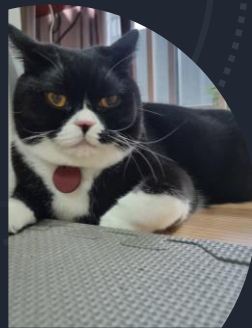




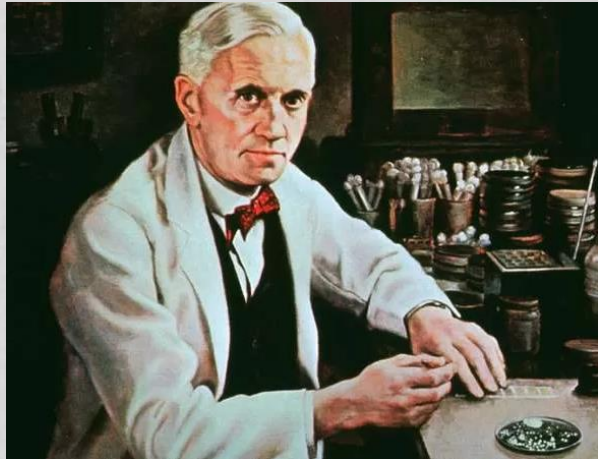
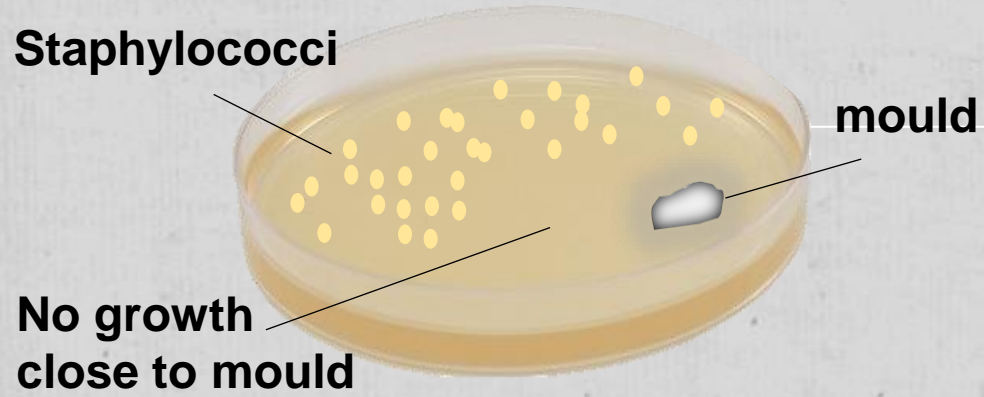
AMR IN ONE HEALTH PERSPECTIVE

Rungtip Chuanchuen DVM, MS PhD

Faculty of Veterinary Science, Chulalongkorn University



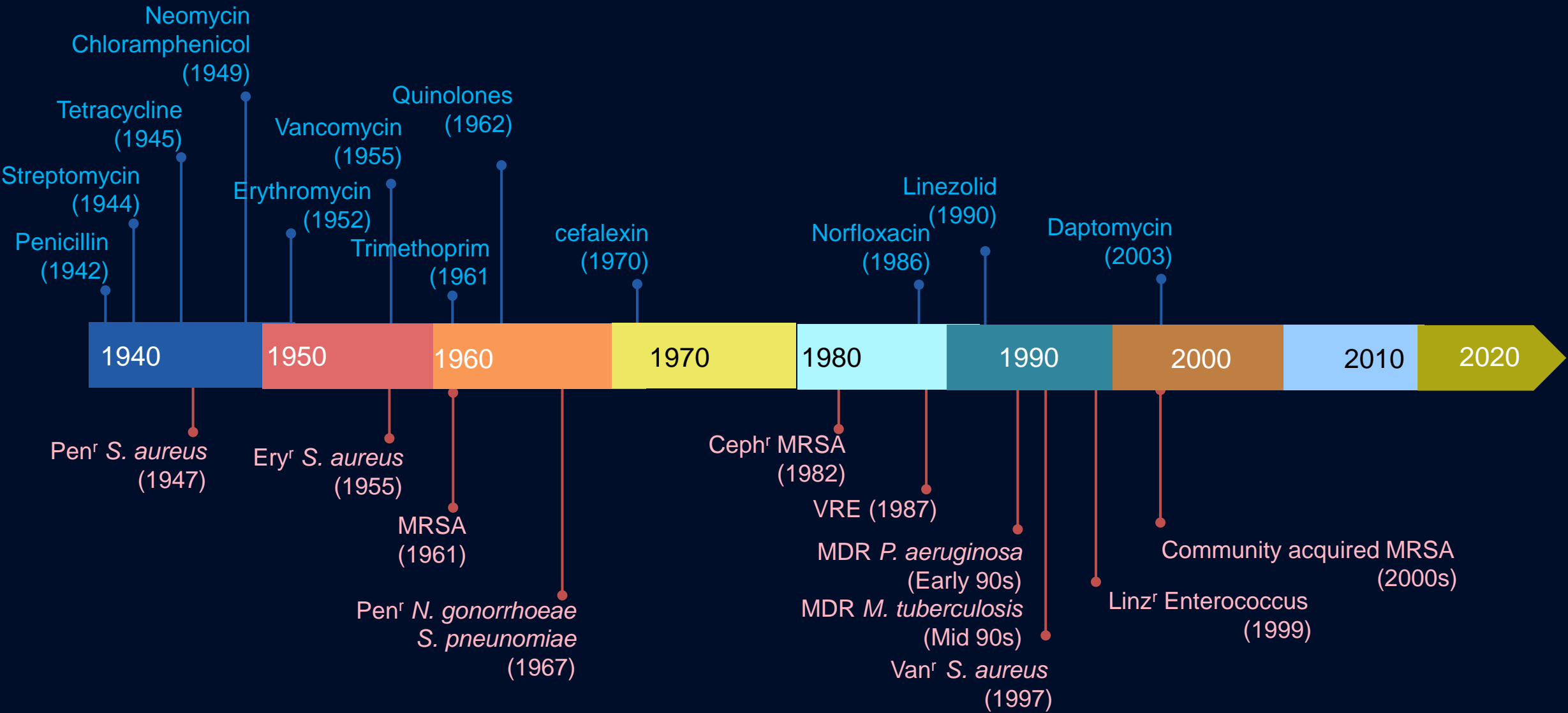
AMR in bacteria is not a new issue.



Alexander Fleming's
discovery of penicillin in 1928

“It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body.....”

AMR dynamically develops.



AMR dynamically spreads.

Global spread of NDM-1 superbugs

E. coli and *K. pneumoniae* harboring New Delhi metallo β -lactamase (NDM-1)



AMR dynamically spreads.

Global spread of NDM-1 superbugs

E. coli and *K. pneumoniae* harboring New Delhi metallo β -lactamase (NDM-1)

First report of a *K. pneumoniae* isolate carrying NDM-1 India

- **May**-*E. coli* with NDM-1 in UK
- **June**-First report in Enterobacteriaceae the US
- **July**-*A. baumannii* with NDM-1 in Chennai, India
- **August**-First report in Ontario, Canada
- **September**-First case in Japan

- **May**-A patient died in Edmonton, Alberta due to Acinetobactor with NDM-1
- **October**-First report in Iragi referred to Lebanon

2008

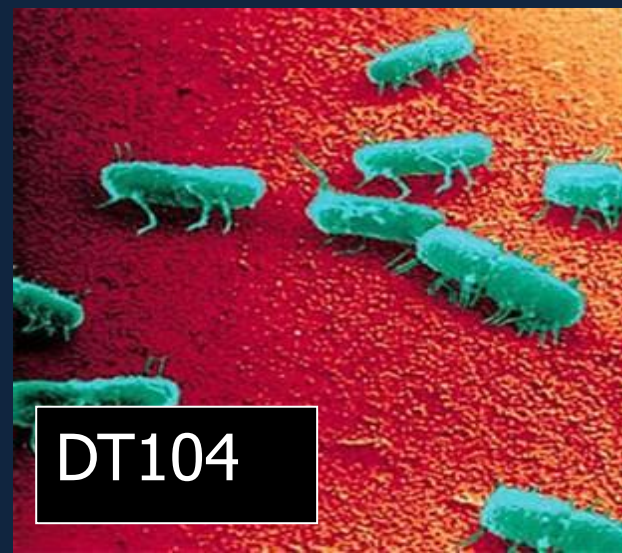
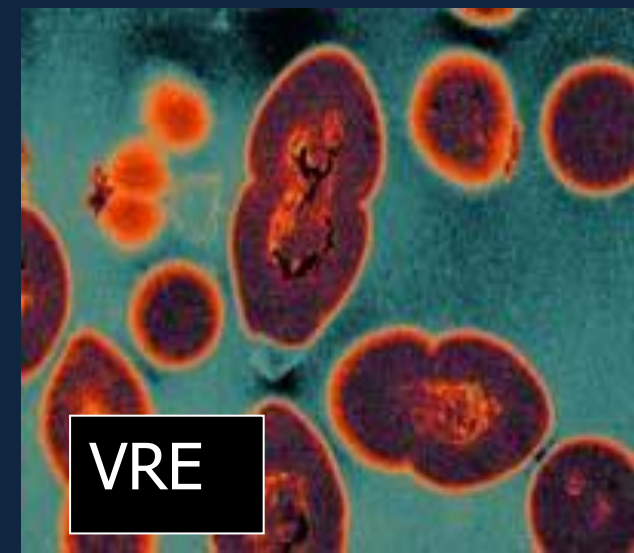
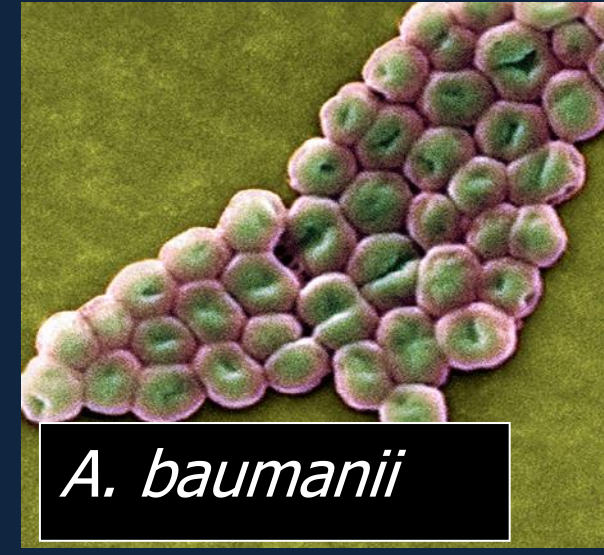
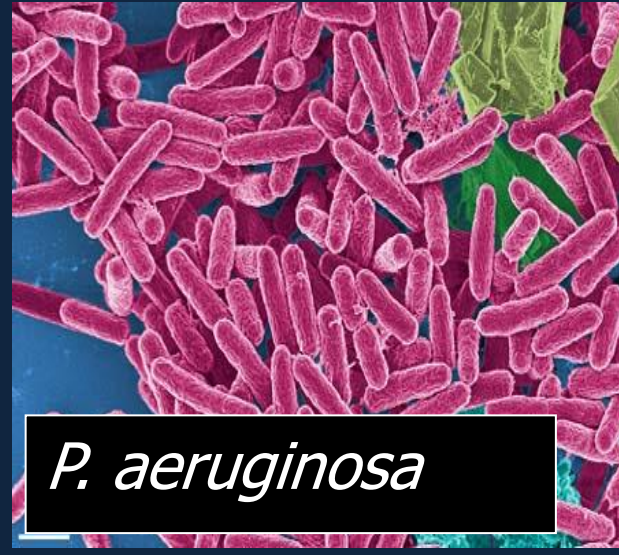
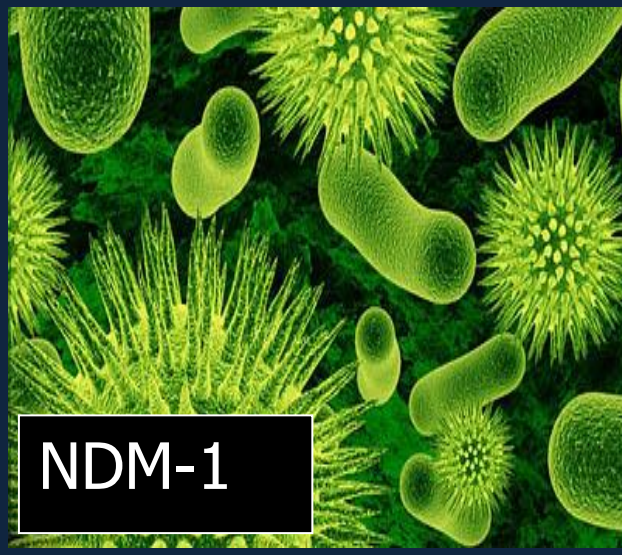
2009

2010





2011

2012

Multidrug resistant (MDR) bacteria “Superbugs”



Antimicrobials are shared in human and veterinary medicine.

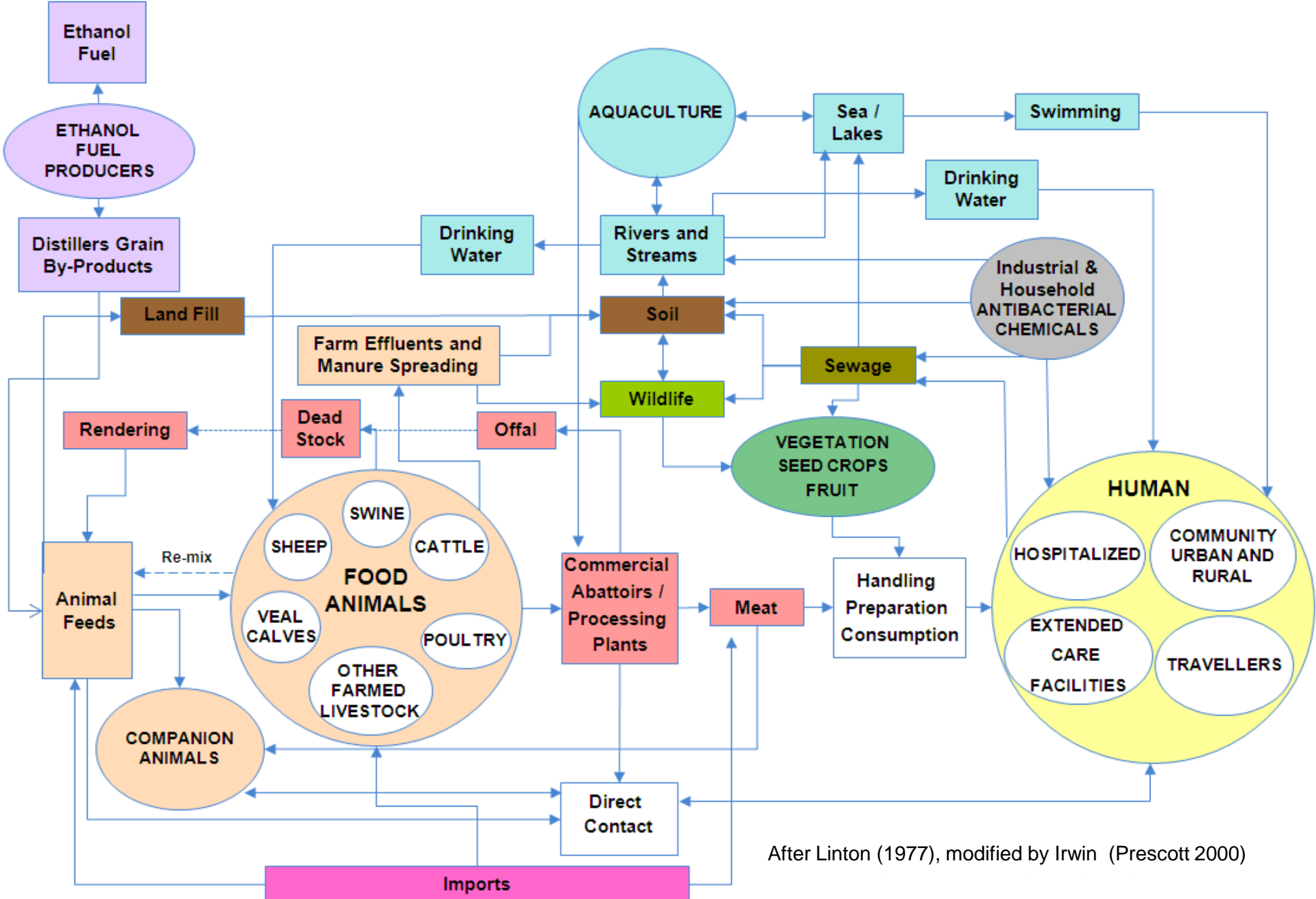
 ABO	Food animals 				Humans 	
	Species	Treatment	Prevention			AGPs
AMGs (GEN, NEO, STR)	Cattle, Cow, Poultry, Swine, Sheep	✓	✓		✓	✓
AMO, AMP	Cattle, Cow, Poultry, Swine, Sheep	✓	✓	✓	✓	✓
Ceftiofur	Cattle, Cow, Poultry, Sheep, Swine	✓	✓		✓	✓
VAN	Poultry, Swine			✓	✓	✓
ERY, TYL, TIL	Cattle, Poultry, Swine	✓	✓	✓	✓	✓
SPC	Poultry, Swine		✓		✓	✓
TET, OXY, CHL	Cattle, Cow, Poultry, Swine, Sheep	✓	✓	✓	✓	✓



AMR is One Health issue.



One Health complexity of AMR



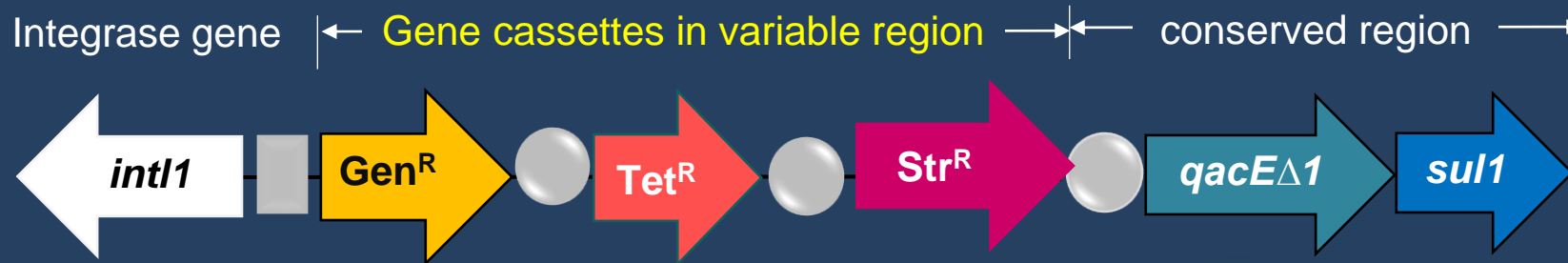
After Linton (1977), modified by Irwin (Prescott 2000)

Our Research on epidemiology & mechanisms of AMR in foodborne pathogens in Thailand & other Southeast Asian countries

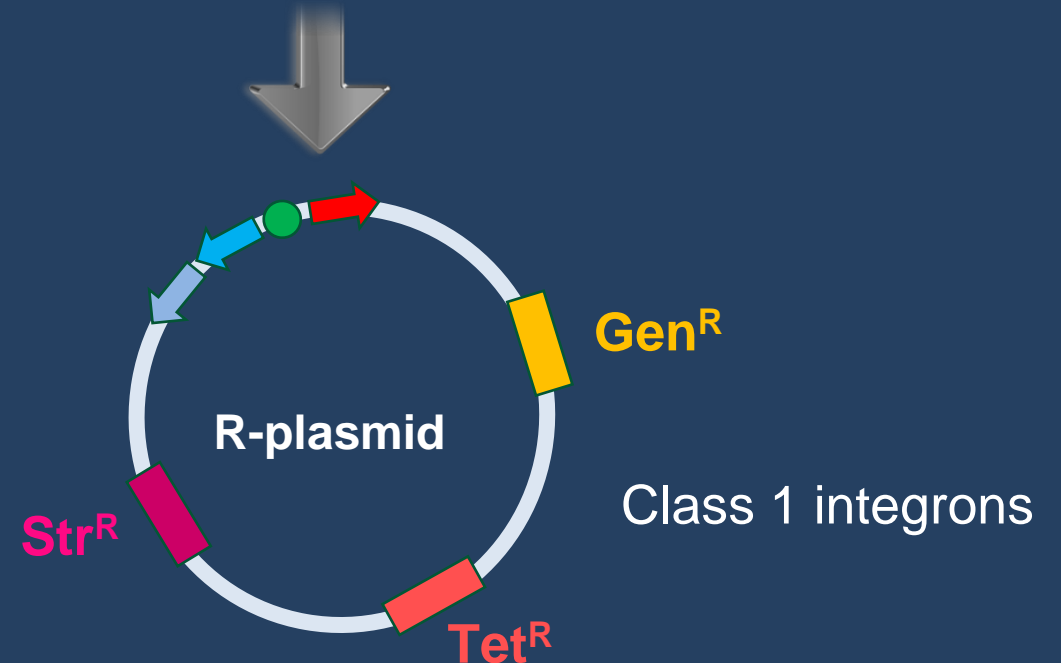


Class 1 integrons as a mean for MDR bacteria dissemination

Class 1 integrons



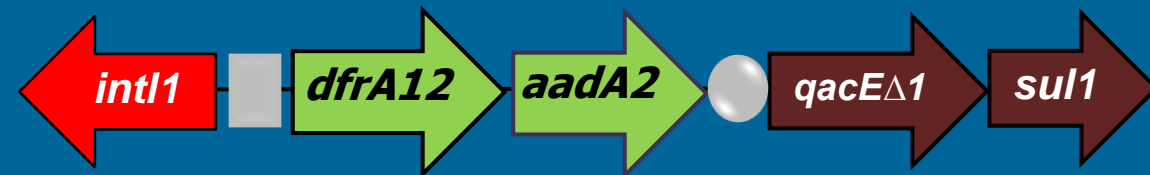
- Most commonly associated with **MDR**
- **Coselection** of many resistance genes by a single antibiotic
- **Horizontal transfer** in the presence of antimicrobials



Gen^R Gentamicin resistance gene; Tet^R Tetracycline resistance gene; Strep^R Streptomycin resistance gene



dfrA12-aadA2 is widespread in Thailand

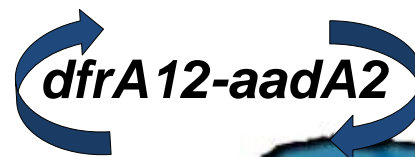


E. coli
Salmonella



A. hydrophila

Salmonella
E. coli



Salmonella, *P. aeruginosa*,
A. baumannii

Salmonella



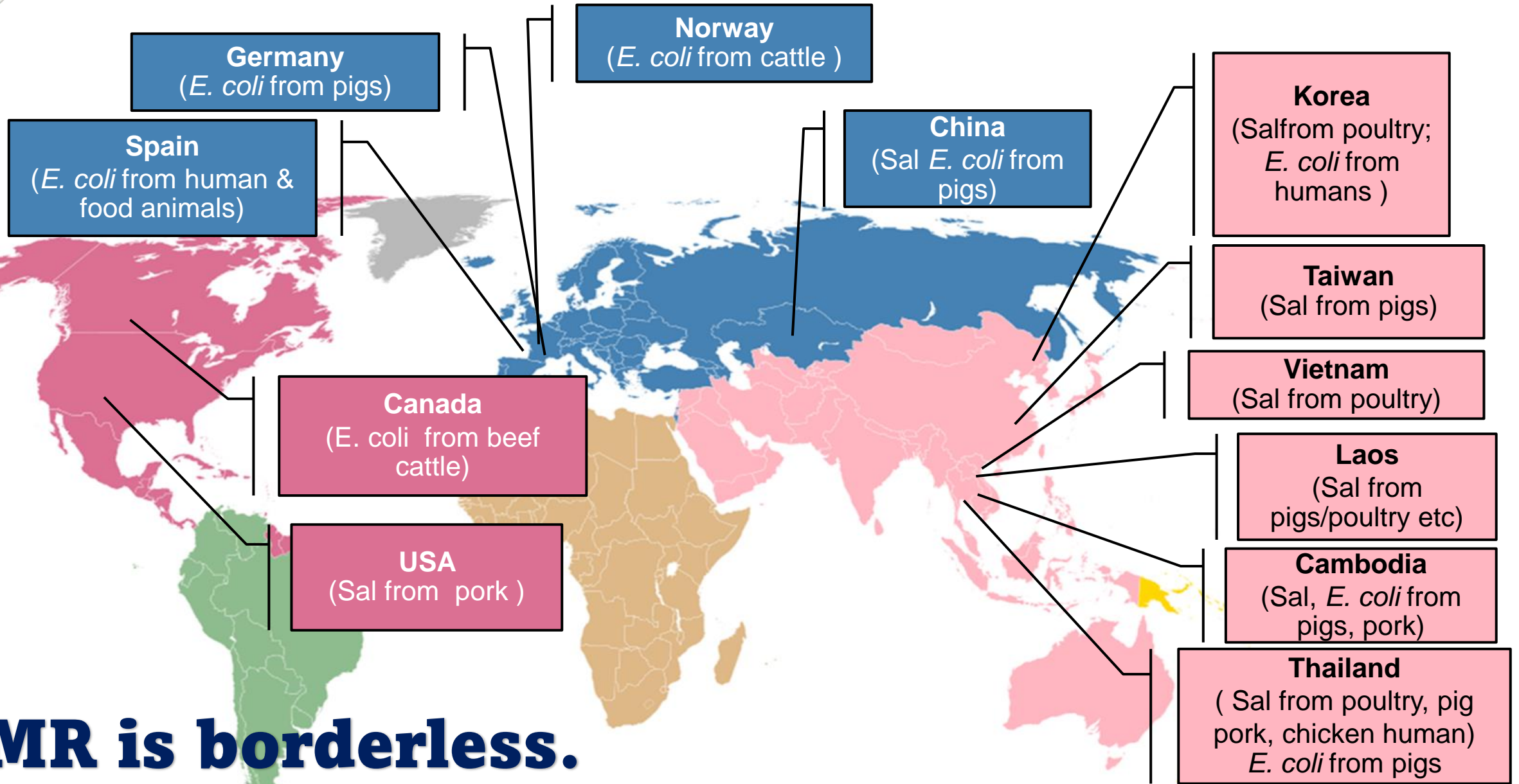
Salmonella

**AMR is
One Health issue.**

dfrA12, resistance to trimethoprim
aadA2, resistance to streptomycin & spectinomycin



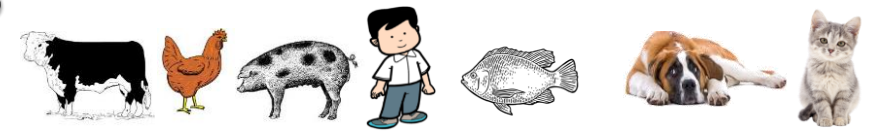
Global spread of *dfrA12-aadA2*



AMR is borderless.



Class 1 integrons-Animals & humans



Bacteria	Source	Gene
<i>Salmonella</i>	Dairy cows	<i>dfrA12-addA2</i> , <i>aadA</i> , <i>aadA1</i>
	Poultry and swine	<i>dfrA1</i> , <i>dfrA12-addA2</i> , <i>aadA4a</i> , <i>bla_{PSE-1}</i>
	Pork, Chicken, humans	<i>dfrA12-addA2</i> , <i>bla_{PSE-1}</i> , <i>aadA2</i>
	Dogs & cats (n=122)	<i>dfrA12-addA2</i> , <i>dfrA12</i>
Commensal <i>E. coli</i>	Pigs	<i>dfrA12-addA2</i> , <i>aadA1</i> , <i>aadA22</i> , <i>aadA2</i>
<i>Aeromonas hydrophila</i>	Nile telapia	<i>dfrA12-addA2</i> , <i>dfrA1</i> , <i>aadA2</i>
<i>Pseudomonas aeruginosa</i>	Humans	<i>dfrA1</i> , <i>aadA1</i> , <i>dfrA12-aadA2</i> <i>aadB</i> , <i>cmlA</i> , <i>aadA1</i>
<i>Acenitobacter baumannii</i>	Humans	<i>dfrA1</i> , <i>aadA1</i> , <i>dfrA12-aadA2</i> , <i>aadB</i> , <i>cmlA</i> , <i>aacA4</i> , <i>catB8</i> ,.....

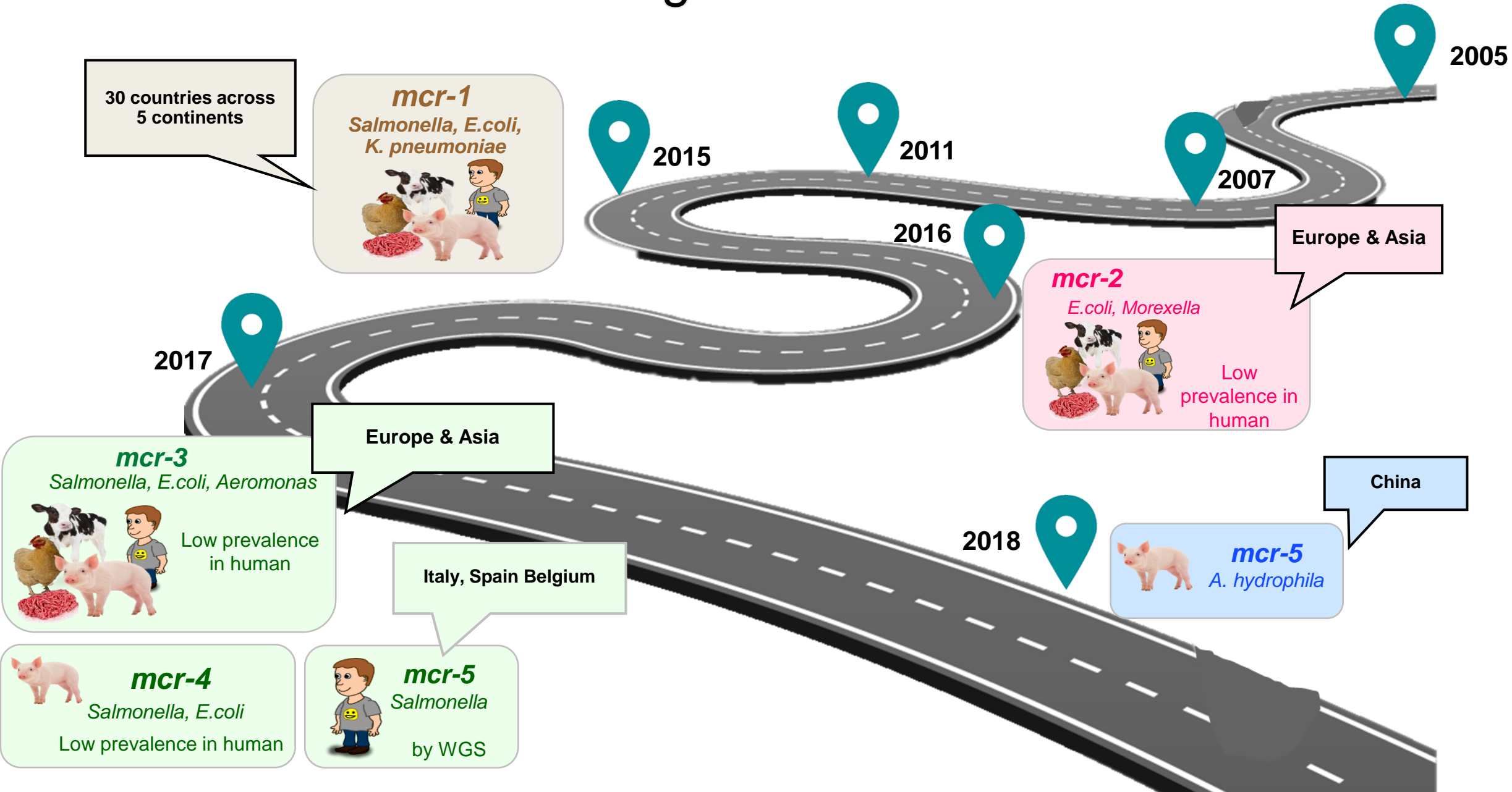
AMR genetically links.

Colistin: What & Why?



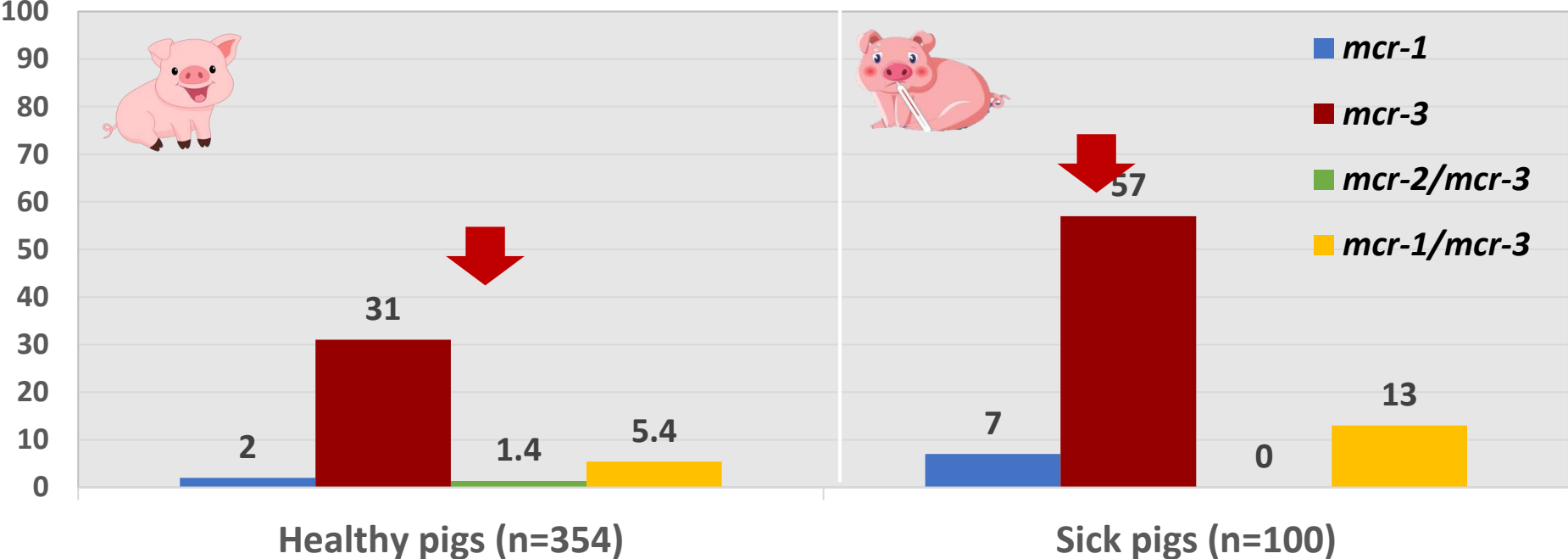
- Polymyxin E, a cationic polypeptide
- Narrow spectrum-bactericidal against most Gram (-) bacilli
- One of the last resort antibiotics for MDR bacterial infections
- Colistin is not used to treat dogs and cats.
- **Plasmid-Encoded Colistin Resistance**
MCR-1 and MCR-2 proteins:
phosphoethanolamine transferase enzyme

Colistin resistance and *mcr* genes



Plasmid-mediated colistin resistance *mcr* in *E. coli* from pigs

% *mcr* genes in *E. coli* (n=454)



mcr-1

- Low prevalence in healthy (7.6%) & sick pigs (20%)

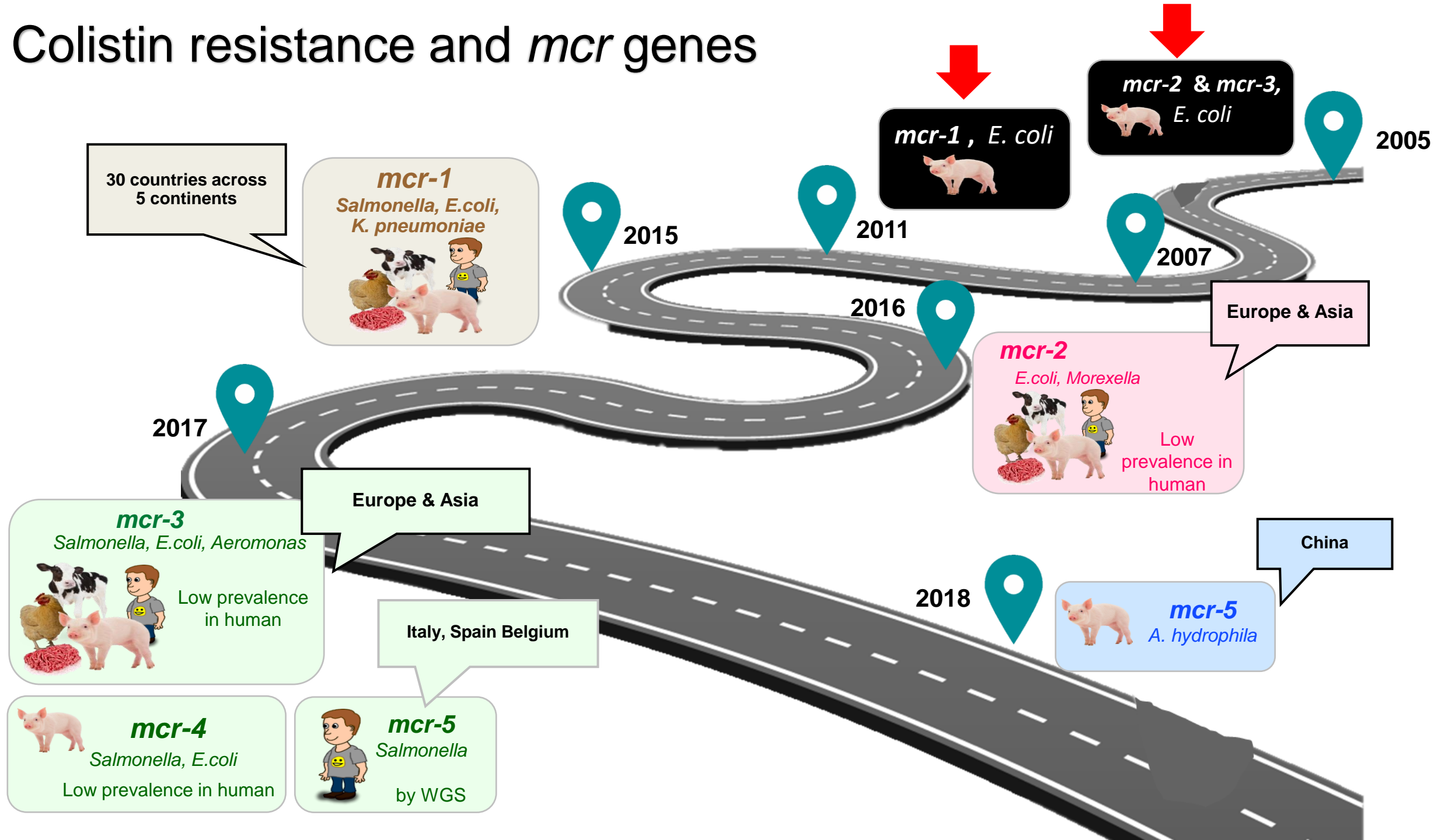
mcr-2

- Five *E. coli* from fattening pigs

mcr-3

- **Most common**
- Can be found in colistin susceptible strains

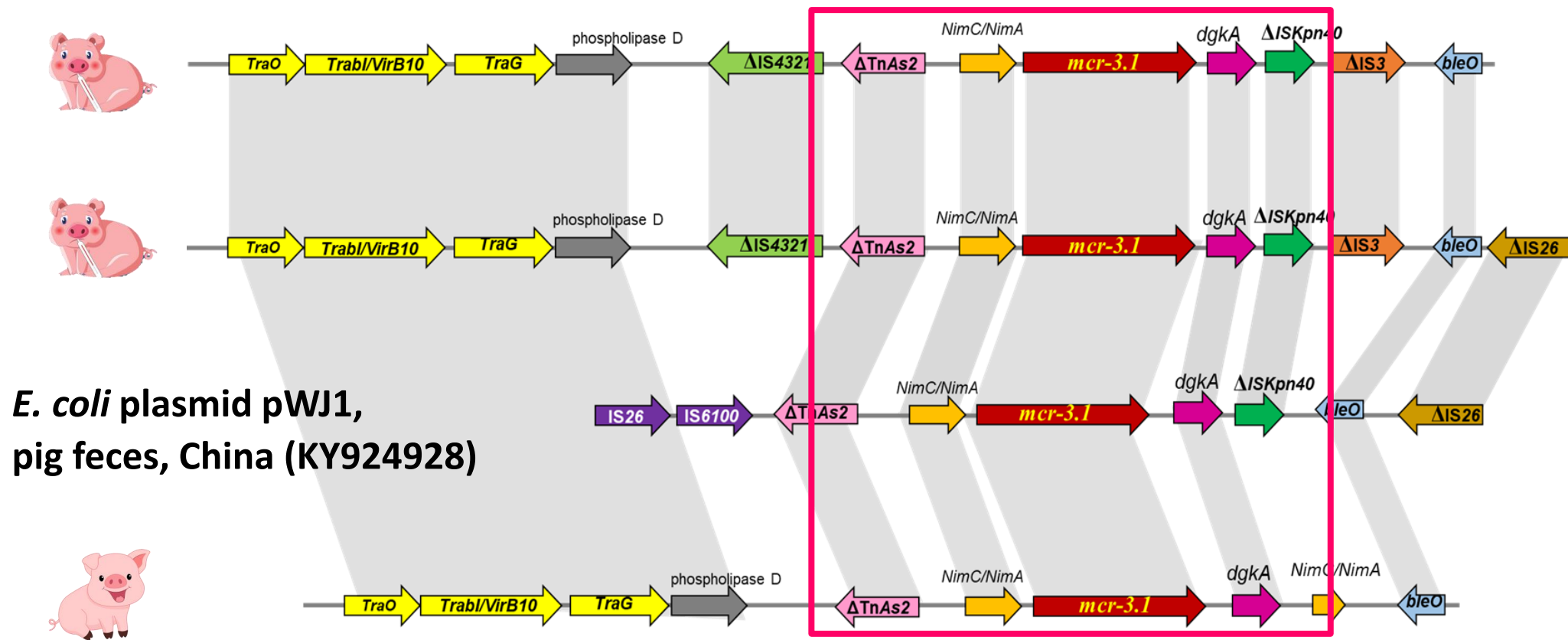
Colistin resistance and *mcr* genes





WGS and characteristics of *E. coli* with coexistence of ESBL and *mcr* genes from pigs

This is why *mcr-3* harboring are widespread.



E. coli plasmid pWJ1, pig feces, China (KY924928)

- The ISAp11 is the main driver of mobilized *mcr-1* by horizontal gene transfer.

mcr-carrying ESBL producing *E. coli* carried both AMR and virulence genes

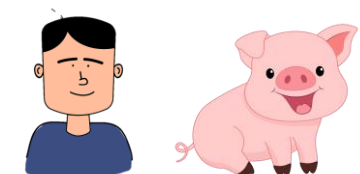
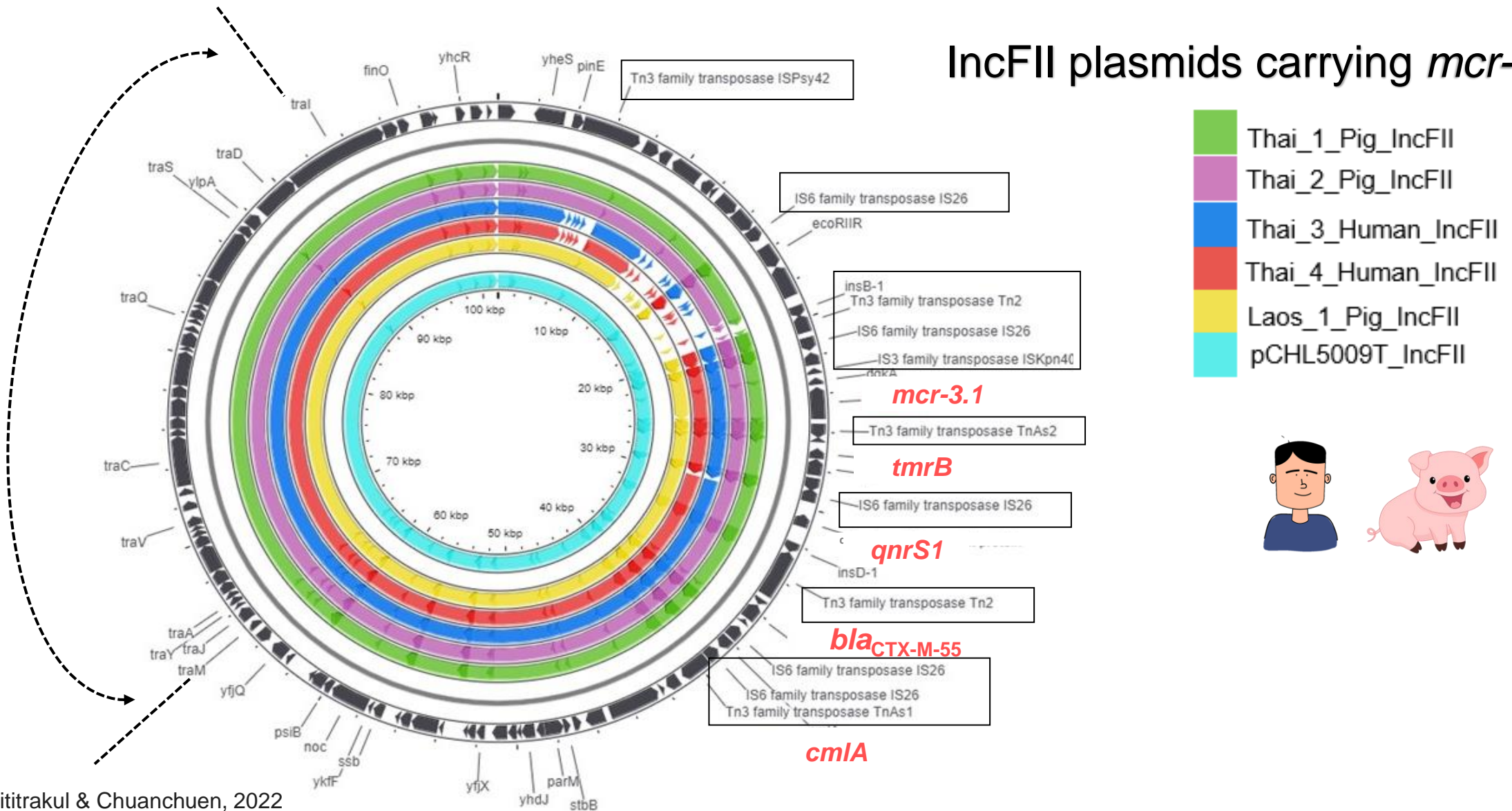
ST	qnrS1	aadA1	aadA2	aac(3)-IId	aph(3'')-Ib	aph(6)-Id	aph(3')-Ia	mcr1.1	mcr3.1	sul2	sul3	dfrA12	tet(A)	tet(B)	tet(M)	cmIA1	catA2	floR	bla _{CTX-M-14}	bla _{CTX-M-55}	bla _{TEM-1}	astA	gad	hra	terC	traT
TH2 6833	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Absent	Present
TH3 6833	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Absent	Present
TH8 48	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Present	Present	Present	Present	Present
TH9 48	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Present	Present	Present	Present	Present
LA1 5708	Present	Present	Present	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present
LA3 10562	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Absent	Present
LA5 10562	Present	Present	Present	Absent	Present	Present	Present	Present	Absent	Absent	Absent	Present	Present	Present	Present	Present	Present	Present	Present	Present	Present	Absent	Absent	Absent	Absent	Present



Genome characterization of *E. coli* carrying ESBL and *mcr* genes from pigs and humans using WGS



IncFII plasmids carrying *mcr-3.1*





M
MOTT
MACDONALD



AMR in One Health perspective


“Prevalence and molecular characterization of colistin-resistant, ESBL/AmpC- and carbapenemase-producing Enterobacterales in humans, animals and in the food chains in Lebanon”

Hiba AL MIR, PhD
Research assistant, DTU


3rd EQAsia Workshop
Chulalongkorn University, Bangkok
7th November 2022




mcr-1 has been isolated from sources other than humans & food animals.



China - *mcr-1*, *E. coli* from diarrhea dogs -2020
mcr-1, *K. pneumonia*, faecal sample from dog – 2021
mcr-1, *E. coli* from rectal swab - 2020
mcr-2, 3, 4, 5, 9, 10, *K. pneumonia*, faecal sample from dog – 2021




China – *mcr-1*, *E. coli*, faecal sample -2020
mcr-1, *E. coli*, rectal swab, – 2017
mcr-1, *E. coli* from diarrhea-2018
mcr-1, *K. pneumonia*, UTI – 2021
France - *mcr-1*, *E. coli*, faecal sample -2020



E. coli from river water, **Switzerland**



E. coli from imported ready-to-eat vegetables



E. coli, herring gull in Lithuania and kelp gulls in Argentina

One health approach to combat colistin resistance

All sectors

- Monitor AMU & AMR
- Determine susceptibility
- Contamination prevention
- Scientific research to manage residue in waste

Environment



- Monitor waste from pharmaceutical industry & aquaculture
- Sentinel animals
- Management of manure

Human



- Monitor for colistin resistance in patients
- Evaluate combination therapy
- Re-evaluate use

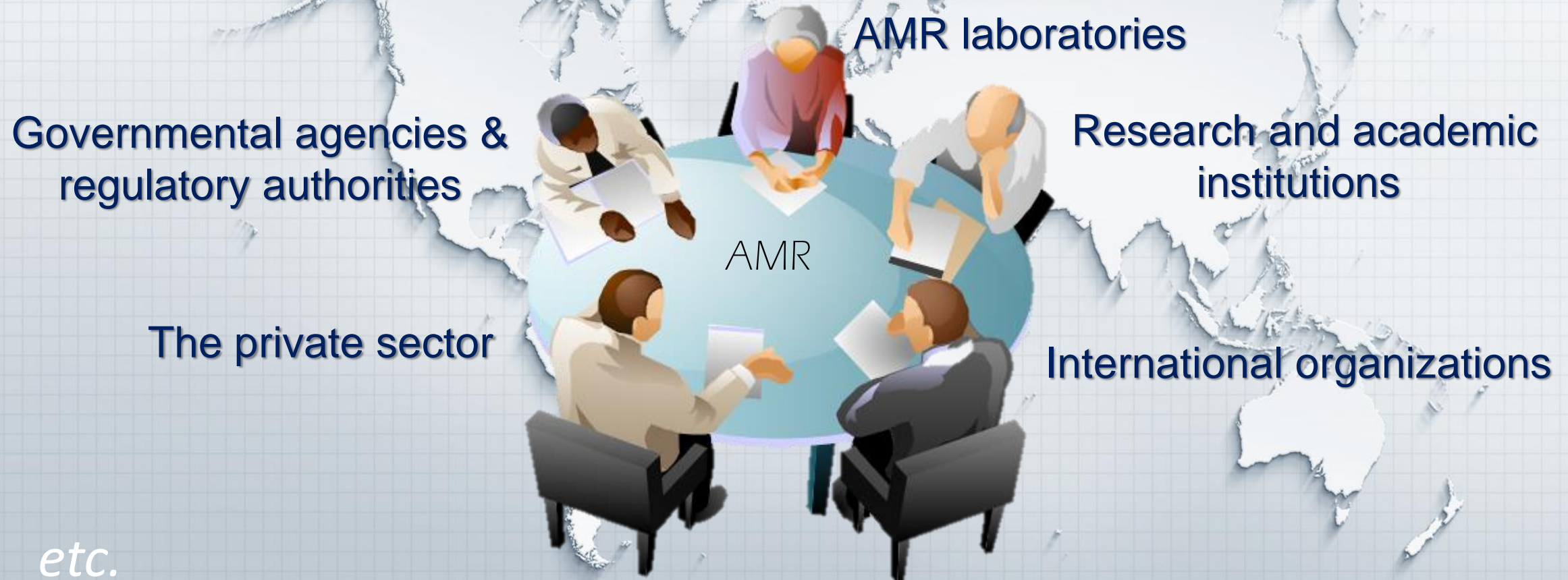
Animal



- Improve farm management
- Prudently use of ABO
- Stop use for growth promoter & prophylactic purposes
- Apply microbiological withdrawal period

Final thought

A multidisciplinary ONE HEALTH approach involving a wide range of partners is needed to manage AMR.



Final thought

To initiate One Health approach to combat AMR,

1

- bring AMR into the spotlight at a high-level visibility and establish national governance framework at an early stage.

2

- Strengthen capacity for less developed sector & build the lacking capacity.

3

- Build trust and respect between focal points to build sustainable multisectoral collaboration.

4

- Get all key stakeholders involved at the beginning.

5

- build AMR NAP using a 'plan of plans'

6

- Always build evaluation platform in parallel with implementation.

Thank you



International
Vaccine
Institute



This programme is being funded by the UK Department of Health and Social Care.
The views expressed do not necessarily reflect the UK Government's official policies.