

Bioinformatics

CS300

**Horizontal Gene Transfer
Database, Tools, Multiseq Alignment**

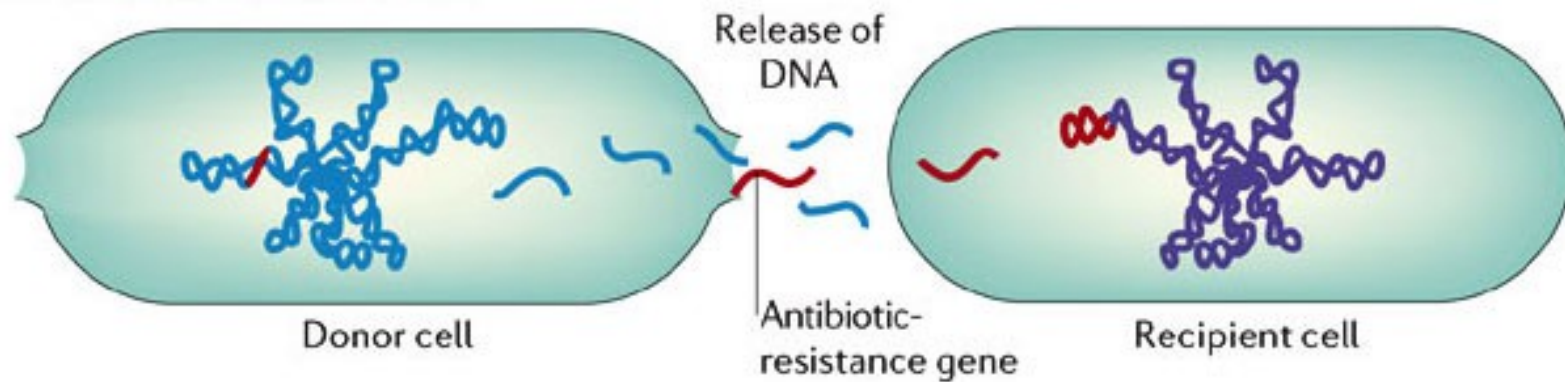
Fall 2017

Oliver Bonham-Carter

Horizontal Gene Transfer

Horizontal gene transfer (HGT) refers to the **transfer of genes** between organisms in a manner other than traditional reproduction.

a Bacterial transformation



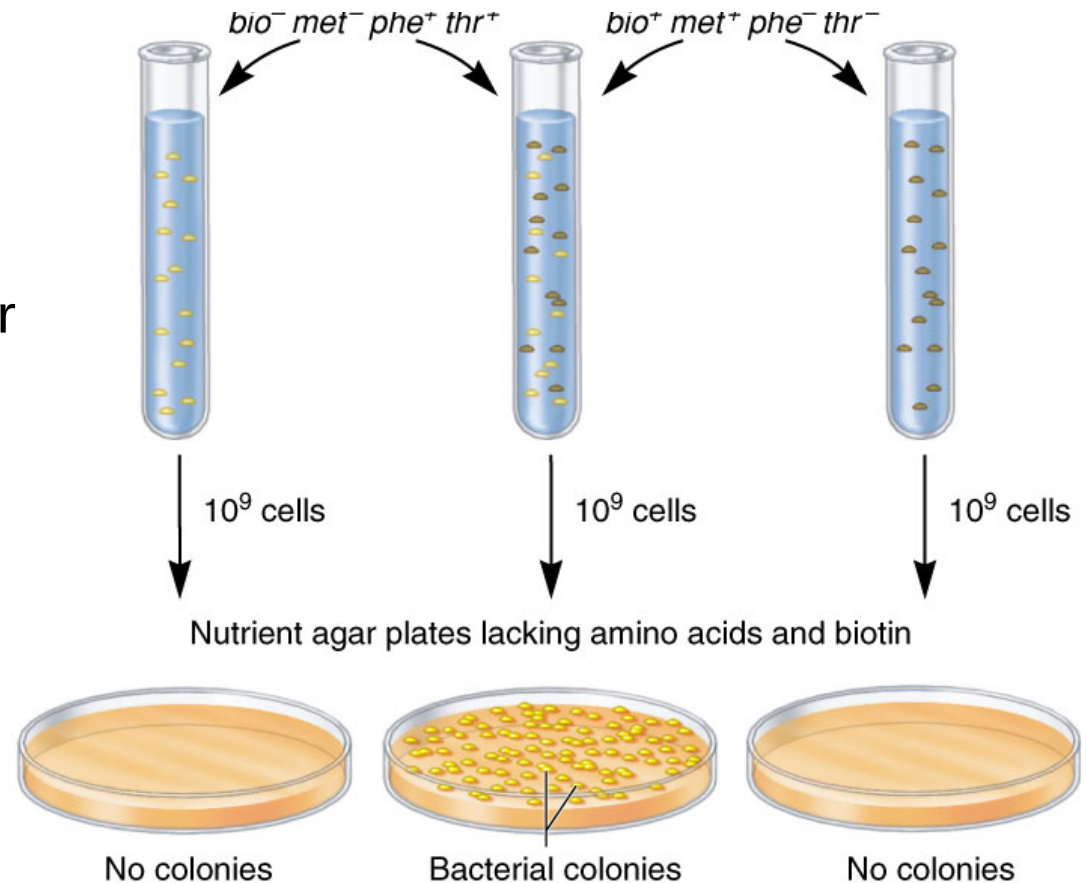
What is HGT (Horizontal Gene Transfer)

- The transmission of portions of genomic DNA between organisms
- A process decoupled from vertical inheritance (no mating).
- Various fragments of the genome are the result of different evolutionary histories and come from unrelated organisms.
- This can therefore complicate the investigations of evolutionary relatedness of lineages and species

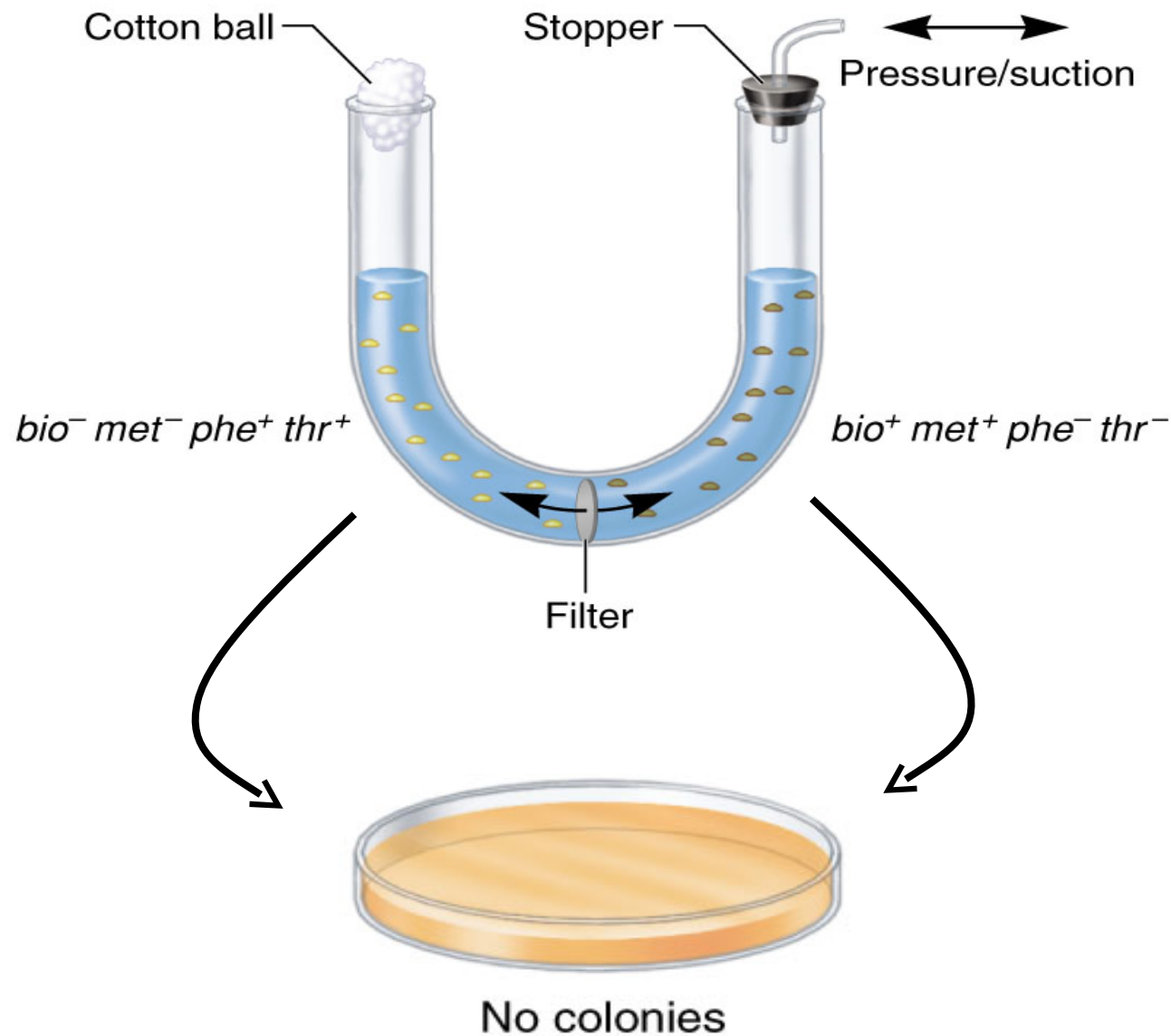
Genetic Sharing

	<i>bio</i>	<i>met</i>	<i>phe</i>	<i>thr</i>
Strain 1	+	+	-	-
Strain 2	-	-	+	+

- Colonies have opposing growth requirements
- Each colony requires two extra genes to survive under conditions.
- In the experiment, colonies randomly share missing genes with each other.
- Cells with HGT survive to make a new colony.



Transfer of Genes From Physical Contact



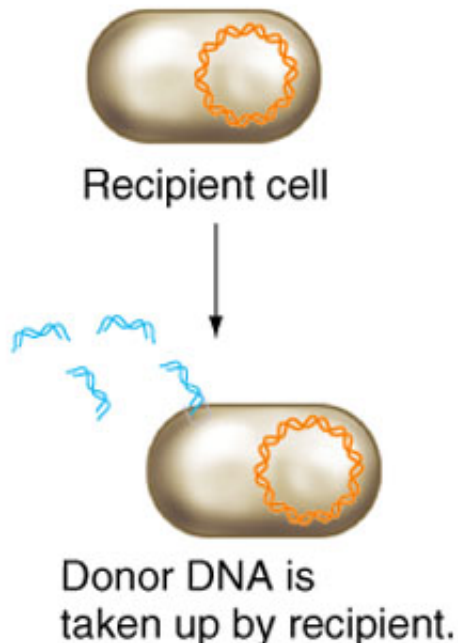
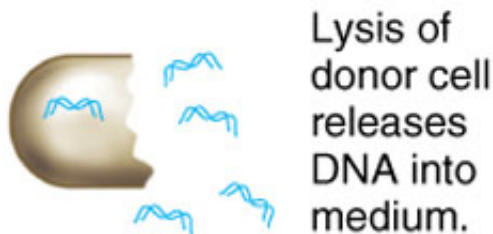


Mechanisms of DNA Transfer

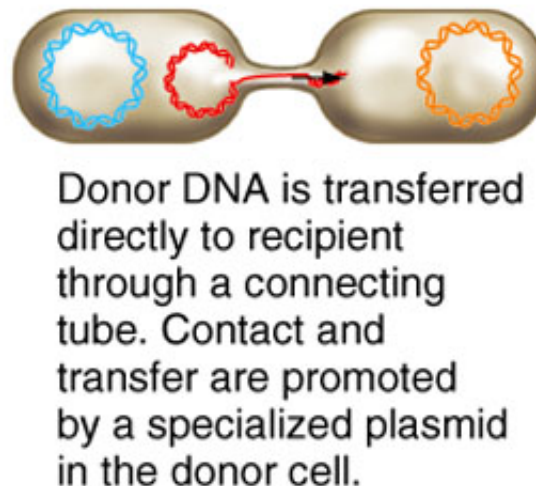
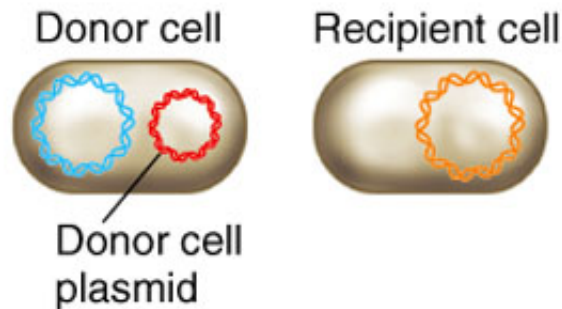
- Conjugation
 - Physical interaction between cells
- Transduction
 - Virus mediated transfer of DNA between bacteria
- Transformation
 - Requires release of DNA into the environment and then the manual take-up of the DNA by bacteria

Mechanisms of DNA Transfer

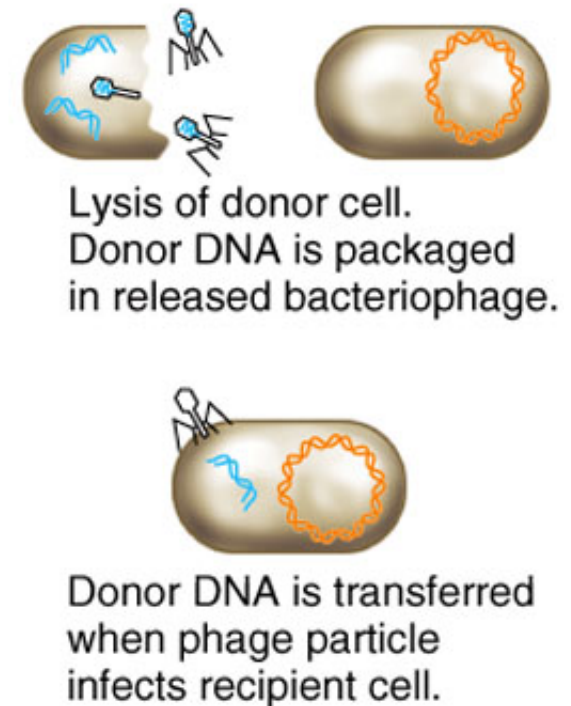
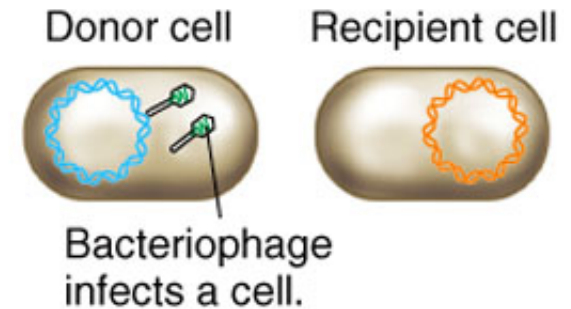
Transformation



Conjugation

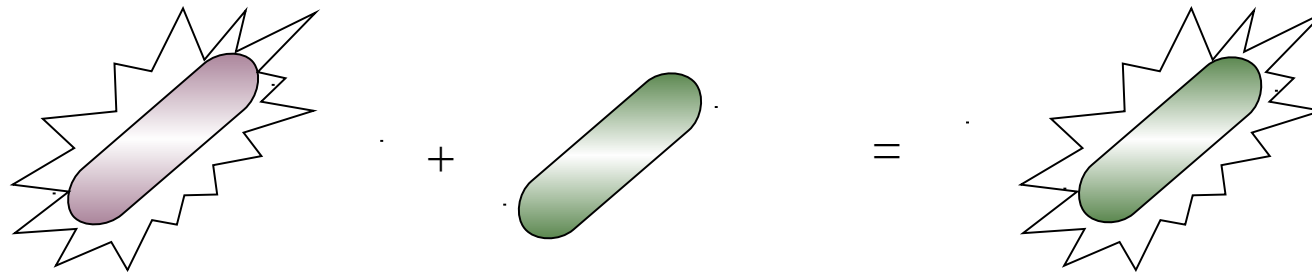


Transduction



Bacterial Conjugation

- Only specific bacteria can serve as donors
 - Arber, Werner. *"Horizontal gene transfer among bacteria and its role in biological evolution."* Life 4.2 (2014): 217-224.
- Five per cent of *E. coli* are naturally donors
- Can be converted when incubated first with a donor strain.



Donor +

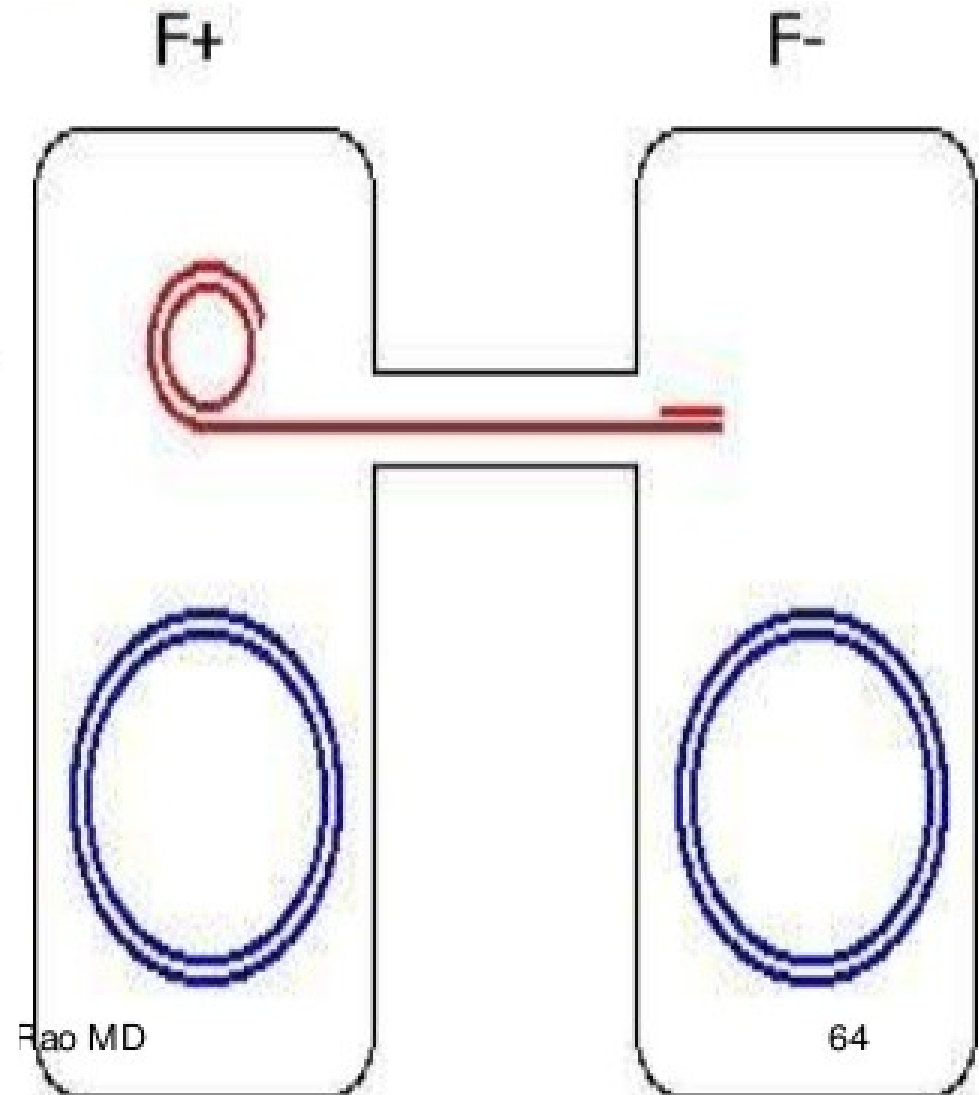
Donor -

Donor+

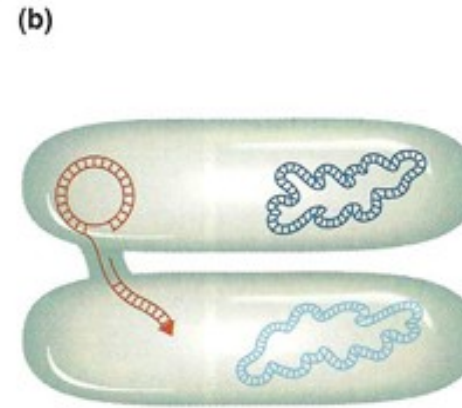
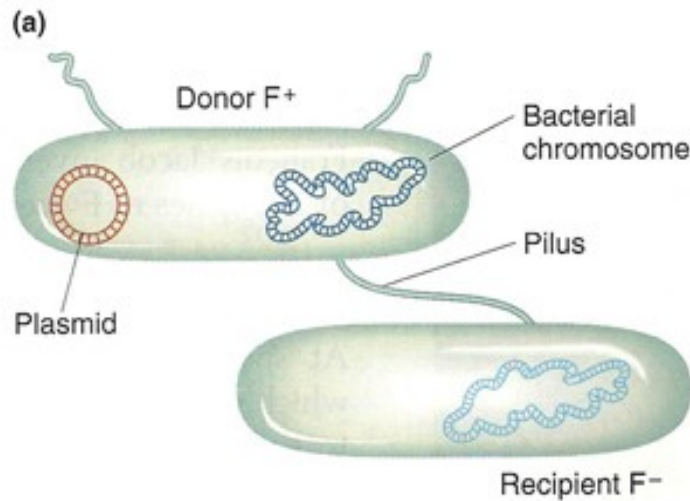
Transfer of genetic material

F Factor

- Transfer factor that contains the genetic information necessary for synthesis of Sex Pilus and for self transfer without any other identifiable genetic materials such as drug resistance

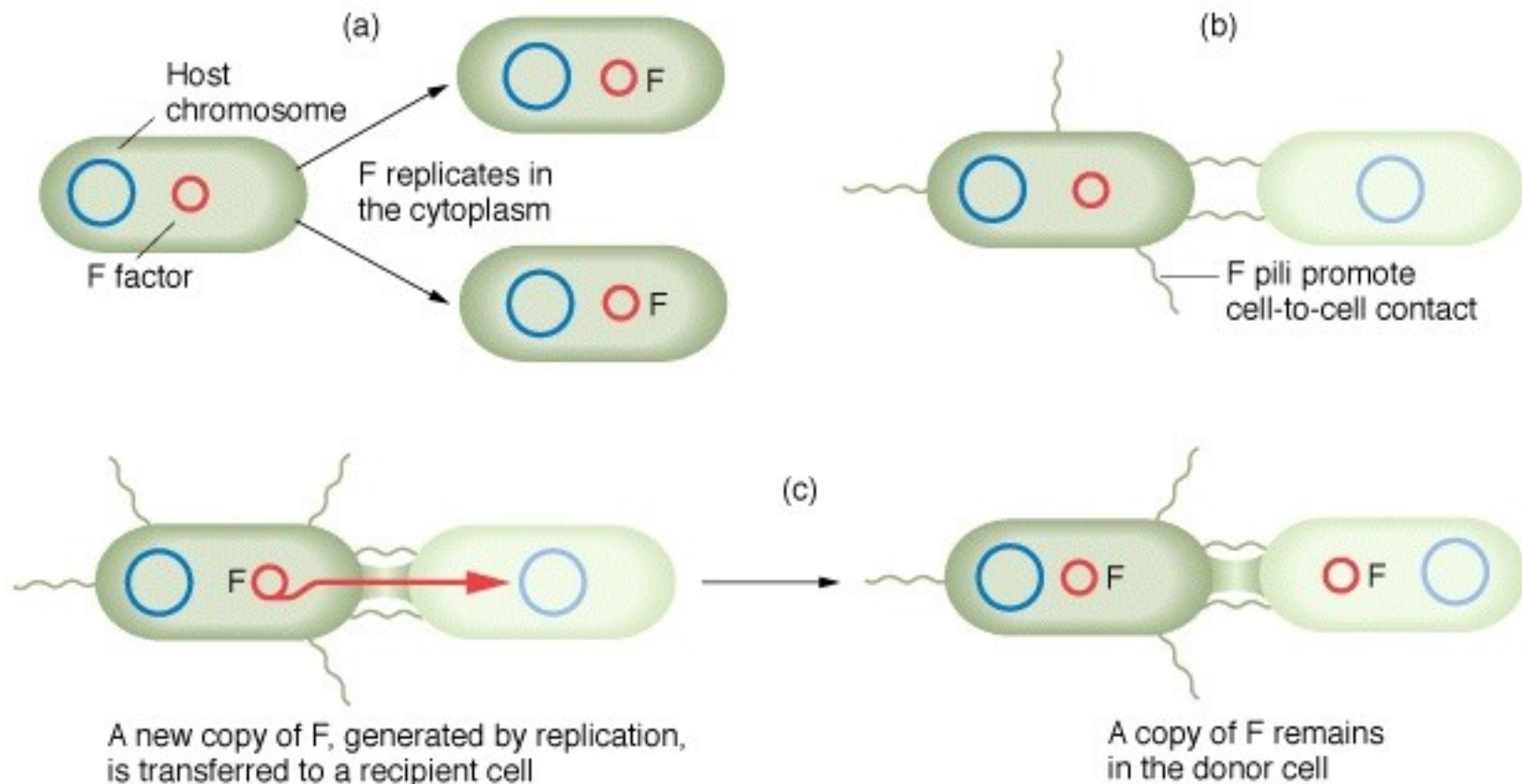


F Factor Is a Plasmid



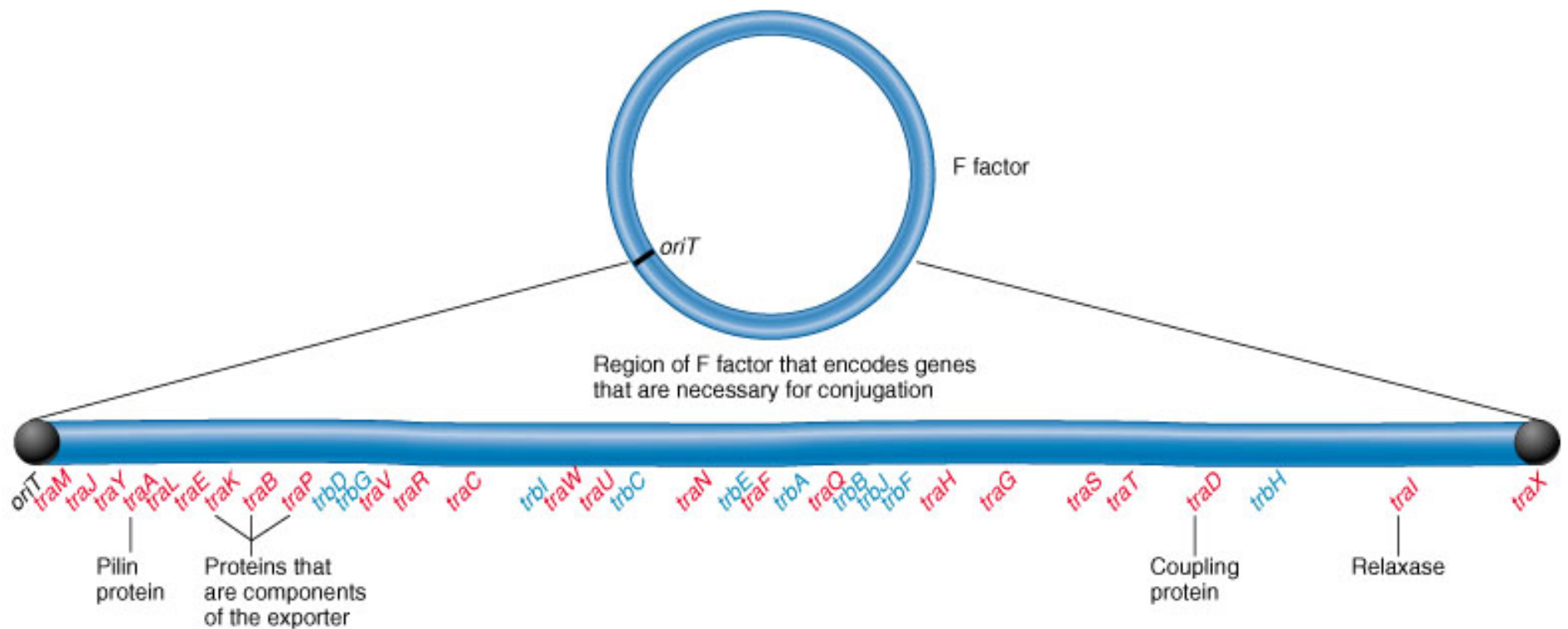
Conjugation Mechanism

- F-Factor: a material that is encoded on the plasmid (bacterial DNA). F⁺ (has) F⁻ (does not have)
- Plasmids are transferred containing genes of sender to receiver



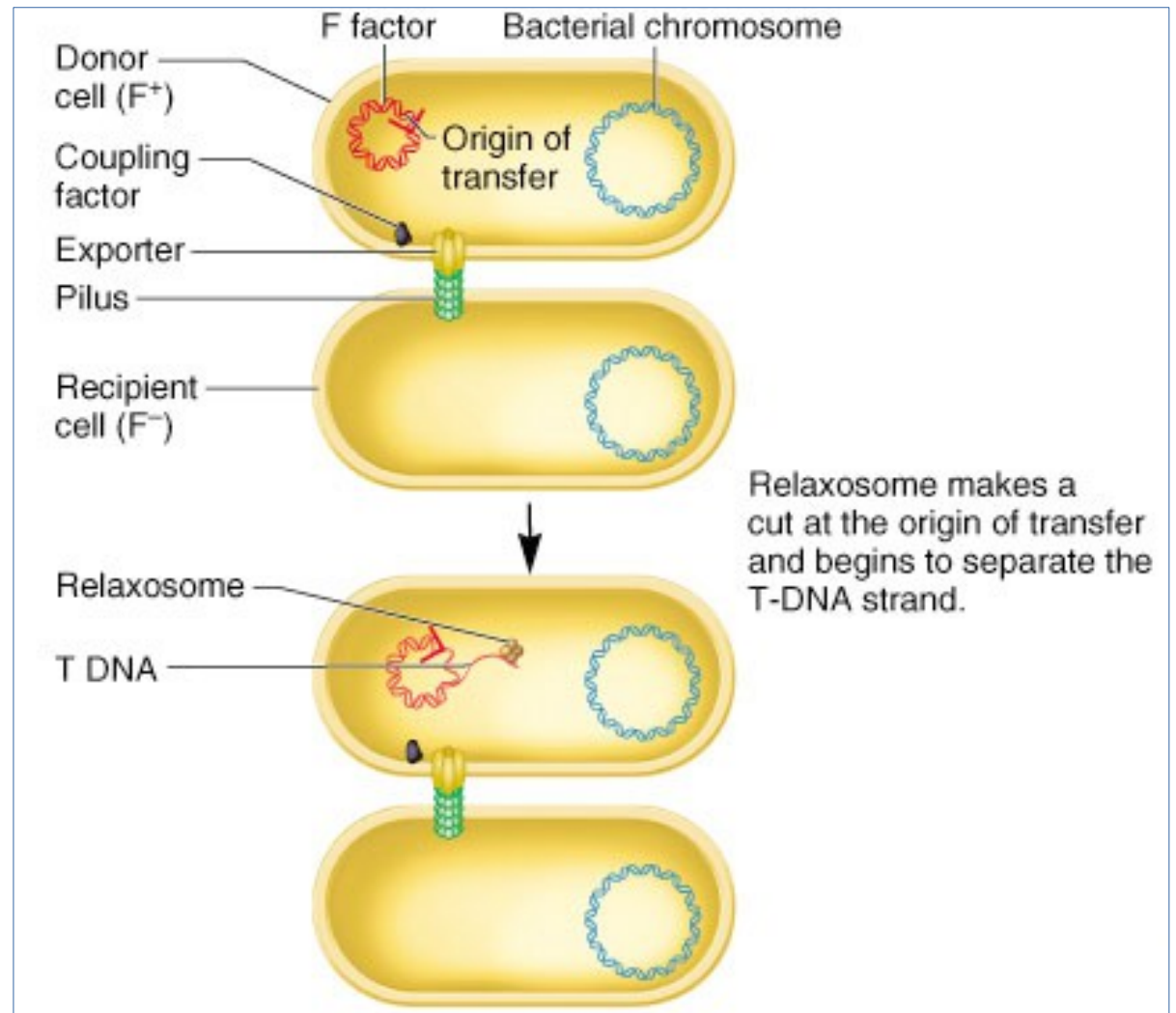
Conjugation Apparatus

- Physical contact is made between strains and the bacteria are brought together.
- Gene sharing possible if F Factor present.



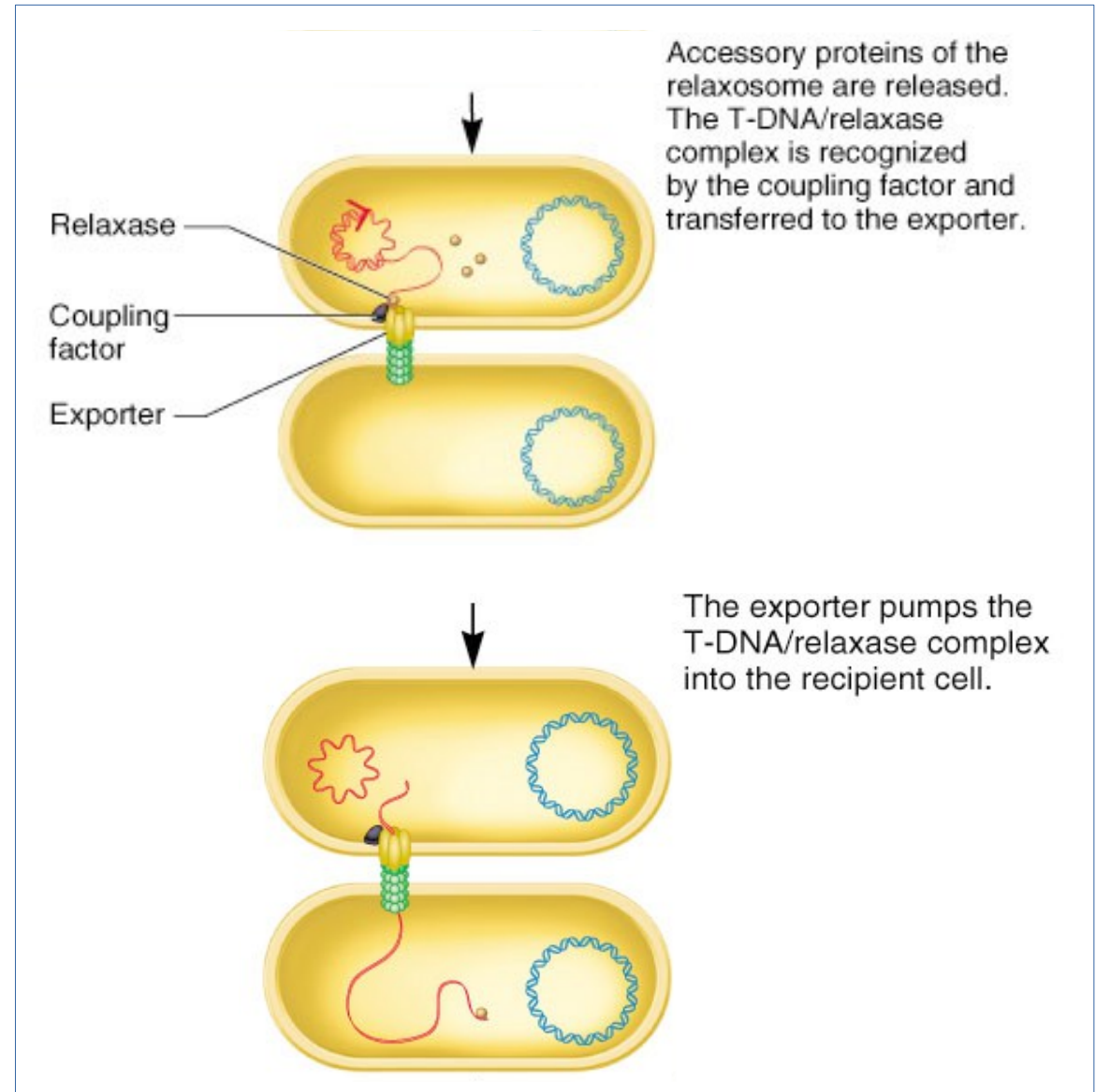
Mechanism of Transfer

- Relaxosome is produced
- Relaxosome recognizes the origin of the transfer
- One DNA strand is cut and transferred over the conjugation tube (T DNA).



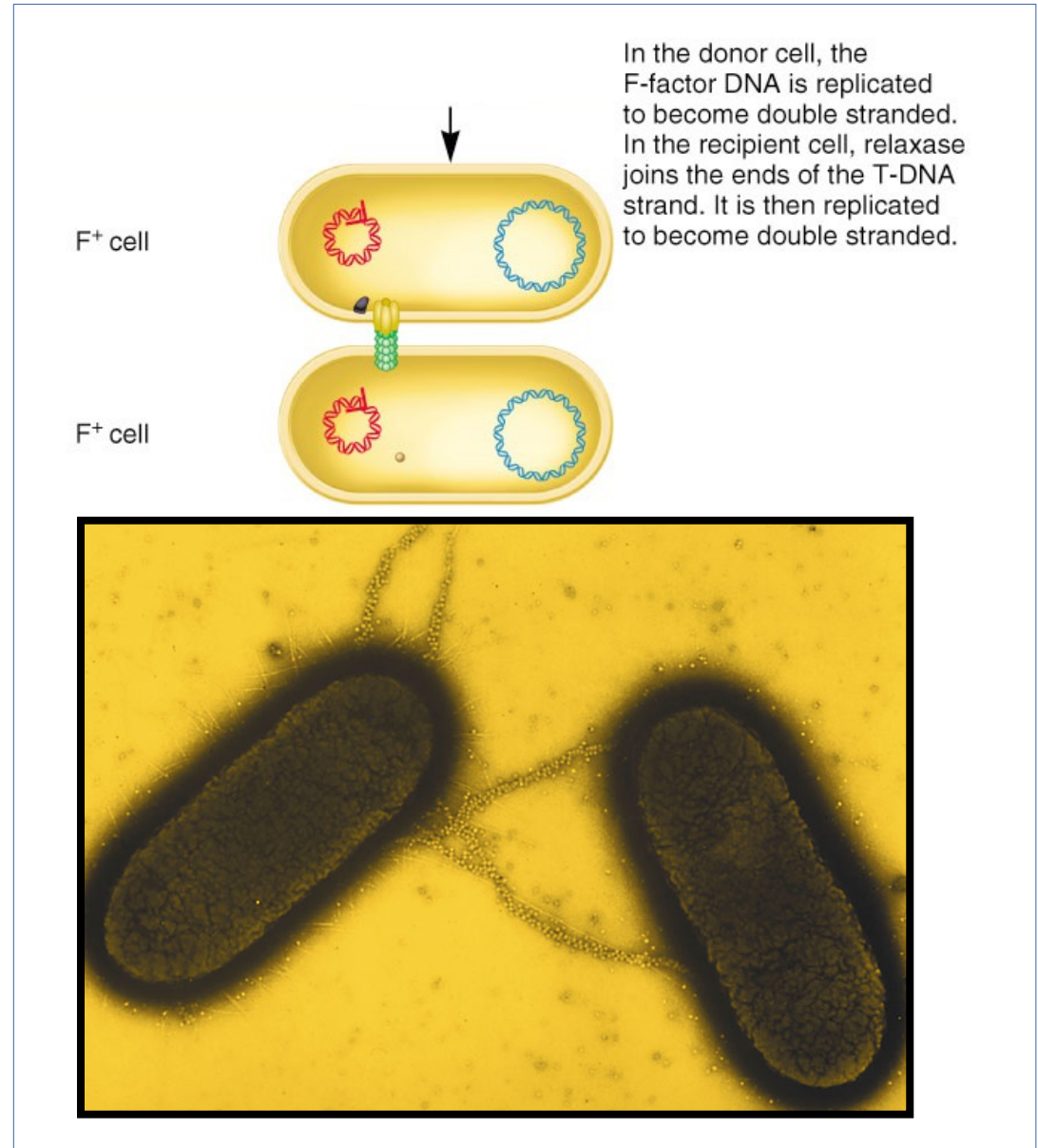
Mechanism of Transfer

- T DNA is separated but bound to relaxase protein.
- Complex called nucleoprotein
- Complex is recognized by a coupling factor, fed through exporter (conjugation tube)



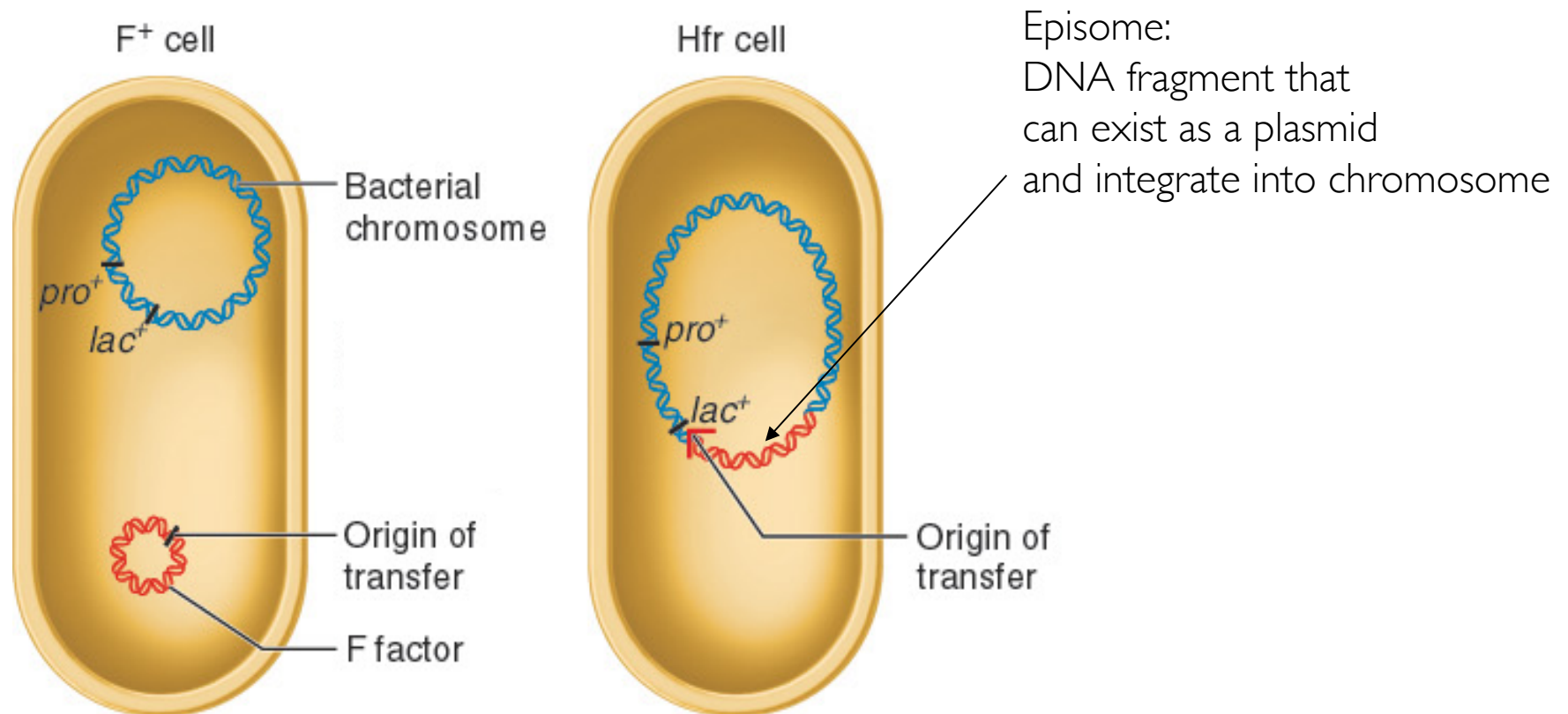
F Factor Transfer

- Relaxase joins ends to produce circular molecule
- Single strands of F Factor are in both cells (DNA replication)



Integration of DNA into Chromosome

- Genes encoded on F Factor can integrate into host DNA and alter its genotype (genetics) and phenotype (look-like)
- An *Hfr* strain was derived from an F⁺ strain





Did You Say, *Hfr* Strain?

- E. Coli strain discovered as Hfr (high frequency of recombination)
- Hfr strain transfers chromosomal DNA from F-strains
- Transfer begins at the origin of the transfer
- The amount of DNA transferred depends on the time allowed for conjugation



Known Instances of HGT

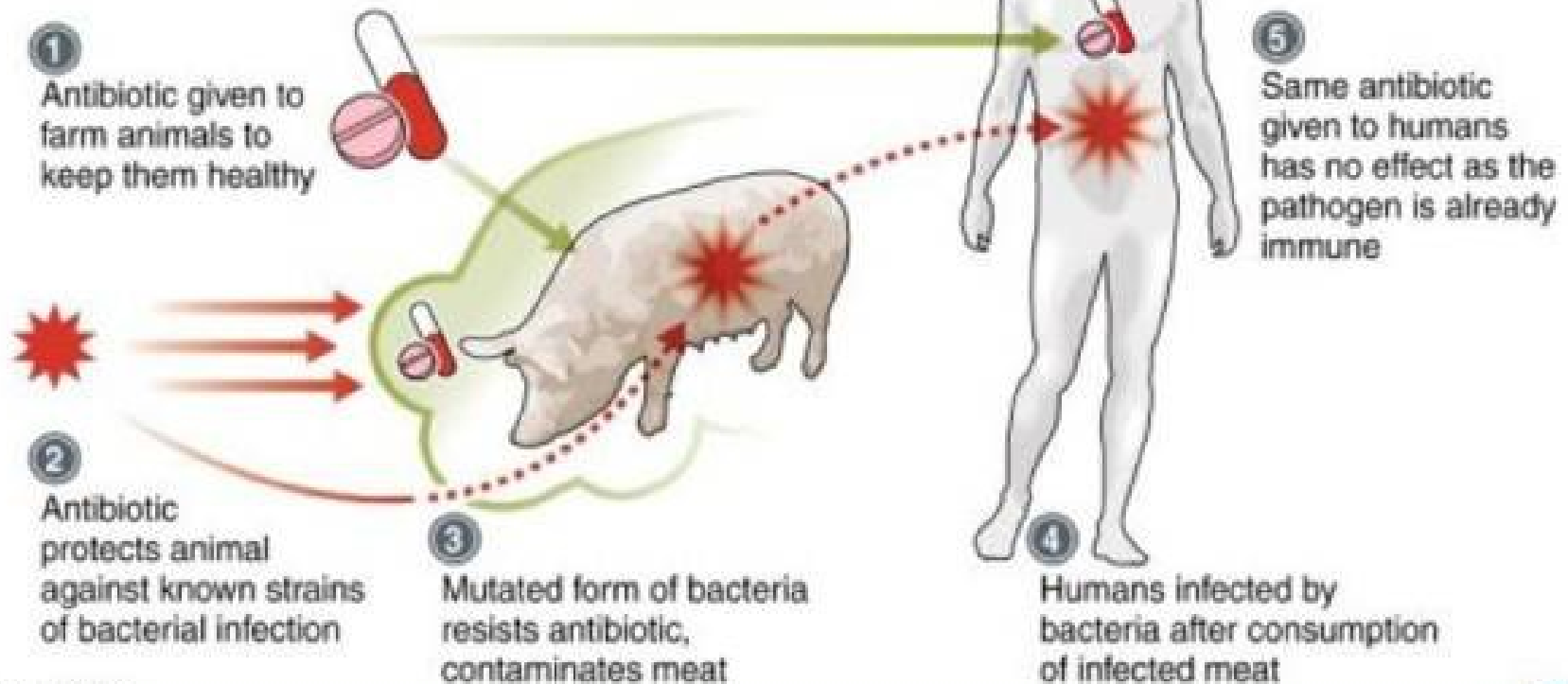
- Antibiotic resistance genes on plasmids
- Insertion sequences
- Pathogenicity islands
- Toxin resistance genes on plasmids
- Viruses and viroids
- Organelle to nucleus transfers

From Farm-to-Fork Spread of Antibiotic Resistance

Antibiotic drug abuse

Overuse of antibiotics in agriculture is widening the spread of superbugs that are immune to common drugs

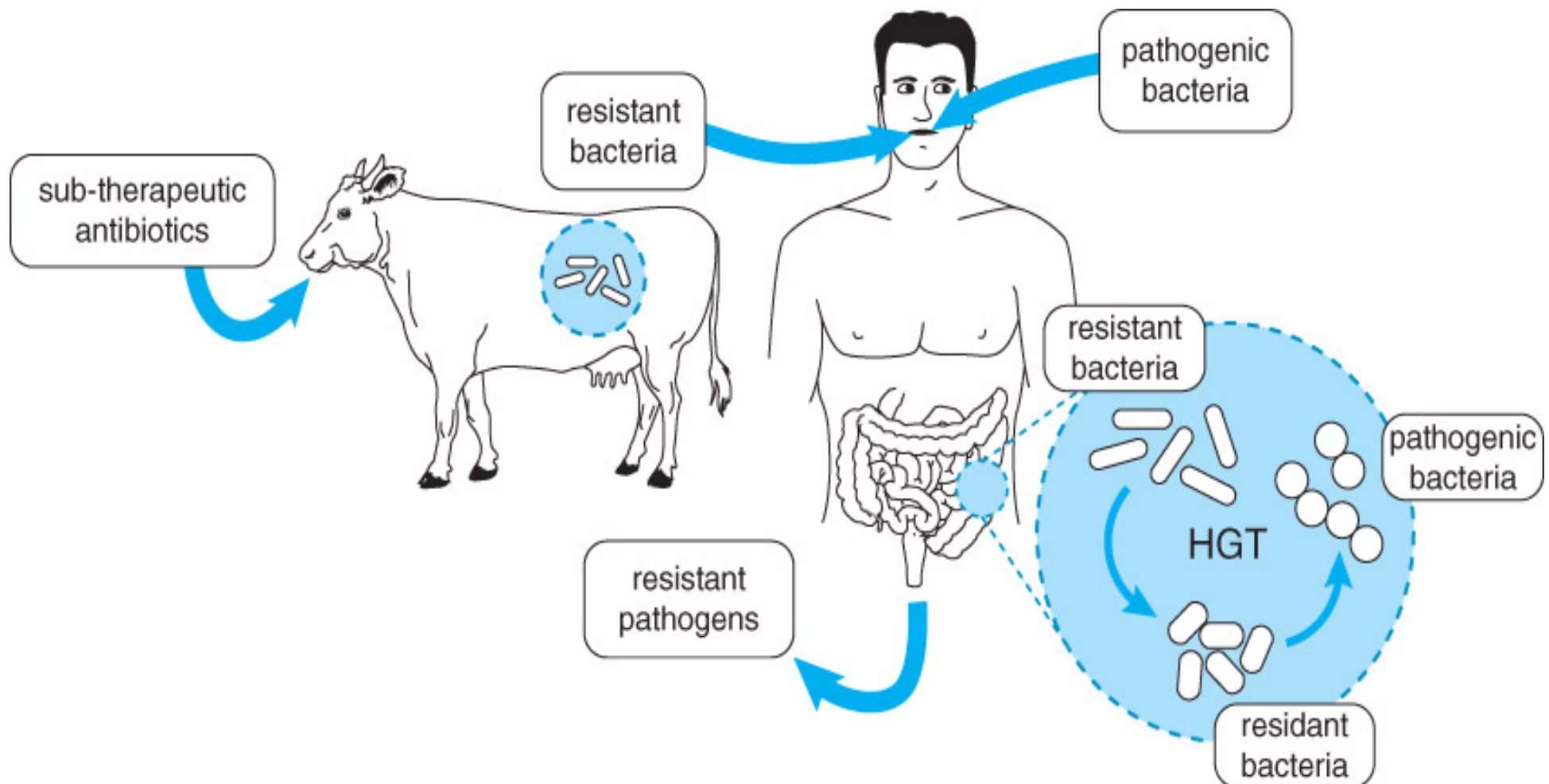
Path of resistance



Source: WHO

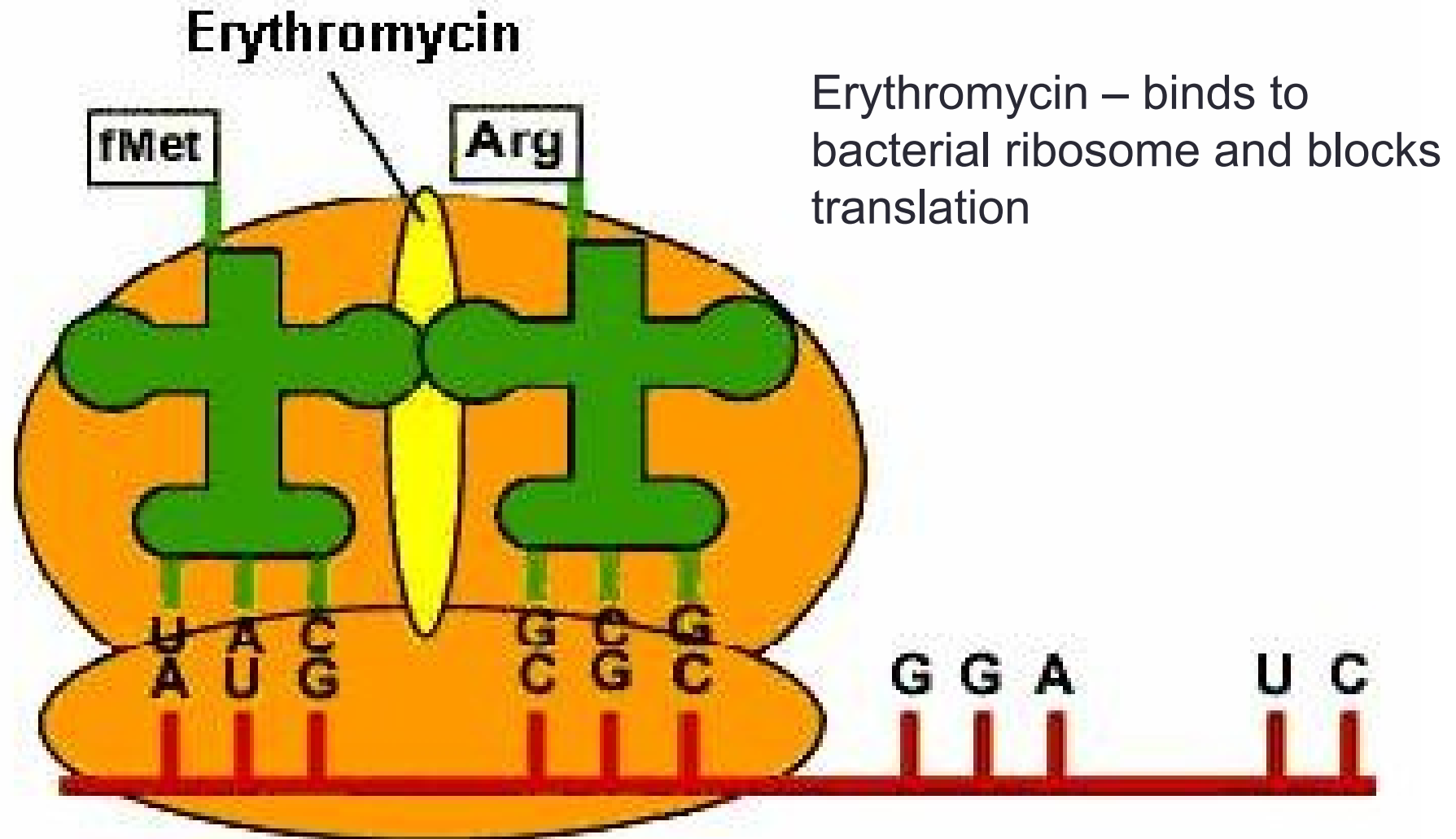
AFP

Horizontal Gene Transfer of Antibiotic Resistance



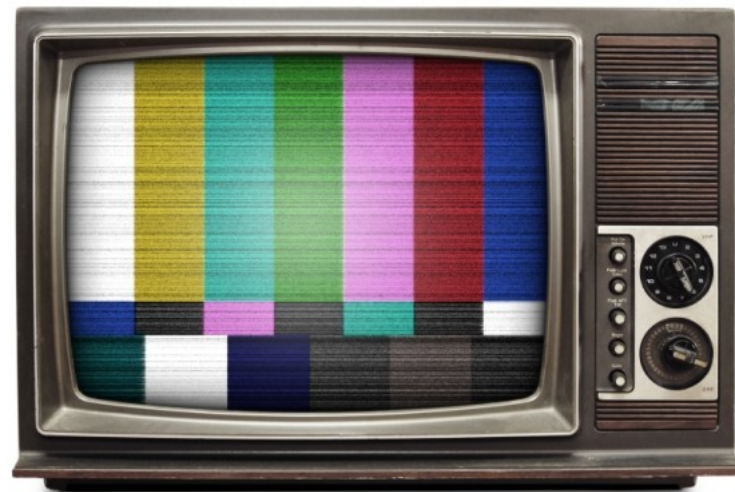
Why Use Multi-Sequence Alignment?

To searching for Resistance Genes



Supporting Video

- Horizontal gene transfer (4mins)
 - <https://www.youtube.com/watch?v=Nunq1yg9Ea0>
- Antibiotic Resistance (4mins)
 - <https://ed.ted.com/lessons/how-antibiotics-become-resistant-over-time-kevin-wu>



Multi-Sequence Alignment

- Clustal Omega: MultiSequence Alignment
- <https://www.ebi.ac.uk/Tools/msa/clustalo/>

Where are the
chunks of
common
genes?

Are these
chunks from
horizontal gene
transfers?

[Input form](#)
[Web services](#)
[Help & Documentation](#)

Tools > Multiple Sequence Alignment > Clustal Omega

EMBL-EBI to be HTTPS by default from 1st October

On the 1st October the majority of services hosted on www.ebi.ac.uk will be served over HTTPS by default. automatically redirect users accessing the site on insecure HTTP URLs to secure HTTPS URLs. Users of EMBL-EBI services may wish to update links, bookmarks or API clients to use the HTTPS URLs.

Results for job clustalo-l20171005-050706-0613-19128639-oy

[Alignments](#)
[Result Summary](#)
[Phylogenetic Tree](#)
[Submission Details](#)

[Download Alignment File](#)
[Send to Simple_Phylogeny](#)

```

CLUSTAL O(1.2.4) multiple sequence alignment

AB011005.1  -----
X95927.1    -----GGGAGG-CAAGAATCAGGC-CTCAAAACCCCTCAAACCTCTA
X95928.1    TATTATTTTCATGAAACTAATGTGAGGAGAAAAATTAGGCAGACGTATAAGTGACAGTAGA
KU325497.1  -----
KU325498.1  -----

AB011005.1  -----
X95927.1    ACCTTGGAACAAACAGCCCTAGTGGGATAGCCCTATCAAACCCCTCCCTTC--AGGGATT
X95928.1    -----

```



Clustal: Load input sequences

Multiple Sequence Alignment

Clustal Omega is a new multiple sequence alignment program that uses seeded guide trees and HMM profile-profile techniques to generate alignments between **three or more** sequences. For the alignment of two sequences please instead use our [pairwise sequence alignment tools](#).

Important note: This tool can align up to 4000 sequences or a maximum file size of 4 MB.

STEP 1 - Enter your input sequences

Enter or paste a set of

DNA

sequences in any supported format:

Or, upload a file: No file chosen

BLAST: A Heuristic Approach to Database Searching

- <https://blast.ncbi.nlm.nih.gov/Blast.cgi>
- Basic Local Alignment Search Tool
 - NCBI – DNA and protein sequence
 - Compares one sequence to database of > 100 million
 - Finds best hits (optimal alignments) in a matter of seconds
 - (would take >3 years using Needleman-Wunsch algorithm)





BLAST: A Heuristic Approach to Database Searching

[Edit and Resubmit](#)



[Save Search Strategies](#)

[▶ Formatting options](#)

[▶ Download](#)

[You Tube](#) [How to read this page](#)

Job title: NZ_CP010184.1 Escherichia coli strain M3

Results for: 1:|cl|Query_91397 NZ_CP010184.1 Escherichia coli strain M3 plasmid A, complete sequence(200925bp)  

RID [XBC0VYV801R](#) (Expires on 10-06 12:07 pm)

Query ID |cl|Query_91397

Description NZ_CP010184.1 Escherichia coli strain M3 plasmid A,
complete sequence

Molecule type nucleic acid

Query Length 200925

Database Name nr

Description Nucleotide collection (nt)

Program BLASTN 2.7.0+ [▶ Citation](#)

Other reports: [▶ Search Summary](#) [\[Taxonomy reports\]](#) [\[Distance tree of results\]](#)

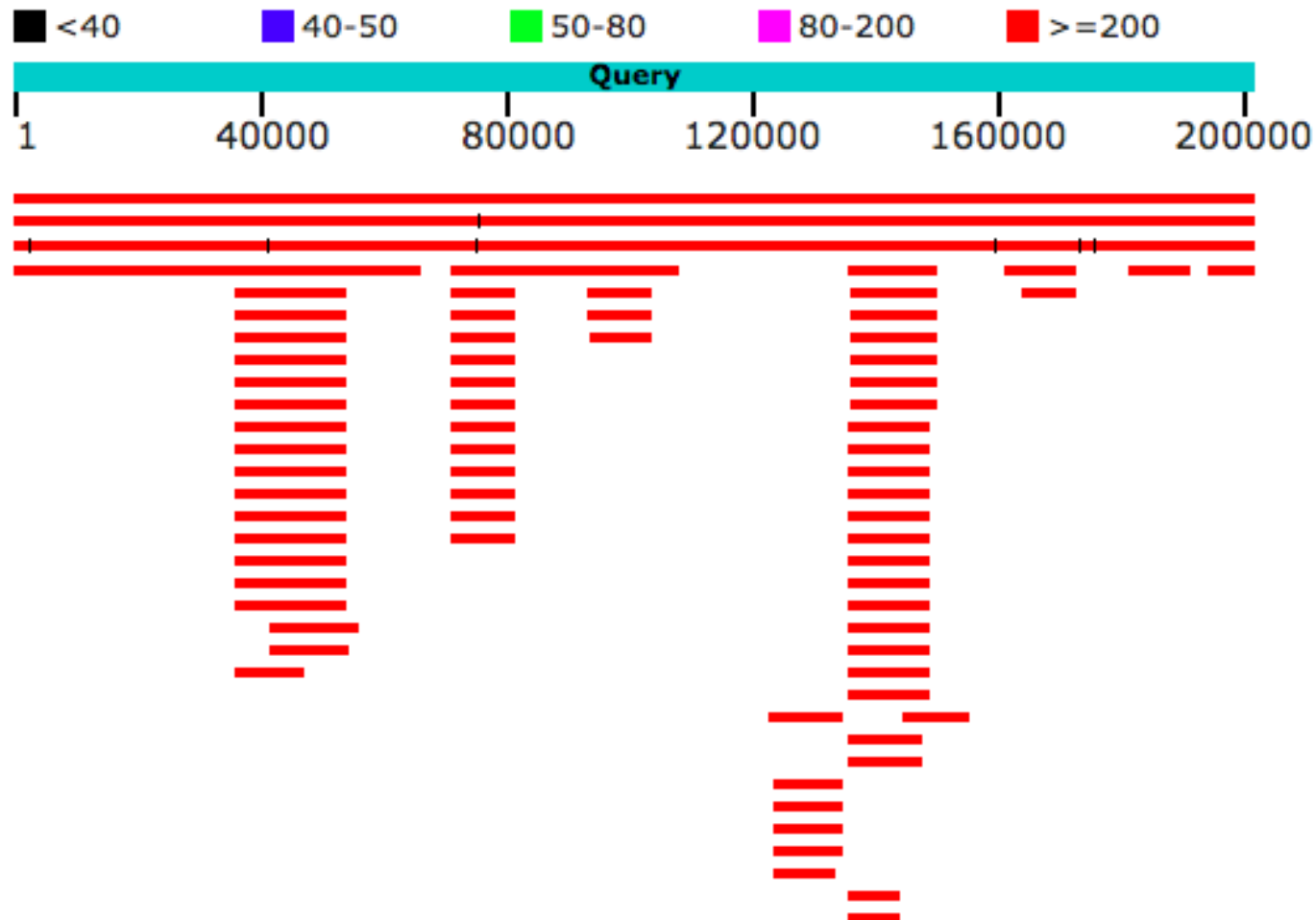


BLAST: Output

Distribution of the top 200 Blast Hits on 100 subject sequences 

Mouse over to see the title, click to show alignments

Color key for alignment scores



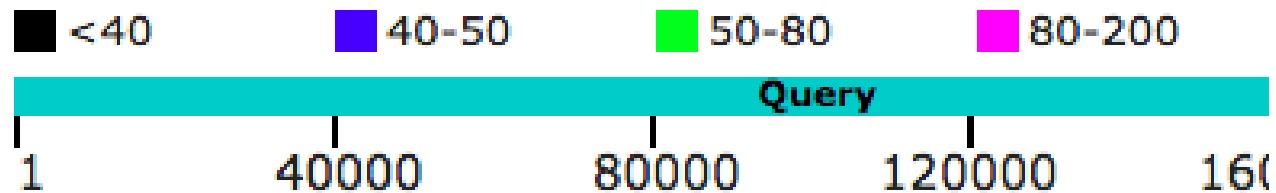


BLAST: Output

Distribution of the top 200 Blast Hits on 100 subject sequen

Mouse over to see the title, click to show alignments

Color key for alignment scores



Escherichia coli strain M18, complete genome

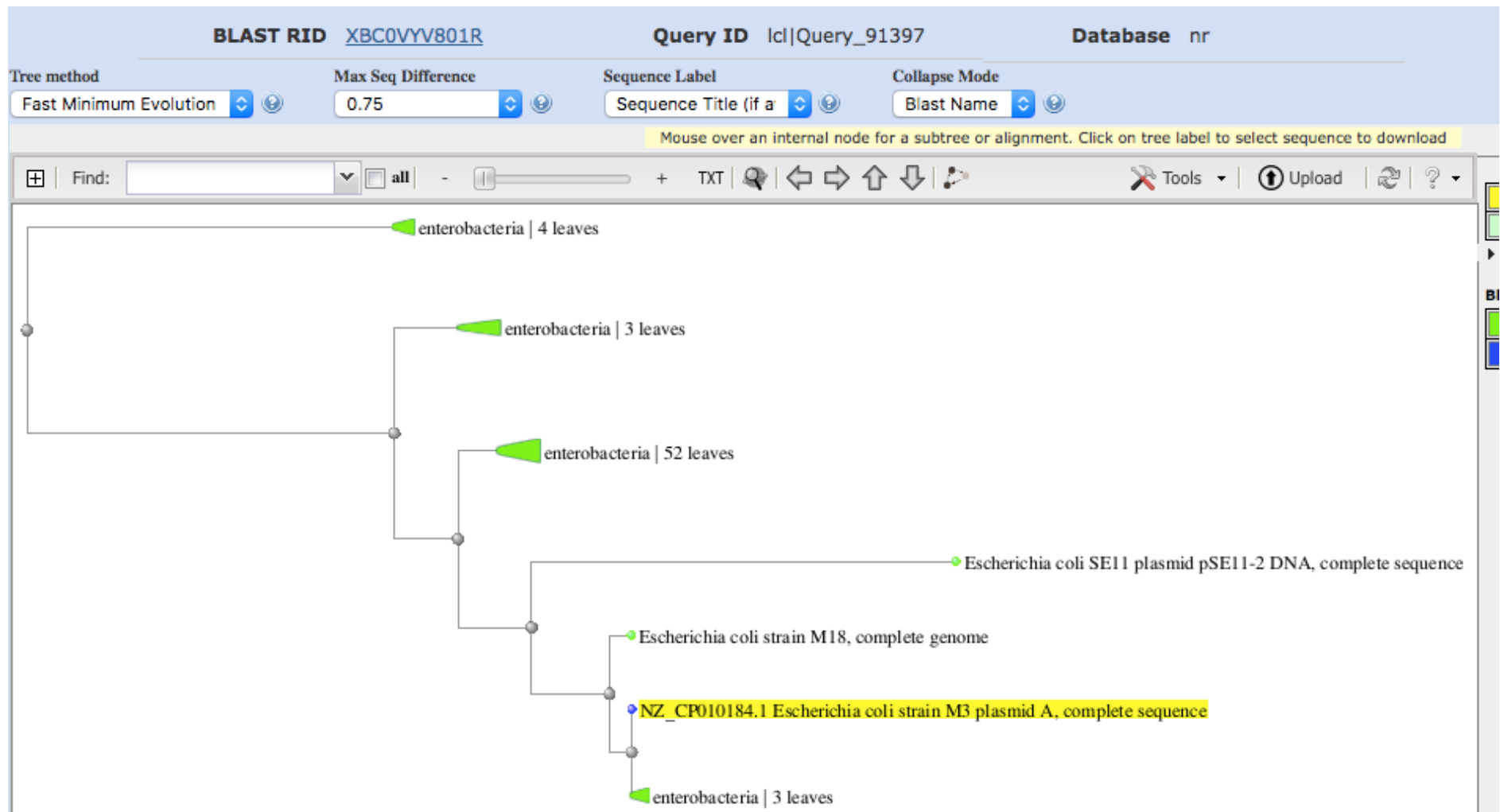
Score:121353 Evalue:0

Accession:CP010219.1

[Alignment](#)



BLAST: Tree of Relations





On Exam 1

- Questions similar to those on worksheets
- Central Dogma of Biology
 - Transcription, Translation
- Mutations: types, causes and effects
- Genetic disorders and their inheritance
- Algorithms: design and implementation in python
- Basic python programming: syntax, keywords and definitions
- Tracking influenza by sequence study
- Sequence alignment
- Topics from recent lessons