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Canada

Characterization of Colistin-Resistant *Enterobacteriaceae* Harbouring *mcr-1* Identified from Food and Human Sources in Canada

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Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

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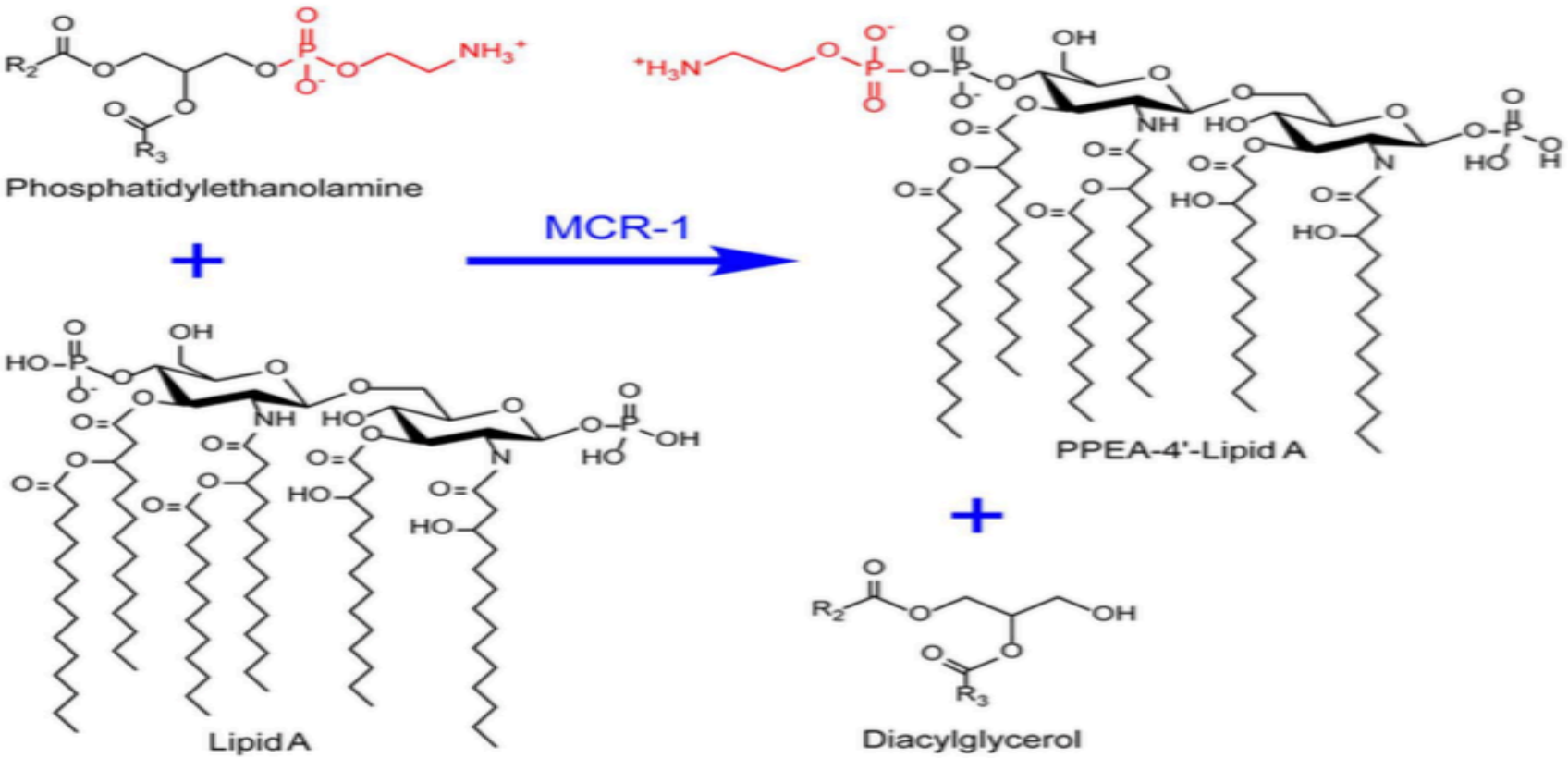
mcr-1 Global Identification

32 countries, possible linkage to Peru

Mcr-1 is a phosphoethanolamine transferase

- Reservoir appears to be in *Moraxella catarrhalis*



Gao et al. 2016. PLOS Pathogens. 12: e1005957

Background

- Found in *Salmonella, Klebsiella pneumoniae*, *Enterobacter* spp., and *Pseudomonas aeruginosa* (experimental conjugation)

- Found in many plasmid types: IncI2, IncX4, IncIH1B, IncHI2, IncIH2A, IncFII, and IncIFB

- Initial Canadian report of *E. coli mcr-1* from retail beef (n=2; ground beef) and a human case also OXA-48 positive

  Mulvey et al. Lancet Infect Dis 2016. 16:289-90.

- *mcr-1* identified from *E. coli* isolates from the 1980s in China

  Shen et al. Lancet Infect Dis 2016. 16:293.

Methods

- CANWARD; 2008-16; 10-15 hospital sites (>6,000 isolates)
  Walkty *et al*. CMAJ. 2016. 4:641-645.
- CNISP Carbapenemase Surveillance; 2007-16 (>500 isolates)
- CIPARS in 2016 and screened all human (n=4200) and agri-food *Salmonella* (n=3271) and *E. coli* (n=4507)
- Reference Services
- PulseNet WGS Analysis of existing *E. coli and Salmonella* (>5000)
- Toronto area sewage/recreational beach

Methods

- Developed screen plate for colistin-R
  - Mueller Hinton, 2 mg/L colistin;
  - 1/10 dilution of 0.5 MacFarland dilution
  - Spot 2 ul on plate
  - validated on 100 *Enterobacteriaceae*

- Multiplex PCR
  - TEM, SHV, CTX, CMY, OXA-1
  - *mcr-1* and *mcr-2*

Canadian *mcr-1* (n=19)

- **Human cases (7 cases; 10 isolates)**
  - *E. coli* Toronto, Ontario (2010); blood isolate from ER; CANWARD
  - *E. coli* Vancouver, British Columbia (2010); blood isolate from ER; CANWARD
  - *E. coli* Ottawa, Ontario (2011); OXA-48 positive, pan-drug resistant; Lived in Egypt for previous 5 years; Reference Services
  - *S*almonella Typhimurium Ontario (2012); CIPARS
  - *E. coli* isolated in Jan. 2016 in BC; obtained health care in China; Reference Services
  - *E. coli* isolated in Jan. 2017 in BC; NDM pos, colonization, recent travel to China; Reference Services
    - 2 additional cases from this patient MCR-1 positive
  - *2 E. coli* isolated 2017 in BC from same patient; Reference Services

Canadian *mcr-1* (n=19)

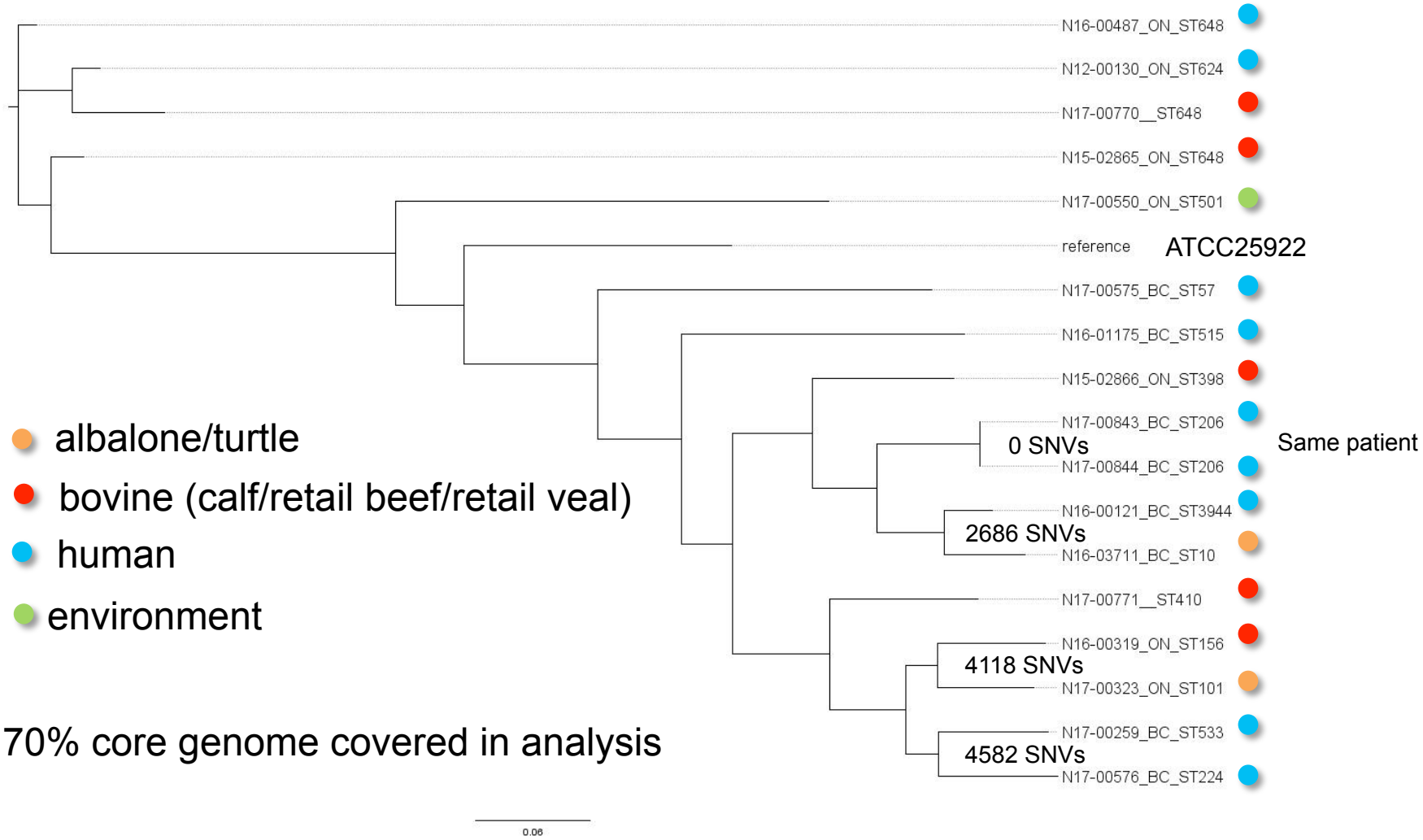
- **Food/Animal (8 isolates)**
  - 2 *E. coli* retail ground beef (2010) Ontario; different retail locations; CIPARS
  - *E. coli* from retail veal (2012) Ontario; CIPARS
  - *E. coli* from soft shell turtle, (2015) Vancouver BC; U of SK study
  - *Salmonella* I:4,[5],12i:- isolated in 2016 from bovine (Ontario); CIPARS
  - *E. coli* from abalone (Mollusk), (2016) Ontario; CIPARS
  - 2 *E. coli* isolated in 2016 from bovine (Quebec); U of Montreal (FMV)/CIPARS

- **Environment (1 isolate)**
  - *E. coli* isolated from sewage (2012) Ontario; 1 confirmed and 5 others PCR positive, 1 from *Vibrio paraheamolyticus*; WGS GRDI study

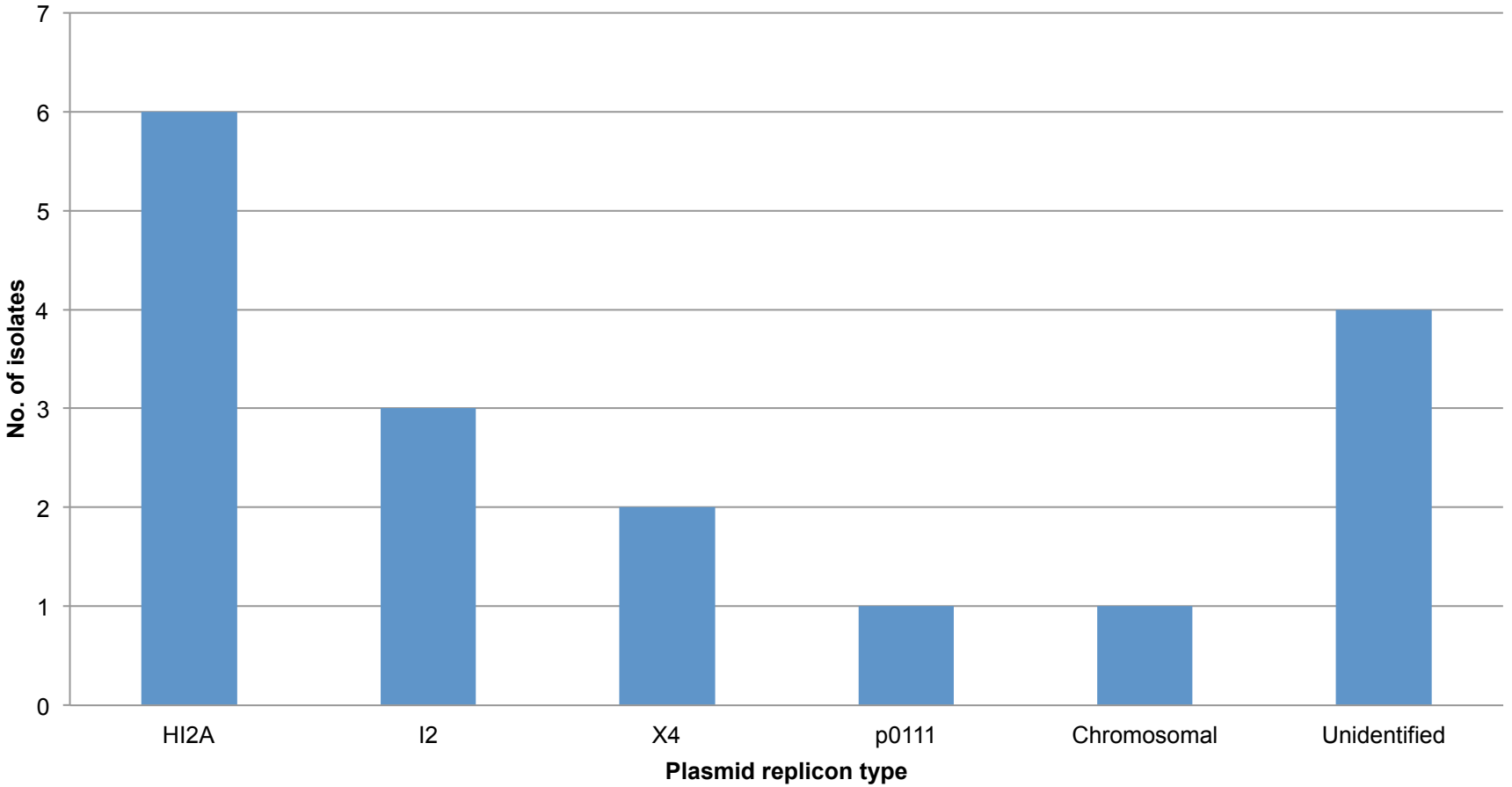
Resistance Profiles of *mcr-1* Positive Isolates

Sensititre GNX2F	Food Isolates					Clinical Isolates								
	CIPARS Ground Beef (2010) N15-02865	CIPARS Ground Beef (2010) N15-02866	CIPARS Veal (2012) N16-00319	Reference Soft shell Turtle (2015) N16-03711	CIPARS Abalone (2017) N17-00323	N17-00259 (2017) **NDM-1**	N12-00130 (2011) **OXA-48**	N17-00259 (2017) **NDM-1**	CANWARD (2010) N16-00121	CANWARD (2010) N16-0487	CANWARD (2016) N16-01175	CIPARS S. Typhimurium 12-7209	Reference Isolate 1 (2017) N17-843	Reference Isolate 2 (2017) N17-844
Aztreonam	≤2	≤2	4	>16	2	8	> 16	8	8	≤2	≤2	≤2	4	4
Cefepime	≤2	≤2	4	8	≤2	>16	16	>16	4	≤2	≤2	≤2	≤2	≤2
Cefotaxime	≤1	≤1	4	>32	≤1	>32	> 32	>32	>32	≤1	≤1	≤1	32	16
Ceftazidime	≤1	≤1	>16	8	≤1	>16	16	>16	16	≤1	≤1	≤1	2	2
Ertapenem	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25	>4	>4	>4	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25
Meropenem	≤1	≤1	≤1	≤1	≤1	8	2	8	≤1	≤1	≤1	≤1	≤1	≤1
Imipenem	≤1	≤1	≤1	≤1	≤1	4	≤1	4	≤1	≤1	≤1	≤1	≤1	≤1
Doripenem	≤0.12	≤0.12	≤0.12	≤0.12	≤0.12	>2	0.5	>2	≤0.12	≤0.12	≤0.12	≤0.12	≤0.12	≤0.12
Doxycycline	> 16	> 16	>16	>16	>16	16	> 16	16	>16	>16	≤2	>16	8	4
Minocycline	> 16	> 16	>16	4	16	>16	16	>16	>16	16	≤2	>16	≤2	≤2
Gentamicin	≤1	>8	≤1	>8	≤1	≤1	>8	≤1	>8	>8	≤1	8	≤1	≤1
Amikacin	≤4	≤4	≤4	>32	≤4	≤4	≤ 4	≤4	≤4	≤4	≤4	≤4	≤4	8
Tobramycin	≤1	>8	4	>8	≤1	≤1	4	≤1	8	> 8	1	>8	≤1	≤1
Ciprofloxacin	>2	>2	>2	>2	≤0.25	>2	>2	>2	>2	>2	0.5	1	>2	>2
Levofloxacin	>8	8	>8	>8	≤1	>8	8	>8	>8	>8	≤1	≤1	8	8
Piperacillin/ tazobactam	≤8	≤8	≤8	≤8	≤8	>64	> 64	>64	≤8	≤8	≤8	≤8	≤8	≤8
Ticarcillin/clavulanic acid	≤ 16	≤ 16	32	64	≤16	>128	>128	>128	≤16	128	≤16	32	≤16	≤16
Tigecycline	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25	≤0.25	0.5	≤0.25	≤0.25	≤0.25	≤0.25
Trimethoprim/ sulfamethoxazole	>4	>4	>4	>4	≤0.5	>4	>4	>4	>4	> 4	≤0.5	>4	>4	>4
Colistin	>4	>4	>4	>4	>4	>4	>4	>4	>4	>4	4	>4	>4	>4
Polymixin B	>4	>4	>4	>4	4	4	>4	4	>4	> 4	4	>4	>4	>4

WGS *E. coli* harbouring mcr-1 in Canada (n=17)

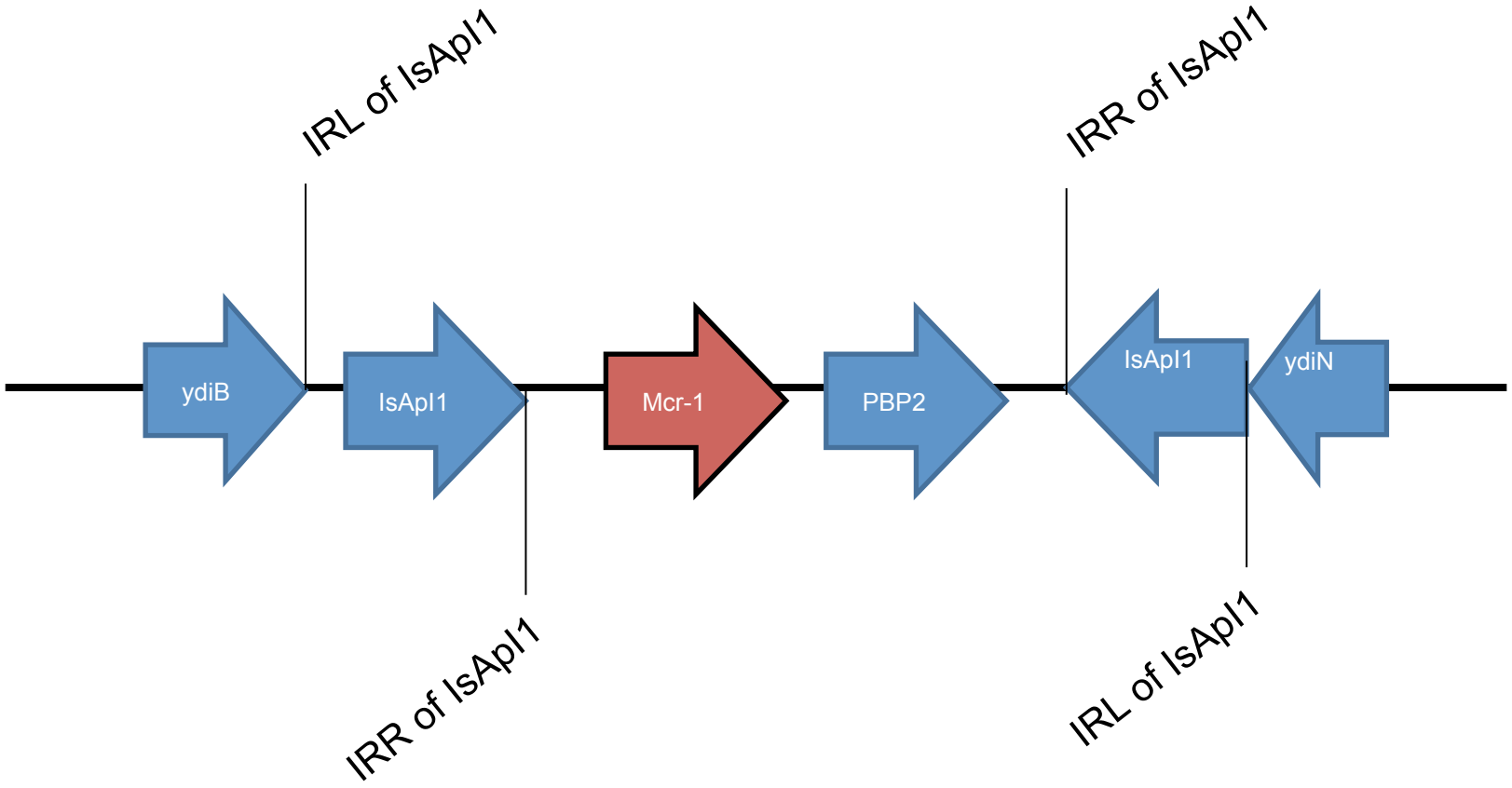


MCR-1 plasmids



Plasmids were identified using either plasmidFinder where *mcr-1* gene and replicon type were on same DNA contig or *mcr-1* contig was >99% identity to known *mcr-1* plasmid on NCBI

Chromosomal Location of *mcr-1*



Summary

- Colistin resistance now mobile
- *mcr-1* seems widespread but not common and has been circulating since at least 2010 in Canada
- *E. coli* isolates not closely related except for two isolates from a single patient
  - No outbreaks or patient to patient transmission observed
  - No linkage between human and agri-food isolates
- Need to reconsider the use of colistin in agriculture
  - In Canada colistin not approved for use in animals but is imported as an API for compounding and extra label use in veal calves

THANK YOU

@superbugfighter