Antimicrobial resistance Can we talk about reservoirs ?

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3 authors, including:

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Some of the authors of this publication are also working on these related projects:

Project AMR OI View project

Project Mechanisms underlying the evolution of sexual isolation in the house mouse View project

Antimicrobial resistance

Can we talk about reservoirs ?

Noellie Gay
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Back to the basics

Reservoir of a disease= any person, animal, plant, soil or substance in which an infectious agent normally lives and multiplies. The **reservoir** typically harbors the infectious agent without injury to itself and serves as a source from which other individuals can be infected.
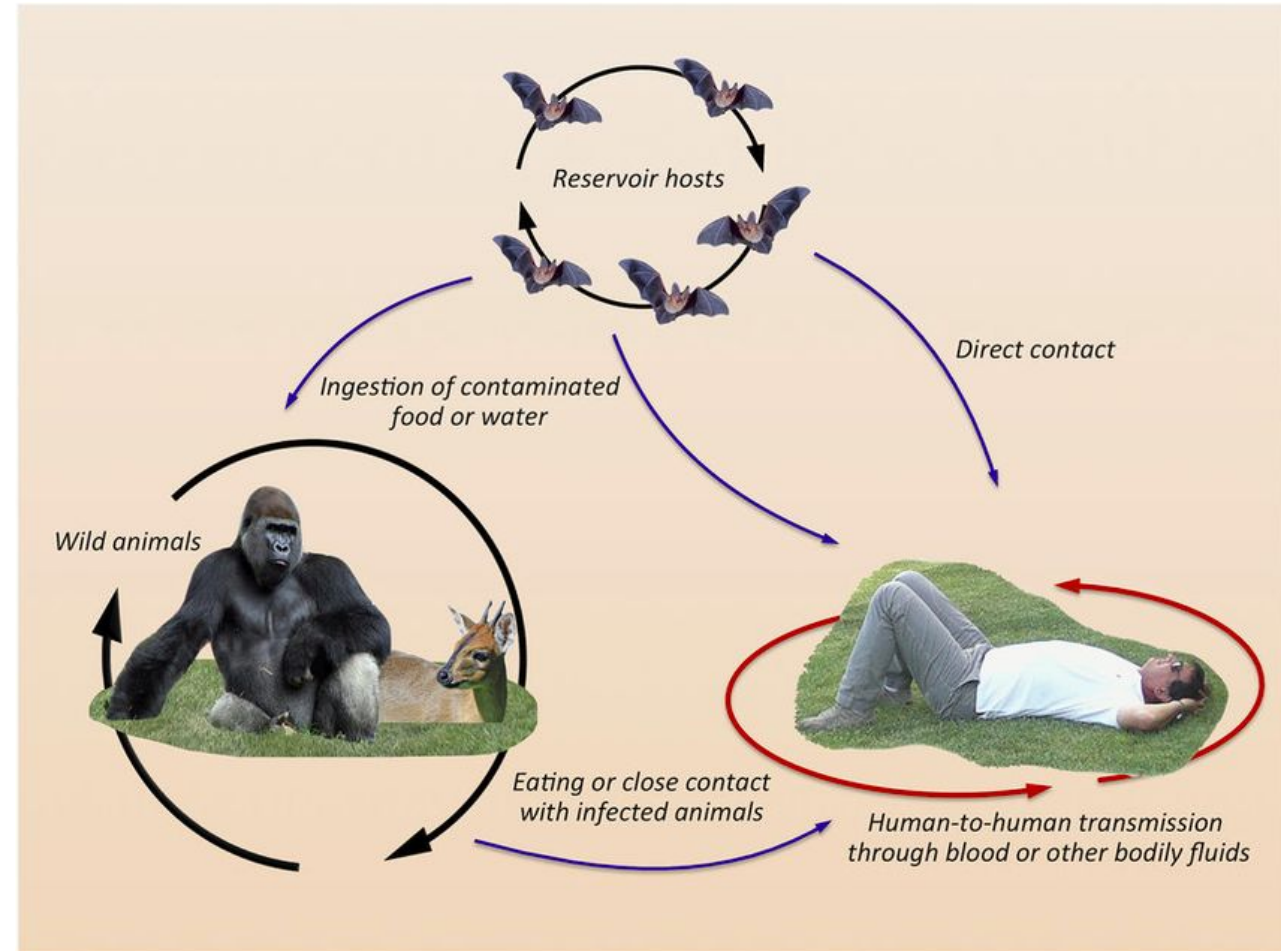
Not so basics: the AMR case

Reservoir of a disease= any person, animal, plant, soil or substance in which an infectious agent?? normally lives and multiplies. The **reservoir** typically harbors the infectious agent?? without injury to itself and serves as a source from which other individuals can be infected.
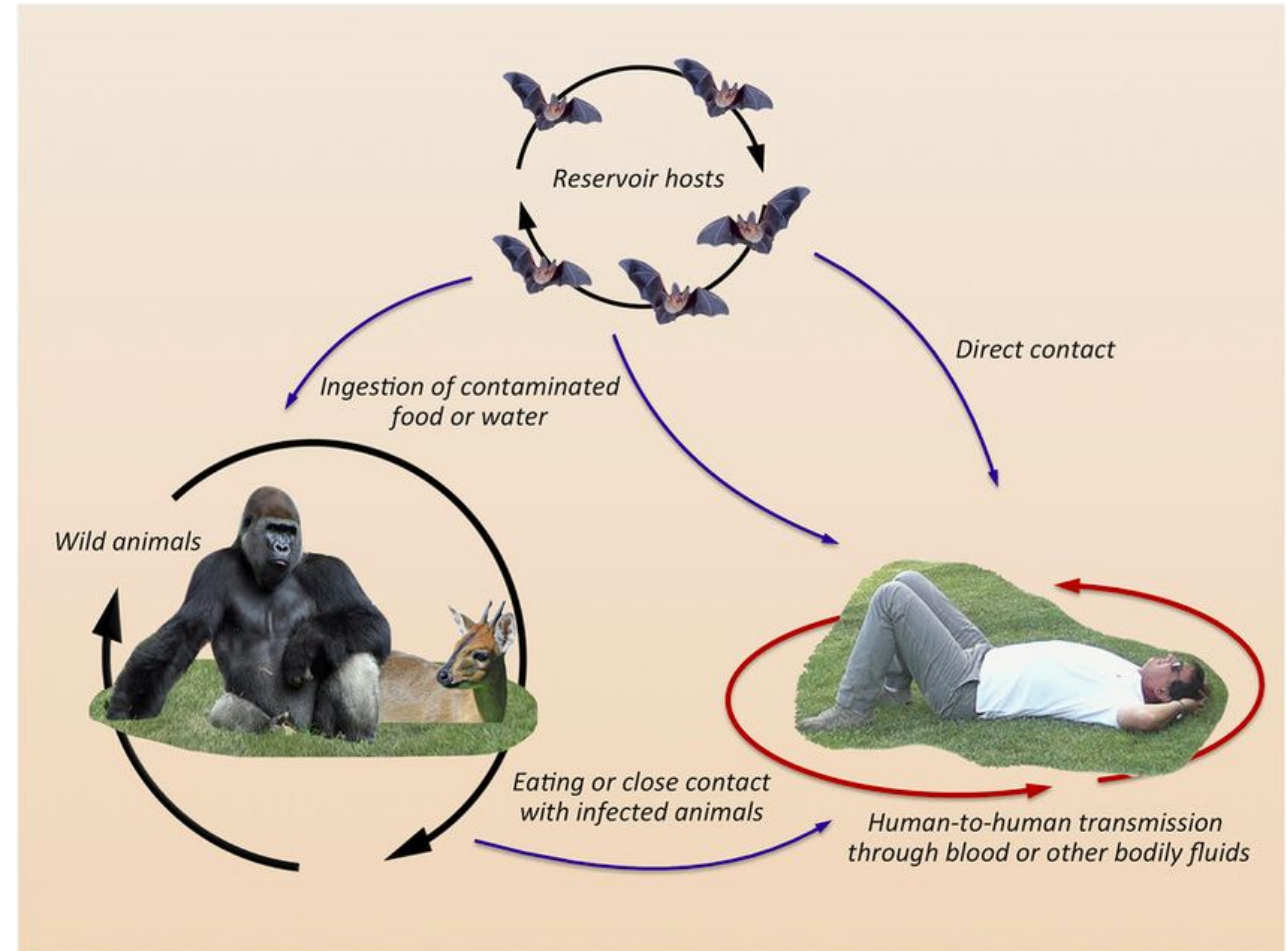
Glossary

- ARG = Antimicrobial resistance gene
  DNA fragment / gene coding for protein involved in the resistance to an antimicrobial compound. It's a GENOTYPE

- ARB = Antibiotic-resistant bacteria
  A BACTERIA, pathogenic or not, hosting an ARG

- AMR = Antimicrobial resistance:
  A TRAIT or PHENOTYPE of an ARB conferred by the expression of an ARG, usually as a result of a selective pressure exerted by the ENVIRONMENT
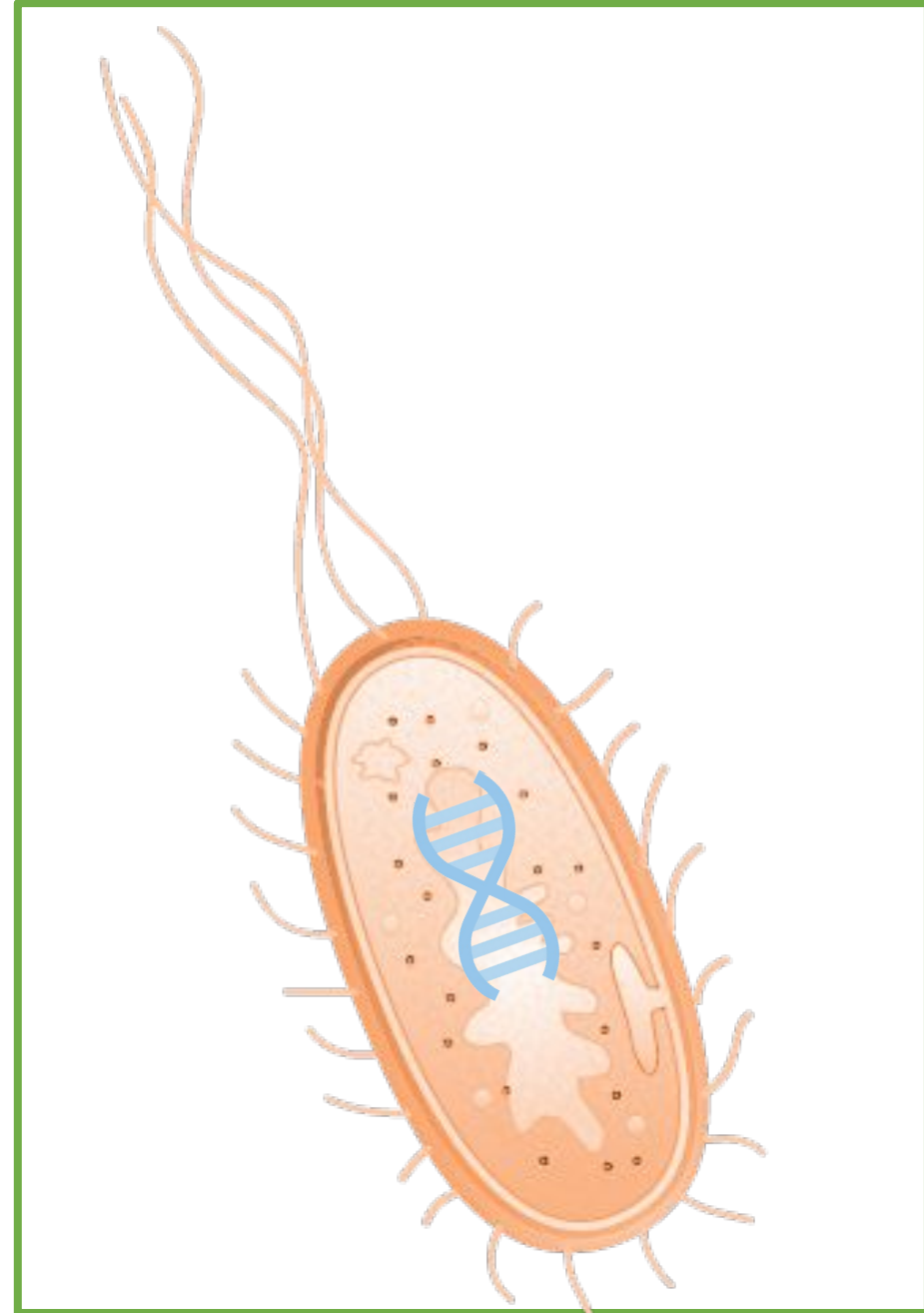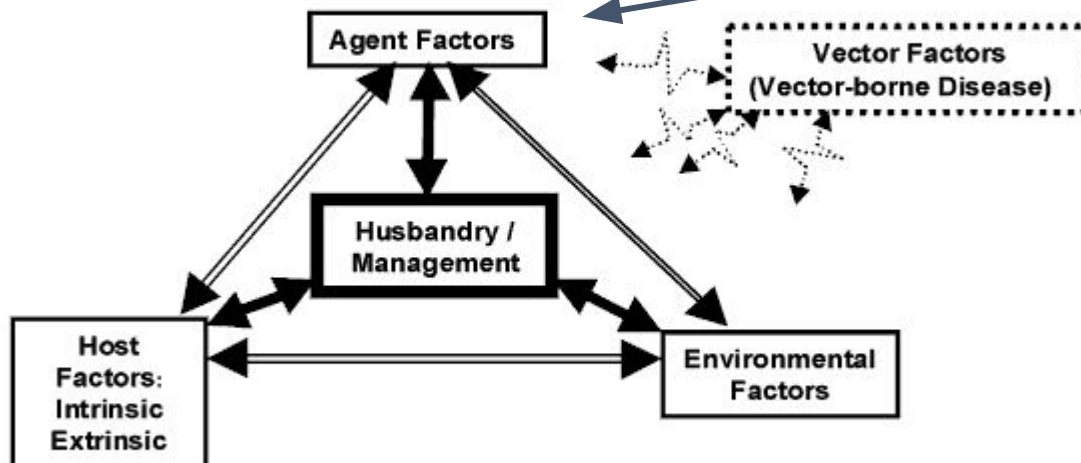
AMR (Antimicrobial resistance) is not an infectious agent.
Some ARB (Antibacterial resistant) are.

The "classical" epidemiological models holds - as well as the reservoir definition - if AMR is just an ARB, *i.e.* a resistant strain of a pathogenic bacteria.
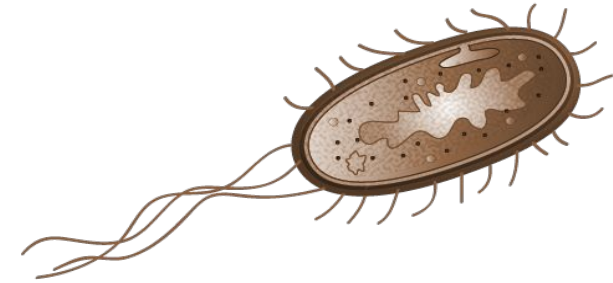
Pathogenic bacteria carrying a resistant gene, agent of an infectious disease that will prove hard to treat with antibiotics

The Epidemiologic Triad

Agent Factors

Vector Factors
(Vector-borne Disease)

Husbandry /
Management

Host
Factors:
Intrinsic
Extrinsic

Environmental
Factors

The components of medical ecology

Reservoir of ARG ?

- Genes are subject to molecular evolution

- Bacteria reproduce rapidly in large populations and thus experience fast paced evolutionary

- ARG evolve from genomic content through a rapid adaptation to an environmental pressure
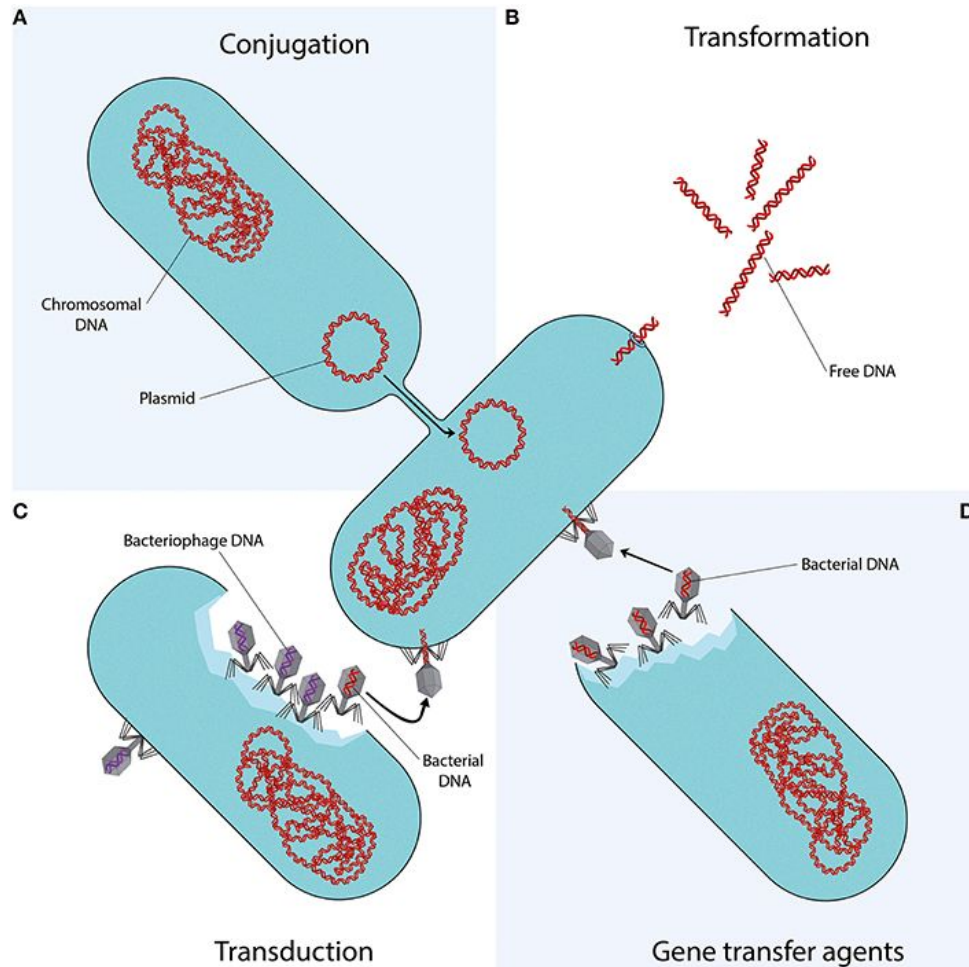
Reservoir of ARG ?

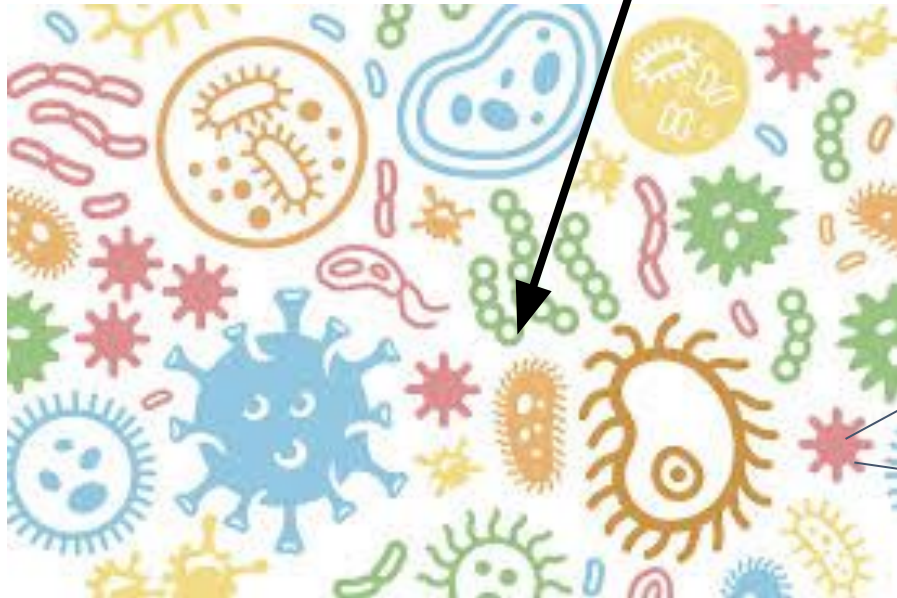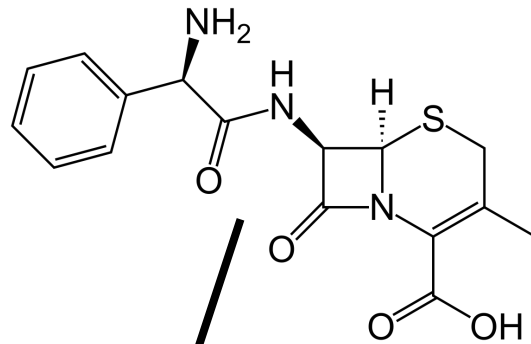Every bacterial **genome** in microbial community can be considered as a potential reservoir of ARG

microbiome

rapid mutation/selection

ARG
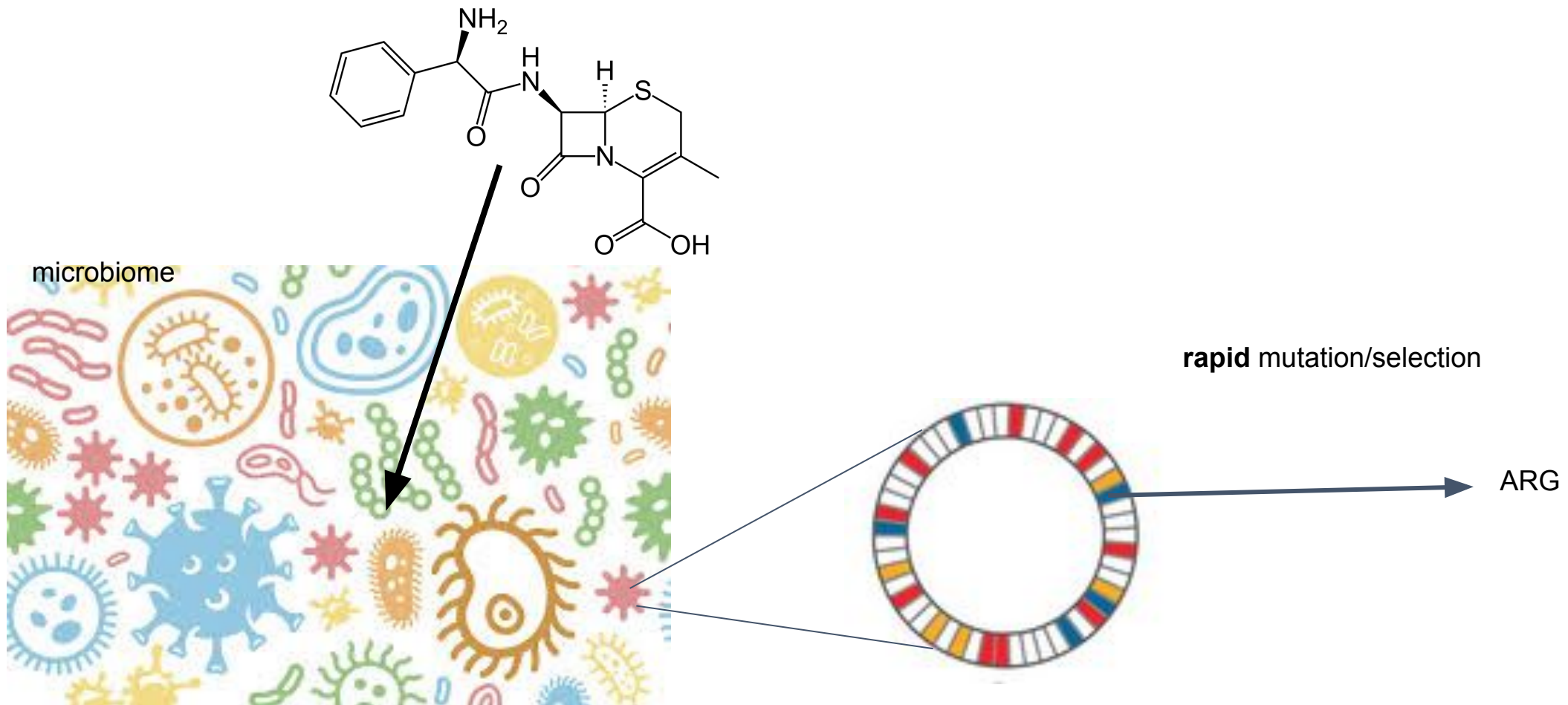
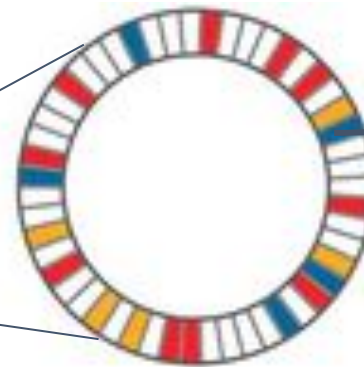# Additional complexity: Horizontal gene transfer

- Each component of a bacterial community hosting an ARG can be considered as a ARG reservoir

- ARG have vectors too ! (MGE: plasmid, phage, GTA)

- Emergence can occur through lateral transfer from an ARB which can be:
  - of the same species
  - of a related species

Reservoir of ARG ?

Every bacterial genome in microbial community can be considered as a potential reservoir of ARG
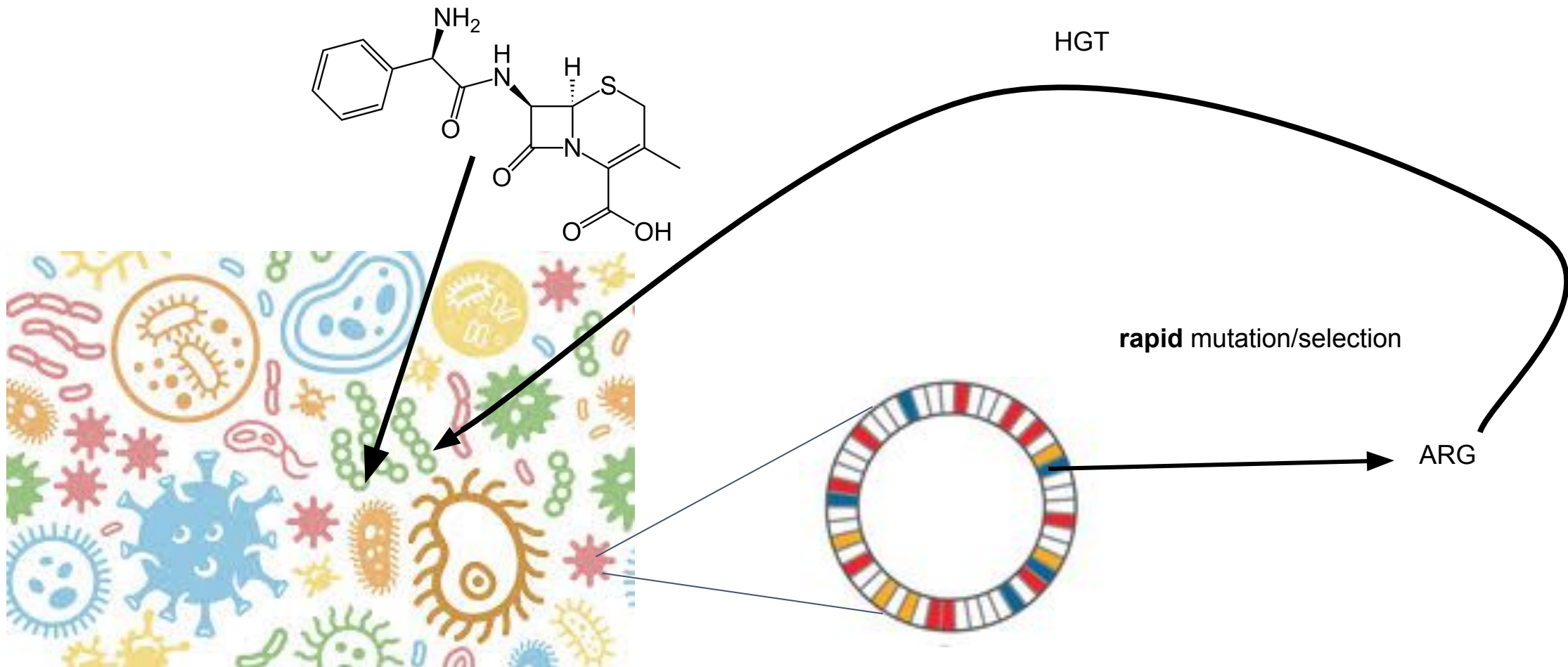

rapid mutation/selection

ARG

Reservoir of ARG ?

Every bacterial genome in microbial community can be considered as a potential reservoir of ARG
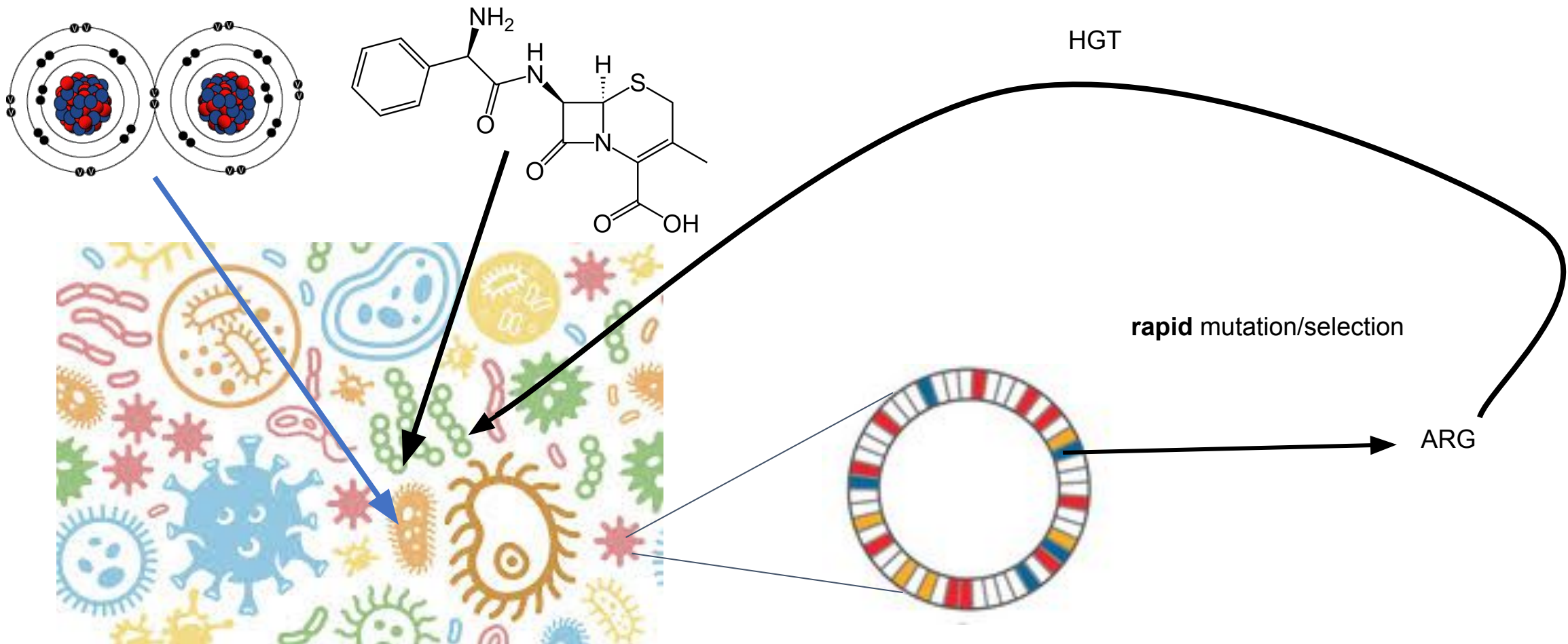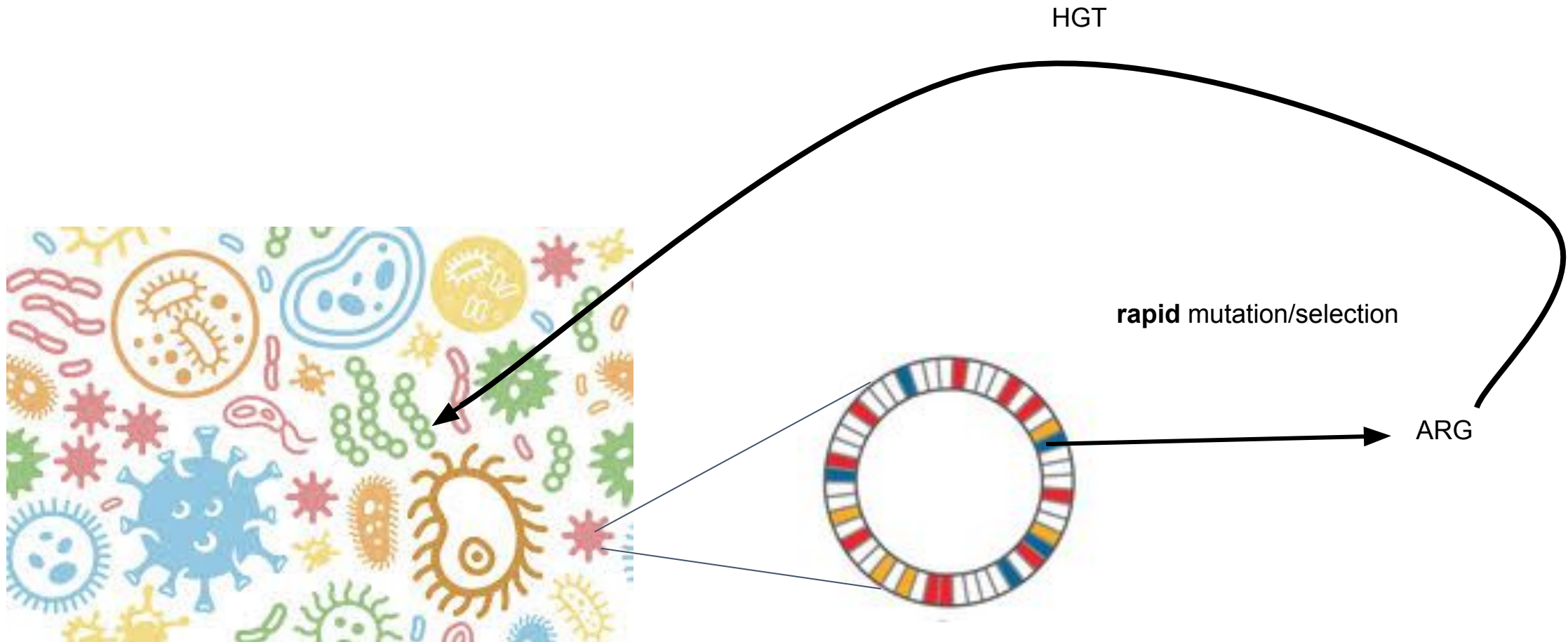
HGT

rapid mutation/selection

ARG

Reservoir of ARG ?

HGT

rapid mutation/selection

ARG

Reservoir of ARG ?

Need for constant selective pressure to maintain resistance ?

HGT

rapid mutation/selection

ARG

Reservoir of ARG ?

STRAIN ACQUISITION FROM ENVIRONMENT

CONTACT & CONSUMPTION

K. pneumoniae

CONTACT & CONSUMPTION

CONTACT

K. pneumoniae strains acquire AMR genes and plasmids in all niches, which they can carry between niches and donate to other human pathogens.

ENVIRONMENT

ANIMALS

HUMANS

HORIZONTAL GENE TRANSFER

Plasmid

Gene

K. pneumoniae

Other species

STRAIN DEPOSITION IN ENVIRONMENT

EFFLUENT

SEWERAGE

Chromosome

Plasmid

Gene

Current Opinion in Microbiology
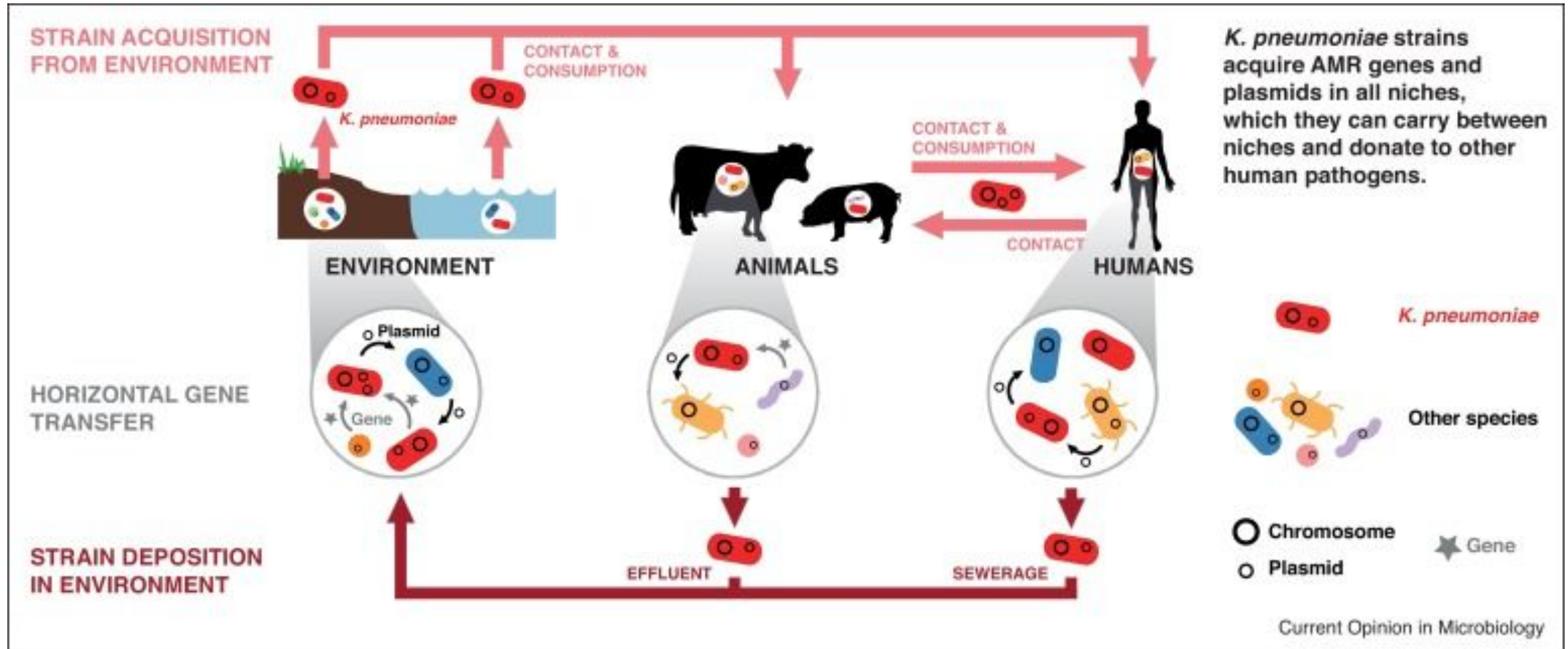
ARB **AND/OR** ARG transmission can occur from another epidemiological compartment/reservoir

AMR in the context of epidemiological reservoir

- The epidemiological unit (atom) can be a gene, not an infectious agent

- "Classical" epidemiological definition are thus sometimes useless in the AMR context

- Even in the AMR context, most epidemiological models will compound ARB (antibiotic resistant bacteria) and ARG (antibiotic resistant gene) as a single epidemiological unit
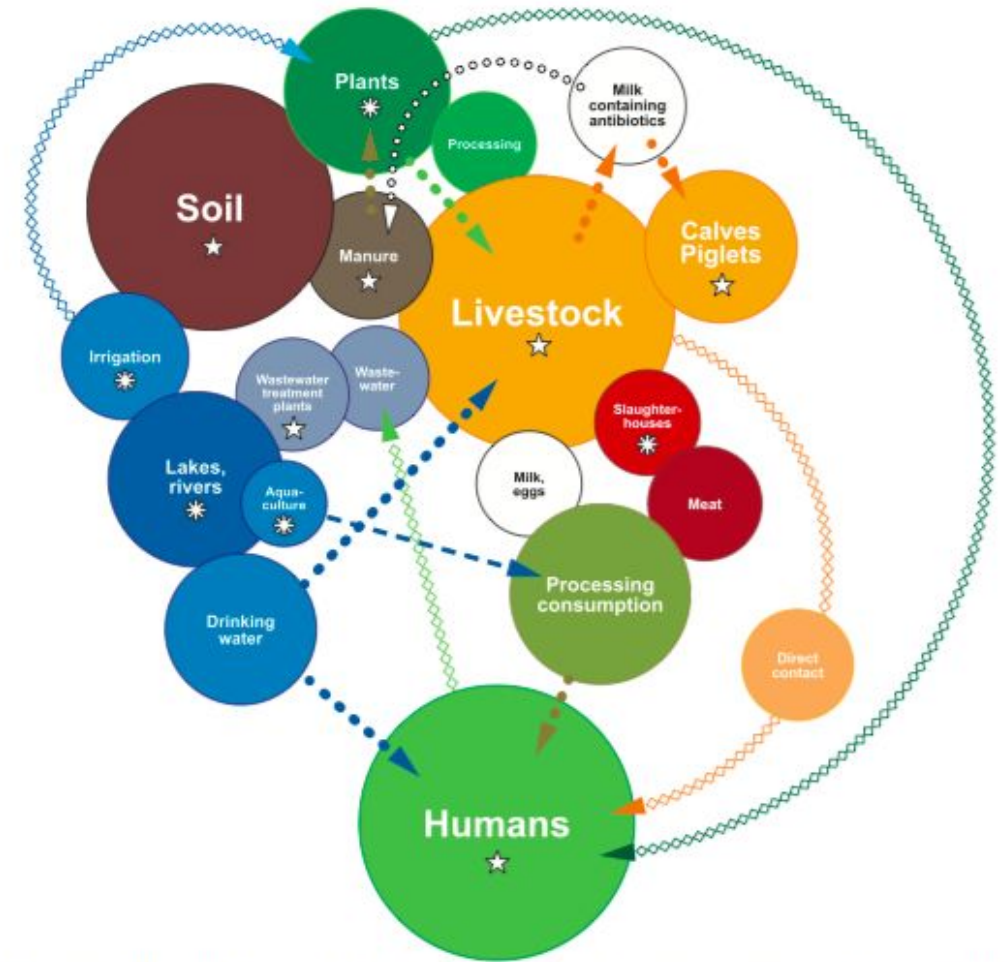

FIG 1 Pathway map of AMA and AMR dissemination within agriculture, the environment, and the food processing industry. Movement of AMA or AMR is indicated by overlapping circles and arrows, respectively; different colors define different groups of reservoirs. Stars indicate the hot spots of ARG and ARB with high bacterial densities, nutrient availability, and selective pressure in the digestive tract of livestock and humans, in manure storage facilities, wastewater treatment plants, and in the rhizosphere. Asterisks indicate possible hot spots of ARG and ARB in water, sediments, and biofilms in aquaculture, rivers, lakes, and irrigation systems, as well as in slaughterhouse facilities and on plant surfaces.
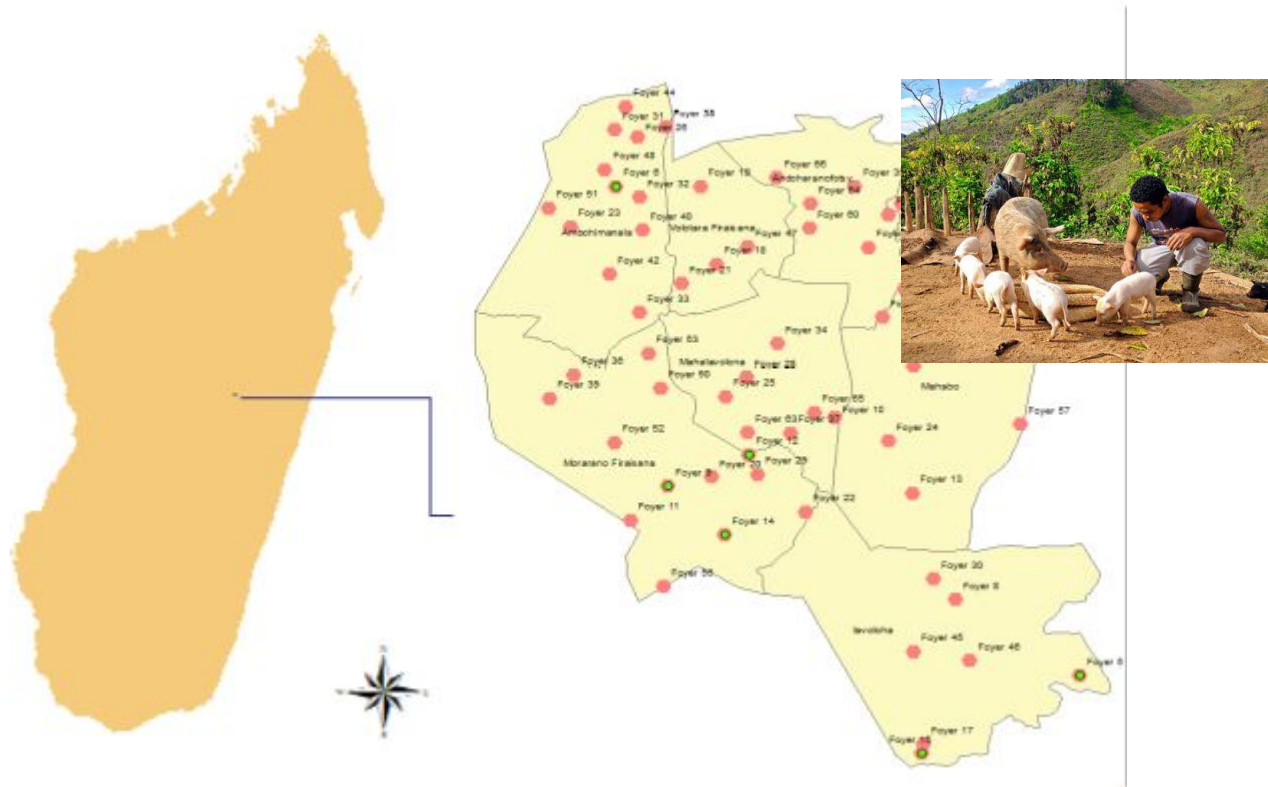
CASE Study in Madagascar:
    Can we highlight transmission between compartment/reservoir ?
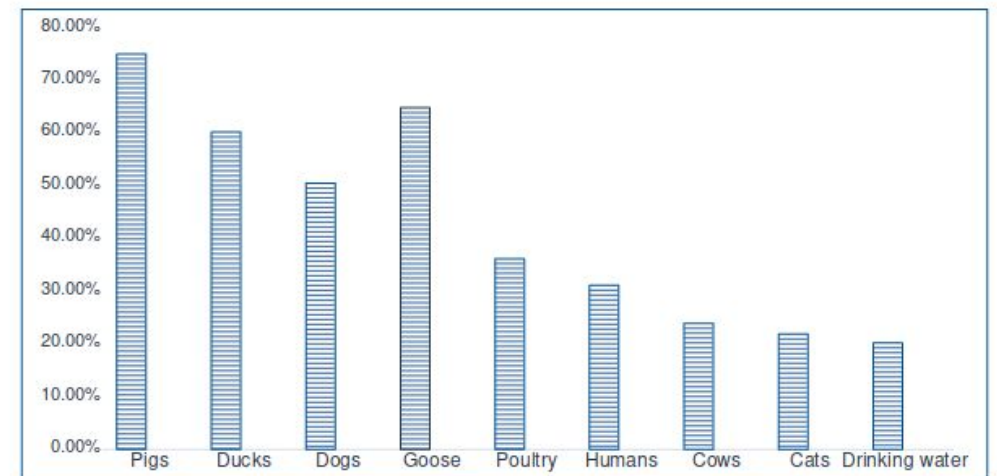   Are we looking at transmission of ARB / ARG and what factors drives them ?

Sampling in the different potential compartments

Prevalence of ESBL-producing E. coli in reservoirs

May-October 2018, 350 humans, and 1002 animals (70 households) sampled.
Prevalence ranged from **21.9% to 75.0%** for **cats** and **pigs** respectively.

* Only animal species with > 20 individual sampled were presented.

CASE Study in Madagascar:
    Can we highlight transmission between compartment/reservoir ?
    Are we looking at transmission of ARB / ARG and what factors drives them ?
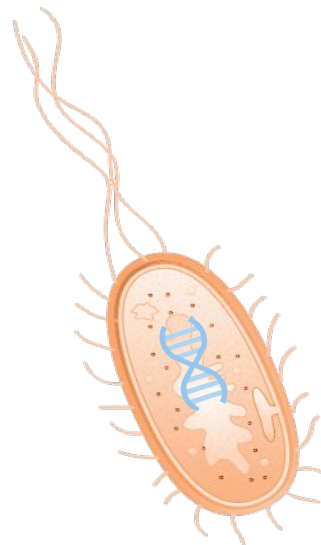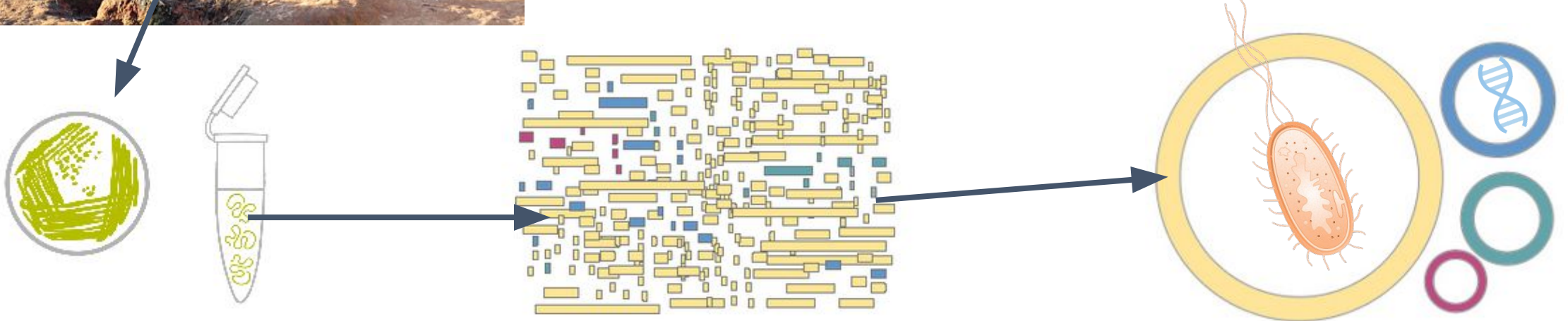

AND / OR ?

CASE Study in Madagascar:
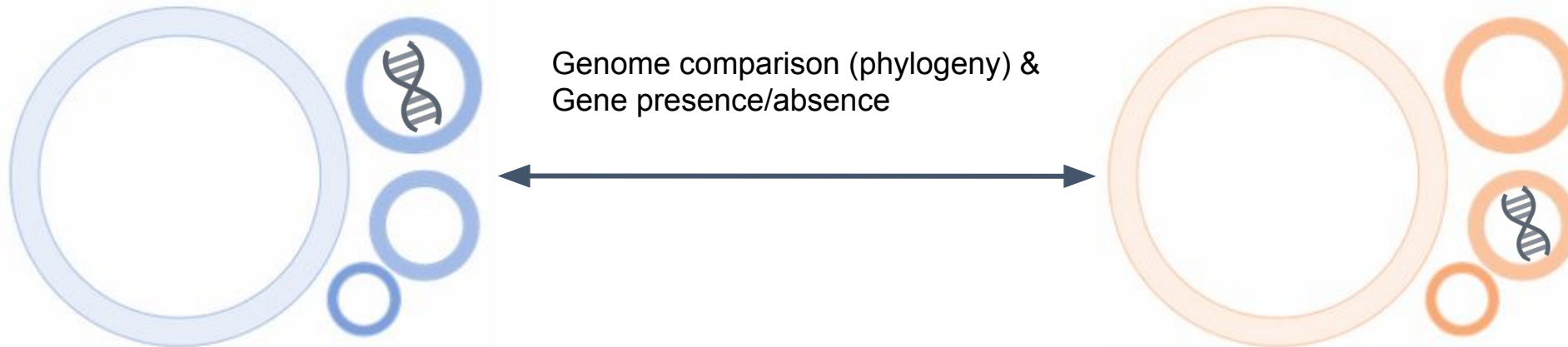   Can we highlight transmission between compartment/reservoir ?
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CASE Study in Madagascar:
  Can we highlight transmission between compartment/reservoir ?
  Are we looking at transmission of ARB / ARG and what factors drives them ?

Genome comparison (phylogeny) &
Gene presence/absence

CASE Study in Madagascar:
    Can we highlight transmission between compartment/reservoir ?
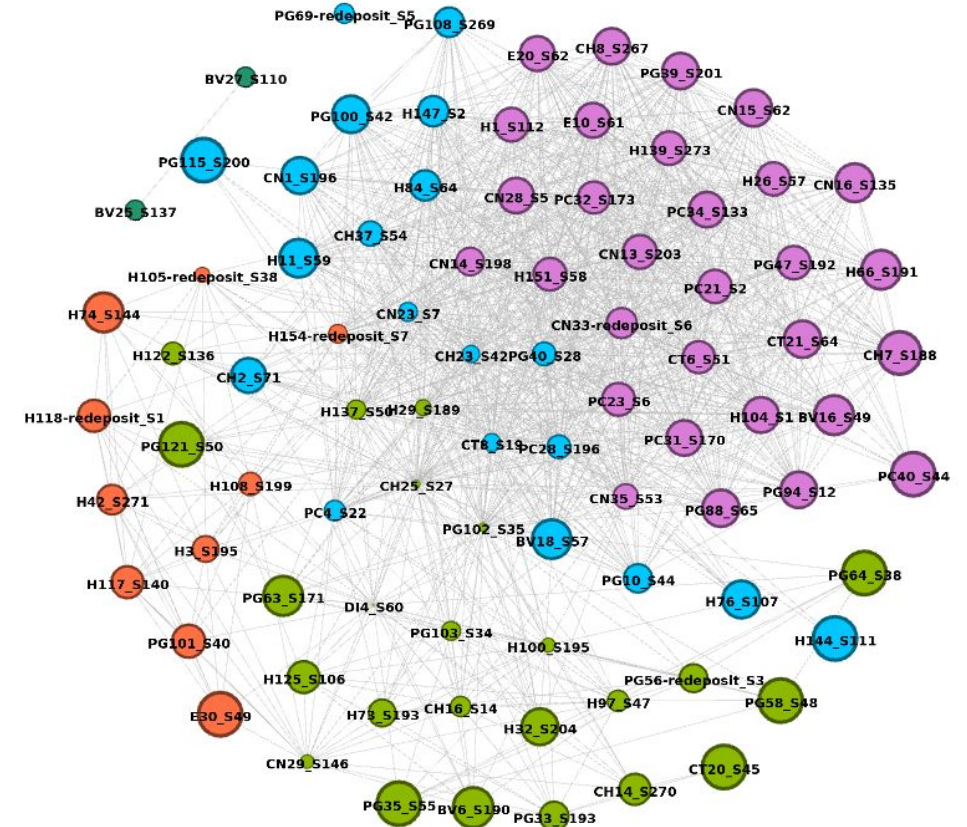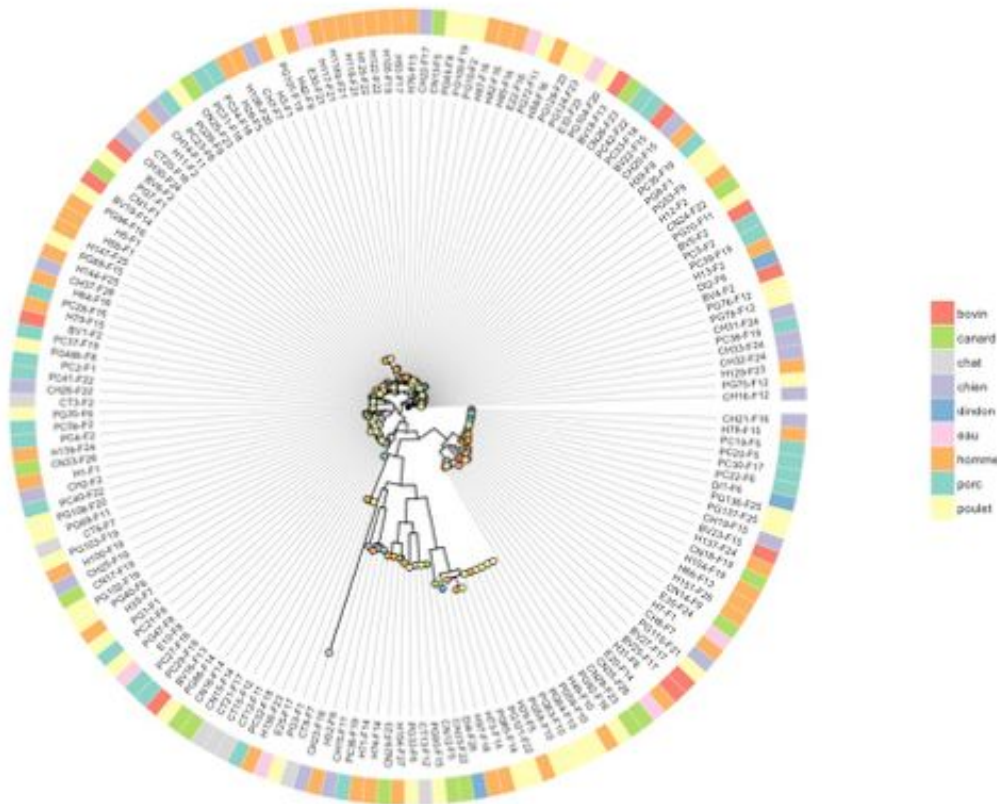   Are we looking at transmission of ARB / ARG and what factors drives them ?

Disentangling vertical vs horizontal transmission of ARG: first results:

Thanks for your attention

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

CASE Study in Madagascar:
    Can we highlight transmission between compartment/reservoir ?
    Are we looking at transmission of ARB / ARG and what factors drives them ?

Sampling in the different potential compartments

AMR :

- MRB: ESBL-E/SARM/EPC etc.
- Resistant genes: mcr1, CTX-M-15, NDM-1, AmpC, etc…
- Plasmidic vs chromosomic
- Compatible groups of plasmids
- Bacterial species
- Can be carried by pathogenic bacteria / « nice bacteria » of the microbiota
- ATB selective pressure increase the phenomenon

hosts:

- Animals: domestic, livestock, wildlife

- Humans: ills at hospital/ healt care centers or in community (gut)

- Environment: water, soil

- Plants: rizosphere, stem

- Certain bacteria: peut-on parler de certaines bact réservoirs de gènes?

A case study

- ESBL-E
- Genes: mainly CTX-M (widespread)
- Originated in *Kluyvera* spp. bacteria from the water/soil/sewage
- Different *Kluyvera* = different CTX-M (1/15/etc).
- Plasmidic resistance (groupes d'incompatibilité)
- Bacterial species: genus Enterobacteriaceae
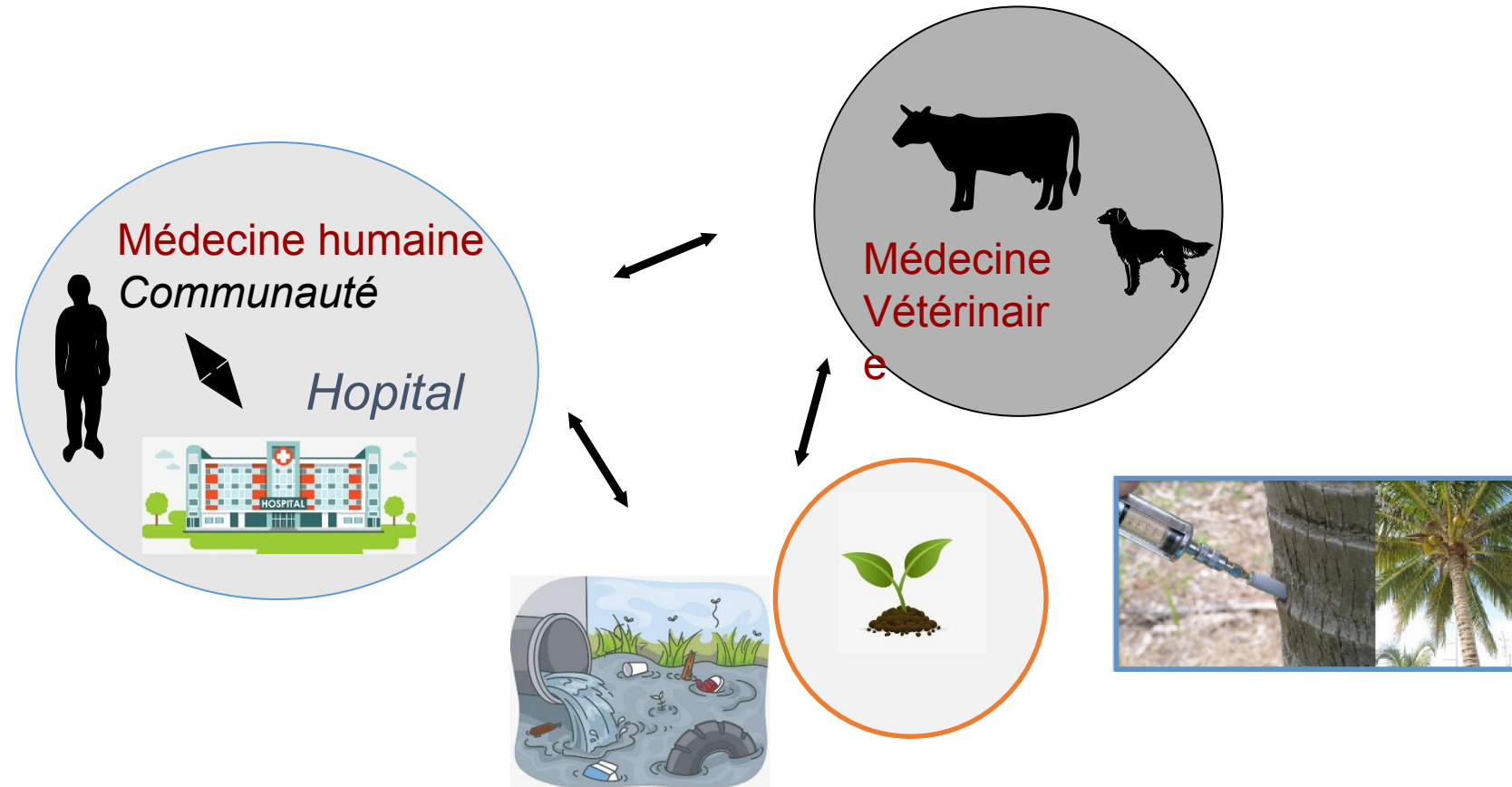- Bactéries concernées: E. coli/klebsiella spp./Enterobacter spp.

Bactéries sensibles

Bactéries résistantes

Antibiotiques
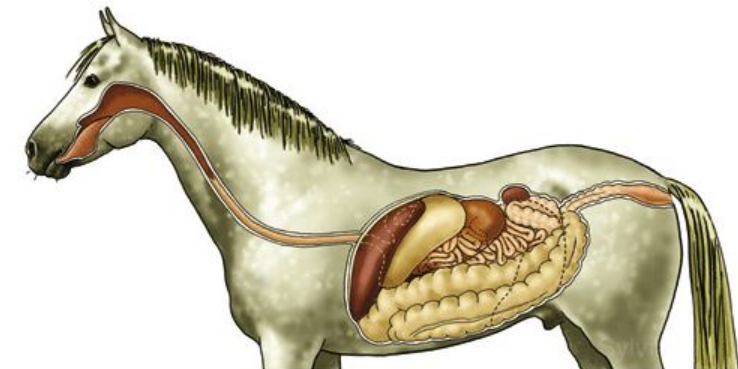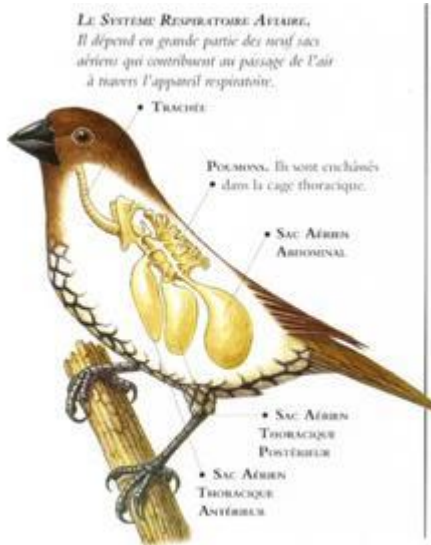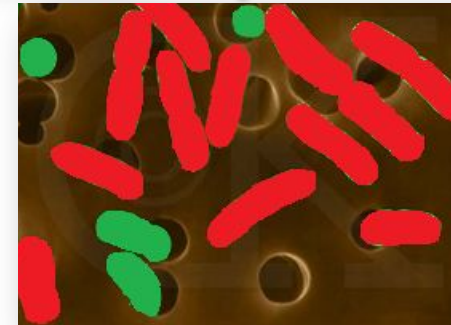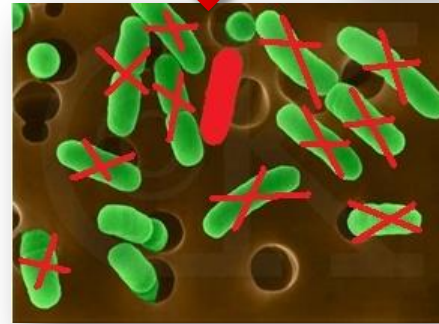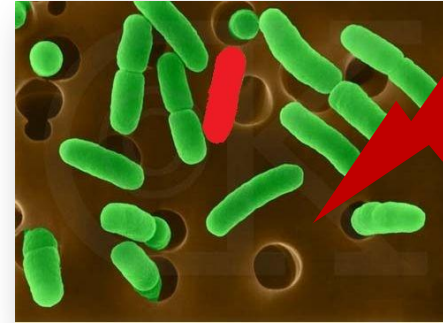
Les pressions de sélection: atb

Médecine humaine
Communauté
Hopital

Médecine Vétérinaire

Reservoir

- Pas de symptômes: portage (microbiote)
- Multiplication dans l'hôte ok mais environnement + plantes?

Conceptual framework

Pathogen	Target	Non-target	Main transmission route	High genetic similarity	High fonctional similarity	Spatial and temporal connectivity	Pathogen involvement	Maintening pathogen viability	Time factor
Escherichia coli	human	Animals (wildlife, livestock, pets)	Fecal/oral Foodborne others	No/Yes	Yes(ATB)	X			
Resistant genes (CTX-M, mcr-1, NDM-1, etc.)	human		Air? Water ?						

DIAPO NONO