Jumping Genes

Barbara McClintock’s Legacy

Barbara McClintock
1983 Nobel Prize

Orthodox Facts

- Genes have fixed positions on chromosomes. These positions are stable over the life of the organism.
- McClintock discovered transposition, and this discovery established the fact that genes change position on chromosomes, and their change in position changes their expression in the phenotype.

Transposition

- A process like mutation which reorganizes the genome, but it arises and is expressed within the phenotype within the lifetime of a single generation (individual).
- The phenotypic expression of a gene is inhibited or activated by the presence or absence of a dissociator (Ds element).
- Differentiation and development are the result of genes expressing their effects at different points in the maturation process (e.g. puberty and the expression of (secondary sexual characteristics).

Transposition

- The presence of a Ds element inhibit the normal functioning of a gene.
- The absence of a Ds element restore the phenotypic expression of a gene.
- Ds elements change location along the length of a chromosome to activate or inhibit the expression of various genes.
Transposition

• Is a two step process, involving the release of a chromosomal element (Ds) from its original position and its insertion into a new position.
  • The Ds locus will undergo dissociation only when a dominant factor called the activator (Ac) is absent.
  • The number of units at an Ac locus can change over time.
  • Changes in the Ac locus result in a release of the Ds element from its preceding location on the chromosome.

Transposition

• If two breaks are induced on opposite sides of the Ds locus a fragment of chromosome is released and becomes available for insertion at any other point on the chromosome where a concurrent break might have occurred.
  • Thus Ds elements jump or change position within the chromosome.

Transposition

• Occasionally the split at the Ds locus is imprecise and some adjacent genetic material is carried with the Ds element and it may be inserted in new locations in either the same or reverse orientation.
  • This results in a novel genome – a mutation.

Transposition

• What causes changes in the frequency of dissociation?
  • Internal and external environmental stress can change the Ac dose at any loci, and hence stress may heighten the probability of dissociation and hence mutation.
  • This is a radical idea for in this way the causes of selection and the causes of mutation may not be strictly independent.

Transposition

• McClintock: “There is little doubt that the genomes of some if not all organisms are fragile and that drastic changes may occur at rapid rates”.
  • New species may evolve rapidly followed by a period of stabilization.
  • Genomes may be programmed to “shuffle the deck” when exposed to sufficient levels of stress.

Transposition

• Historically evolution was thought to be the result of slow transitions expressed over long periods of time (many generations).
  • Transposition changes this equation, and opens the possibility of rapid changes in short intervals.
  • Break-run (punctuated equilibrium).
Punctuated equilibrium

- Punctuated equilibrium is a theory in evolutionary biology. It states that most sexually reproducing populations will show little change for most of their geological history, and that when phenotypic evolution does occur, it is localized in rare, rapid events of branching speciation (called cladogenesis).

Punctuated equilibrium

- Punctuated equilibrium is commonly contrasted against the theory of phyletic gradualism, which states that evolution generally occurs uniformly and by the steady and gradual transformation of whole lineages (anagenesis). In this view, evolution is seen as generally smooth and continuous.

Punctuated equilibrium

- Punctuated equilibrium contradicts some of Darwin's ideas regarding the specific mechanisms of evolution, but generally accords with Darwin's theory of evolution by natural selection.

Transpons

- Sequences of DNA that move around to different positions within the genome of a single cell.
- They control developmental processes, and they may cause mutations and change the amount of DNA in the genome.

Transpons

- The Ac/Ds system described by McClintock are now called Class II: DNA transpons.
- These transpons usually move through a deletion and insertion process. The computer analogy is:
  - cut and paste

Class I: Retrotranspons

- Work by copying themselves and pasting copies back into the genome in multiple places.
- Retrotranspons copy themselves to RNA (transcription), and the RNA is copied into DNA by reverse transcriptase and inserted back into the genome.
Transpons

- Transpons may confer some benefit on their **hosts**, but they are generally considered to be selfish DNA **parasites** that live within the genome of cellular organisms.
- Similar to viruses.

Transpons

- Evolution of transpons is a dynamic field of study.
- Transposons are found in all major branches of life. They may or may not have originated in the **last universal common ancestor**, or arisen independently multiple times, or perhaps arisen once and then spread to other kingdoms by **horizontal gene transfer**.

Retroviruses

- Retroviruses were first identified 80 years ago as agents involved in the onset of cancer. More recently the AIDS epidemic has been shown to be due to the HIV retrovirus. In the early 1970s it was discovered that retroviruses had the ability to replicate their RNA genomes via conversion into DNA which became integrated in the DNA of the host cell.

Retroviruses

- Viruses and transposons also share features in their genome structure and biochemical abilities, leading to speculation that they **share a common ancestor**.
- Since excessive transposon activity can destroy a genome, many organisms seem to have developed mechanisms to reduce transposition to a manageable level (genetic deletion).
- Transposons may have been co-opted by the **vertebrate immune system** as a means of producing antibody diversity.

Heredity

- The DNA within any organism is a combination of the genes inherited from their parents, and the DNA injected into the genome via invader transpons.
- Some authorities claim that about 50% of the genes in an organism were derived from invader transpons.
- Once the DNA is in the genome it is passed on to the next generation.
- The invasion is an ongoing process, impacting on the fitness of the phenotype, and then selection can act to favor or reject that genotype.
Transposons are mutagens. They can damage the genome of their host cell in different ways: 

- A transposon or a retroposon that inserts itself into a functional gene will most likely disable that gene.
- After a transposon leaves a gene, the resulting gap will probably not be repaired correctly.
- Multiple copies of the same sequence, such as Alu sequences can hinder precise chromosomal pairing during mitosis, resulting in unequal crossovers, one of the main reasons for chromosome duplication.

Diseases that are often caused by transposons include hemophilia A and B, severe combined immunodeficiency, porphyria, predisposition to cancer, and Duchenne muscular dystrophy.

Additionally, many transposons contain promoters which drive transcription of their own transposase. These promoters can cause aberrant expression of linked genes, causing disease or mutant phenotypes.

Controls differentiation and development.

- Permits reorganization of the genome in response to environmental change.
- Is vulnerable to invasion by selfish DNA parasites.
  - Some invaders may promote antibody diversity and improve survivorship.
  - Others damage the host.
  - Helpful and harmful transposons may share a common ancestor.