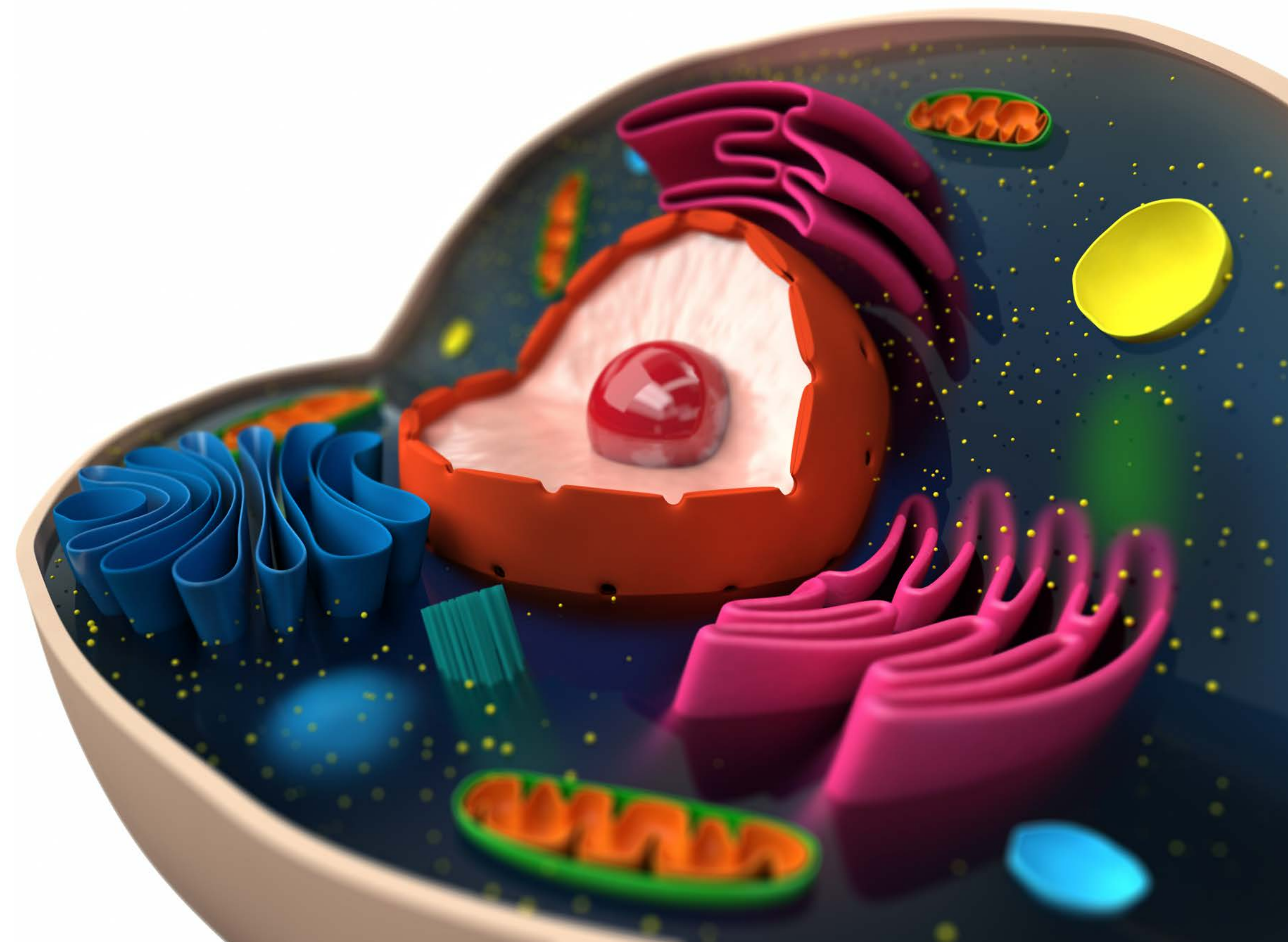


Faith & Science CONFERENCE



EPIGENETICS, ORPHAN GENES AND PSEUDOGENES

Warren Grubb



- Evolution is based on the premise that only a very simple form of life could have spontaneously emerged and that from that simple form more complex forms have developed.
- Living organisms are divided into two structurally different life forms:

1. Prokaryotes

- Bacteria and Archaea

2. Eukaryotes

- Fungi, Algae, Protozoa, Plants & Animals.



- ▶ **Prokaryotes** are the least complex free-living organisms and the Archaea are regarded as being the closest to the earliest forms of life.
- ▶ **Eukaryotes** are quite different structurally but we will only look at the differences in the organisation of the DNA.



Genetic material	Prokaryotes	Eukaryotes
Membrane-bound nucleus	None	Present
Histones with DNA	None	Present
Number of Chromosomes	One [*]	> one
Circular chromosome	Yes ^{**}	No
Introns	Rare	Yes
Nucleolus	None	Yes
Mitosis	No	Yes

^{*}*Some may have > 1. Some have extrachromosomal genes - plasmids.*

^{**}*In B.bergdorferi it is linear*



► For an organism to acquire new phenotypes (features) it has to acquire additional DNA and from this DNA new coding genes have to emerge i.e. genes must arise *de novo*.

► Two processes for acquiring more DNA:

1. Horizontal transfer
2. DNA duplication



1. HORIZONTAL TRANSFER

Eukaryotes - occurs during the sexual process when the fertilised egg acquires DNA from both partners.

Prokaryotes – three processes:

- i. **Transduction** – bacteriophages can occasionally transfer small amounts of DNA, instead of their own DNA, or small amounts of host DNA together with their own DNA. The phages have very high host specificity and the host DNA transferred has to be compatible with the DNA of the new host.



Prokaryotes –three processes cont.

ii. Transformation –DNA released by one cell is taken up by another. Limited in non-laboratory conditions and only between related organisms.

iii. Conjugation - Some bacteria are able to transfer their DNA to another bacterium by cell to cell contact. Once again it only occurs between related organisms.



RELEVANCE

- Only occurs between related organisms and therefore related DNA.
- Except for transposition from incoming DNA these do not add to the amount of DNA in the cell.
- Prokaryotes can acquire plasmids from related organisms.



2. GENE DUPLICATION

➤ Can arise by¹:

- Errors in replication.
- Errors in repair;
- Selfish DNA – DNA that makes copies of itself without making any contribution to the organism.²

“The classic model of evolution is based on duplication, rearrangement, and mutation of genes with the idea of common descent.”³

1. https://en.wikipedia.org/wiki/Gene_duplication
2. https://simple.m.wikipedia.org/wiki/Selfish_DNA
3. https://en.wikipedia.org/wiki/Orphan_gene



GENE

- Different definitions over time. There is agreement that a sequence that codes for a protein is a gene.
- About 1/5 of human genome has been associated with protein coding genes.¹
- In sequencing there are difficulties in distinguishing between protein coding and non-coding sequences.²

1. https://en.wikipedia.org/wiki/Long_non-coding_RNA

2. <https://f1000research.com/articles/6-57/v1>



GENE cont.

- ▶ Many genes are now being found in noncoding genomic regions.¹
- ▶ In addition RNA transcripts of noncoding “junk” DNA have been found to have regulative function.²
- ▶ “All definitions of genes are linked to the notion of function, as it is generally agreed that a genuine gene should encode a functional product, be it RNA or protein.”³

1. <https://www.ncbi.nlm.nih.gov/pubmed/25773713/>

2. <https://www.ncbi.nlm.nih.gov/pubmed/23618400>Pseudogenes: pseudo or real functional elements?

3. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6542195/>



PSEUDOGENES

- Pseudogenes are ubiquitous and abundant in genomes.¹
- Had been regarded as duplicates of ancient protein-coding genes which had mutated over time and lost their function² and that mutation and rearrangement of these could produce new genes - *de novo* genes
- This raises the questions “Why organisms maintain pseudogenes and pay a cost of energy? Replication of these genes over generations is a disadvantageous biochemical process. Why would not natural selection remove these costly DNA segments? What is the potential benefit to keep non-protein-coding sequences?”³

1. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3352212/>

2. <https://www.ncbi.nlm.nih.gov/pubmed/23618400>

3. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3352212/>



PSEUDOGENES

- Many RNA transcripts of the nonprotein-coding sequences, "junk" DNA, and have been found to have regulatory functions.
- micro RNAs (miRNAs) of about 22nt long repress gene expression at the mRNA level.
- There are other nonprotein-coding RNA transcripts [competitive endogenous RNAs (ceRNAs)] which also bind to miRNA and therefore can affect gene expression.
- ceRNAs include: long non-coding RNA (longNC RNAs or lncRNAs); small circular RNA (circRNA) and **pseudogenes**.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5192809/>

[https://en.wikipedia.org/wiki/Competing_endogenous_RNA_\(CeRNA\)](https://en.wikipedia.org/wiki/Competing_endogenous_RNA_(CeRNA))



PSEUDOGENES

- ▶ Pseudogene's RNA transcripts have regulatory function.
- ▶ Transcripts of two types:
 1. **Contain introns.** Considered to be non-coding mutated duplicates of ancestral protein-coding genes. Regarded as the strict definition of a pseudogene.
 2. **No introns.** Considered to be reverse transcriptase DNA copies of the mRNAs of the above.

<http://www.biology-pages.info/P/Pseudogenes.html>
<https://en.wikipedia.org/wiki/Pseudogene>



PSEUDOGENES

- ▶ The fact that similar pseudogenes are found in other organisms isn't surprising considering that all forms of life have some genes in common. E.g. metabolic and synthesis genes. It would be expected that they would have similar regulatory genes.



ORPHAN GENES

- ▶ Orphan genes are distinguished from pseudogenes in that sequences similar to them are only found in closely related organisms and sometimes restricted to a single species.¹
- ▶ Often regarded as orphan genes because they have no evolutionary parents.²
- ▶ ‘A more precise term is “taxonomically restricted genes.”’²
- ▶ Found every time an organism is sequenced.²

1. https://en.wikipedia.org/wiki/Orphan_gene

2. <https://natureecoevocommunity.nature.com/users/24561-richard-%20buggs/posts/14227-the-unsolved-evolutionary-conundrum-of-orphan-genes>



ORPHAN GENES

► Their role is being debated.¹

- Many found to be protein coding and have important functions.^{1,2,3}
- artifacts³
- nonprotein-coding RNAs³
- source of *de novo* genes²

1. https://en.wikipedia.org/wiki/Orphan_gene

2. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6542195/>

3. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4888513/>



ORPHAN GENES

► Evolutionary role?

- Hard problem for evolutionary genomics.¹
- Still being debated, may have no role.²
- Create spurious peptides not maintained by selection.²
- Source of *de novo* genes?

1. <https://natureecoevocommunity.nature.com/users/24561-richard-%20buggs/posts/14227-the-unsolved-evolutionary-conundrum-of-orphan-genes>
2. https://en.wikipedia.org/wiki/Orphan_gene



ORPHAN GENES

► Conundrum?

- If they have no function why would an organism retain them?

It is an energy cost to the cell. Replication of these genes over generations is a disadvantage biochemically. There is no selective pressure to retain them.¹

- A source of *de novo* gene?

The cell/organism doesn't know it needs to retain surplus DNA for future genetic diversity and therefore no selective pressure to retain them - at an energy cost.

1. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3352212/>



ORPHAN GENES

► Explanations?

- As some have been found to have function, perhaps they all have a role in the cell. Just hasn't been elucidated.



EPIGENETICS

- ▶ Heritable phenotypic changes that do not involve the DNA sequence.¹
 - ▶ Caused by chemical modification of DNA and protein.
 - ▶ Once thought that only the protein in the nucleus was sufficiently complex to encode heredity. DNA was too simple.
 - ▶ When DNA was demonstrated to encode for heredity, protein was dismissed as having any heredity role.
 - ▶ Now know protein can have a role.

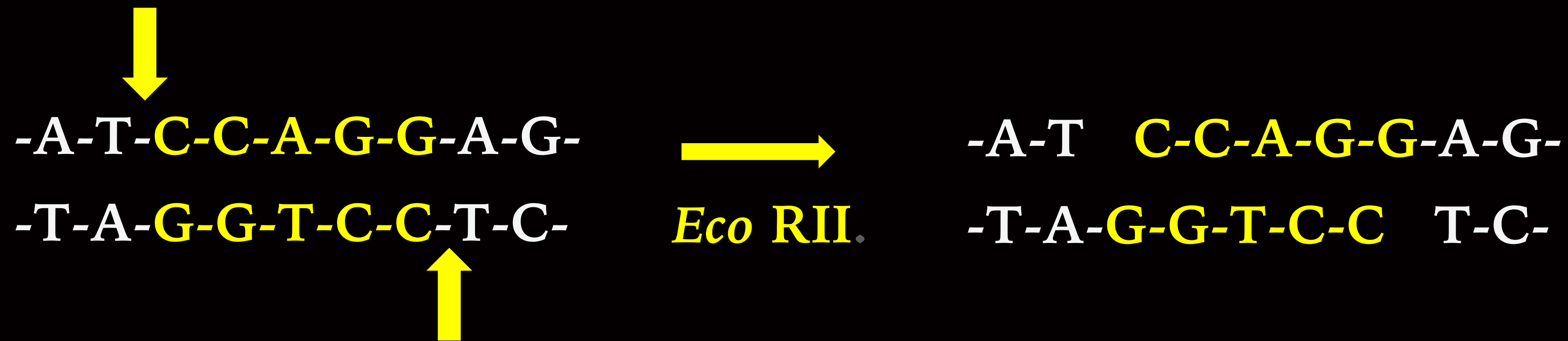
1. <https://en.wikipedia.org/wiki/Epigenetics>



EPIGENETICS

► In prokaryotes.

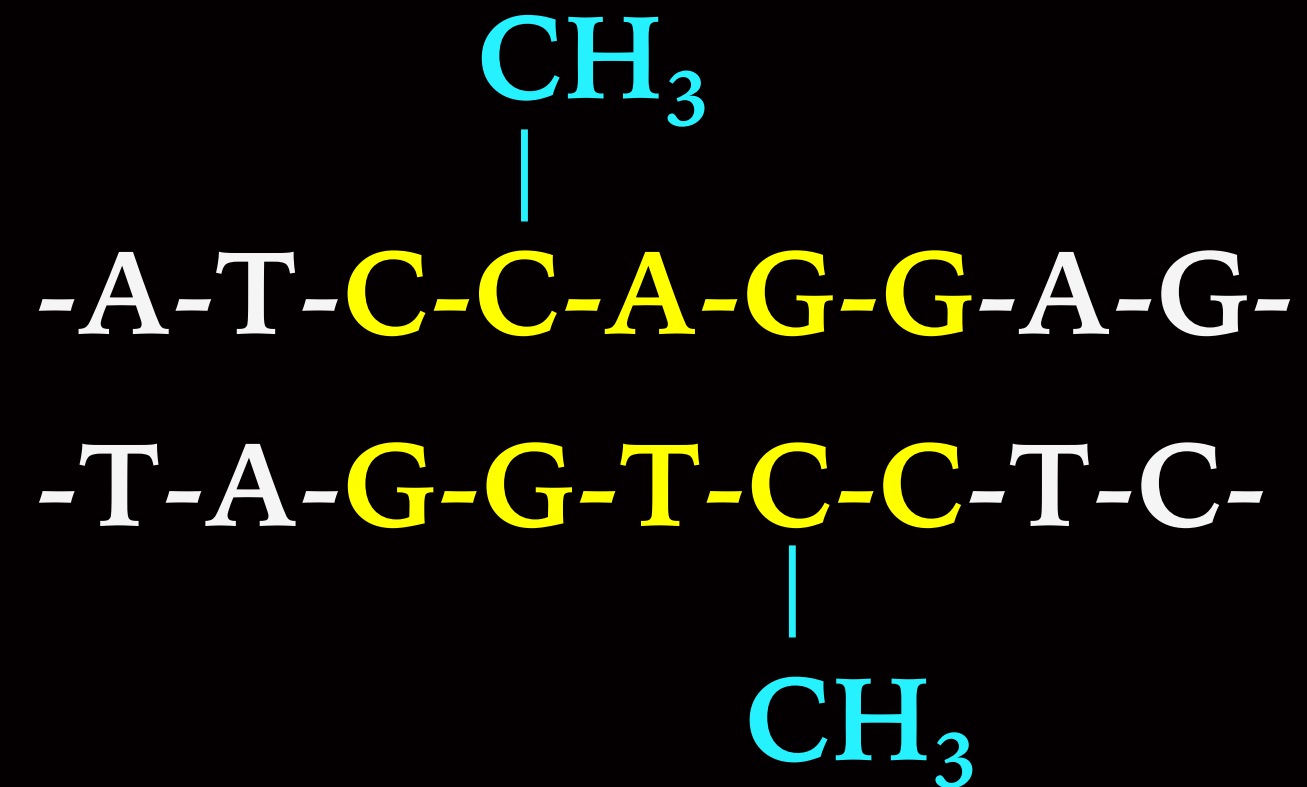
- Bacteria restrict the entry of foreign DNA by cutting it at specific sequences. Different enzymes recognize different sites.



EPIGENETICS

► In prokaryotes.

- To protect its own DNA from being cut the organism modifies the site by methylating a cytosine.



EPIGENETICS

► In eukaryotes.

- Also methylation of DNA.
- In addition modification of histones.
- At least 9 modifications of histones e.g:
 - lysine acetylation
 - lysine and arginine methylation
 - serine/threonine/tyrosine phosphorylation
 - serine/threonine ubiquitylation.

<https://docs.abcam.com/pdf/chromatin/a-guide-to-epigenetics.pdf>



EPIGENETICS

► Significance

- Normal function is to regulate morphogenesis, cellular differentiation and gene expression by turning genes on or off and regulating gene expression.
- Can be affected by external factors resulting in abnormal functions.

<https://en.wikipedia.org/wiki/Epigenetics>



EPIGENETICS

► Significance

► Affected by external factors e.g. in humans.

- diet,
- obesity,
- physical activity,
- tobacco smoking,
- alcohol consumption,
- environmental pollutants,
- psychological stress,
- working on night shifts,
- chemical pollutants,
- temperature changes

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3752894/>
<https://www.nature.com/articles/nrg3142>



EPIGENETICS

► Significance

► Affects in humans of epigenetic changes e.g.

- Possible impact on IQ.
<https://www.sciencedaily.com/releases/2018/09/180924102037.htm>
- Possible impact on autism.
<https://iancommunity.org/ssc/dna-and-environment-what-determines-how-our-genes-work>
- Cancer.
[https://www.ncbi.nlm.nih.gov/pubmed/31049029?log\\$=activity](https://www.ncbi.nlm.nih.gov/pubmed/31049029?log$=activity)
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2802667/>



EPIGENETICS

► Evolutionary implications

- Changes don't provide new DNA.
- Can only alter expression of existing genes.
- Stability of epigenetic changes?

Changes reversible <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2802667/>

► Inheritable but for how many generations?

“--- central question remains: are epigenetic states transmitted over a sufficient number of generations to give rise to natural selection?

<https://www.encyclopédie-environnement.org/en/health/epigenetics-how-the-environment-influences-our-genes/>



EPIGENETICS

► Evolutionary implications

- Externally induced changes appear to be negative for organisms.
- Does not provide new genes – only affects the expression of existing genes.

<https://www.encyclopédie-environnement.org/en/health/epigenetics-how-the-environment-influences-our-genes/>



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