New molecular approaches to AMR testing

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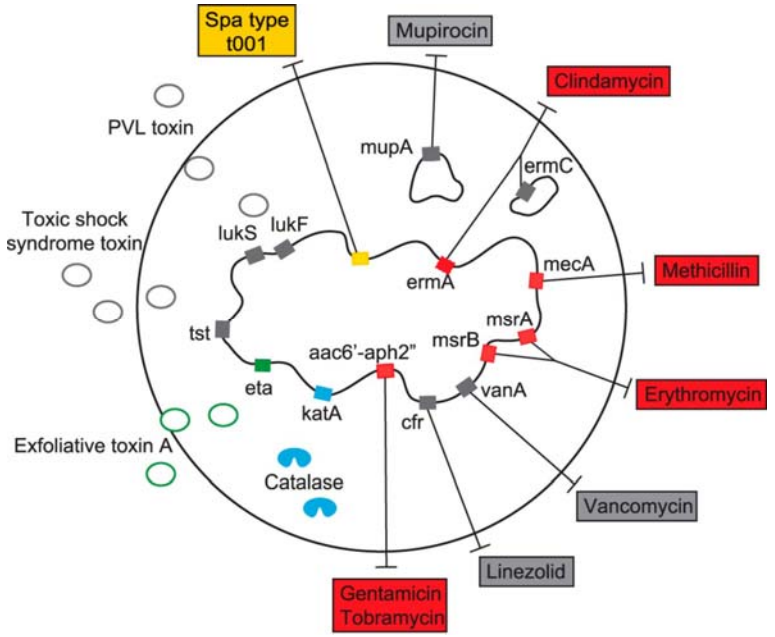
Why do we need to genetically “predict” antimicrobial resistance in animal health?

Bacterial whole genome sequencing in vet diagnostics

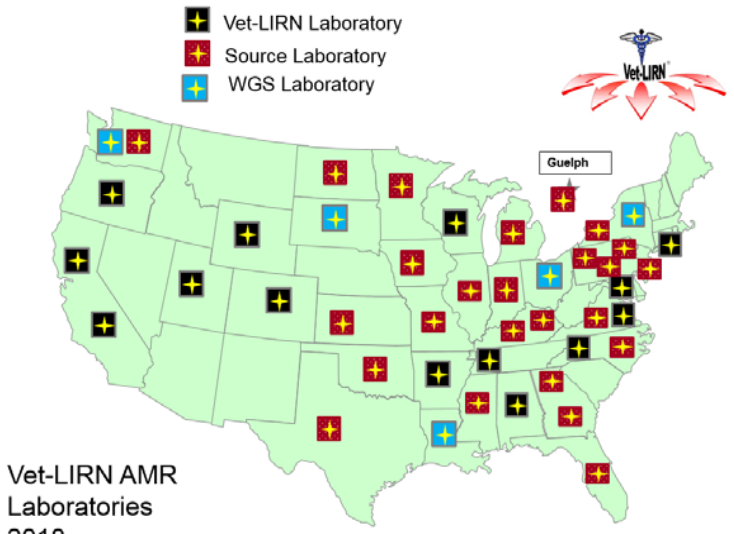
- Performed on cultures (costs ~$200)
- Nationally harmonized lab procedures (with FDA/CDC/state health)
- Confirms species, subspecies, isolate relatedness
- Large databases mined to predict features (functional genomics):
  - Serotype
  - Virulence factors
  - Antibiotic resistance gene (ARG) profile



Leopold et al. J. Clin. Microbiol. 2014

National CARB veterinary surveillance project using WGS

- **FDA Veterinary Laboratory Investigation and Response Network**
  - 25 vet diagnostic source labs
  - ~2,000 isolates collected in 2017
    - *Salmonella* (all hosts)
    - *E. coli* (dogs)
    - *S. pseudintermedius* (dogs)
    - "Other" (2018)
  - Including whole genome sequencing on a subset (done by 5 additional vet labs) uploaded to NCBI in near real-time
  - NARMS integration



Vet-LIRN AMR Laboratories 2018

Metadata protections

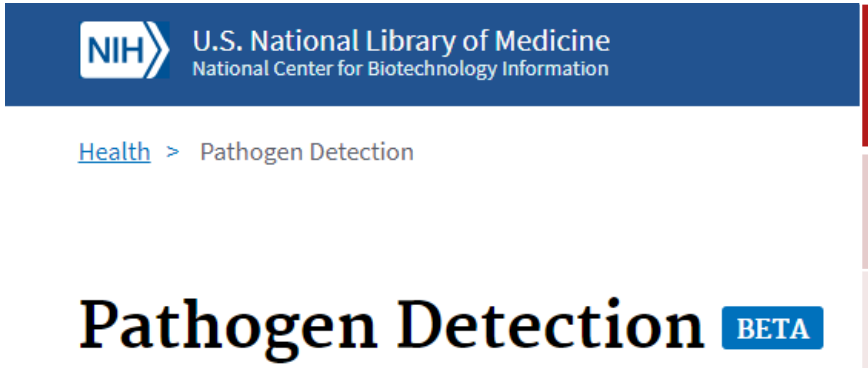
Data included

- Host species
- Sample type (e.g. feces, respiratory, wound swab)
- Collection date
- State of origin
- Case type
- Lab methods

Not included

- VDL accession number
- Referring DVM
- Animal owner
- Animal name

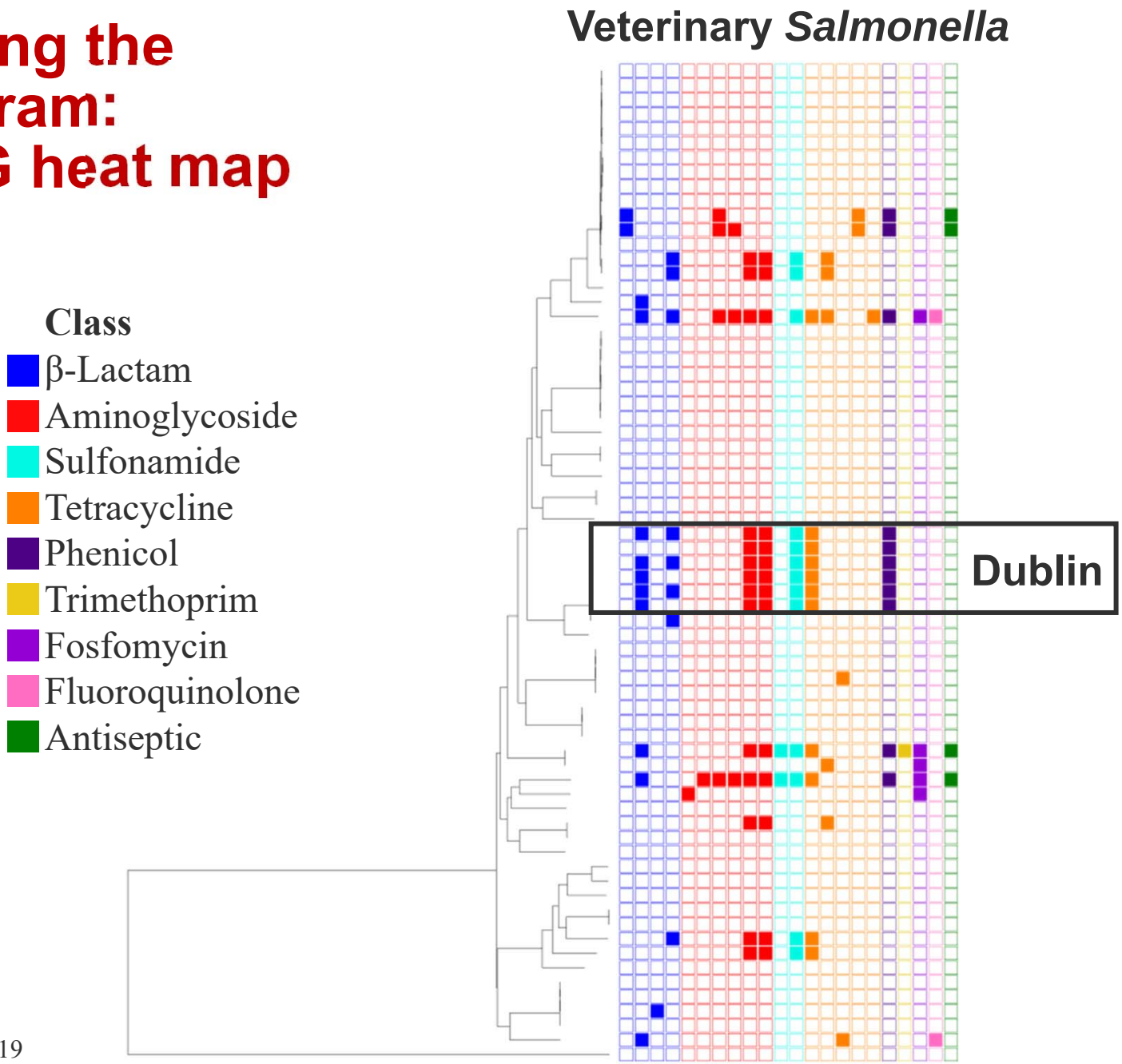
Working towards animal health representation in the NCBI database



Organism	Total isolates (10/22/19)
Salmonella	235,207
E. Coli	87,471
Campylobacter jejuni	44,737
Listeria monocytogenes	29,306
Klebsiella pneumoniae	17,982
Staphylococcus pseudintermedius	695

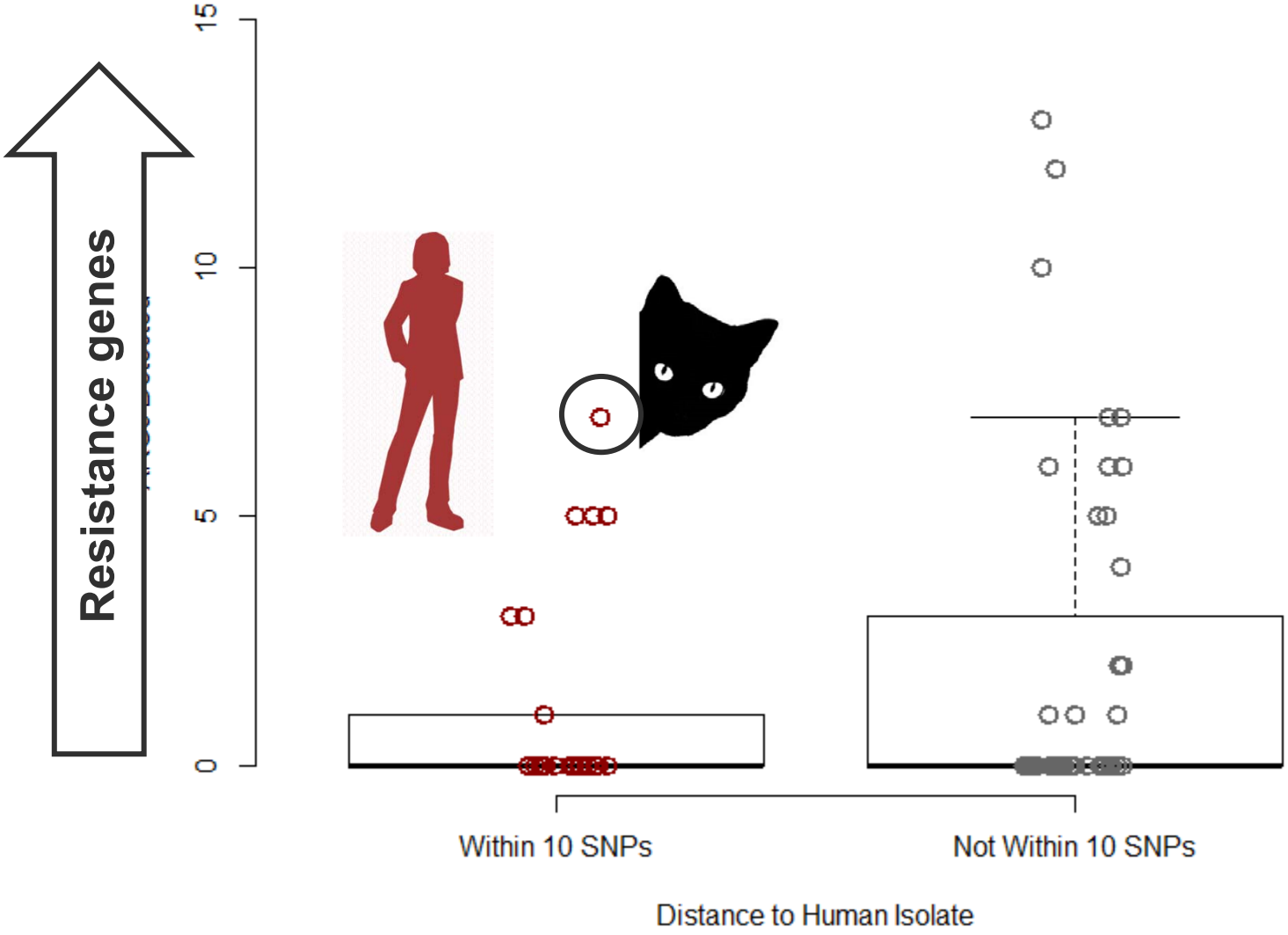
www.ncbi.nlm.nih.gov/pathogens/

Rethinking the antibiogram: The ARG heat map



Ceric et al., BMC Vet 2019
FDA Vet-LIRN, data available at ncbi.nlm.nih.gov/pathogens/

Distribution of ARGs in veterinary *Salmonella* by Distance to Human Cases



FDA Vet-LIRN, data available at ncbi.nlm.nih.gov/pathogens/

Most extreme cases highlight role of companion animals in AMR

Canine lung (2017)
aac(3)-Iid (gentamicin)
aadA1 (streptomycin)
aph(3")-Ib (streptomycin)
aph(3')-Ia (kanamycin)
aph(6)-Id (streptomycin)
blaCMY-2 (penicillins, amoxi-clav, cephalosporins)
blaTEM-1 (penicillins)
catA1 (phenicols)
dfrA14 (trimethoprim)
mph(A) (macrolides)
qacL (disinfectants)
sul2, sul 3 (sulfonamides)
tet(B) (tetracycline)
gyrA mutations (fluoroquinolones)

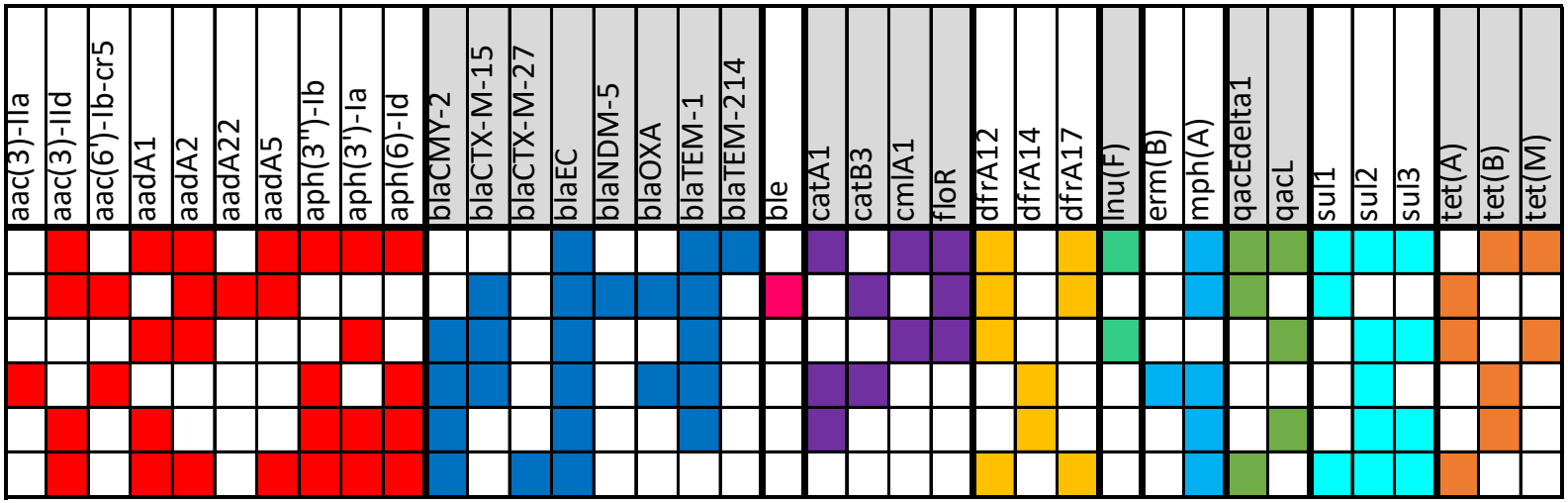
Canine lung (2018)
aac(3)-Iid (gentamicin)
aadA1, A2, A5 (streptomycin)
aph(3")-Ib (streptomycin)
aph(3')-Ia (kanamycin)
aph(6)-Id (streptomycin)
blaEC (cephalosporins)
blaTEM-1 (penicillins)
catA1, cmlA1, floR (phenicols)
dfrA12, 17 (trimethoprim)
Inu(F) (lincosamide)
mph(A) (macrolides)
qacL, qacEdelta1 (disinfectants)
sul1, sul2, sul 3 (sulfonamides)
tet(B, M) (tetracycline)

FDA Vet-LIRN, data available at ncbi.nlm.nih.gov/pathogens/

Most extreme cases

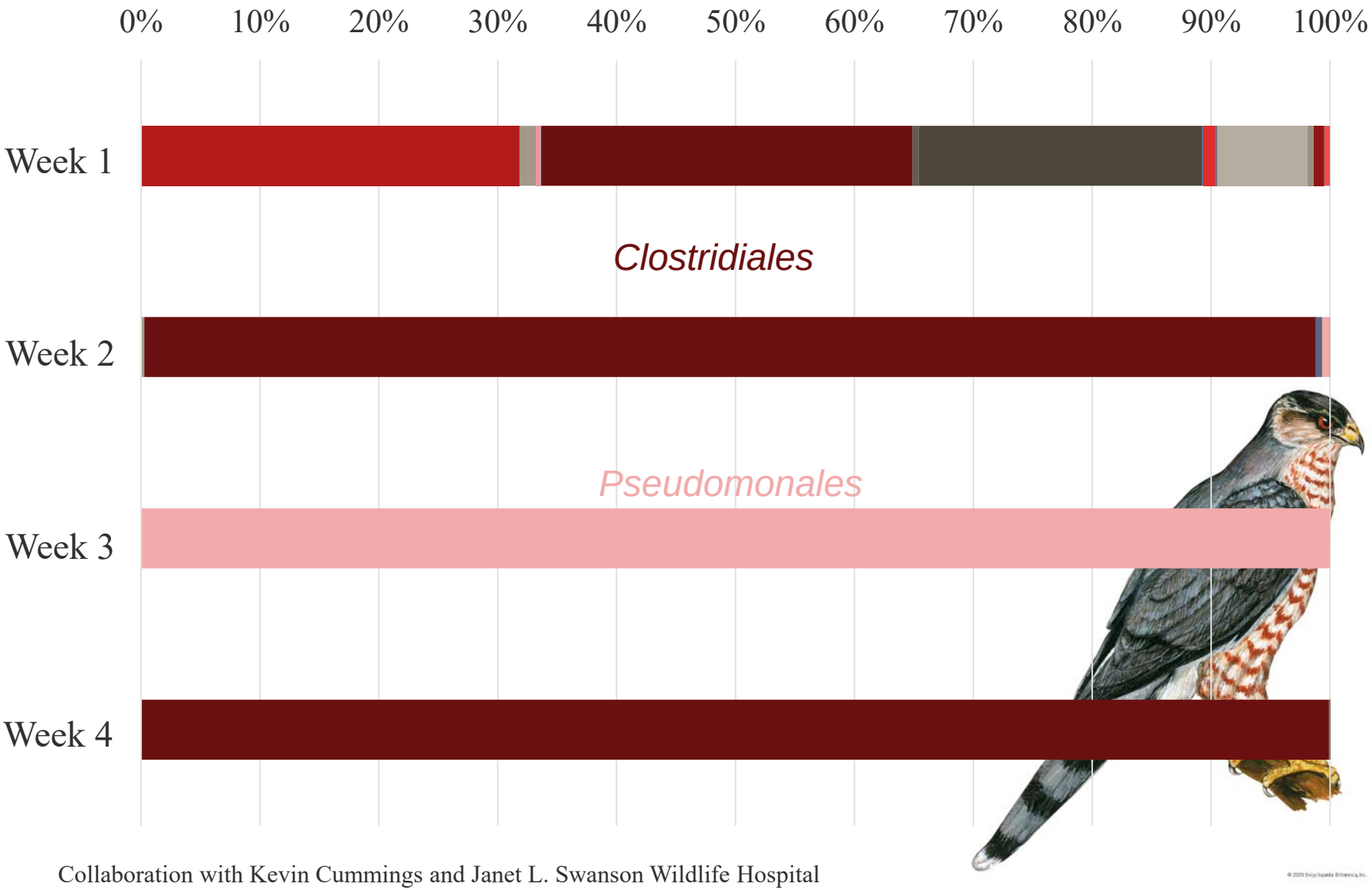
Nearly pan-resistant *E. coli*s from canines

- 6 *E. coli* isolates with ≥ 15 ARGs in Vet-LIRN CARB collection (n = 333)
  - 3* serotypes (O8:H9, O9:H10, O89:H9)
  - 5 different MLST patterns
  - No shared SNP clusters



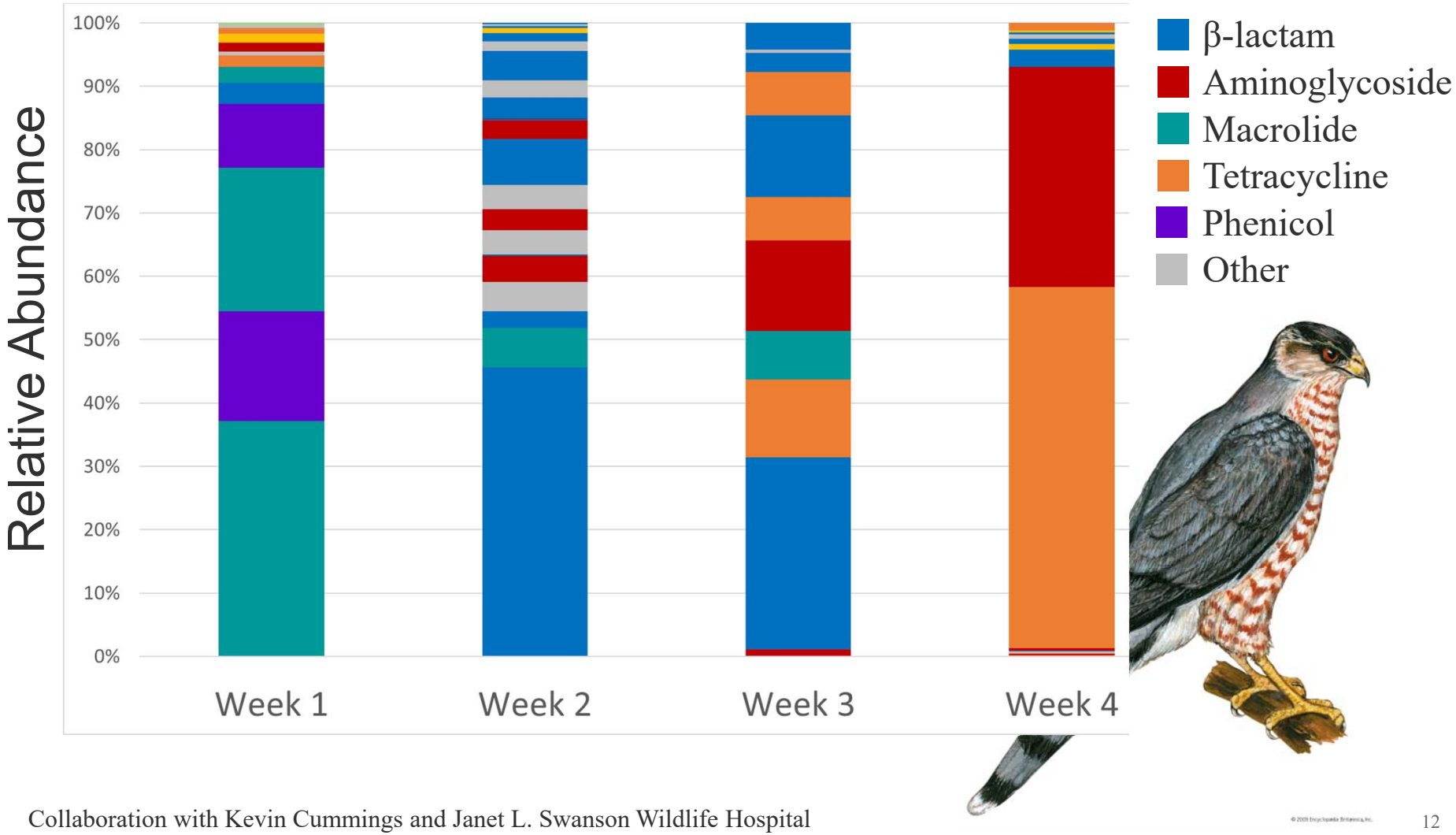
*One only had H antigen predicted (H9)

Culture-independent AMR detection



Collaboration with Kevin Cummings and Janet L. Swanson Wildlife Hospital

Culture-independent AMR detection



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Take-home points

1. People and animals share pathogens and pathogens share genes

2. By monitoring ARGs in animal populations, we can better protect both animal and human health

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