmission of antibiotic resistance genes in bacteria***
- Transposons are ***mobile genetic elements*** that often carry an antimicrobial resistance gene.
- These elements can insert randomly, ***move from plasmids to the chromosome***, and vice versa, and can be moved from one bacterium to another by conjugation, transformation, or transduction.

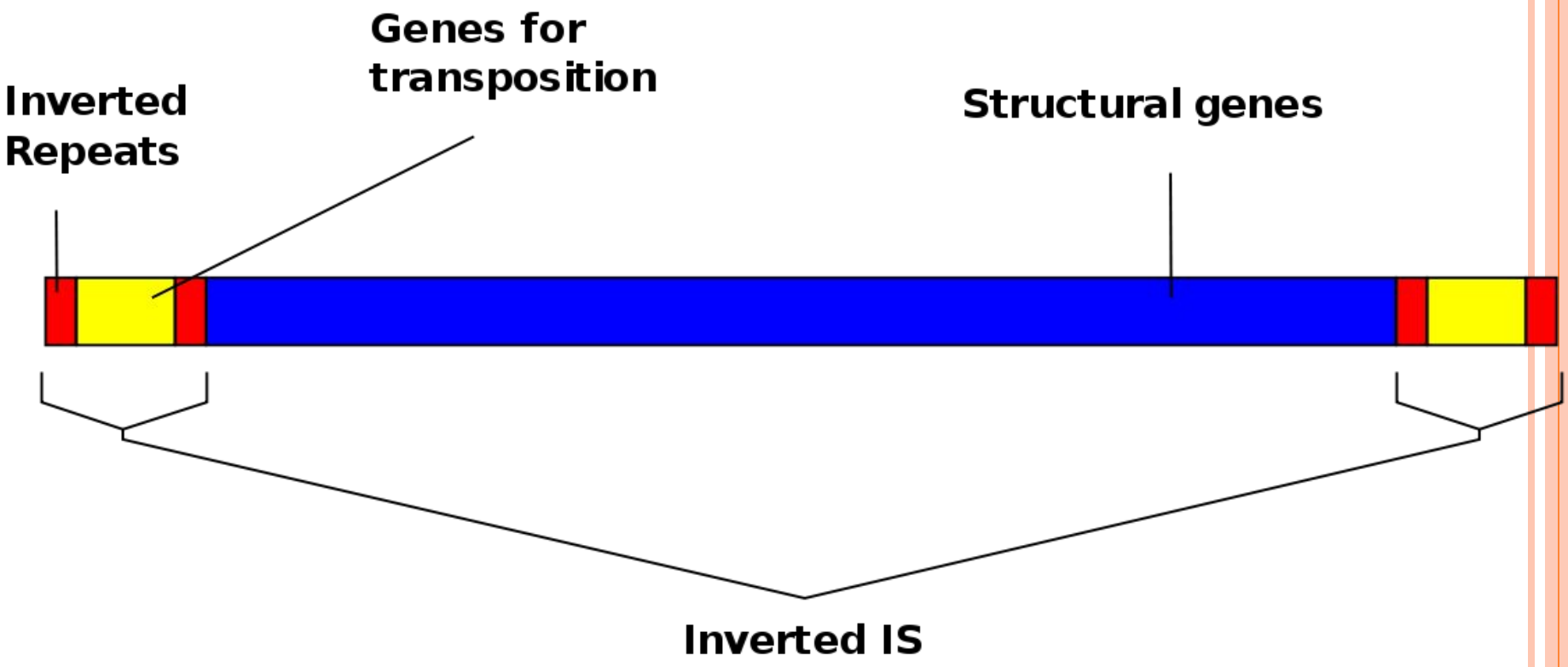
Example of Transposons in bacteria

- **Insertion sequences (ISs)**, which are components of nearly all bacterial genomes, are the simplest forms of transposable elements
- **Tn5** (kanamycin resistance),
- **Tn9** (chloramphenicol resistance), and
- **Tn10** (tetracycline resistance).



Tn5 ***is a composite bacterial transposon that encodes a protein, transposase (Tnp), required for movement of the transposon***

Bacterial composite transposon



AC AND DS ELEMENTS IN MAIZE

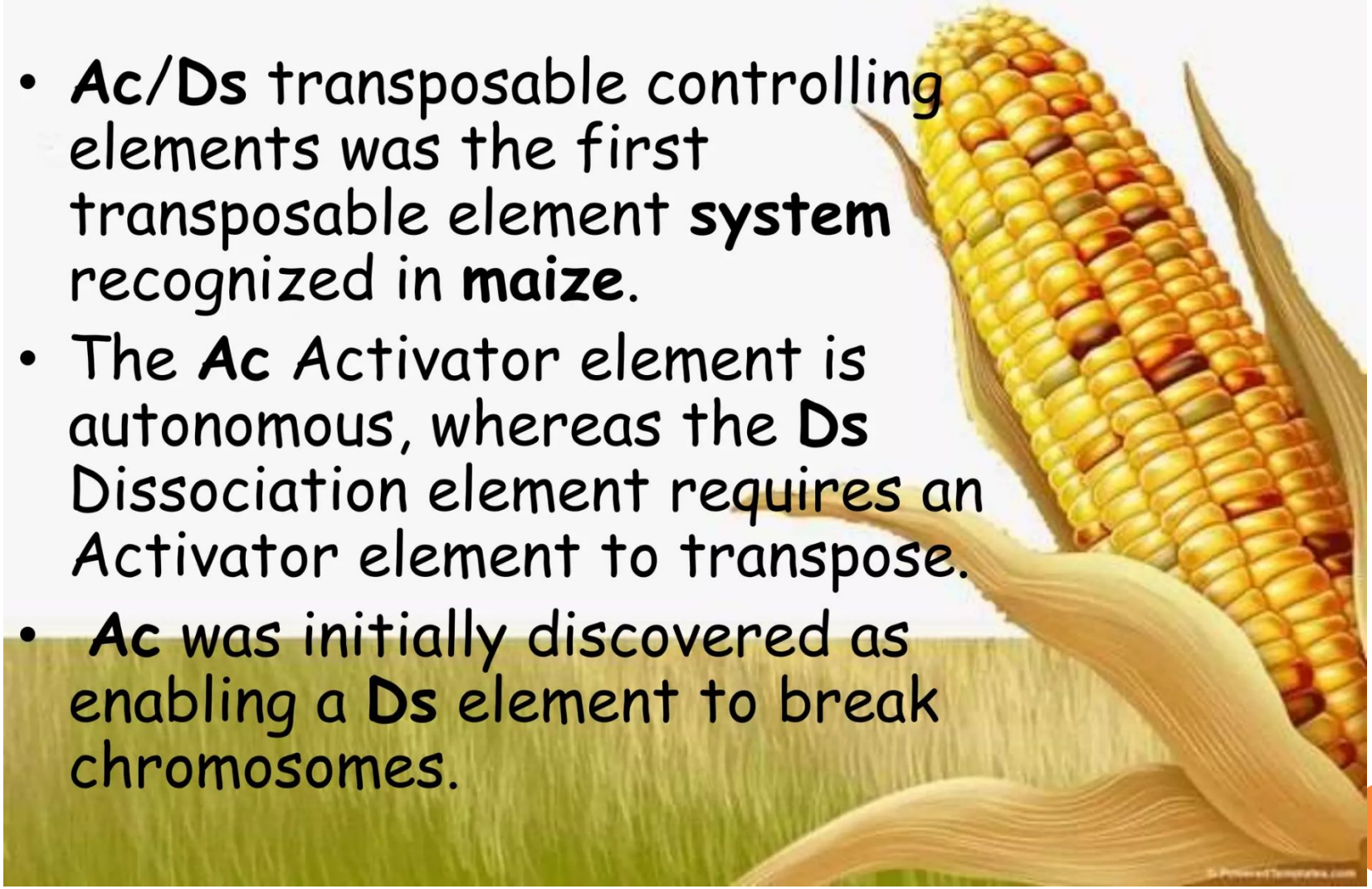
- Transposable elements were first identified in maize (corn), after 50 years by Barbara McClintock.
- McClintock published her conclusion in 1948.
- The significance of McClintock's early discoveries was finally recognized in 1983, when she was awarded the nobel prize in physiology or medicine.

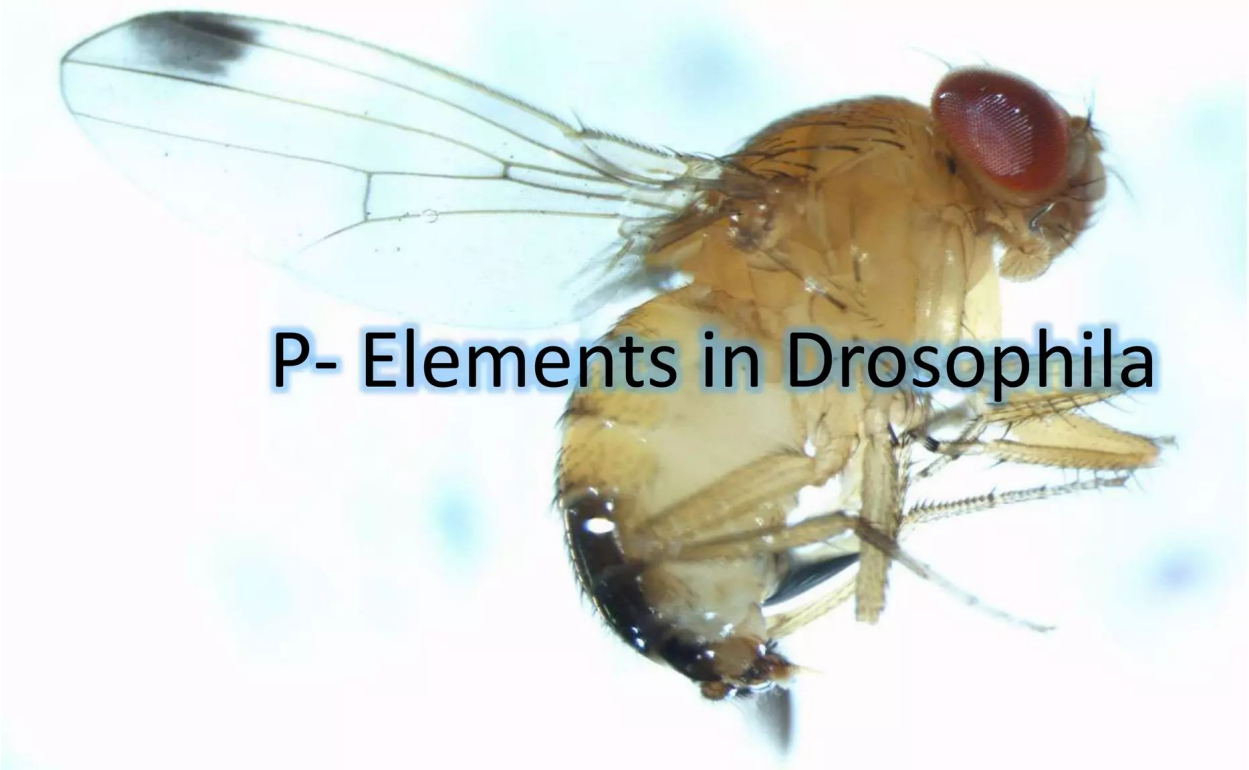
Maize Activator (Ac) is one of the prototype *transposable elements* in plants, fungi, and animals. The *autonomous Ac* and *nonautonomous Dissociation (Ds*) elements are mobilized by the single transposase protein encoded by Ac.

The nonautonomous maize Ds transposons can only move in the presence of the autonomous element Ac.

AC –DS SYSTEM

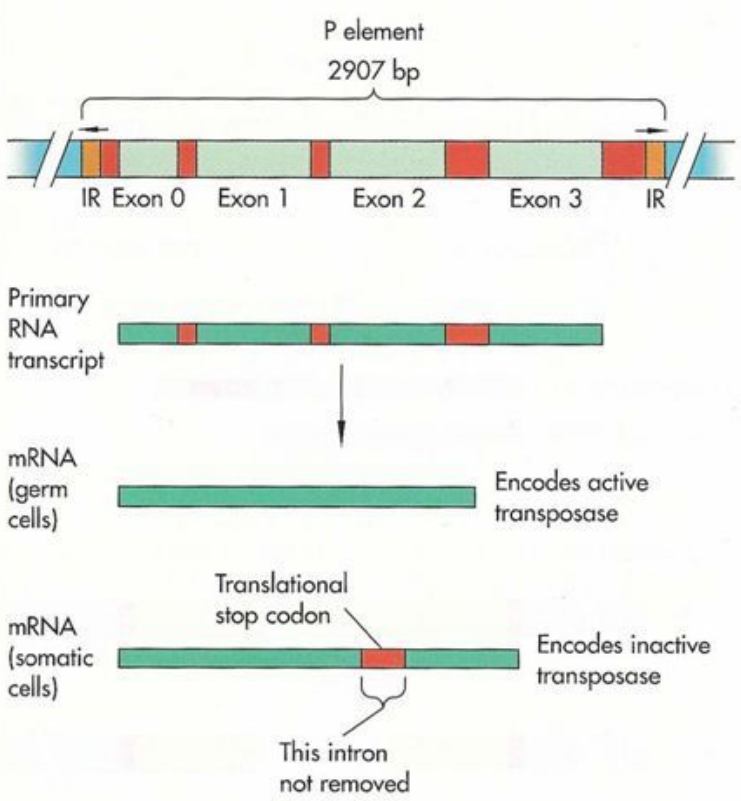
- **Ac/Ds** transposable controlling elements was the first transposable element **system** recognized in **maize**.
- The **Ac** Activator element is autonomous, whereas the **Ds** Dissociation element requires an Activator element to transpose.
- **Ac** was initially discovered as enabling a **Ds** element to break chromosomes.




P- Elements in Drosophila

Drosophila Transposons

- Known as P elements, similar in structure to *Ac* & *Ds*
- P elements can be incomplete (no transposase) or complete (functional transposase) – analogous to *Ac*/*Ds*
- P elements are only active in germ line cells, because a stop codon exists in transposase
- In germ cells, alternative splicing removes exon 2 to remove the codon
- Demonstrated by engineering a P element without intron 3



Transposons in Humans

- Transposable elements comprise at ***least 45% of the human genome while coding sequences occupy <3%*** .
- These ***highly repetitive strands of "junk" DNA*** are capable of generating new copies in the human germline and certain somatic tissues.
- The most common form of transposon in humans is the ***Alu sequence***.

- The ***Alu sequence*** is approximately 300 bases long and can be found between 300,000 and a million times in the human genome.
- ***Mu phage*** transposition is the best known example of replicative transposition.