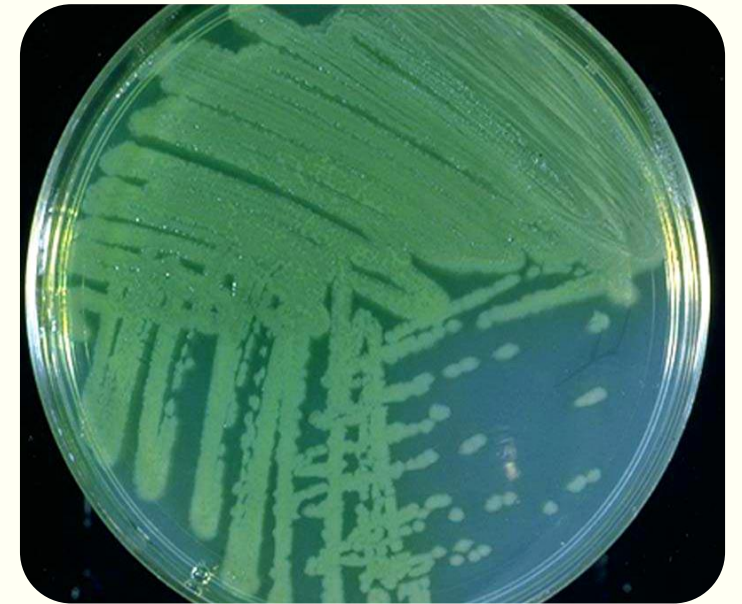


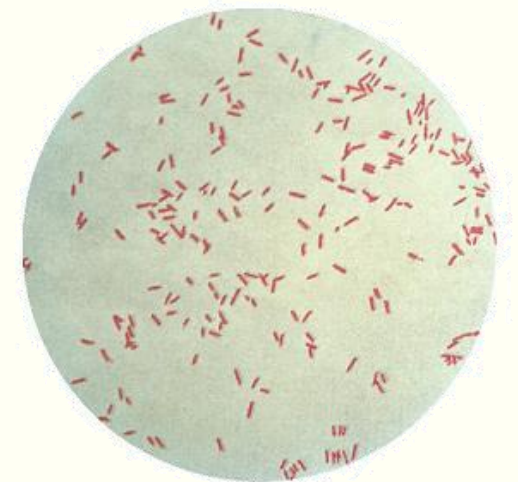
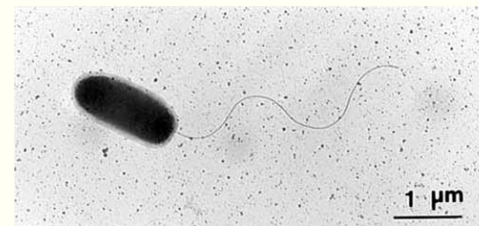
Biologia da
Pseudomonas aeruginosa
CCBH4851



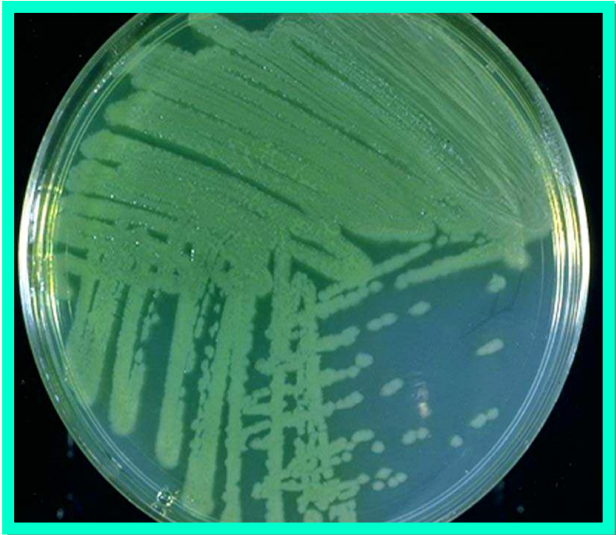
Ana Paula D'Alincourt Carvalho Assef
Laboratório de Pesquisa em Infecção Hospitalar - IOC

P. aeruginosa - Características gerais

- Bacilo gram negativo não fermentador, aeróbio, móvel
- Encontrado, em pequeno percentual na microbiota humana normal
- Presente na água, solo e vegetais (predileção por ambientes úmidos)
- Capaz de utilizar diversos compostos como fonte de energia e carbono, capaz de crescer em desinfetantes
- Resistente a múltiplas drogas
- Patógeno oportunista



P. aeruginosa - Características coloniais



Pigmentos:

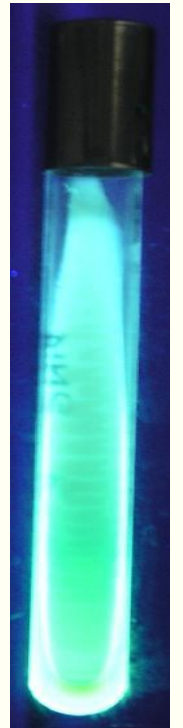
Piocianina

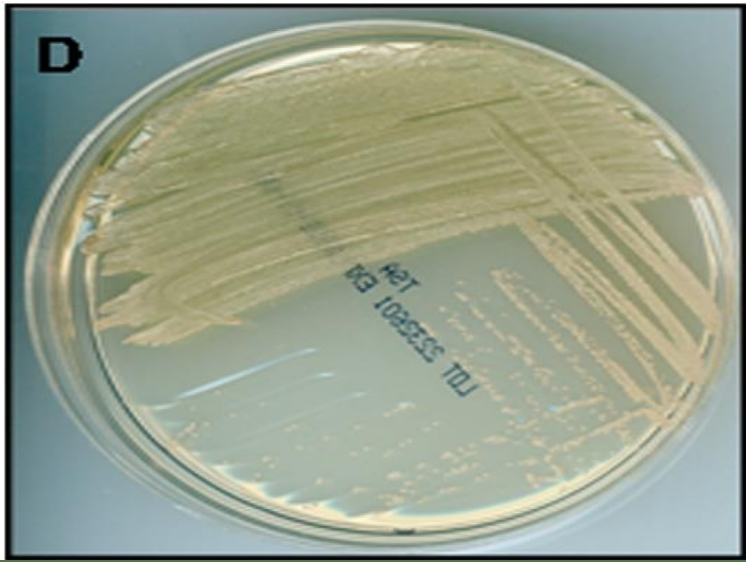
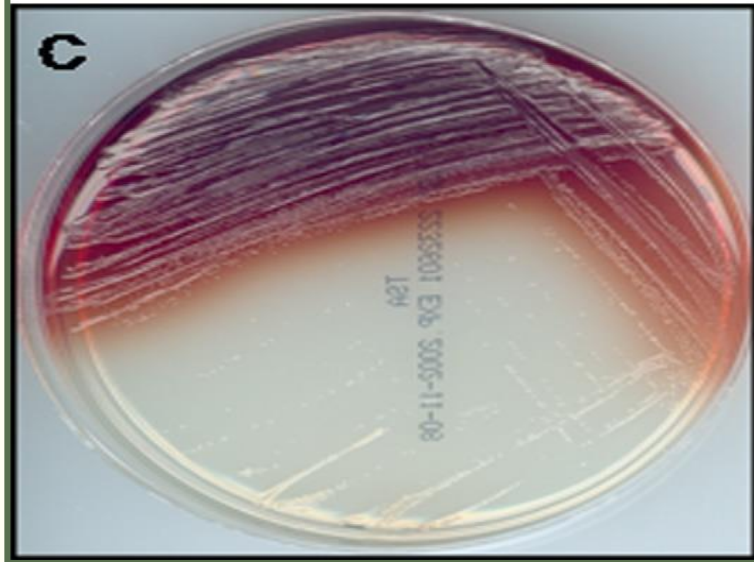
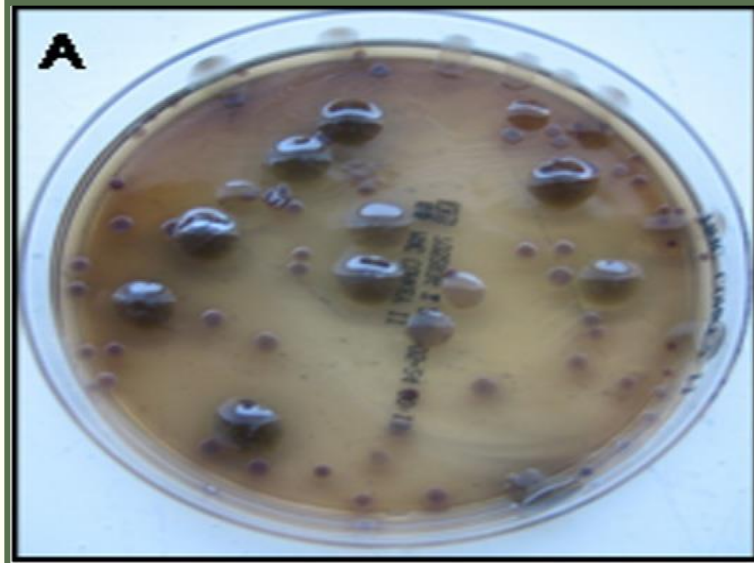
Pioverdina (fluorescente)

Piorrubina (vermelho)

Piomelanina (marron)

Odor adocicado





***P. aeruginosa* - Importância clínica**

Infecções comunitárias:

- Infecção Ocular (lentes de contato)
- Otite externa (água de piscina)
- Endocardite (usuários de drogas injetáveis)
- Foliculite
- Pneumonias (pacientes com Fibrose cística)

Infecções hospitalares:

- Infecções respiratórias
- Infecções urinárias
- Infecções de ferida cirúrgica
- Sepses
- Meningite
- Infecções em queimaduras

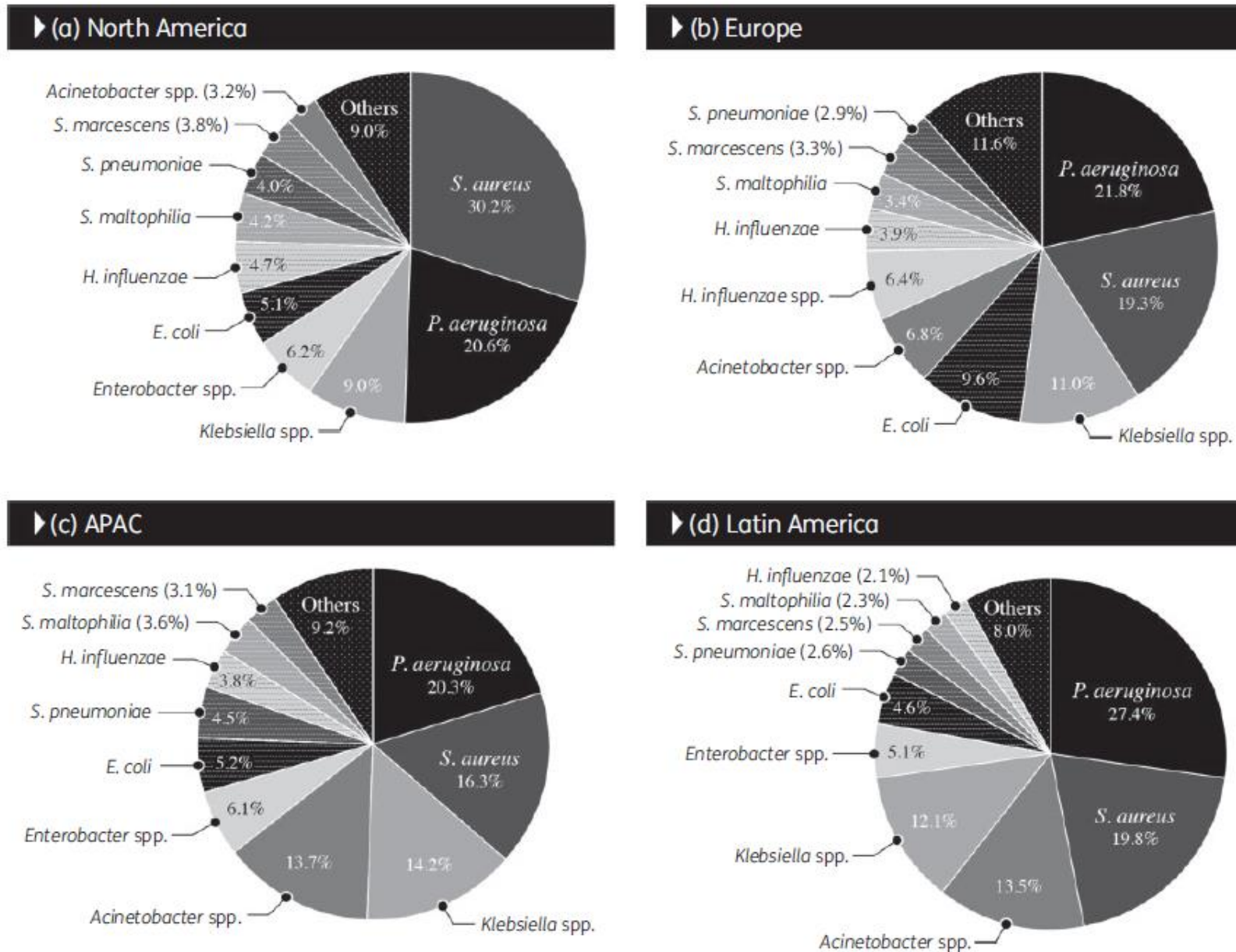
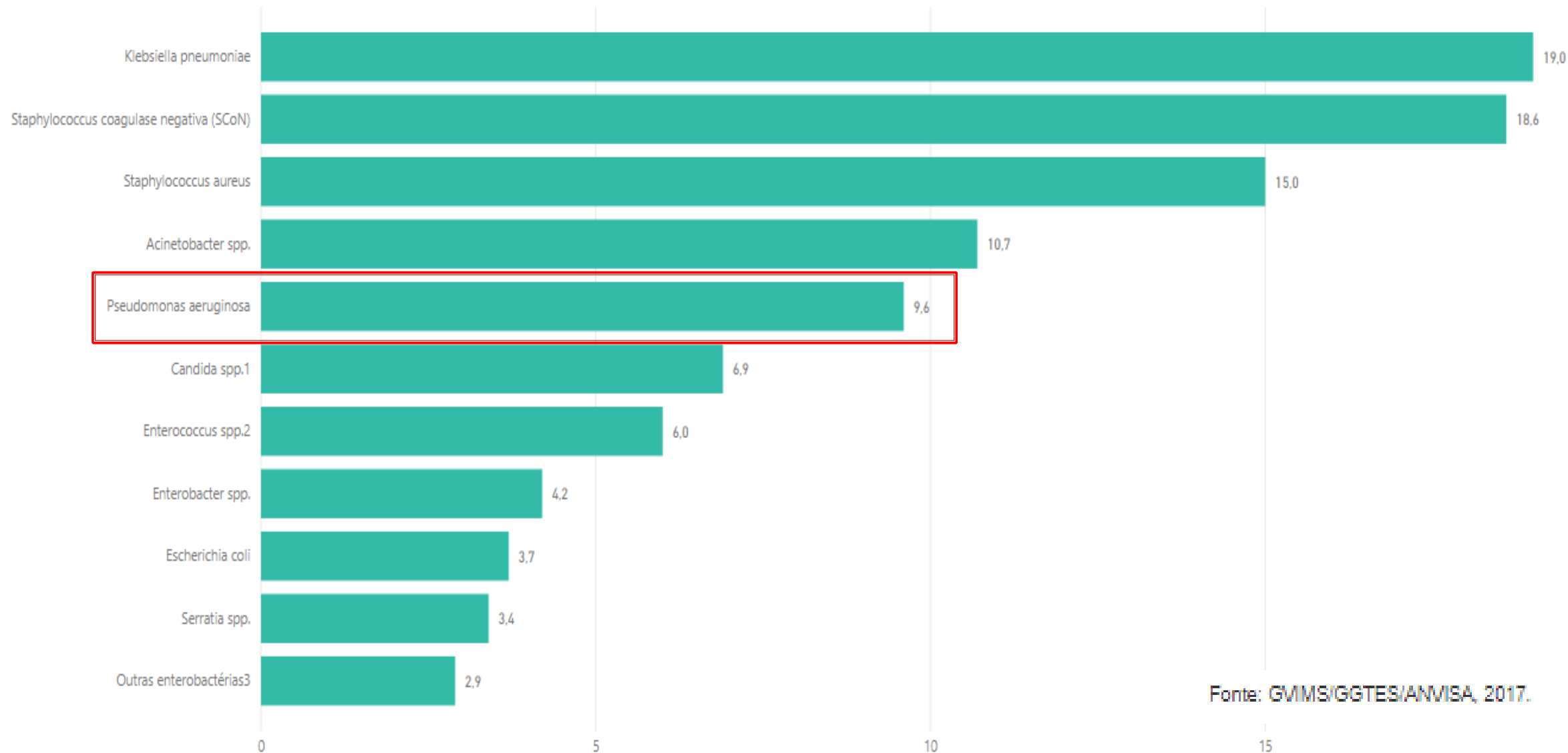


Figure 1. Overall frequency (1997–2016) of occurrence of organisms isolated from patients hospitalized with pneumonia stratified by geographical region. APAC, Asia-Pacific region.

Distribuição percentual dos microrganismos notificados como agentes etiológicos de IPCSL em pacientes hospitalizados em UTI adulto no Brasil em 2017.

TIPO DE UTI ● UTI adulto



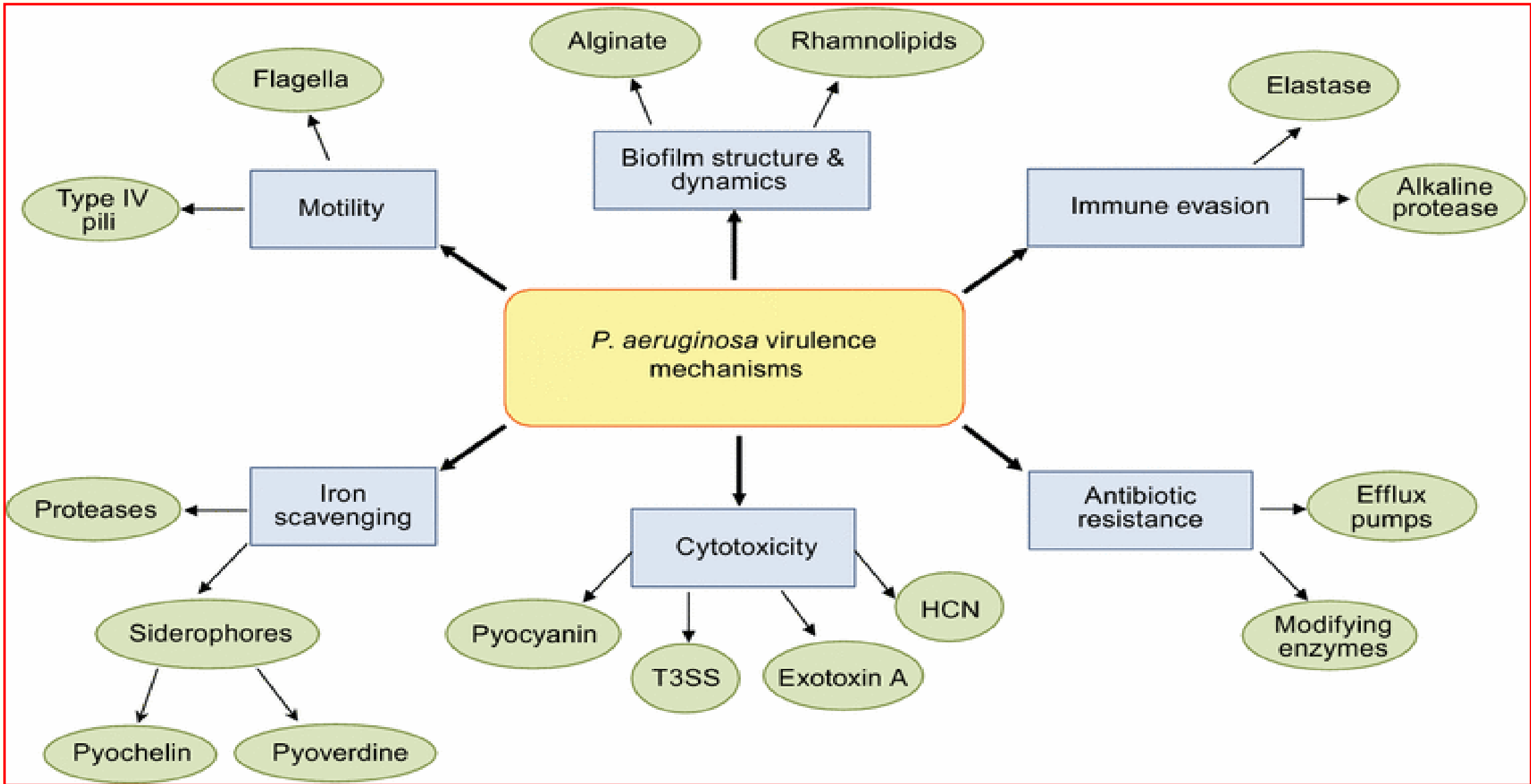
Fonte: GVIMS/GGTES/ANVISA, 2017.

P. aeruginosa - Importância clínica

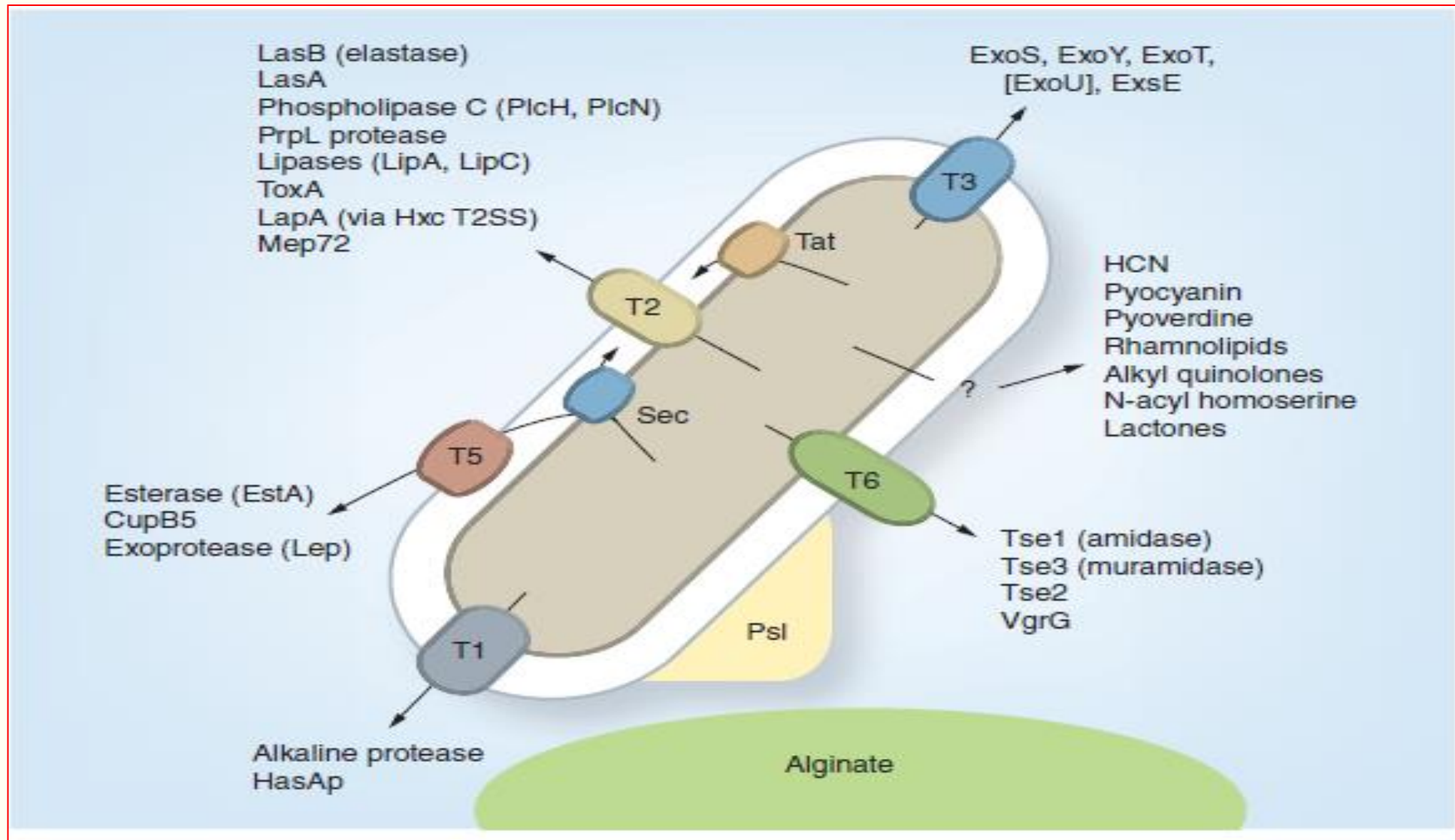




FATORES DE VIRULÊNCIA DE *P. aeruginosa*



Sistemas de secreção





RESISTÊNCIA AOS ANTIMICROBIANOS EM *P. aeruginosa*

Resistência aos antimicrobianos em *P. aeruginosa*

Resistência intrínseca

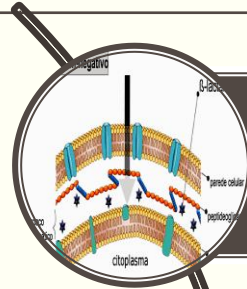
- ✓ Baixa permeabilidade da membrana externa;
- ✓ Sistemas de efluxo;
- ✓ Produção de enzimas



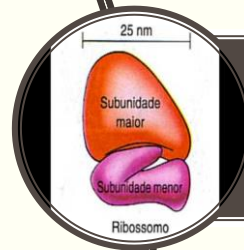
Resistência adquirida

- ✓ Mutações em genes cromossomais (*oprD*, *gyrA*, *parC*, reguladores de bombas de efluxo e *AmpC*,...)
- ✓ Aquisição de genes. (β -lactamases, RNAmetilases, ...)

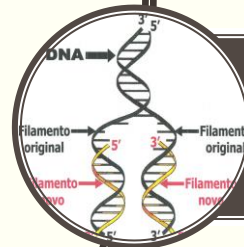
Opções de tratamento para *P. aeruginosa*



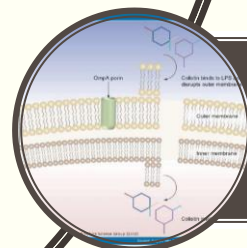
Beta-lactamicos
• Carbapenemas



Aminoglicosídeos
• Amicacina
• Gentamicina

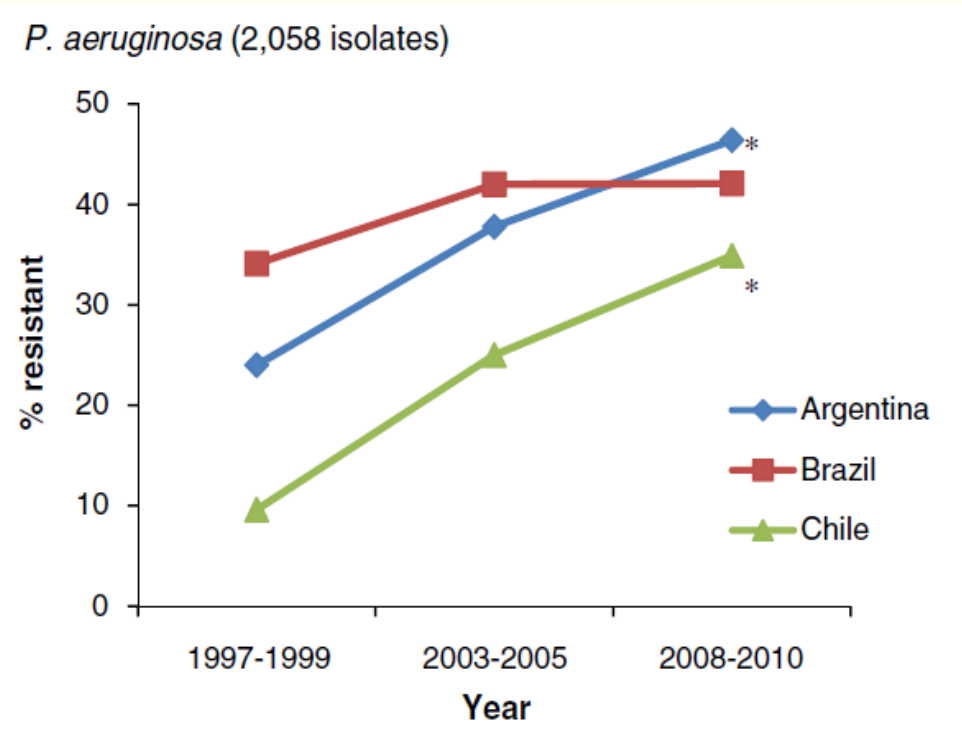
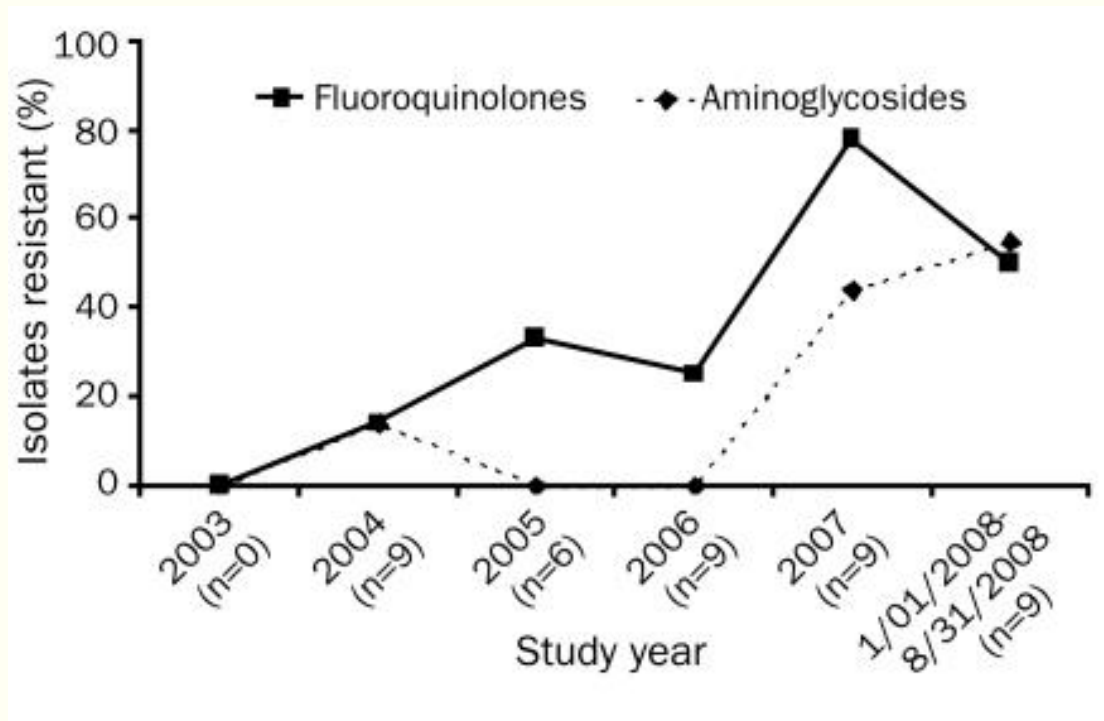


Fluoroquinolonas
• Ciprofloxacina
• Levofloxacina



Polimixina
• Polimixina B

Evolução da resistência em *P. aeruginosa*



Gales et al., Diagn Microbiol Infect Dis. 2012 73:354-60

Resistência aos carbapenemas

Multirresistência



MULTIDRUG-RESISTANT PSEUDOMONAS AERUGINOSA



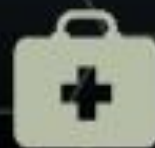
6,700

MULTIDRUG-RESISTANT
PSEUDOMONAS
INFECTIONS



440

DEATHS



51,000

PSEUDOMONAS
INFECTIONS
PER YEAR

THREAT LEVEL
SERIOUS



This bacteria is a serious concern and requires prompt and sustained action to ensure the problem does not grow.



Lista dos 12 patógenos prioritários para pesquisa e desenvolvimento de novas terapias

Priority 1: CRITICAL[#]

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

*Enterobacteriaceae**, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella spp., fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

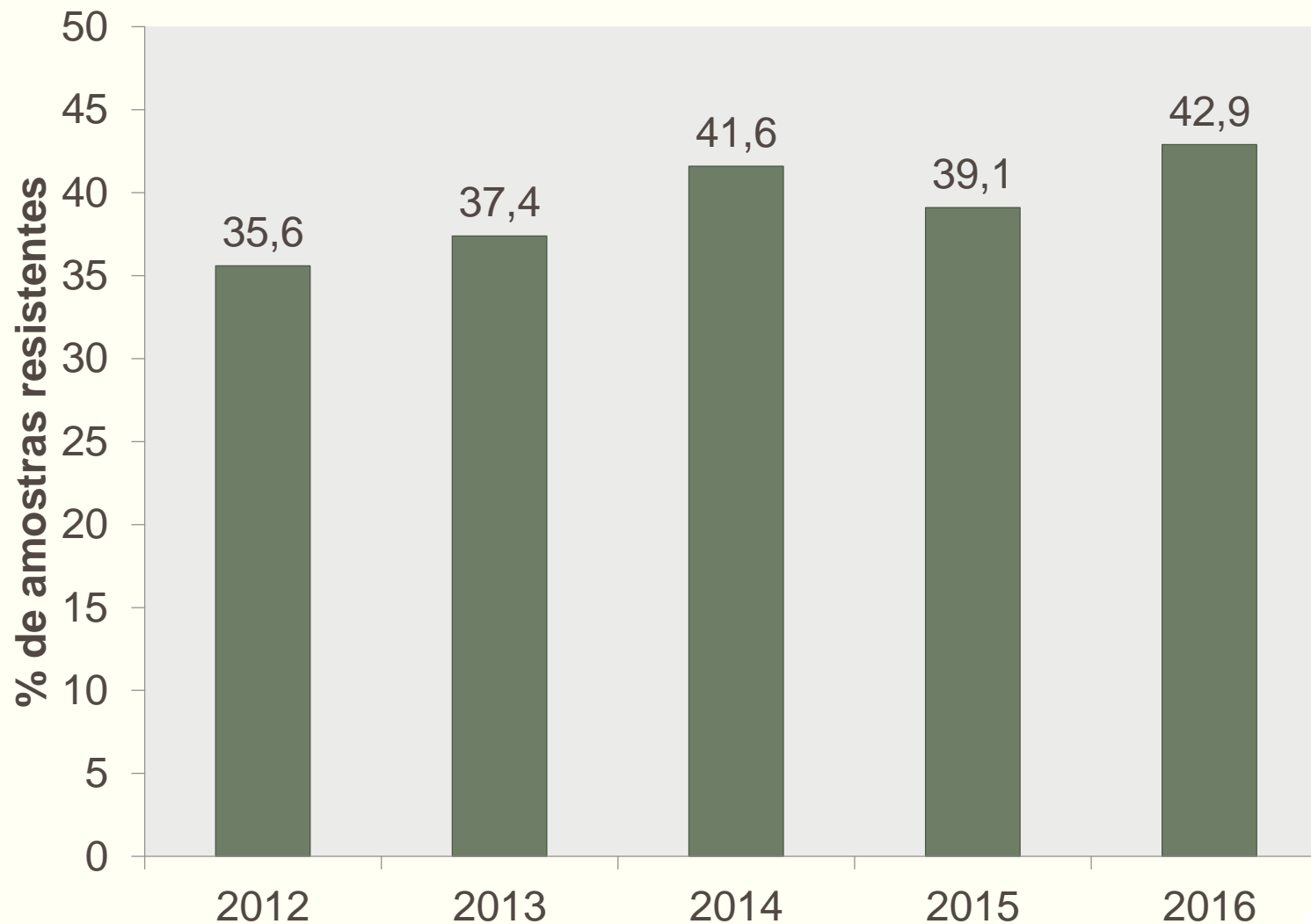
Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

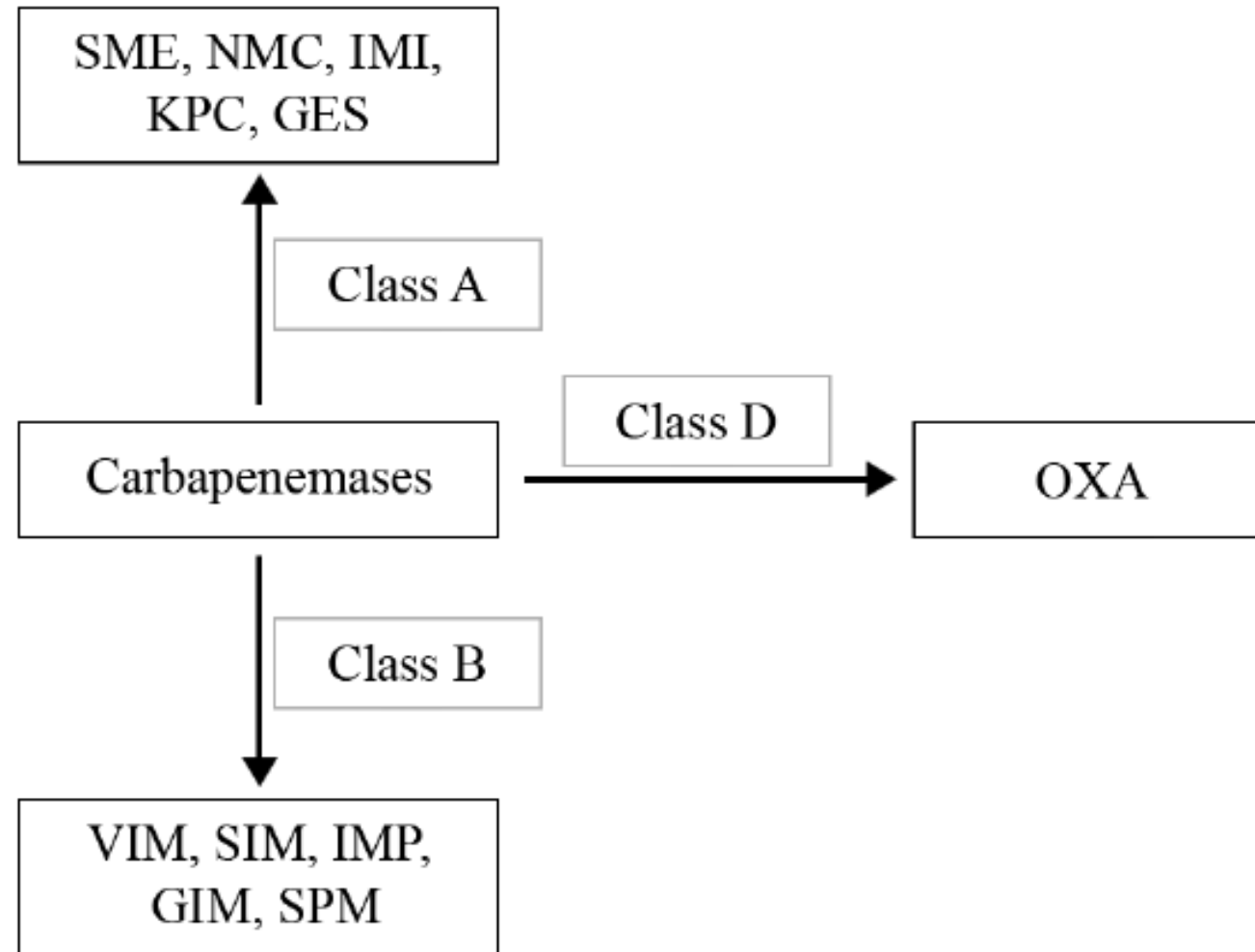
Haemophilus influenzae, ampicillin-resistant

Shigella spp., fluoroquinolone-resistant

Comparação das porcentagens de resistência de *P. aeruginosa* isoladas de IPCSL associada a CVC em pacientes hospitalizados em UTI adulto. Brasil, 2012-2016.



Carbapenemases





***P. aeruginosa* ST277**
produtor de SPM-1

SPM-1 (*São Paulo Metallo- β -lactamase*)

Journal of Antimicrobial Chemotherapy (2002) **50**, 673–679

DOI: 10.1093/jac/dkf210

JAC

Molecular characterization of SPM-1, a novel metallo- β -lactamase isolated in Latin America: report from the SENTRY antimicrobial surveillance programme

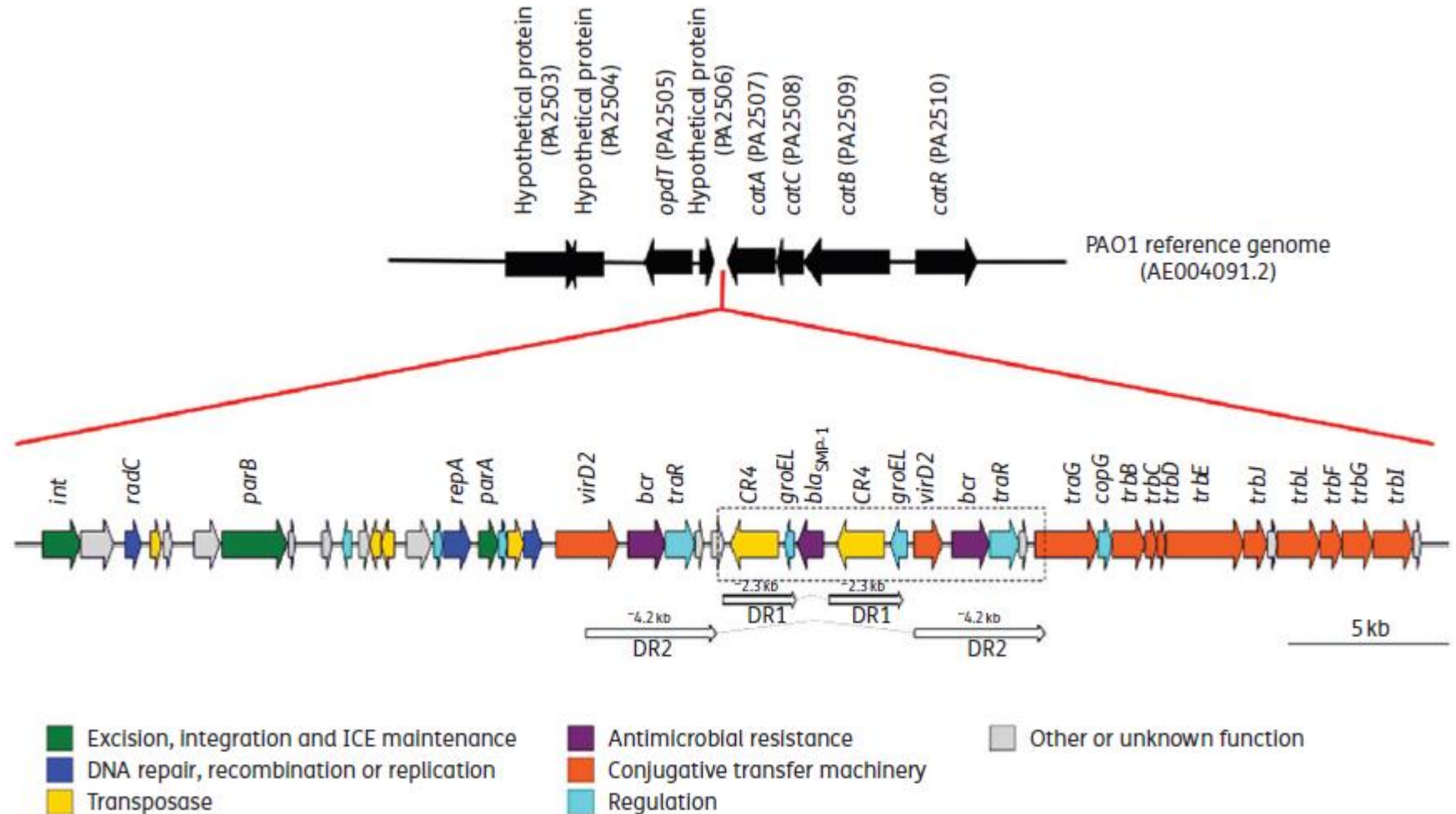
**Mark A. Toleman^{1*}, Alan M. Simm¹, Tanya A. Murphy¹, Ana C. Gales², Doug J. Biedenbach³,
Ronald N. Jones^{3,4} and Timothy R. Walsh¹**

Amostra isolada de urina de paciente internado em São Paulo em 2001

Full characterization of the integrative and conjugative element carrying the metallo- β -lactamase *bla*_{SMP-1} and bicyclomycin *bcr1* resistance genes found in the pandemic *Pseudomonas aeruginosa* clone SP/ST277

Erica L. Fonseca, Michel A. Marin*, Fernando Encinas and Ana Carolina P. Vicente

Elemento integrativo conjugativo ICE_{Tn4371} 6061
(43,8pb)



Clone SP/ST277 produtor de bla_{SPM-1}

- ✓ Disseminado por diferentes estados brasileiros
- ✓ Clone multirresistente;
- ✓ Restrito ao Brasil.



(Gales *et al.* 2003; Poirel *et al.*, 2004; Carvalho *et al.*, 2006; Gonçalves *et al.* 2009; LAPIH 2019)

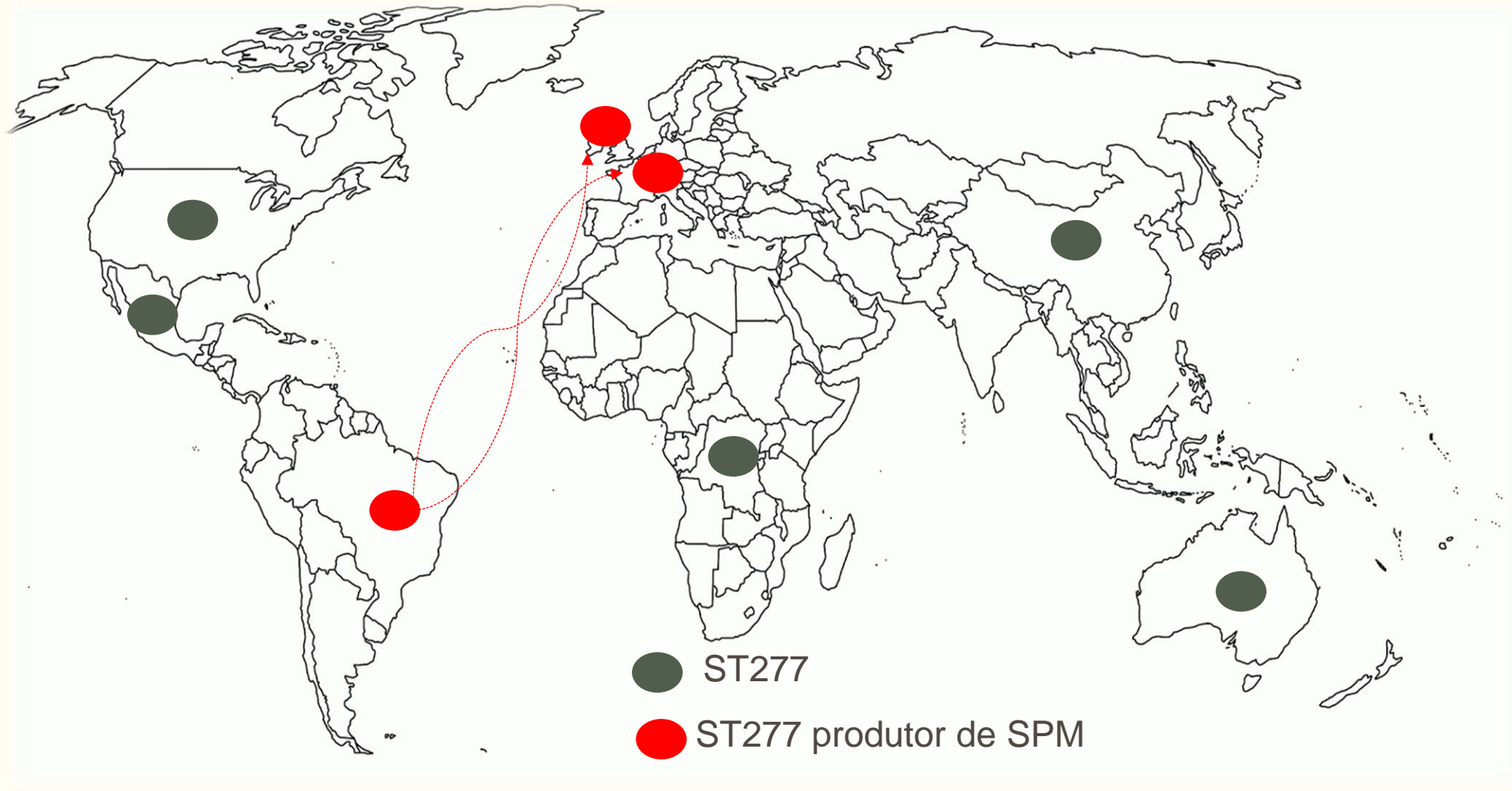


Table 1: Mechanisms contributing to antimicrobial resistance in the ST277 strains.

Mechanism	Resistance	Percentage of positive strains
<i>bla</i> _{OXA-50}	Beta-lactam	100%
PDC-5	Beta-lactam	100%
<i>aph</i> (3')-IIb	Aminoglycoside	100%
<i>cat</i> B7	Chloramphenicol	100%
MexEF-OprN (<i>nfxC</i> mutant)	Fluoroquinolones	100%
	Chloramphenicol	
<i>Bcr</i> 1	Bicyclomycin	100%
<i>fos</i> A	Fosfomycin	100%
<i>gyr</i> A mutation	Fluoroquinolones	93%
<i>aad</i> A7	Aminoglycoside	90%
<i>aac</i> A4	Aminoglycoside	90%
<i>bla</i> _{OXA-56}	Beta-lactam	90%
MexXY-OprM (<i>mexZ</i> deletion)	Macrolides	88%
	Tetracyclines	
	Beta-lactam	
OprD frameshift	Carbapenem	88%
<i>bla</i> _{SPM-1}	Carbapenem	70%
<i>rmt</i> D	Aminoglycoside	65%
<i>crp</i> P	Ciprofloxacin	42%

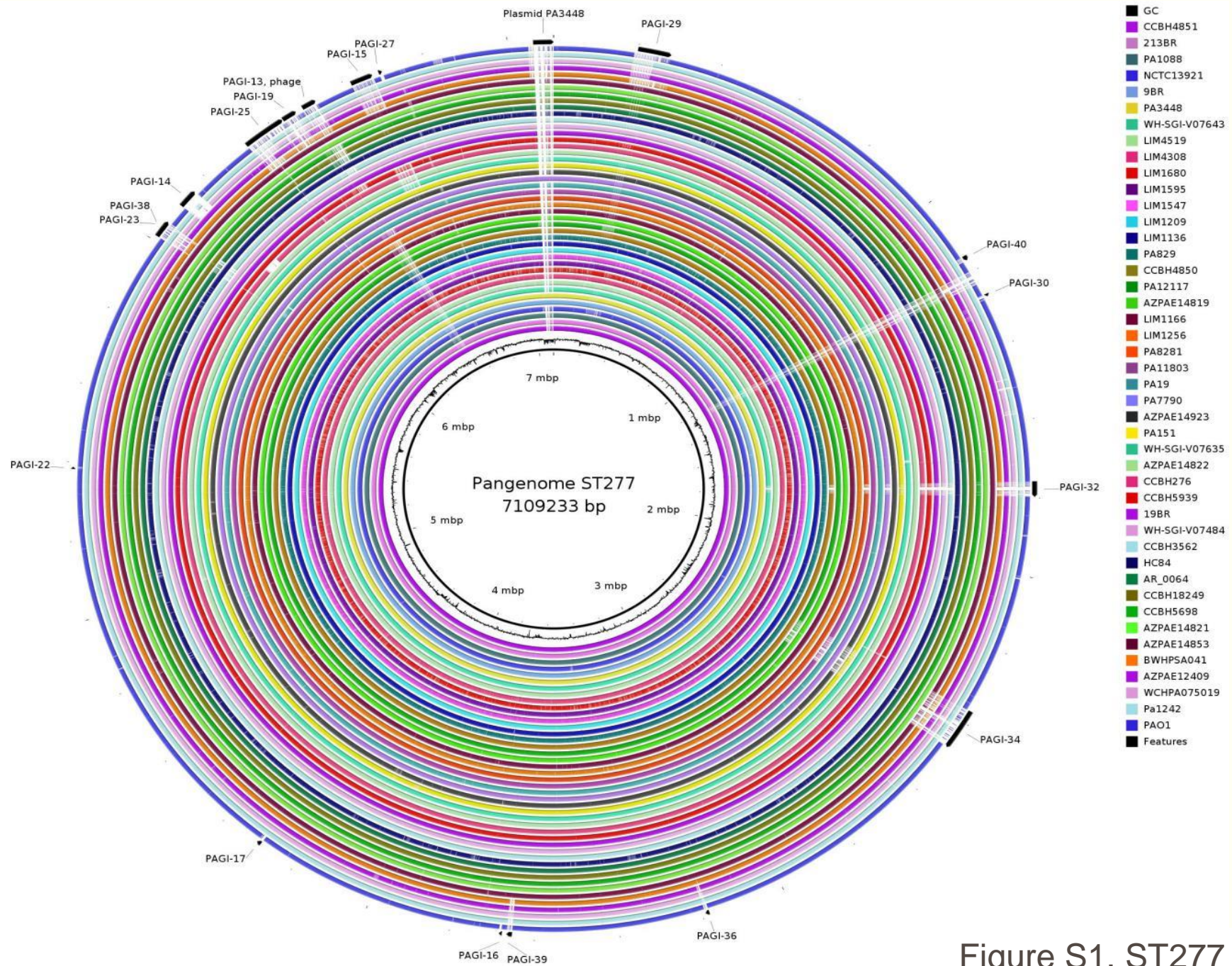


Figure S1. ST277 pangenome.



***P. aeruginosa* CCBH 4851**

Características fenotípicas e moleculares da CCBH4851

MELISE CHAVES SILVEIRA

Caracterização do ambiente genético dos genes de resistência a β -lactâmicos e aminoglicosídeos, *bla_{SPM-1}* e *rmtD*, em amostras de *Pseudomonas aeruginosa* pertencentes ao clone ST277, epidêmico no Brasil.

Dissertação apresentada ao Instituto Oswaldo Cruz como parte dos requisitos para obtenção do título de Mestre em Biologia Celular e Molecular

CCBH4851:

Amostra isolada de ponta de cateter de paciente internado em um hospital em Goiás em 2008

Clone SP/ST277

Tabela 4.3: Dados das amostras que entraram na etapa de sequenciamento total do genoma

Amostras	Ano	PCR para <i>bla_{SPM-1}</i> , <i>rmtD</i> e <i>In163</i>	PCR para									
			AK	ATM	CAZ	FEP	CIP	GEN	IPM	MER	TZP	PB
CCBH276	2004	-/-+	S	R	R	R	R	R	R	R	R	S
CCBH3462	2007	+/-+	S	R	R	R	R	R	R	R	S	S
CCBH4850	2008	+/>+	R	I	R	R	R	R	R	R	R	S
CCBH4851	2008	+/>+	R	I	R	R	R	R	R	R	R	S
CCBH5698	2010	+/>+	R	I	R	R	R	R	R	R	R	S
CCBH5939	2010	-/>+	R	R	R	R	R	R	R	R	R	S

Legenda: AK-amicacina, ATM-aztreonam, CAZ-ceftazidima, FEP-cefepime, CIP-ciprofloxacina, GEN-gentamicina, IPM-
imipenem, MER-meropenem, TZP-piperacilina-tazobactam, PB-polimixina B.

The draft genome sequence of multidrug-resistant *Pseudomonas aeruginosa* strain CCBH4851, a nosocomial isolate belonging to clone SP (ST277) that is prevalent in Brazil

Melise Silveira^{1/+}, Rodolpho Albano², Marise Asensi¹, Ana Paula Carvalho Assef¹

¹Laboratório de Pesquisa em Infecção Hospitalar, Instituto Oswaldo Cruz-Fiocruz, Rio de Janeiro, RJ, Brasil

²Departamento de Bioquímica, Universidade do Estado do Rio de Janeiro, Rio de Janeiro, RJ, Brasil

Infection, Genetics and Evolution 42 (2016) 60–65



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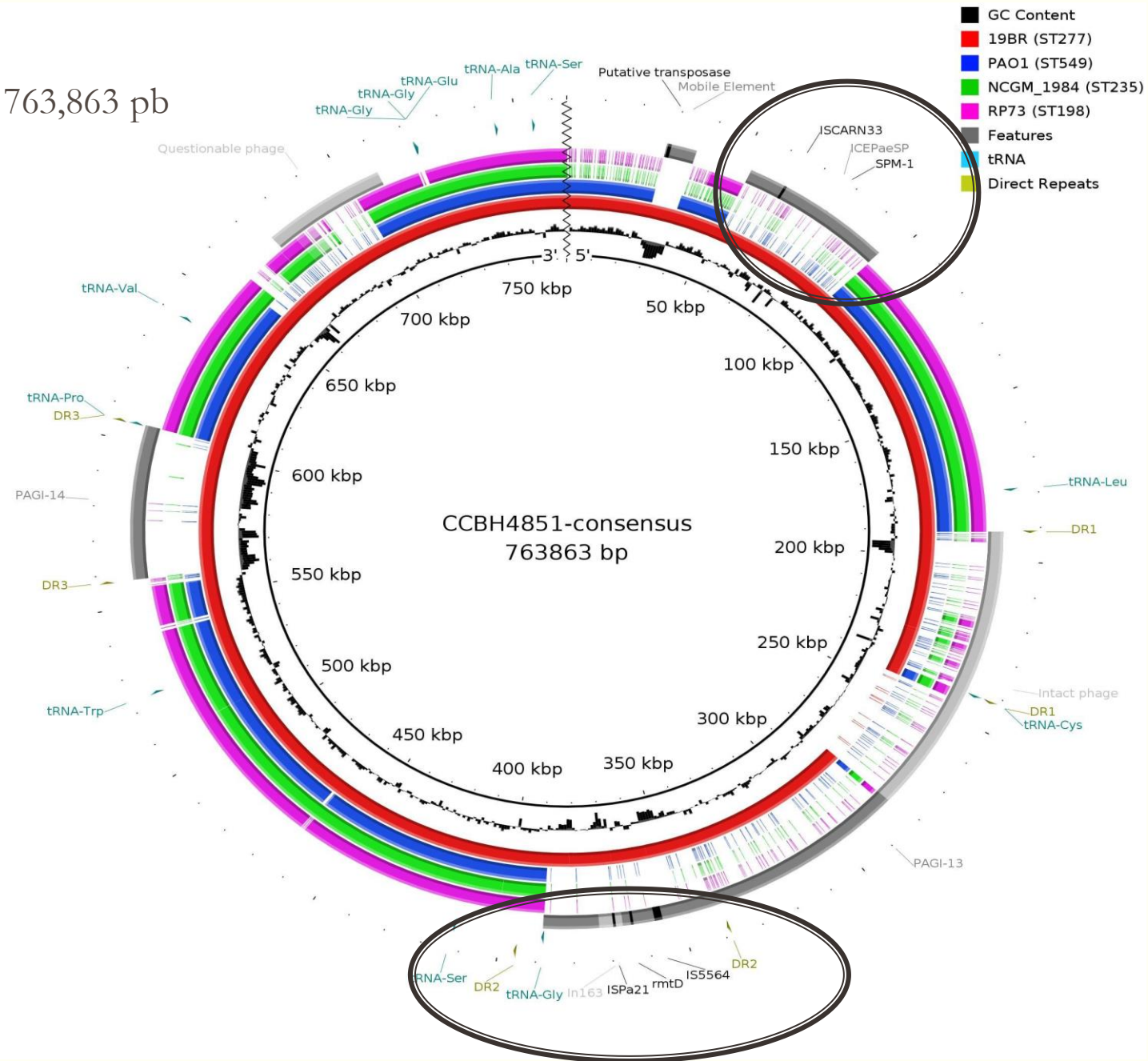
Short communication

Description of genomic islands associated to the multidrug-resistant *Pseudomonas aeruginosa* clone ST277

Melise Chaves Silveira^{a,b,*}, Rodolpho Mattos Albano^c,
Marise Dutra Asensi^a, Ana Paula D'Alincourt Carvalho-Assef^a



763,863 pb



Comparative genome analysis of the multidrug-resistant *Pseudomonas aeruginosa* Brazilian isolate belonging to ST-277

Ana Paula Barbosa do Nascimento¹✉, Fernando Medeiros Filho¹, Hério Sousa², Hermes Sanger², Rodolpho Mattos Albano³, Marcelo Trindade dos Santos⁴, Ana Paula D'Alincourt Carvalho-Assef⁵, and Fabricio Alves Barbosa da Silva¹

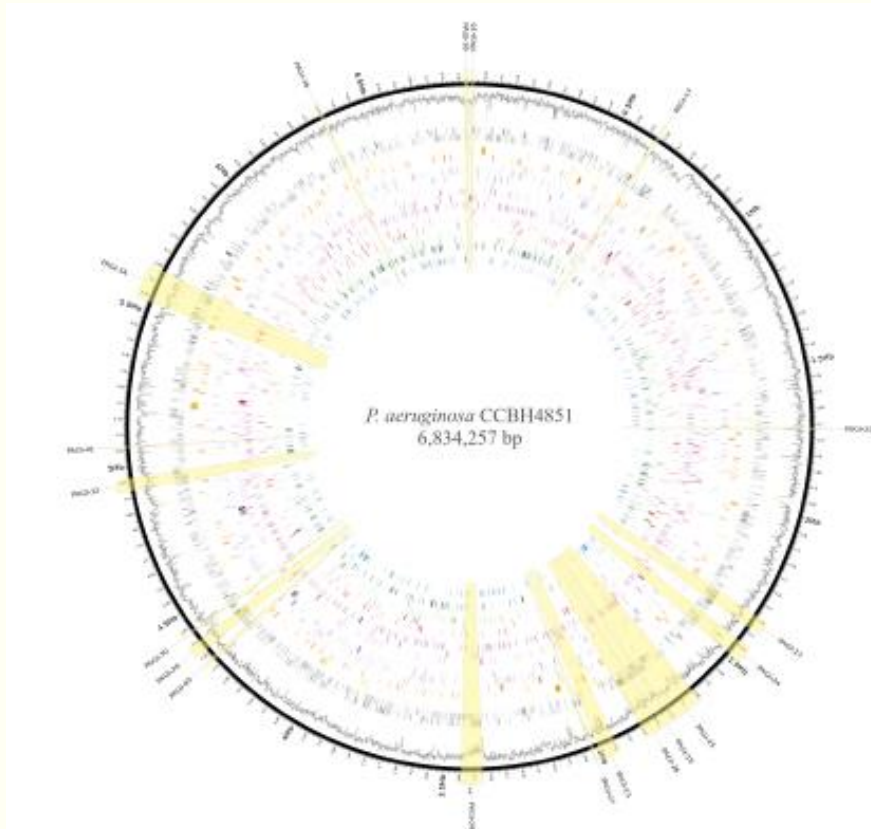


Table 2. Genome features of *P. aeruginosa* CCBH4851 compared to *P. aeruginosa* PAO1 reference strain.

Feature	Strain	
	CCBH4851	PAO1
Genome status	complete	complete
Source	catheter tip	wound
Country	Brazil	Australia
Year	2008	unknown
Genome size (bp)	6,834,257	6,264,404
G+C content (%)	66.08	66.56
No. of total genes	6,319	5,697
No. of pseudogenes	78	19
No. of total CDSs	6,211	5,572
No. of hypothetical proteins	2,476	2,256
No. of rRNAs	13	13
No. of tRNAs	64	63
No. of other RNAs	29	30

OBRIGADA!!!!

anapdca@ioc.fiocruz.br



<https://loonylabs.files.wordpress.com/2015/01/super-bugs.jpg?w=590>