

Evolution and dynamics of CRISPR

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CRISPR

- First description

Ishino *et al.* 1987

- CRISPR are widespread

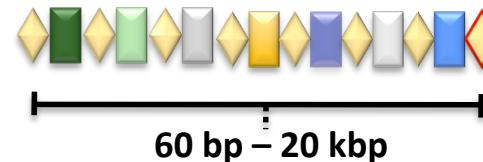
Mojica *et al.* 2000

- The number of loci per genome

can vary from 1 to 18

Bult *et al.* 1996

Clustered Regularly Interspaced Short Palindromic Repeats



Repeat



Spacer

CGGTTTATCCCCGCTGGCGCGGGGAACA

CGGTTTATCCCCGCTGGCGCGGGGAACA

ATGTGCACGGCAGCGTTATGCATTATGCGTAC

TGAGTAAGTCCTGACGTGCATATCTGCCATG

CGGTTTATCCCCGCTGGCGCGGGGAACA

ATGGTTATCCCCGCTGACGCGGGGAACAT

GGCCTAGTCGGAGTCGAGGTACCATGTACGA

Repeats :

Mostly invariable sequence

20 to 50 bp

2 to 375 per locus *Grissa et al. 2007*

12 groups of repeats *Kunin et al. 2007*

Spacers:

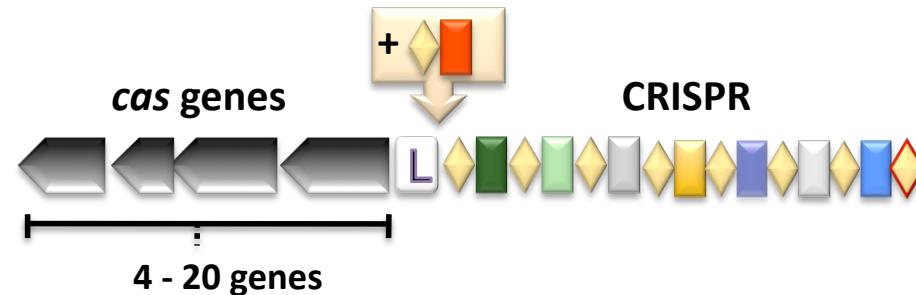
Variable sequence

25 to 75 bp

1 to 374 per locus

CRISPR System

Clustered Regularly Interspaced Short Palindromic Repeats



L

- Leader : AT-rich, 200-550bp, lack ORF, not conserved between species

Mojica et al. 2000; Jansen et al. 2002

- **Recognition sequence for the addition of new spacers** Bolotin 2005; Barrangou et. al 2007
 - **Promote transcription towards the repeats** Brouns et al. 2008



- **CAS genes (CRISPR-Associated Sequence): 10 subtypes of *cas* genes operon.**
 - **Functional domains identified : endonuclease and exonuclease domain, helicases, RNA- and DNA-binding domains, and domains that are involved in transcription and regulation**

Makarova 2005; Ebihara 2006; Barrangou 2007; Brouns 2008

CRISPR function

cas genes (repeats + spacers) n

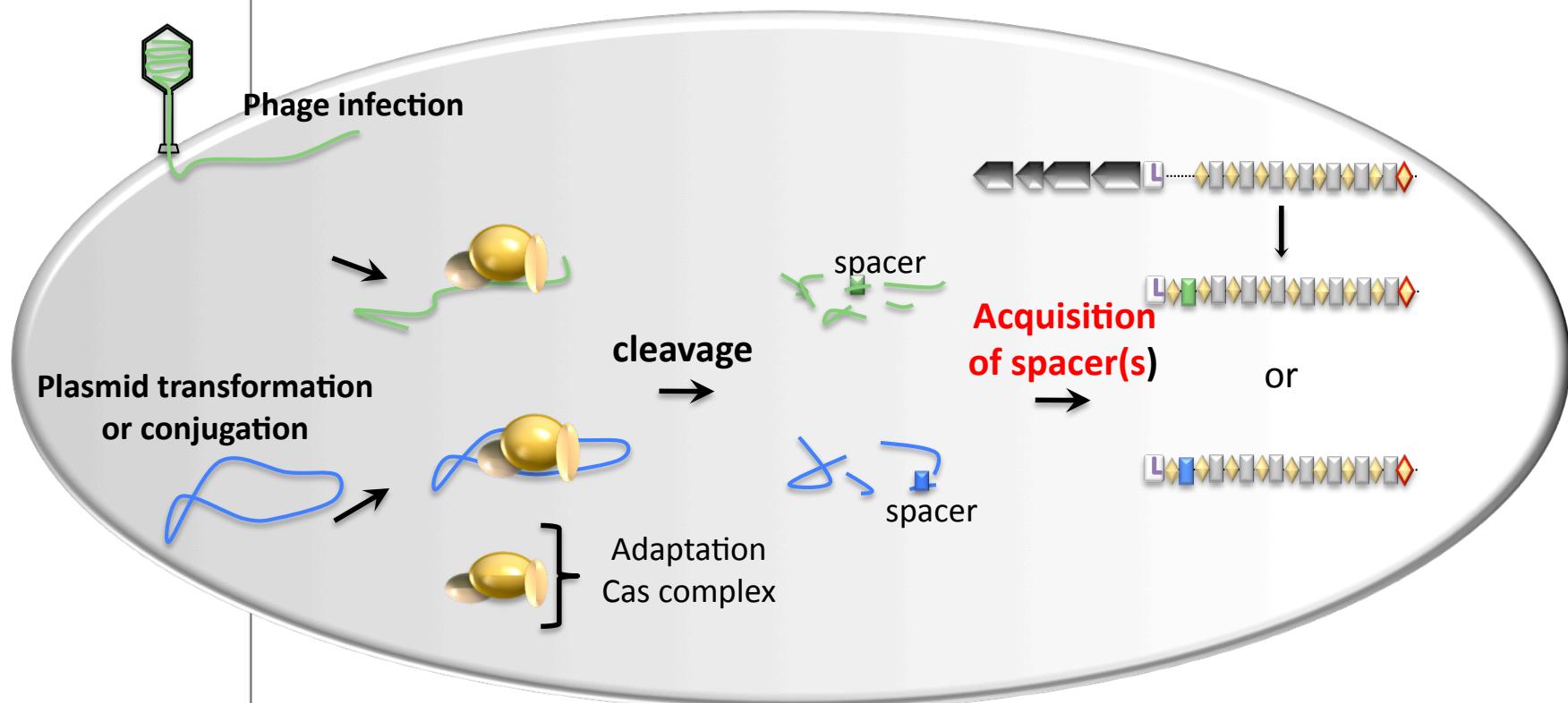


Brief history

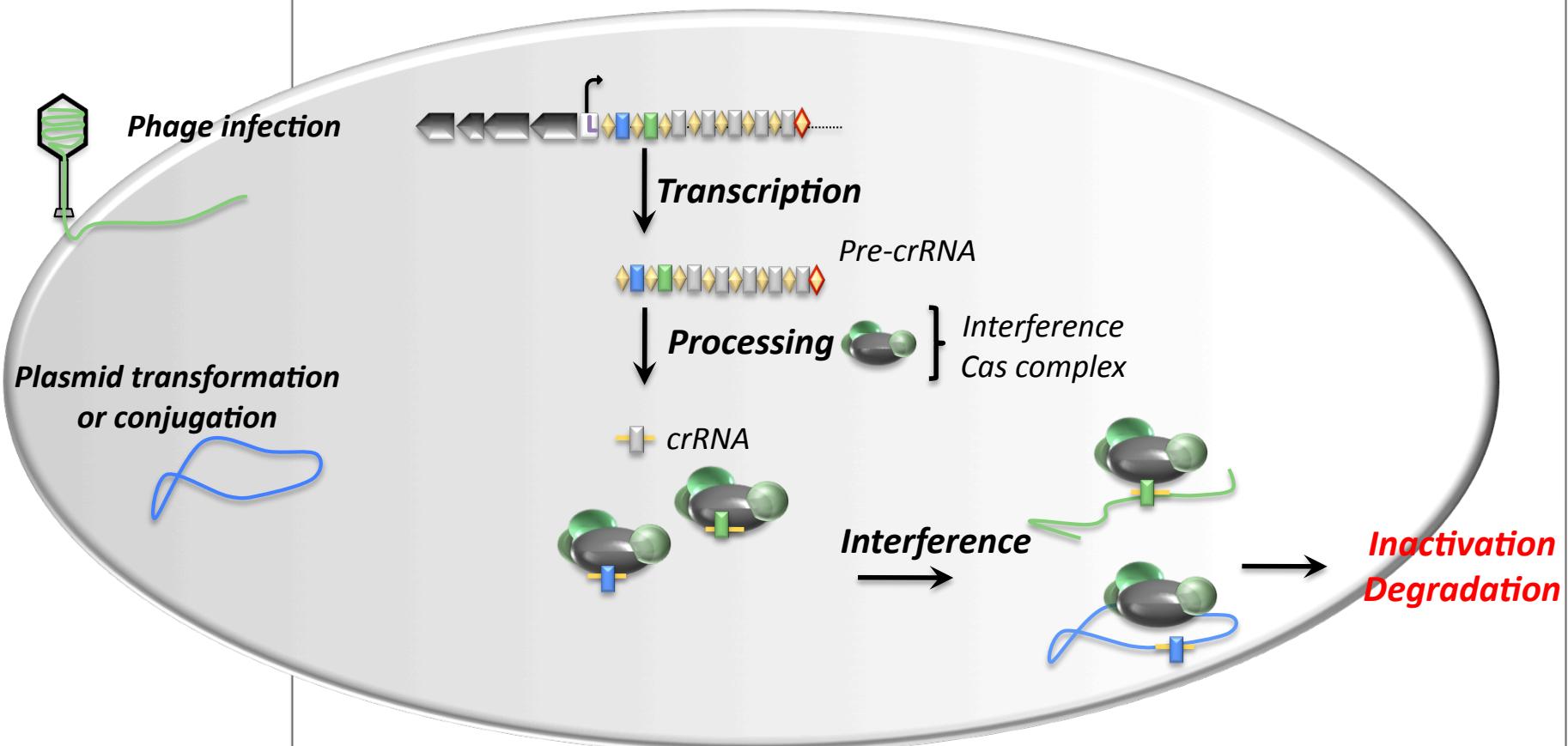
The involvement of the CRISPR system in several processes has been proposed, including :

- 1995 : replicon partitionning *Mojica et al.*
- 2001 : thermal adaptation *Riehle et al.*
- 2002 : DNA repair *Makarova et al.*
- 2006 : chromosome rearrangements *DeBoy et al.*
- 2005 : CRISPR mediate immunity against infection by extrachromosomal agents *Mojica; Pourcel, Bolotin*
- 2007 : CRISPR is an antiphage defense system (experimentally) *Barrangou et al.*

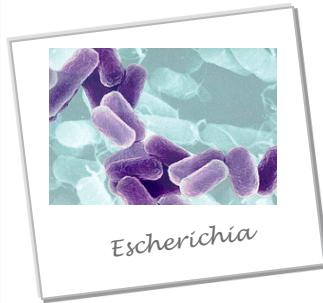
Stage I : Adaptation



Stage II : Interference



Comparative genomics & phylogeny



Escherichia



Salmonella

- ✓ 50 complete genomes *Escherichia* and *Salmonella*
- ✓ 300 *E. coli* strains + 600 *Salmonella* strains
- ✓ Many phages and plasmids genomes of these species

To elucidate :

- ✓ the mechanisms of CRISPR evolution and dynamics
- ✓ link with pathogenicity and antibiotic resistance ...
- ✓ the mechanisms involved in immunity against infection by extrachromosomal agents

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