

McClintock 1953

Home

Biol 4241

Luria-Delbruck 1943

Hershey-Chase 1952

Meselson-Stahl 1958

Garapin et al. 1978

McClintock 1953

King-Wilson 1975

Sanger et al. 1977

Jeffreys et al. 1985

Rothberg et al. 2011

Hamer et al. 1993

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Induction of Instability at Selected Loci in Maize

Background and Introduction



- [Barbara McClintock](#) discovered transposable elements (“[Jumping Genes](#)”) in 1953, while working with [Maize](#)
- First half of 20th century (Thomas Hunt Morgan):
 - Genes thought of as “[beads](#)” along a chromosome
 - [Genes](#) inviolate objects with [fixed positions](#)
- Major discovery considering gaps in the story of genes and their workings
- “[Classic Paper](#)” because:
 - [Standard Mendelian crosses](#) to infer molecular genetics
 - [Little cytological evidence](#) - conclusions about [chromosomes behaviour](#)
- Contributes to molecular genetics by explaining how [chromosome functioning can alter genotypes and phenotypes](#)
- 1972 - Peter Starlinger and Heinz Seadler “[re-discovered](#)” transposable elements in bacteria
- Brought McClintock’s 1953 work to the attention of the scientific community
 - Received [Nobel Prize](#) in [Physiology or Medicine](#) in 1983

Theory



Dissociation-Activator (Ds-Ac) System

- Nuclear two-unit system capable of **controlling gene expression**
- Both **Ds** and **Ac** are **single chromosomal units**
- Both are **able to move** from one location to another within the chromosome

The Nature of the Chromosome Break

- The **Dissociation factor (Ds)** initiates changes in **genic expression**
- **Ds** provides a point for the **chromosome to break**
- Chromosome breakage results in the **loss of all downstream loci**
- The **alleles remaining** after the break are **phenotypically expressed**

Activation of the Dissociation Factor

- **Ac** is inherited as a single unit
- **Ds** only **causes a chromosome break** if the **Activator factor (Ac)** is present
 - **Ds AND Ac** both present at a locus - gene's action can further change
 - Re-introduction of **Ac** leads to further mutations
 - Phenotype produced is **stable** in the **absence of Ac**
- **Ac** can exert control over **Ds** at **any time**
 - Degree of expression **dependent** on the point in the **developmental cycle** when **Ac** acts on **Ds**
 - The earlier the change occurs, the greater the expression
- If alterations occur in sporogeneous cells, derived plant cells will present mutations

Implications of the Ds-Ac Interaction

- Interaction of the Ds-Ac system can result in **phenotypes unpredictable by traditional Mendelian genetics**
- Ds-Ac interaction may also result in:
 - Dicentric chromatid formation
 - Genic action deficiency
 - Duplication of segments
 - Inversions
 - Ring-chromosomes
 - Reciprocal translocations between chromosomes
- **Phenotype produced depends** on the how **Ds exerts its effects** on the chromosome (breakage VS disruption)
- McClintock's idea that **Ds factor could behave in numerous ways** led to her correctly interpret the results!!!

In short

- Ds-Ac controlled mutations are
 - NOT a change in genic action potential,
 - BUT **chromosomal modifications** at a locus affecting **type** and degree of genic expression
- Changes at gene locus caused by units NOT at the gene à “**extragenic chromatin units**”
 - These units exert **control** over the gene they associate with
 - Can transpose (“**move**”) from location to location on a chromosome
 - Act in a **similar way** on all genes it associates with
 - Example: Dissociation-Activator (**Ds-Ac**) two-unit system in maize

Materials and Methods

Purpose:

To demonstrate that Ac-controlled mutations may **act on any loci** of **known genic action** (Eg: chromosome 9)

Predictions:

- 1) Mutations only occur when **Ac** is present in the nucleus
- 2) Phenotypes are stable in the absence of **Ac**
- 3) Phenotypes become unstable when **Ac** returns
- 4) Dosage of **Ac** plays a factor in phenotypes produced
- 5) **Ds** may enter any location, **Ac**-regulated mutation arises at a **number of loci** of known action

Approach:

- 1) **Cross plants** of **known genotypes** in a **Mendelian fashion** and analysed the results
- 2) **Compare** **obtained phenotypic** ratios with the **expected phenotypic** ratios to draw conclusions about genic action

Pigmentation gene selected to test predictions

- **Ac** factor can have **numerous effects** on **behaviour** of **Ds** factor

· McClintock reasoned:

- In the **absence** of **Ac** à phenotypes predicted by **Mendelian genetics**
- In the **presence** of **Ac** à two **variegated patterns** could result

· Variegation pattern due to either:

- 1) **Loss** of alleles downstream from the **Ds** factor
- 2) **Interruption** of alleles when the **Ds** inserts into the allele

Expected Phenotypic Ratios and Interpretation

Expected Results from Crosses

Results



Action of Ac factor on Ds factor affecting phenotypes

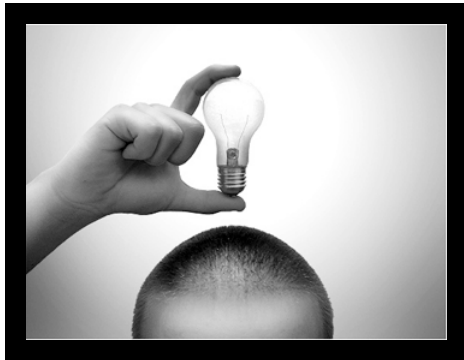
- Crossed “unknown” plants with “tester plants” to determine their Ac constitution
- “Tester Plants”:
 - Had genetic markers on the short arm of [Chromosome 9](#)
 - Had NO Ac factor
- Finding: [Graded potential](#) of Ac

Support for predictions by crossing known "tester plants" with plants of known genotype

- Performed [numerous crosses](#) with plants of varying phenotypes
- Obtained ratios to draw inferences about genic action
- Why colored plants???
 - “cross plants” were either heterozygous (**colorless**) or homozygous recessive (**coloured**)
 - “tester plants” were exclusively homozygous dominant (**colorless**)
 - Neither of these genotypic combinations should produce **colored** plants ... how did they arise??
- McClintock suggests that changes [late in development](#) at this locus are responsible for completely **colored kernels**.
- Is it possible that instability caused by [something other than Ac](#) may have caused this??

Conclusion

- Genes previously believed to be relatively static only undergoing rearrangement with mutations triggered during meiosis
- **BUT genes have a dynamic structure!!**



Continuation of Barbara's Work

Other organisms have transposable elements:

- 1) *Zea mays* (corn) - Ds
- 2) *Caenorhabditis elegans* (roundworm) - Tc₁
- 3) *Drosophila melanogaster* (common fruit fly) - P₁
- 4) *Homo sapiens* (Human) - Alu

Further research has told us that:

- 1) Mobile DNA is not an exception but is **abundant** (composes up to 50% of human genome and >60% of Maize)

genome)

II) Serves valuable function in DNA expression, genome structural recognition, and mutation generation

III) Three types of transposons (jumping genes have been identified):

1. DNA transposons (like the one identified by McClintock)

2. LTR (viral- like) Retrotransposons (have RNA phase)

3. Poly-A (non- LTR) Retrotransposons (have RNA phase)

IV) There are **autonomous** (synthesize transposase) and **non-autonomous** transposons

Areas of Continued Study:

-In the human genome most mobile DNA sequences are not active, however 1 of 600 human disease causing mutations are caused by retrotransposon jumping

- **Specific functions of Transposons currently under investigation:**

I) Important component of centromeres

II) Maintain the ends of *Drosophila* chromosomes

III) Arrangement of immunoglobulin genes

Additional information and educational videos



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