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

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, IncH2A, IncFII, and IncFIB

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

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

- *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
- Salmonella 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
<table>
<thead>
<tr>
<th>Sensititre GNX2F</th>
<th>Food Isolates</th>
<th>Clinical Isolates</th>
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<tbody>
<tr>
<td>Aztreonam</td>
<td>≤2 ≤2 4 &gt;16 2</td>
<td>8 8</td>
</tr>
<tr>
<td>Cefepime</td>
<td>≤2 ≤2 4 8 ≤2</td>
<td>&gt;16</td>
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<tr>
<td>Cefotaxime</td>
<td>≤1 ≤1 4 32 ≥1</td>
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<td>Ceftazidime</td>
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<td>Ertapenem</td>
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<td>Imipenem</td>
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<td>Doripenem</td>
<td>≤0.12 ≤0.12 ≤0.12 ≤0.12 ≤0.12 &gt;2 0.5 &gt;2 0.12 ≤0.12 ≤0.12 ≤0.12 ≤0.12 ≤0.12 ≤0.12</td>
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<td>Doxycycline</td>
<td>&gt;16 &gt;16 &gt;16 &gt;16 &gt;16 &gt;16 &gt;16 &gt;16 ≥16 ≥16 ≥16 ≥16 ≥16 ≥16 ≥16 ≥16</td>
<td>8 4</td>
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<td>Minocycline</td>
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<td>8 2 2 2 2 2 0.5 1 &gt;2 &gt;2 8 4</td>
</tr>
<tr>
<td>Gentamicin</td>
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<td>Amikacin</td>
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<td>Tobramycin</td>
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<tr>
<td>Ciprofloxacin</td>
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<td>Levofloxacin</td>
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<tr>
<td>Piperacillin/ tazobactam</td>
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<td>Ticarcillin/clavulanic acid</td>
<td>≤16 ≤16 32 64 ≤16 ≥128 ≥128 ≥128 ≥16 ≥16 ≥16 ≥16 ≥16 ≥16 ≥16 ≥16</td>
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<tr>
<td>Tigecycline</td>
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<tr>
<td>Trimethoprim/ sulfamethoxazole</td>
<td>≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4 ≥4</td>
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<td>Colistin</td>
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<td>Polymixin B</td>
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WGS E. coli harbouring mcr-1 in Canada (n=17)

70% core genome covered in analysis
Plasmids were identified using either plasmidFinder where \textit{mcr-1} gene and replicon type were on same DNA contig or \textit{mcr-1} contig was >99\% identity to known \textit{mcr-1} plasmid on NCBI
Chromosomal Location of \textit{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