Résistance croisée et résistances associées : les voies d'acquisition de la multirésistance

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Hôpital Européen Georges Pompidou et

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Résistance croisée et résistances associées

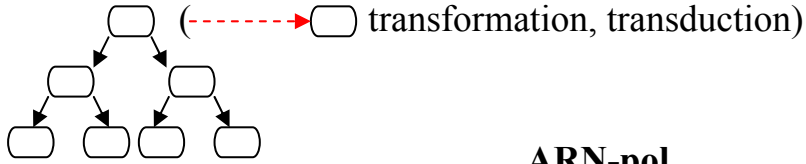
- **Résistance croisée : un mécanisme**

erm	**MLS_B : méthylation de l'ARN 23S**	
acrA/B*, *mex	**β-lactamines, quinolones, chloramphénicol tétracyclines**	**: efflux**
BLSE, carbapénémase		

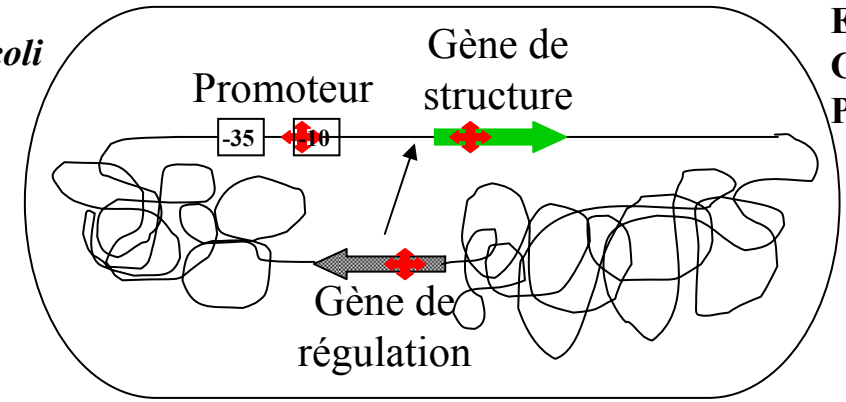
- **Résistances associées : plusieurs mécanismes**

Acquisition de la résistance

- **Mutation chromosomique**



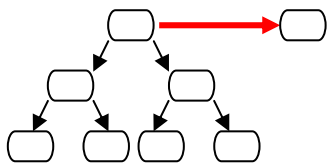
Case de *E. coli*



ARN-pol : Rifampicine
EFG : Acide fusidique
GyrA/B; ParC/E : Quinolones
PLP; porine : ß-Lactamines

Case de *E. cloacae*
Efflux

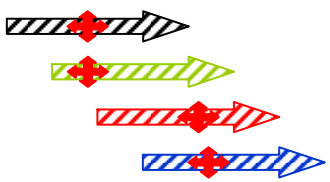
- **Acquisition de matériel génétique**



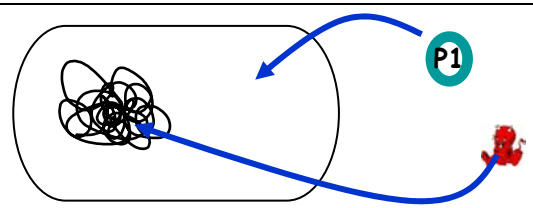
Quasiment tous les ATB (*qnr*, *arr*, *fus*…)

Mutation dans des gènes acquis : BLSE (bla_{SHV}, bla_{TEM})

Mycobactéries

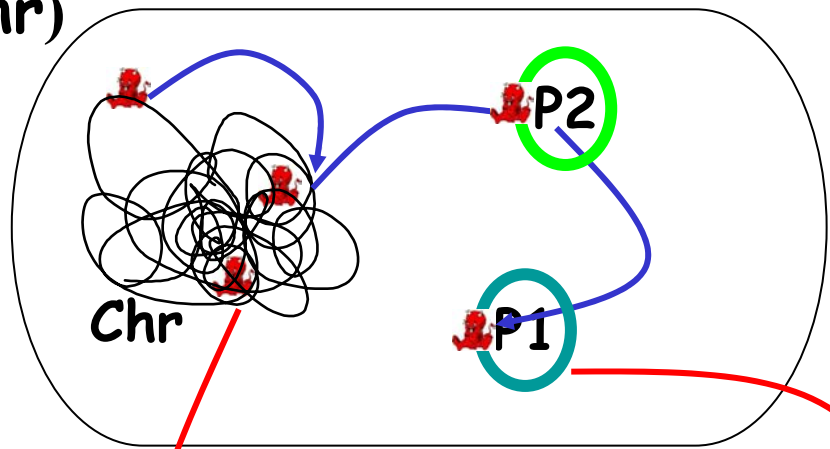


Entérobactéries



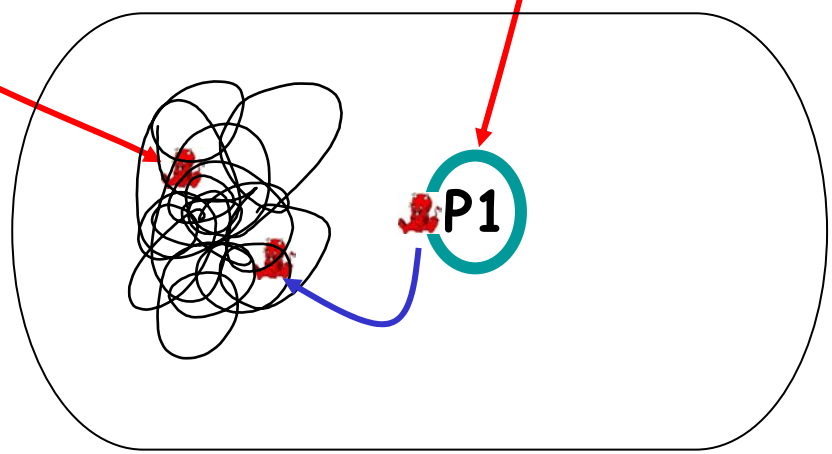
Les supports génétiques de la multirésistance

- **Le chromosome (Chr)**
- **Les plasmides (P)**
- **Les transposons**
- **Les intégrons**

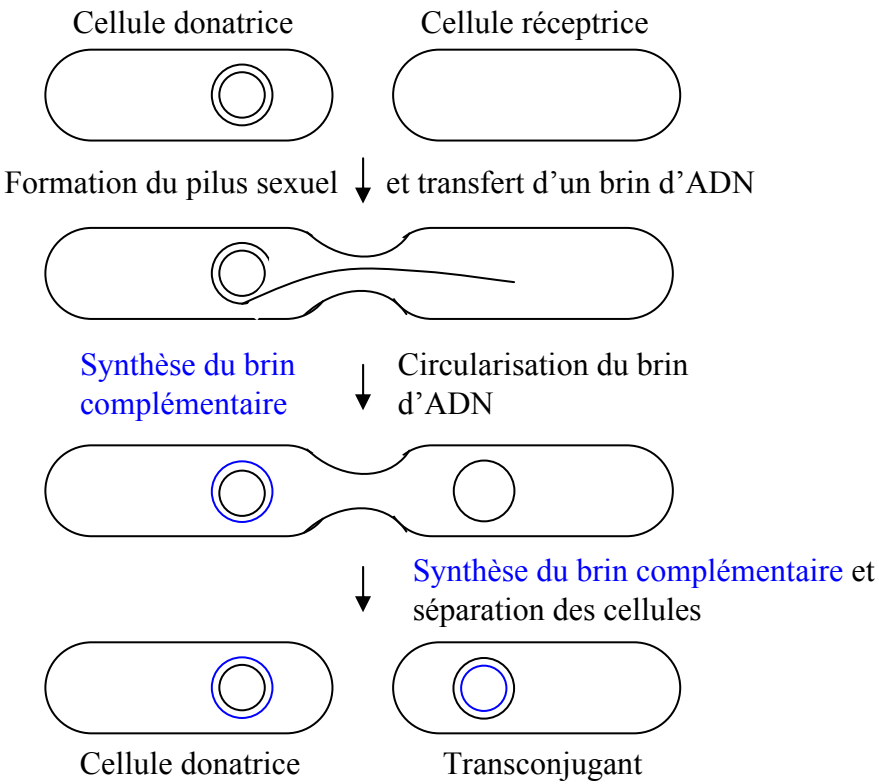


Les modes de transfert de la multirésistance

- **La conjugaison**
- La transformation
- La transduction



La conjugaison



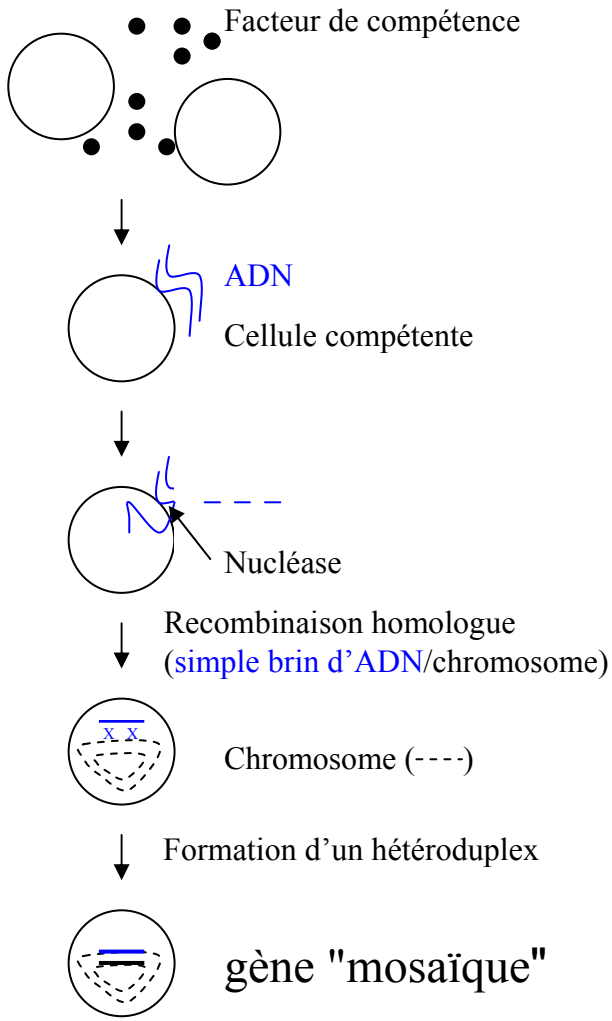
La transduction

Ex : SGI, *S.* Typhimurium DT104

La transformation

Résistance aux β-lactamines

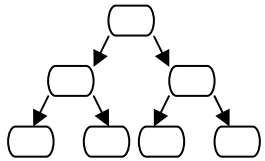
S. pneumoniae*, *N. meningitidis

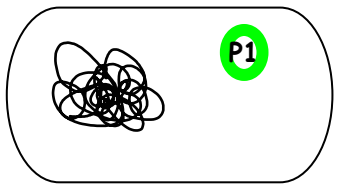


Plasmides (spectre d'hôte)

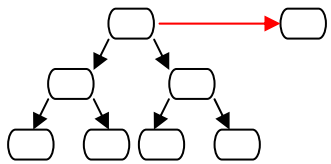
β-lactamines
Aminosides
MLS_B
Tétracyclines
Glycopeptides
Chloramphénicol
Sulfamides

Plasmides non conjugatifs

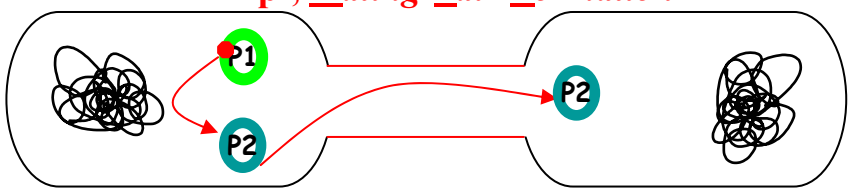


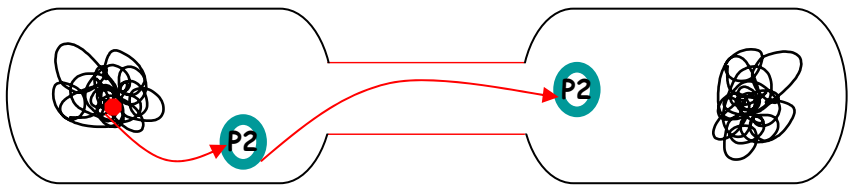


Plasmides mobilisables



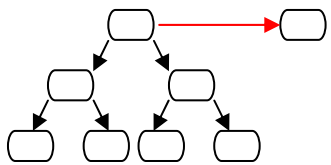
Mpf, *Mating-Pair Formation*

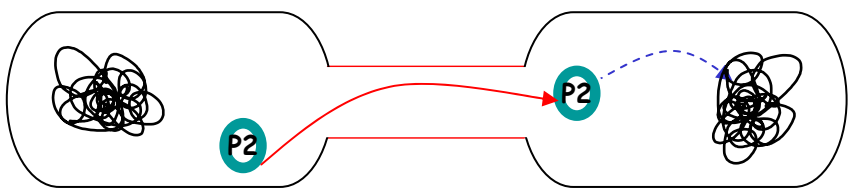




Dtr, *DNA Transfer and Replication* (*mob*)

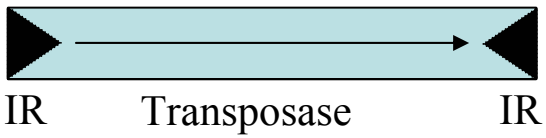
Plasmides conjugatifs ou autotransférables

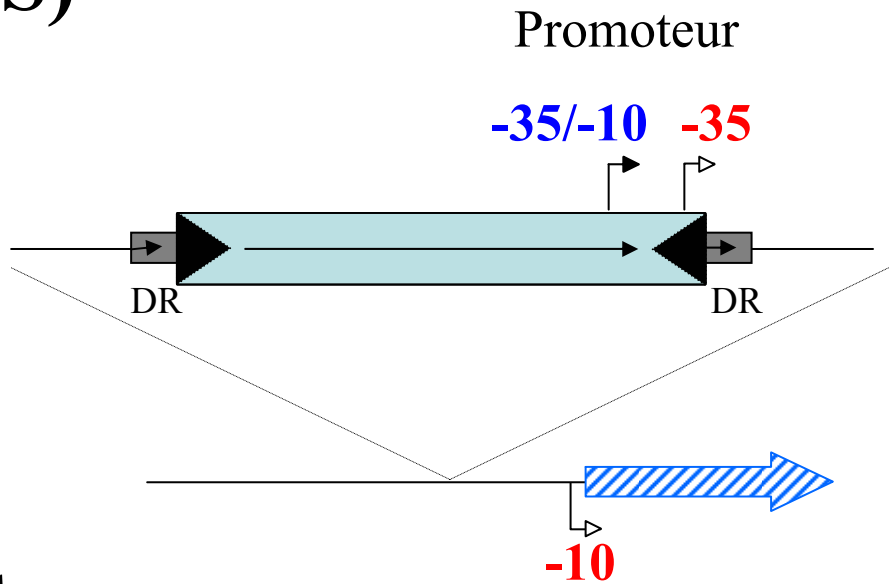




Mpf + Dtr (gènes *tra*)

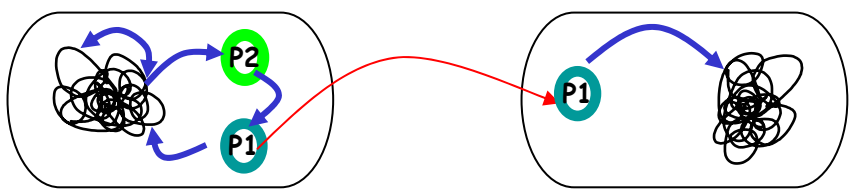
Séquences d'insertion (IS)





Transposons composites

Gène de résistance

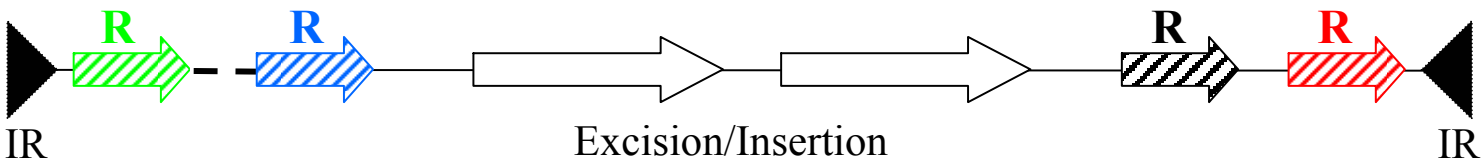


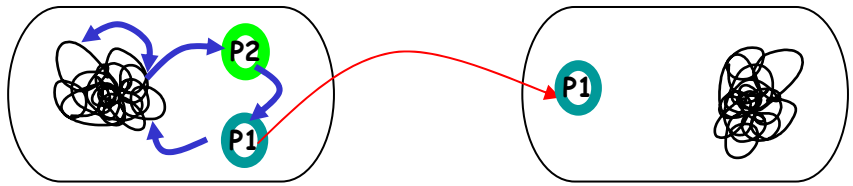
Exemples de transposons composites

Transposon	Taille (kb)	IS	Phénotype de résistance
Bactéries à Gram négatif			
Tn*5*	5,7	IS*50*	Kan, Str
Tn*9*	2,5	IS*1*	Chl
Tn*10*	9,3	IS*10*	Tet
Tn*903*	3,1	IS*903*	Kan
Tn*1548*	16,6	IS*6*	(Kan, Tob, Gen, Net/*armA)*, (Str, Spe), Sul, Tmp
Tn*4351*	6	IS*4351*	MLS_B, (*tetX*)
Bactéries à Gram positif			
Tn*4001*	4,7	IS*256*	Gen, Tob, Kan
Tn*4003*	3,6	IS*257*	Tob
Tn*5432*	4,5	IS*1249*	MLS_B

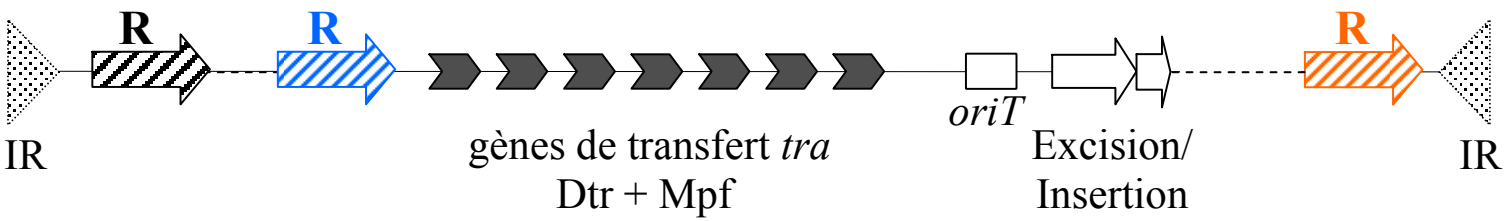
D'après Bennett, Methods in Molecular Biology

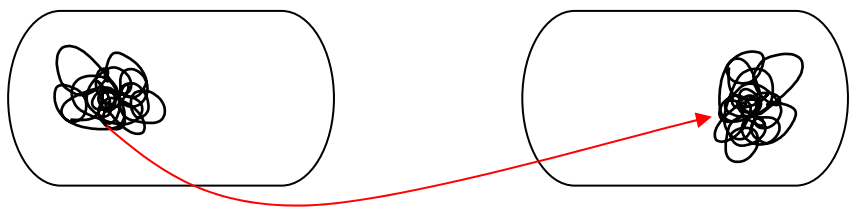
Transposons non composites (non conjugatifs)





Transposons conjugatifs (éventuellement slt. mobilisables)

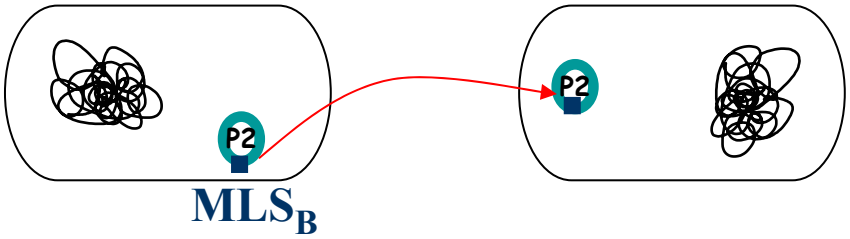




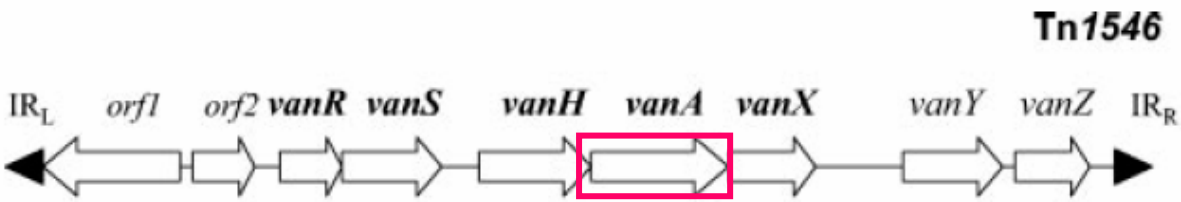
Exemples de transposons non composites

Transposon	Gène porté (phénotype R)	Distribution
Tn*3*	*bla*$_{TEM}$ (Amp)	Entérobactéries, *P. aeruginosa*
Tn*1546*	*vanA* (Van, Tei)	Entérocoques
Tn*21*	*merA* (Hg) *sul1* (Sul) *aadA1* (Str, Spc)	Entérobactéries

Transposon non composite Tn*1546*

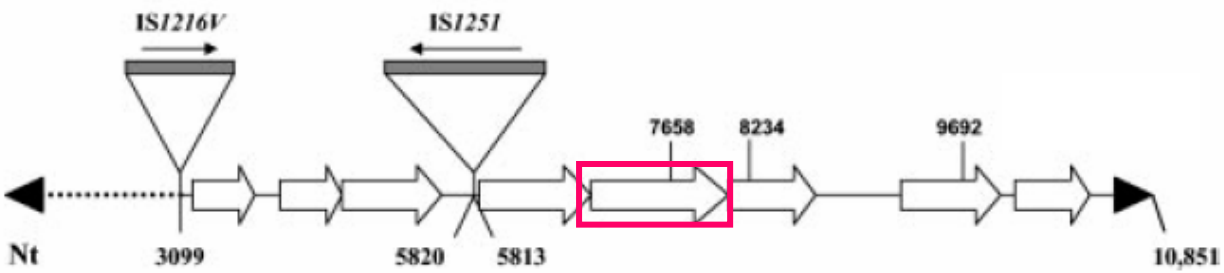


vancomycine
+
teicoplanime



E. faecium

Quelques cas rarissimes



***S. aureus* VRSA**
Michigan

***S. aureus* VRSA**
Pensylvanie

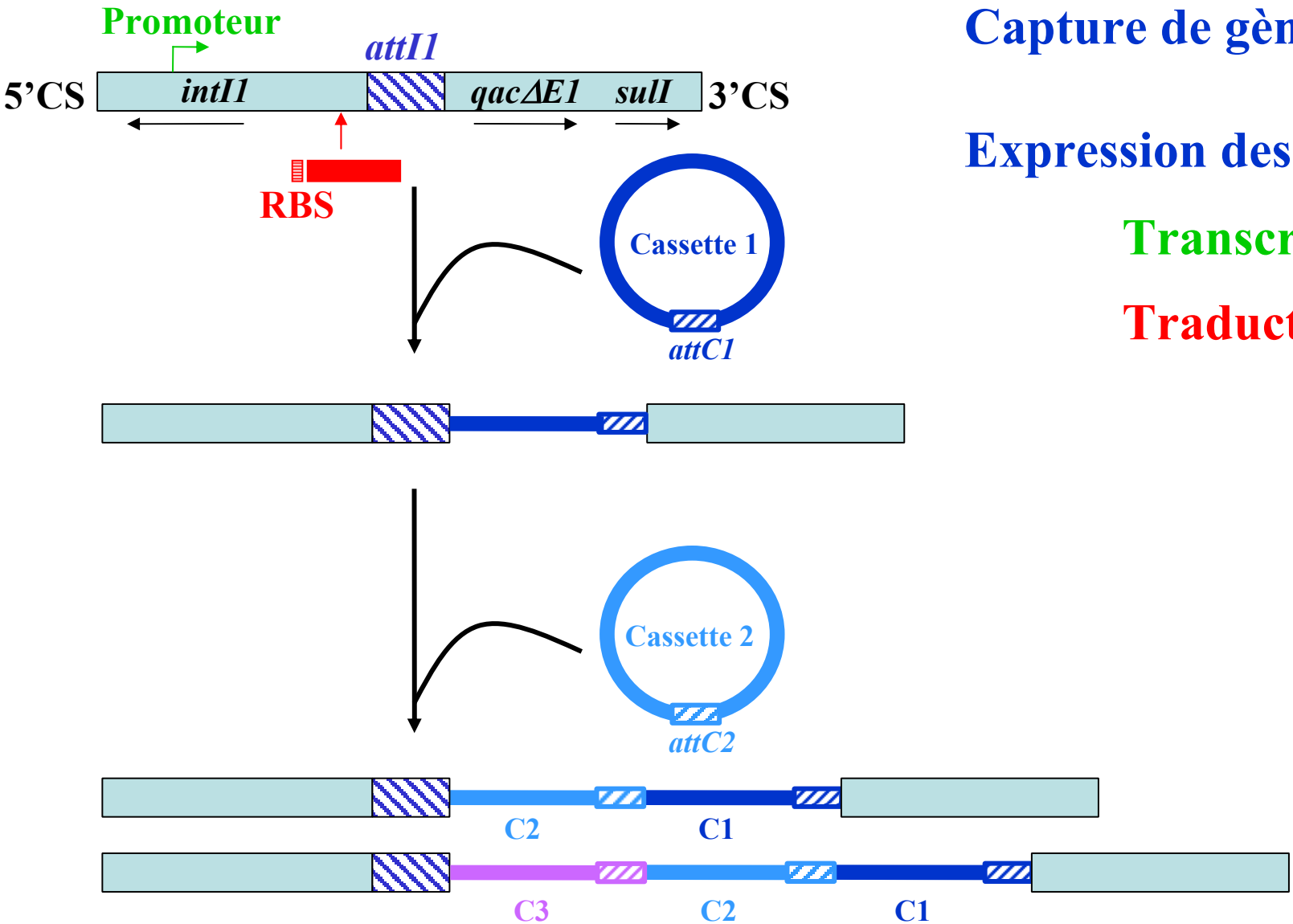
D'après Clark *et al*., Antimicrobiol. Agents Chemother. 2005

Exemples de transposons conjugatifs

Transposon		Gène porté (phénotype de résistance)		Description initiale
Tn conjugatif				
Tn*916*		*tetM*	(Tet, Min)	*E. faecalis*
Tn*1545*		***tetM*** ***ermAM*** ***aphA-3***	**(Tet, Min)** **(MLS_B)** **(Kan)**	***S. pneumoniae***
Tn*5253*[a]	Tn*5251* Tn*5252*	*tetM* *cat*	(Tet, Min) (Chl)	*S. pneumoniae*
Tn*3701*[b]	Tn*3703*	*tetM* *erm*	(Tet, Min) (MLS_B)	*S. pyogenes*
CTnDOT		*tetQ*	(Tet)	*B. fragilis*
Tn*5397*		*tetM*	(Tet, Min)	*C. difficile*
Tn*5398*		*ermB*	(MLS_B)	*C. difficile*
SXT		*sulII* *strA-strB* *cat*	(Sul, Tmp) (Str) (Chl)	*Vibrio cholerae*
Tn mobilisable				
Tn*4555*		*cfxA*	(Cfx)	*B. fragilis*

Intégrons de classe 1

Entérobactéries, *Pseudomonas*, *Acinetobacter*



Capture de gènes R

Expression des gènes R

Transcription

Traduction

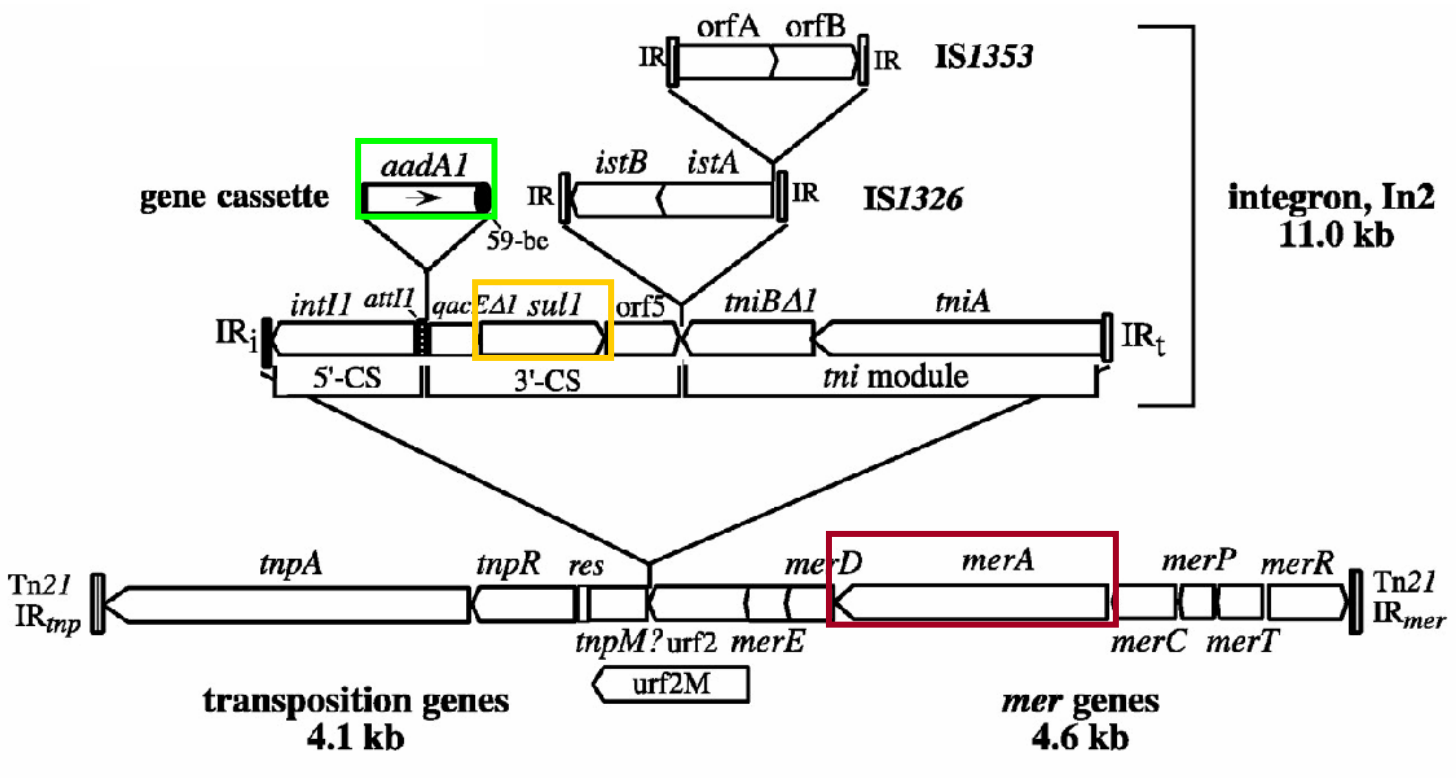
Gènes de résistance décrits dans des intégrons

β-Lactamines	**: *bla*$_{IMP}$, *bla*$_{VIM}$, *oxa*, *bla*$_{CTX_M}$ (inactivation)**
Aminosides	**: *aad*, *aac*, *aph* (inactivation)**
Chloramphénicol	**: *cml* (efflux)**
Rifampicine	**: *arr* (inactivation)**
Triméthoprime	**: *dfr* (substitution de cible)**
Quinolone	**: *qnr* (blocage de cible)**
Erythromycine	**: *ere* (inactivation)**
Amonium quaternaire	**: *qac* (efflux)**

Des "classiques"

Transposon non composite Tn*21* (plasmidique)

Tn*21*, Flagship of the floating genome; Liebert *et al*

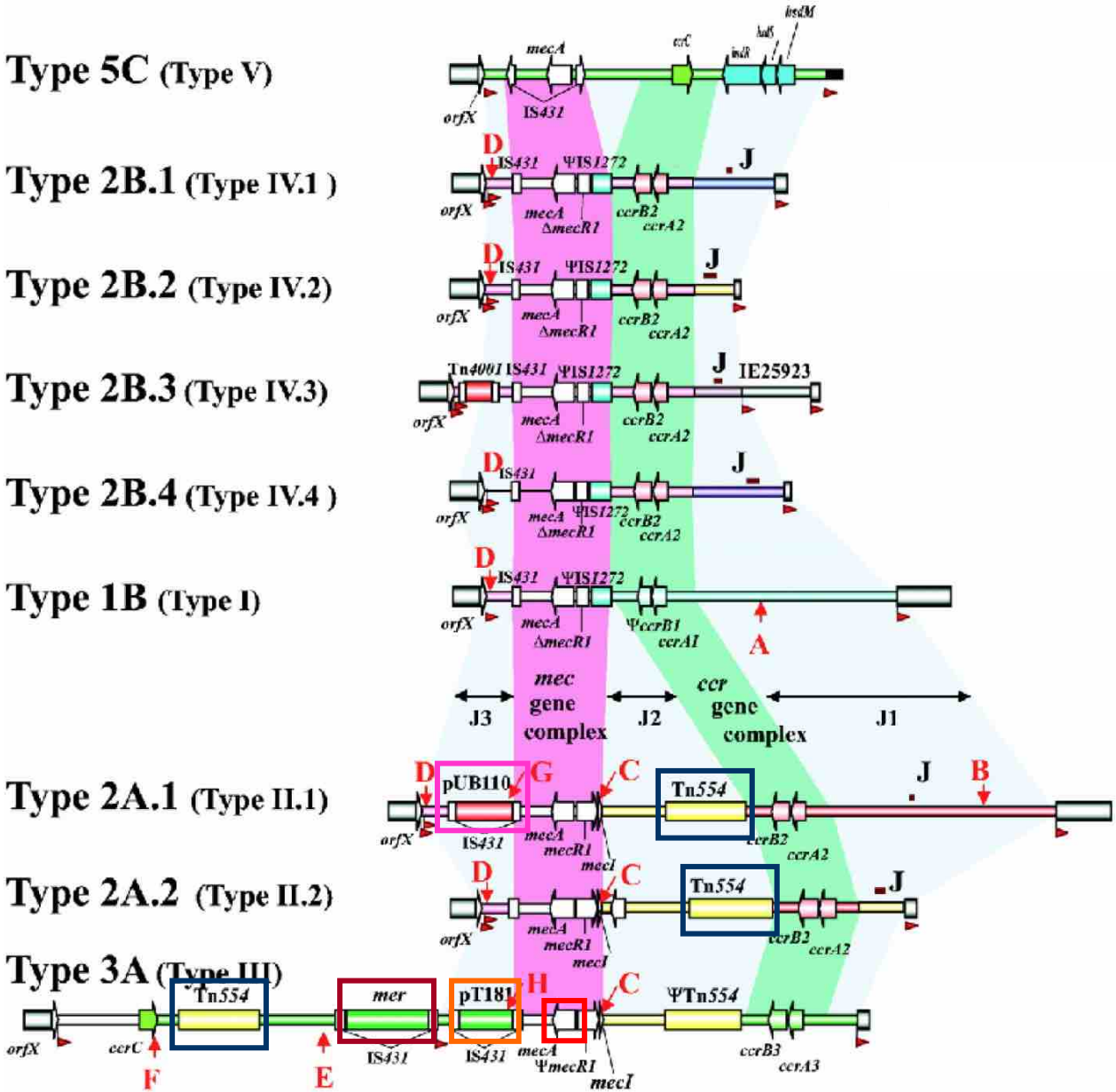


Streptomycine + Spectinomycine, **Sulfamides**, **Dérivés mercuriques**

Microbiol. Mol. Biol. Rev., 1999

Des "classiques" …

SCC*mec*, staphylococcal cassette chromosome *mec*



Méticilline

pUB110 plasmide intégratif

Chloramphénicol

pT181 plasmide intégratif

Tétracyclines

Tn composite

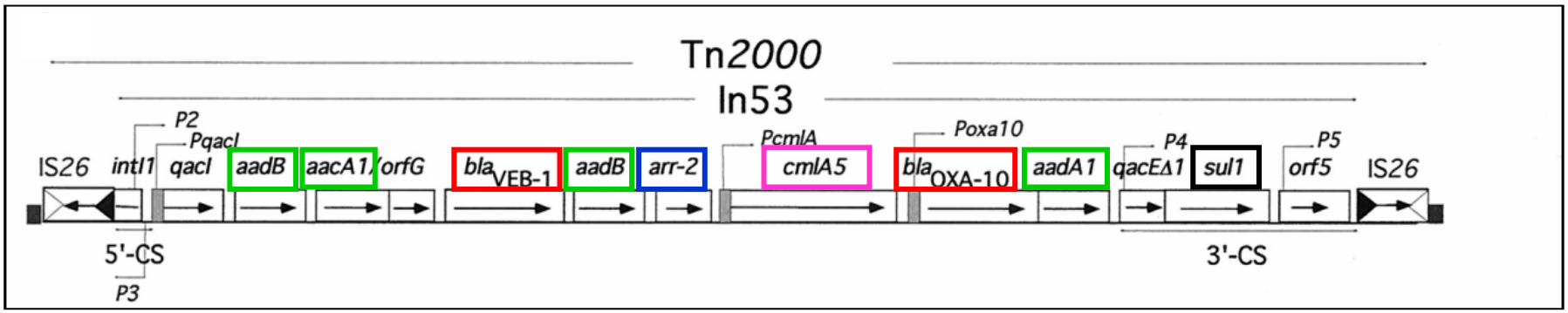
Dérivés mercuriques

Tn*554* non composite non conjugatif

MLS_B (*ermA*) + spectinomycine (*spc*)

Chongtrakool *et al.*, Antimicrobiol. Agents Chemother. 2006

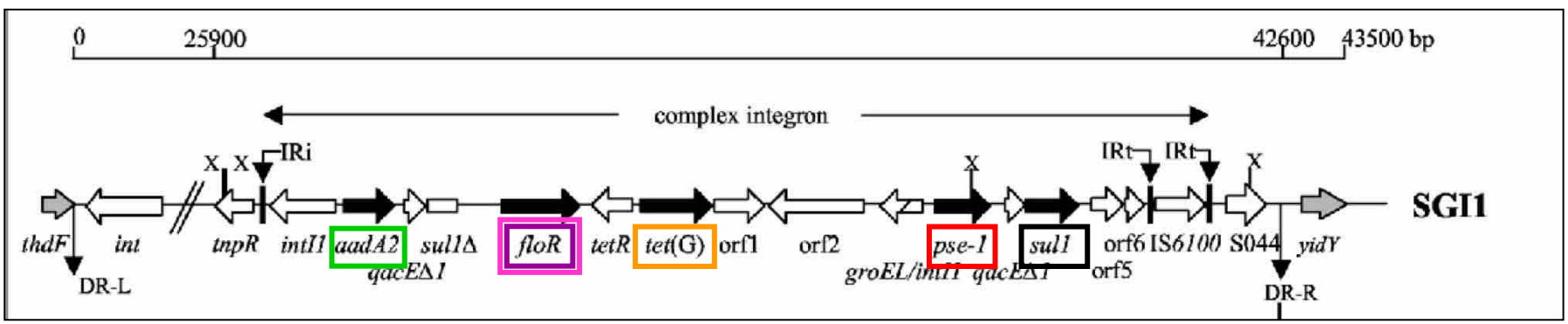
… et des "monstres"



Transposon composite (plasmidique) Naas *et al.*, J. Bacteriol. 2001

E. coli

aminosides, β-lactamines, rifampicine, chloramphénicol, florphénicol, sulfamides, tétracyclines



Îlot de résistance (chromosomique) Doublet *et al.*, Mol. Microbiol. 2001

S. enterica

Séquences contrôlant l'initiation de la transcription et de la translation