Michigan One Health Antimicrobial Resistance Summit

Statewide Activity Talks, Lab

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Prevent Disease – Promote Wellness – Improve Quality of Life

Overview

- Zoonotic and AMR diseases account for 95% of all emerging diseases reported in the 2nd half of the 20th century (USAID)
- Estimated 700,000 world-wide die annually from drug resistant TB, malaria, and HIV (USAID)
- WHO's One Health aim is to:
  - Ensure antimicrobial agents continue to be effective and useful
  - Promote prudent and responsible use of antimicrobial agents
  - Ensure global access to medicines of good quality

3 examples of Lab Data

- **CRE**
- **TB Complex**
- **Sequencing**

(Salmonella and Gonorrhea)

CRE

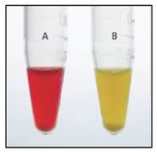
CRE

- Detecting and distinguishing CP-CRE vs. non-CP-CRE is important because: CP-CRE disseminate between patients more readily than non-CP CRE and warrant implementation of more intensive infection control.

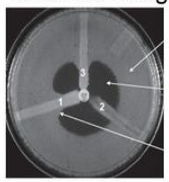
Laboratory CRE Testing

- Phenotypic testing for carbapenemase production
  - Modified-Hodge (outdated – NOT recommended)
  - CarbaNP
  - mCIM – current method at BOL
- Antimicrobial susceptibility testing
  - Broth microdilution
- Mechanism testing
  - Polymerase Chain Reaction (PCR)
  - Whole Genome Sequencing (WGS)

Carba NP



Modified Hodge Test



A lawn of carbapenem susceptible *E. coli* ATCC 25922

Zone of inhibition of *E. coli* ATCC 25922 by ertapenem

Indentation of *E. coli* ATCC 25922 growth (clover leaf appearance) around the streak line of the carbapenemase-producing *K. pneumoniae* ATCC BAA-1705.

Modified Carbapenem Inactivation Method (mCIM)

F.

G.

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Susceptibility Testing

- GNX2F Trek Sensititre broth microdilution plates
- Limitations: May lose the plasmid and therefore will look different than submitter; repeat with meropenem disk to try and recover
- Epidemiological purposes only – NOT intended for patient treatment purposes
- Extended testing from WI ARLN site for clinical testing for combo therapy: ceftazidime + avibactam, aztreonam; aztreonam + avibactam
  - Send directly to WI

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Real-time PCR

- BOL detects the following mechanisms of resistance:
  - KPC
  - NDM
  - VIM
  - OXA-48-like
  - IMP
  - MCR-1
  - MCR-2
  - Oxa-23 (coming soon)

- Whole Genome Sequencing available in outbreak situations based upon special request of state epidemiologists

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Colonization Screening

- For human clinical specimens - Bureau of Epidemiology approval is required
- Rectal swab in Aimes Transport
- Screening performed via real-time PCR for gene of interest
- Turn-around Time: based on time of receipt, but generally within 48hrs

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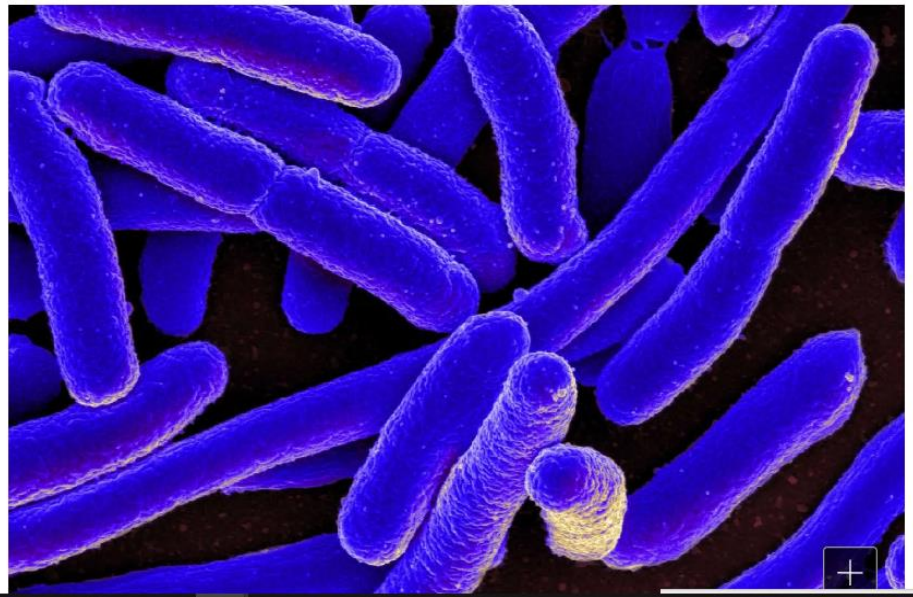
One Health Example - CRE

The Philadelphia Inquirer

Drug-resistant bacteria identified in 15 animal patients at Penn Vet Hospital

by Mari A. Schaefer, Updated: July 9, 2019



- 15 Companion animals
  - 14 dogs and 1 cat
- NDM-5
  - Previously found in China and Europe
  - First reports of this strain in the US
- Reported cases to human health partners

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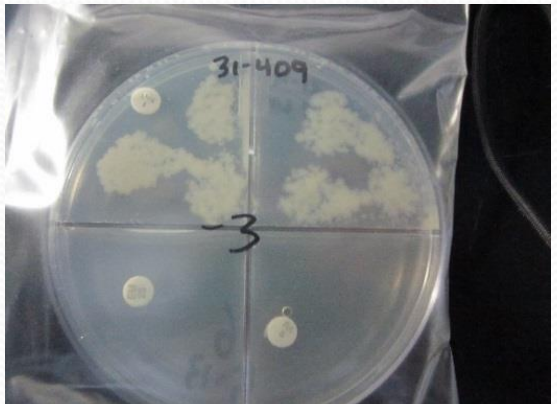
TB Complex

TB Susceptibility Testing Primary

Results are available within 7-14 days of *M. tuberculosis* complex identification

- Isoniazid
- Rifampin
- Ethambutol
- Pyrazinamide

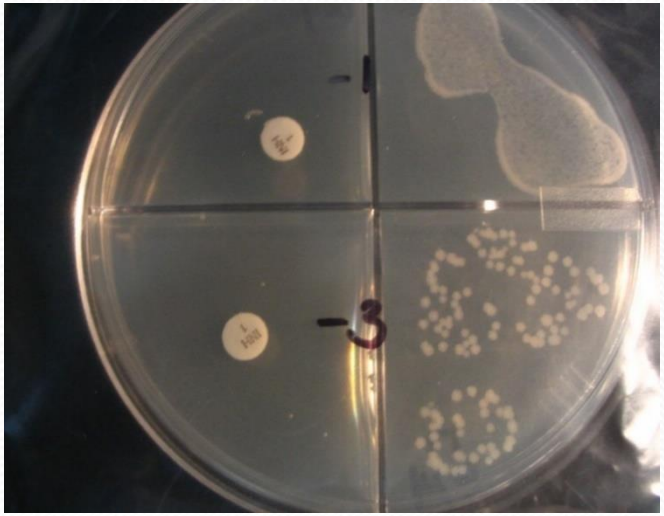


Repeat testing if cultures are still positive after 90 days

Susceptibility Testing-Secondary

If there is any resistant to the four primary drugs, another agar proportion plate test will be set up using secondary antibiotics:

- Fluoroquinolone (ciprofloxacin, ofloxacin)
- Ethionamide
- Cycloserine
- Capreomycin
- Amikacin
- Kanamycin
- Streptomycin



Results are **available 3 weeks** from detection of resistance on Primary susceptibility testing

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MDDR Susceptibility by CDC

- Testing performed by CDC
- PCR (+) sputum sediment or growth-based culture isolates
- 3-4 day turn-around-time
- Only requested by state health lab
- Submission criteria :
  - ✓ Known Rifampin resistance
  - ✓ Known MDR
  - ✓ High risk of Rifampin resistance or MDR-TB (e.g. previous TB, MDR-TB contact, foreign born)
  - ✓ High profile patient (e.g. daycare worker, nurse)
  - ✓ Mixed or non-viable culture
  - ✓ Adverse reaction (e.g. RIF allergy)

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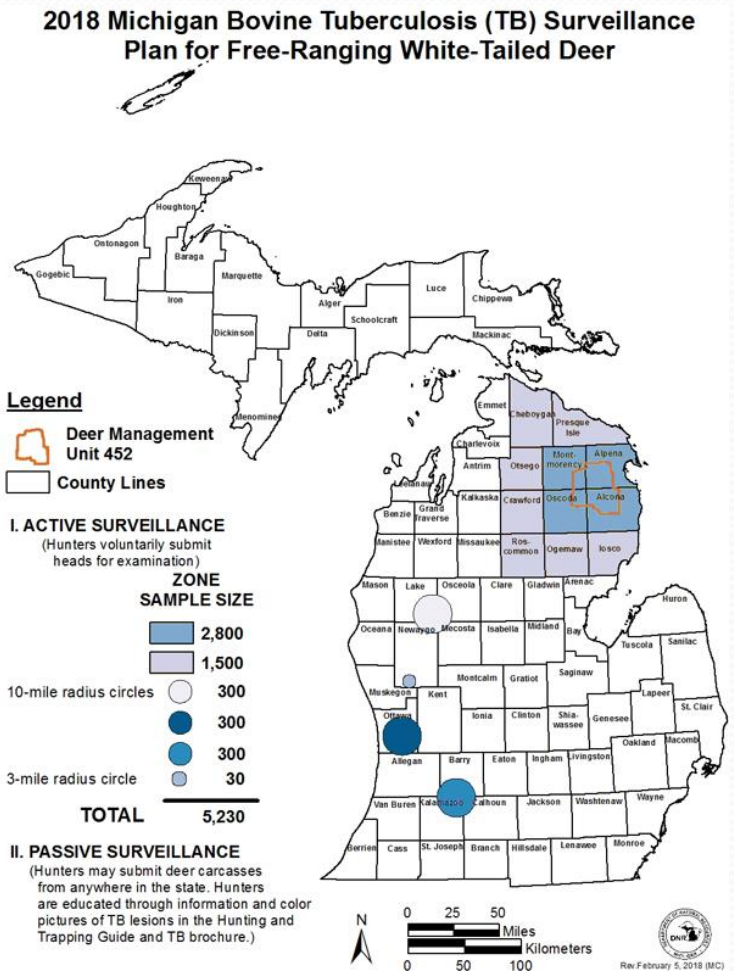
TB Complex Resistance Counts

ALL TB COMPLEX	2018	2019 (Jan-Jun)
Number MTBC cultures:	78	54
# all susceptible:	62	42
# R to 1 drug:	7	5
# R to 2 drugs:	4	5
# R to 3 drugs:	1	0
# R to 4 drugs:	1	0
# MDR:	3	2
# drugs R for MDRs		
5 drugs:	1	2
6 drugs:	1	0
8 drugs:	1	0

DEER 2018	
Number tested:	112
Number M. bovis:	28

One Health Example – M. bovis

- Bovine TB has been found in MI white-tailed deer, elk, black bear, bobcat, coyote, opossum, raccoons, and red fox



Sequencing

Sequencing

Antibiotic Resistance Profiles:

		AR Gene							
		mtrCDE (multidrug efflux complex)	mtrR (mutation increases resistance of mtrCDE)	macAB (macrolide)	farAB (antibacterial fatty acids)	patA (fluoroquinolone)	TEM-104/106/135 (beta-lactamase)	tetM (tetracycline)	penA (penicillin)
Strain	CL18-186008	y	y	y	y	y	y		y
	CL18-186027	y	y	y	y		y		y
	CL19-186061	y	y	y	y		y		y
	CL19-186063	y	y	y	y			y	y
	CL19-186093	y	y	y	y				y
	CL19-186098	y	y	y	y				y
	CL19-186099	y	y	y	y				y
	CL19-186100	y	y	y	y				y
	CL19-186102	y	y	y	y				y

Example shown is from gonorrhea cases

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Sequencing Cont.

Heat Maps

.	CL18-186008	CL18-186027	CL19-186061	CL19-186063	CL19-186093	CL19-186098	CL19-186099	CL19-186100	CL19-186102
CL18-186008	-	3490	678	3957	3171	3131	3128	2720	3182
CL18-186027	3490	-	3665	4050	2852	2847	2829	2516	2843
CL19-186061	678	3665	-	4024	3382	3357	3334	2921	3396
CL19-186063	3957	4050	4024	-	4220	4151	4144	3592	4255
CL19-186093	3171	2852	3382	4220	-	-	12	-	5
CL19-186098	3131	2847	3357	4151	-	-	12	-	5
CL19-186099	3128	2829	3334	4144	12	12	-	5	17
CL19-186100	2720	2516	2921	3592	-	-	5	-	4
CL19-186102	3182	2843	3396	4255	5	5	17	4	-

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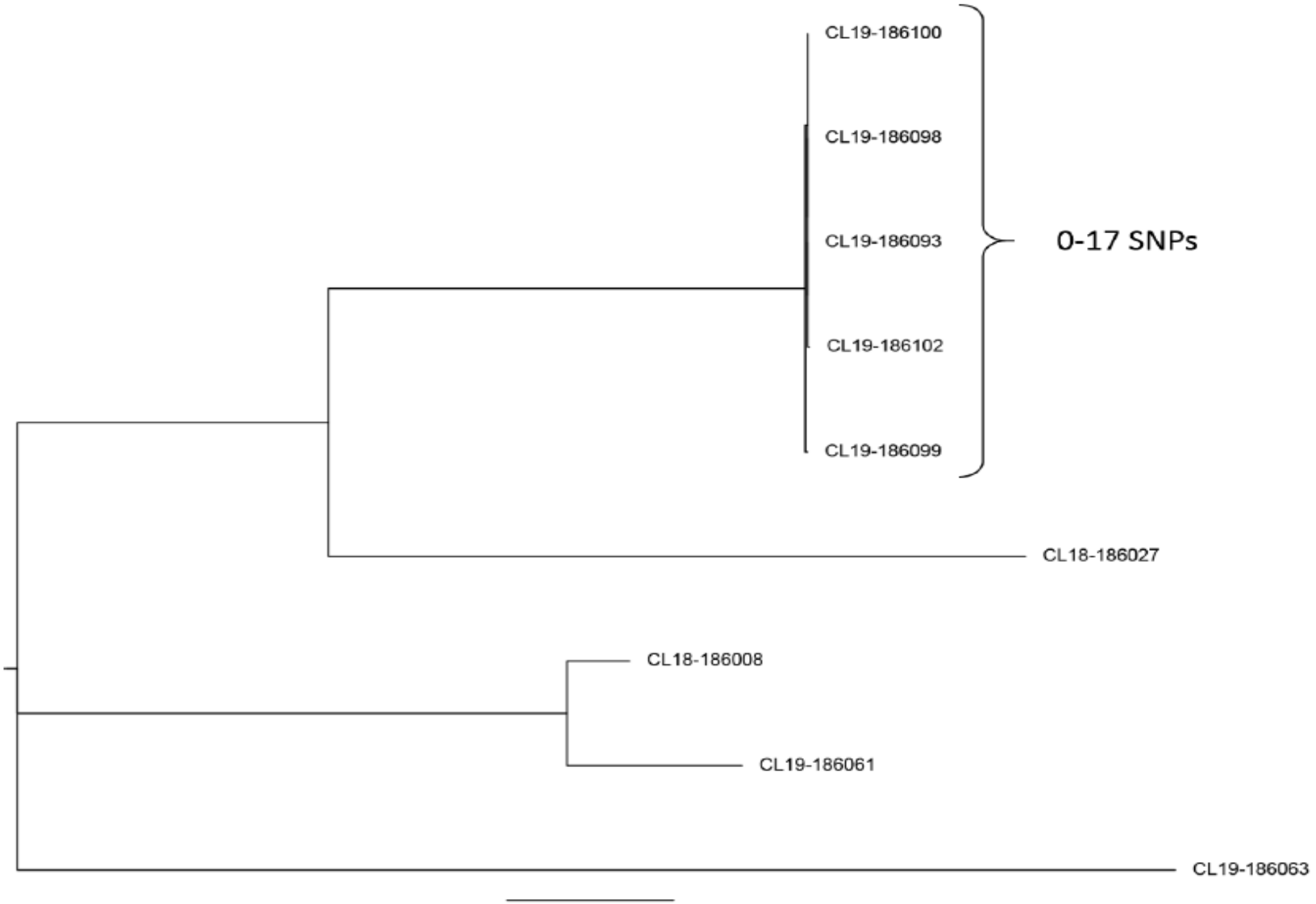
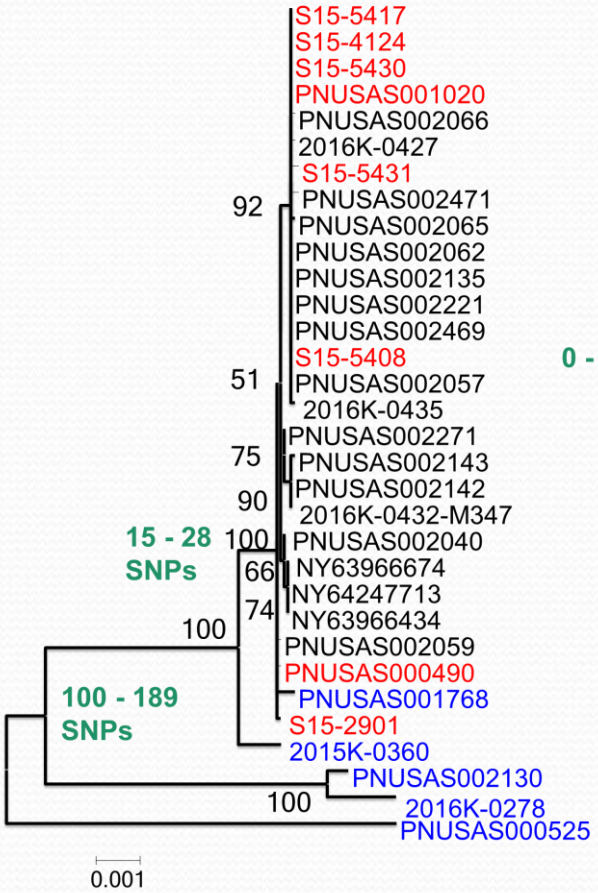
Phylogenetic Trees



One Health Example - Sequencing

Salmonella serovar Enteritidis clusters
Associated with a Michigan hatchery



	2015K-0360	2016K-0278	2016K-0427	2016K-0432	2016K-0435	NY63966434	NY63966674	NY64247713	PNUSAS000490	PNUSAS000525	PNUSAS001020	PNUSAS001768	PNUSAS002040	PNUSAS002057	PNUSAS002059	PNUSAS002062	PNUSAS002065	PNUSAS002066	PNUSAS002130	PNUSAS002135	PNUSAS002142	PNUSAS002143	PNUSAS002221	PNUSAS002271	PNUSAS002469	PNUSAS002471	S1502901	S1504124	S1505408	S1505417	S1505430	S1505431
2015K-0360	0	156	27	26	26	25	25	25	23	174	24	27	24	22	15	26	27	25	134	26	24	27	25	24	26	28	20	24	25	26	25	27
2016K-0278	156	0	158	158	158	156	159	159	156	210	158	153	158	140	116	157	158	146	24	160	139	161	157	155	160	163	146	152	154	152	152	158
2016K-0427	27	158	0	7	2	6	6	6	6	172	1	10	5	1	5	1	2	2	138	1	7	8	1	5	1	3	6	1	1	1	1	3
2016K-0432	26	158	7	0	6	5	5	5	4	174	6	9	4	5	4	6	7	7	138	6	0	1	6	2	6	8	5	6	5	6	6	8
2016K-0435	26	158	2	6	0	5	5	5	5	177	1	9	4	1	4	1	2	2	137	1	5	7	1	4	1	3	5	1	1	1	1	3
NY63966434	25	156	6	5	5	0	0	0	4	175	5	8	1	4	2	5	6	6	136	5	5	6	5	3	5	7	4	5	4	5	5	7
NY63966674	25	159	6	5	5	0	0	0	4	184	5	8	1	4	2	5	6	6	138	5	5	6	5	3	5	7	4	5	4	5	5	7
NY64247713	25	159	6	5	5	0	0	0	4	181	5	8	1	4	2	5	6	6	138	5	5	6	5	3	5	7	4	5	4	5	5	7
PNUSAS000490	23	156	6	4	5	4	4	4	0	172	5	6	3	4	2	5	6	6	132	5	4	5	5	3	5	7	2	5	4	5	5	7
PNUSAS000525	174	210	172	174	177	175	184	181	172	0	172	173	180	147	116	182	179	148	183	183	151	189	177	180	182	181	158	165	172	169	168	170
PNUSAS001020	24	158	1	6	1	5	5	5	5	172	0	9	4	0	4	0	1	0	137	0	6	7	0	4	0	2	5	0	0	0	0	2
PNUSAS001768	27	153	10	9	9	8	8	8	6	173	9	0	7	7	6	9	10	10	137	9	9	10	9	7	9	11	6	9	8	9	9	11
PNUSAS002040	24	158	5	4	4	1	1	1	3	180	4	7	0	3	1	4	5	5	139	4	4	5	4	2	4	6	3	4	3	4	4	6
PNUSAS002057	22	140	1	5	1	4	4	4	4	147	0	7	3	0	3	0	1	1	127	0	5	5	0	3	0	2	4	0	0	0	0	2
PNUSAS002059	15	116	5	4	4	2	2	2	2	116	4	6	1	3	0	4	4	4	100	4	4	4	4	2	4	6	1	4	3	4	4	6
PNUSAS002062	26	157	1	6	1	5	5	5	5	182	0	9	4	0	4	0	1	1	139	0	6	7	0	4	0	2	5	0	0	0	0	2
PNUSAS002065	27	158	2	7	2	6	6	6	6	179	1	10	5	1	4	1	0	1	140	1	7	8	1	5	1	3	6	1	1	1	1	3
PNUSAS002066	25	146	2	7	2	6	6	6	6	148	0	10	5	1	4	1	1	0	131	1	7	8	1	5	1	3	6	1	1	1	1	3
PNUSAS002130	134	24	138	138	137	136	138	138	132	183	137	137	139	127	100	139	140	131	0	140	127	139	136	135	139	142	128	135	136	135	134	140
PNUSAS002135	26	160	1	6	1	5	5	5	5	183	0	9	4	0	4	0	1	1	140	0	6	7	0	4	0	2	5	0	0	0	0	2
PNUSAS002142	24	139	7	0	5	5	5	5	4	151	6	9	4	5	4	6	7	7	127	6	0	1	6	2	6	8	5	6	5	6	6	8
PNUSAS002143	27	161	8	1	7	6	6	6	5	189	7	10	5	5	4	7	8	8	139	7	1	0	7	3	7	9	6	7	6	7	7	9
PNUSAS002221	25	157	1	6	1	5	5	5	5	177	0	9	4	0	4	0	1	1	136	0	6	7	0	4	0	2	5	0	0	0	0	2
PNUSAS002271	24	155	5	2	4	3	3	3	3	180	4	7	2	3	2	4	5	5	135	4	2	3	4	0	4	6	3	4	3	4	4	6
PNUSAS002469	26	160	1	6	1	5	5	5	5	182	0	9	4	0	4	0	1	1	139	0	6	7	0	4	0	2	5	0	0	0	0	2
PNUSAS002471	28	163	3	8	3	7	7	7	7	181	2	11	6	2	6	2	3	3	142	2	8	9	2	6	2	0	7	2	2	2	2	4
S1502901	20	146	6	5	5	4	4	4	2	158	5	6	3	4	1	5	6	6	128	5	5	6	5	3	5	7	0	5	4	5	5	7
S1504124	24	152	1	6	1	5	5	5	5	165	0	9	4	0	4	0	1	1	135	0	6	7	0	4	0	2	5	0	0	0	0	2
S1505408	25	154	1	5	1	4	4	4	4	172	0	8	3	0	3	0	1	1	136	0	5	6	0	3	0	2	4	0	0	0	0	2
S1505417	26	152	1	6	1	5	5	5	5	169	0	9	4	0	4	0	1	1	135	0	6	7	0	4	0	2	5	0	0	0	0	2
S1505430	25	152	1	6	1	5	5	5	5	168	0	9	4	0	4	0	1	1	134	0	6	7	0	4	0	2	5	0	0	0	0	2
S1505431	27	158	3	8	3	7	7	7	7	170	2	11	6	2	6	2	3	3	140	2	8	9	2	6	2	4	7	2	2	2	2	0

- 2015 chick outbreak
- 2016 chick outbreak
- Unrelated to chick outbreaks

Sidge et. al. 2019 MMWR
Hardy et. al. 2019 MMWR
Robertson et. al. 2019 Poultry Science

Final Thoughts

How to select good laboratory tests

What Considerations when selecting:

- Costs
- Turn-around-time
- Intended final use of results
- What type of interpretation is needed
- Screening vs Diagnostic value
- Phenotypic vs Genotypic

Common things that lead to inappropriate test results

- Serum vs. Plasma
- Anticoagulant used

(i.e. EDTA vs Heparin)

- Storage conditions
- Loss of plasmid

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Key contact information

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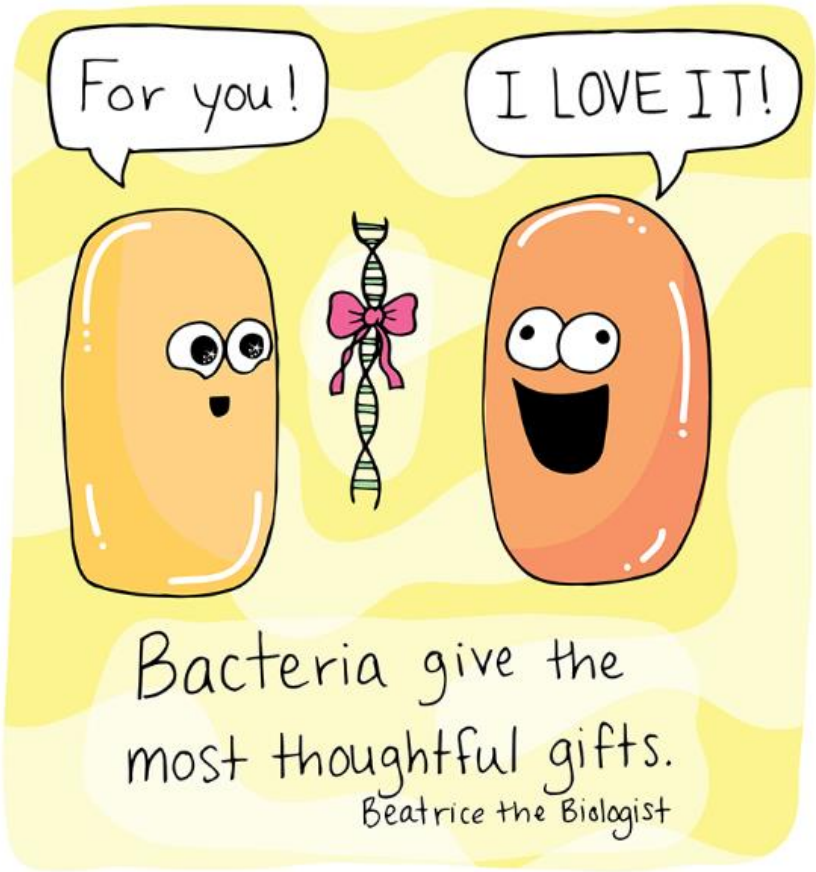
Questions?

- Many types of antimicrobial resistant organisms are of interest to One Health prevention efforts
- When in doubt reach out to colleagues on the other side (either human or veterinary)



WHO's World Antibiotic Awareness Week 2019: November 18th – 24th

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