

Antibiotic resistance genes are everywhere! Meet the environmental resistome

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AMR Arenas



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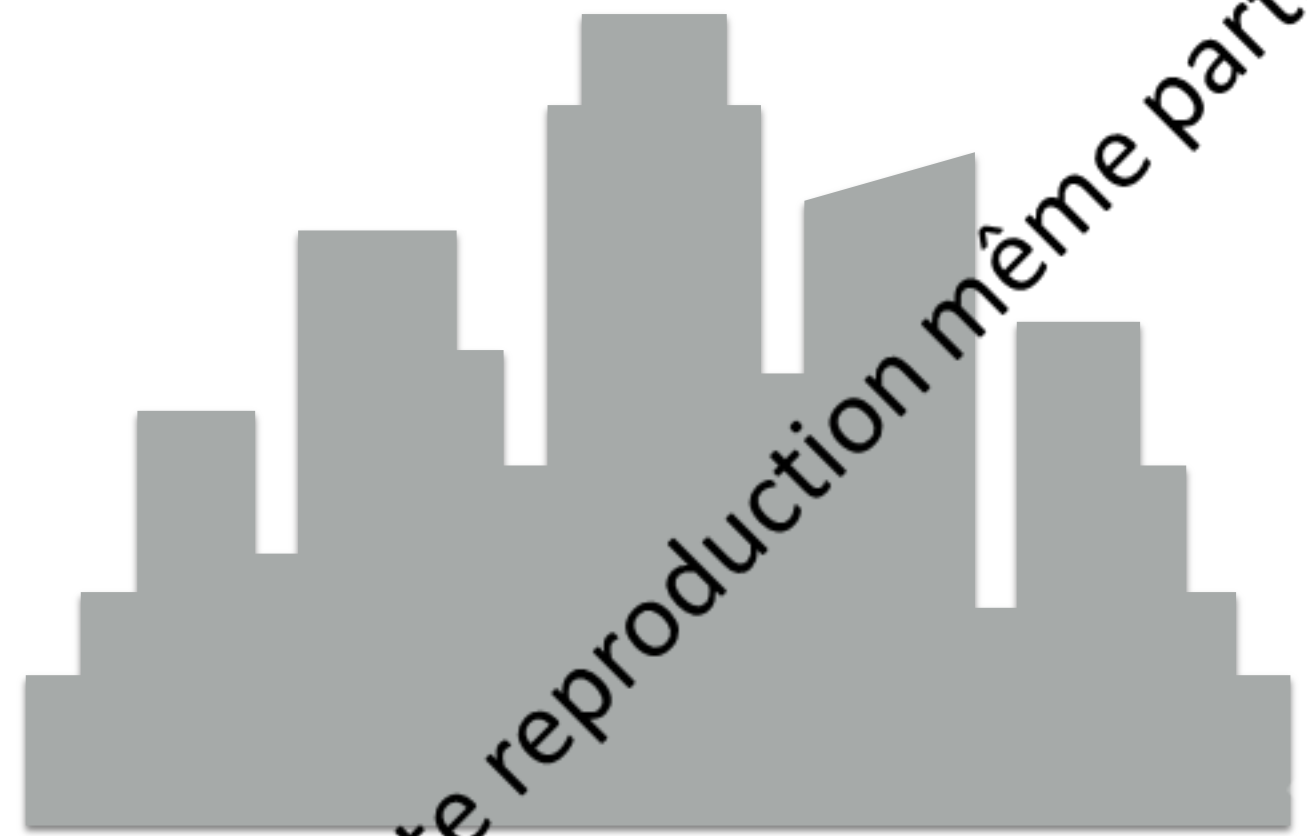


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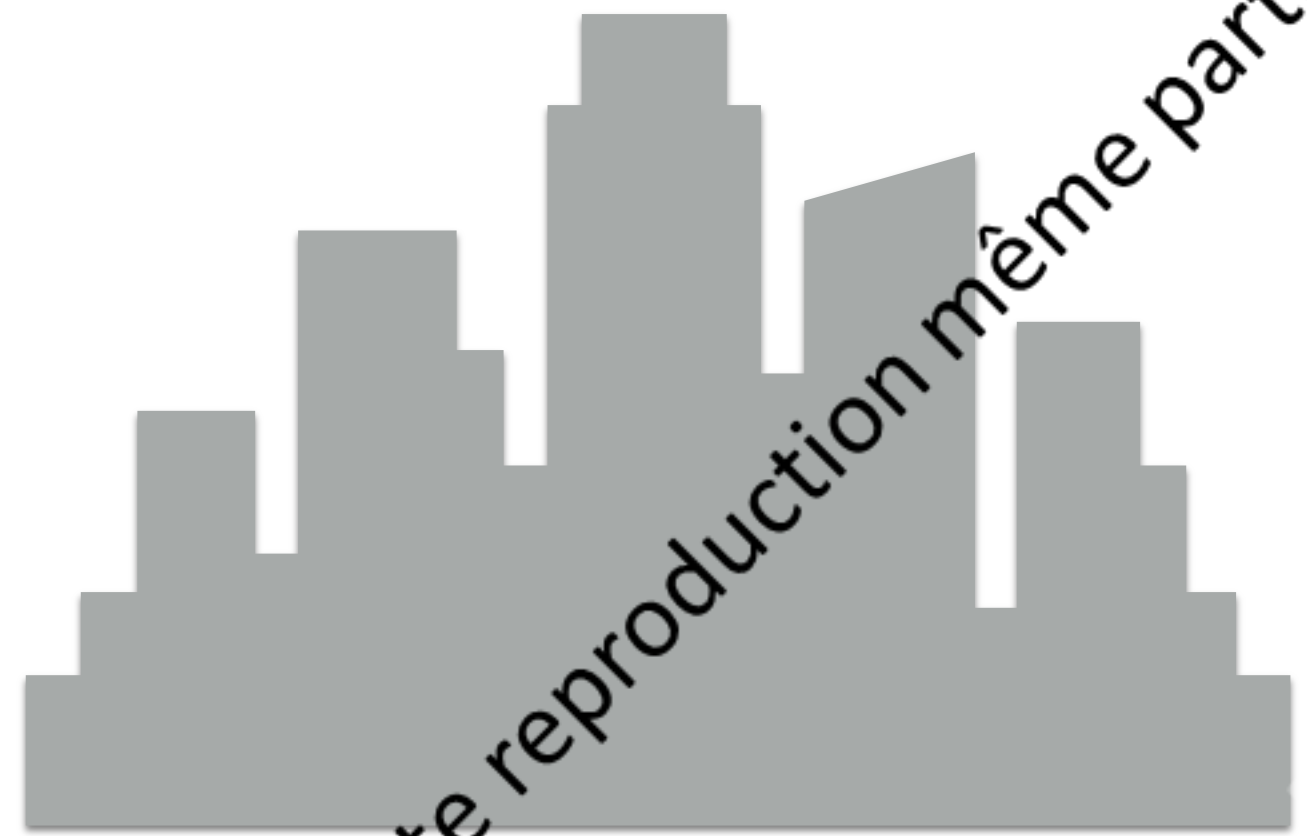
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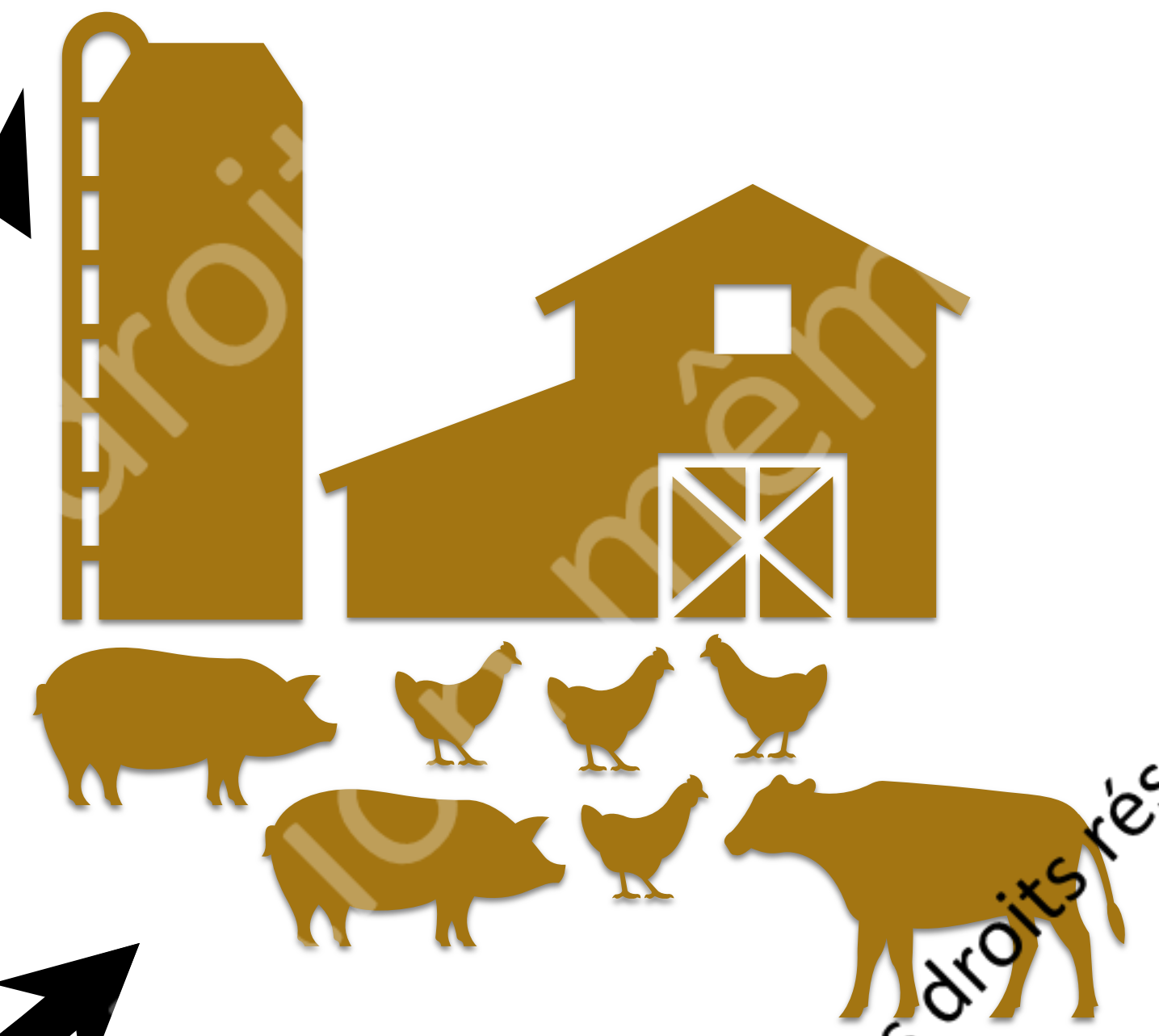
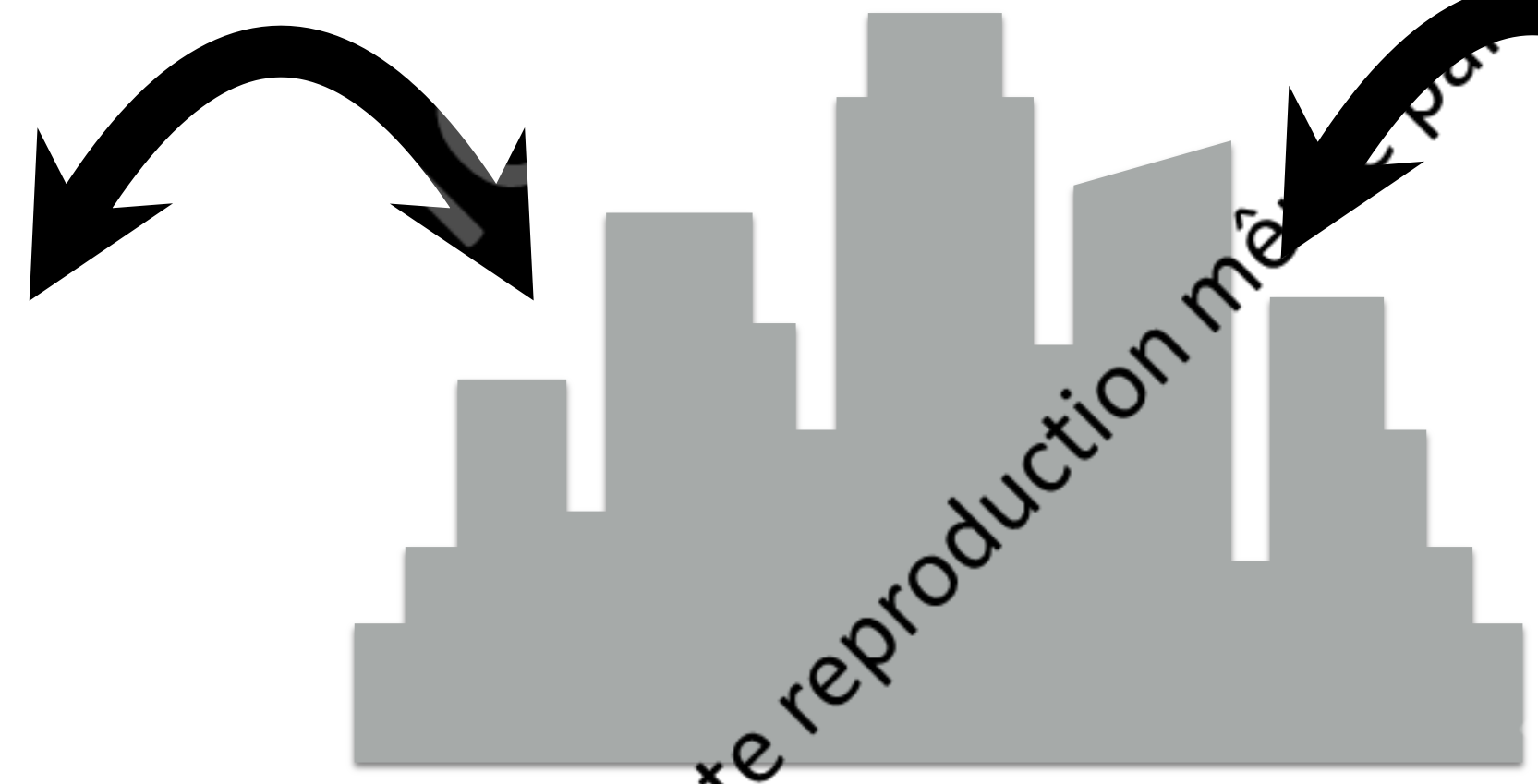
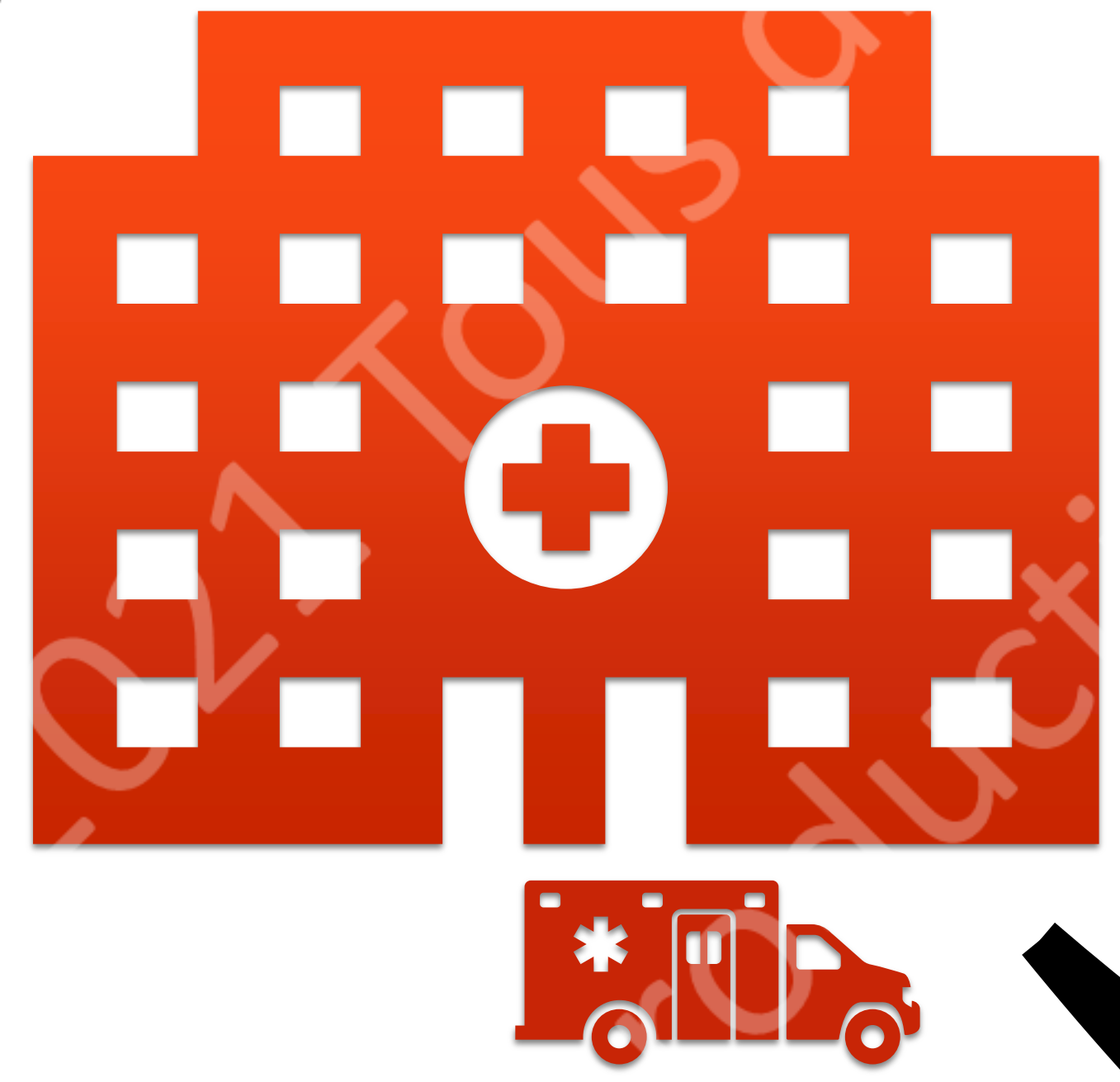


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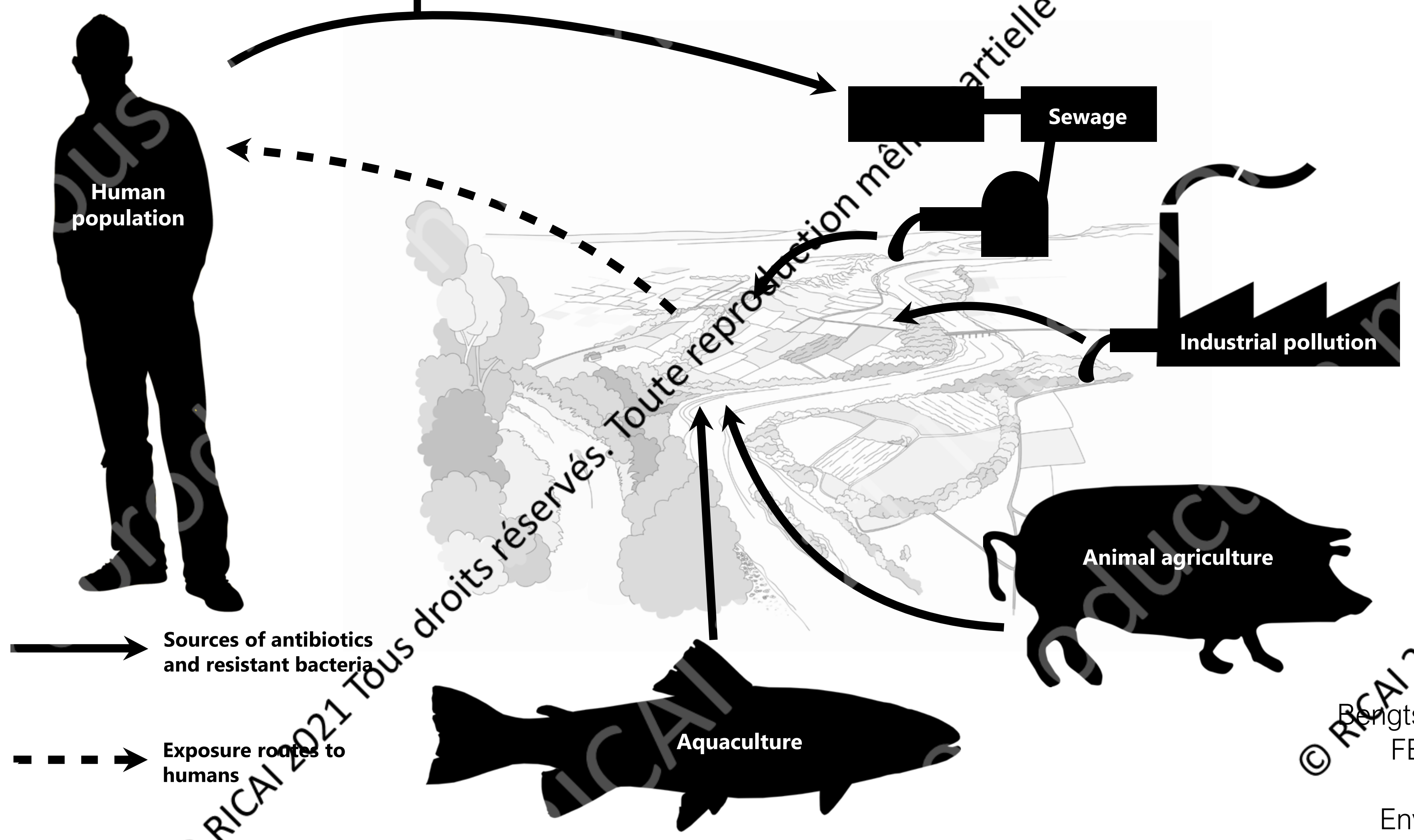


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AMR Arenas



Exposure to AMR



Bengtsson-Palme et al. 2018
FEMS Microbiol Reviews
Larsson et al. 2018
Environment International

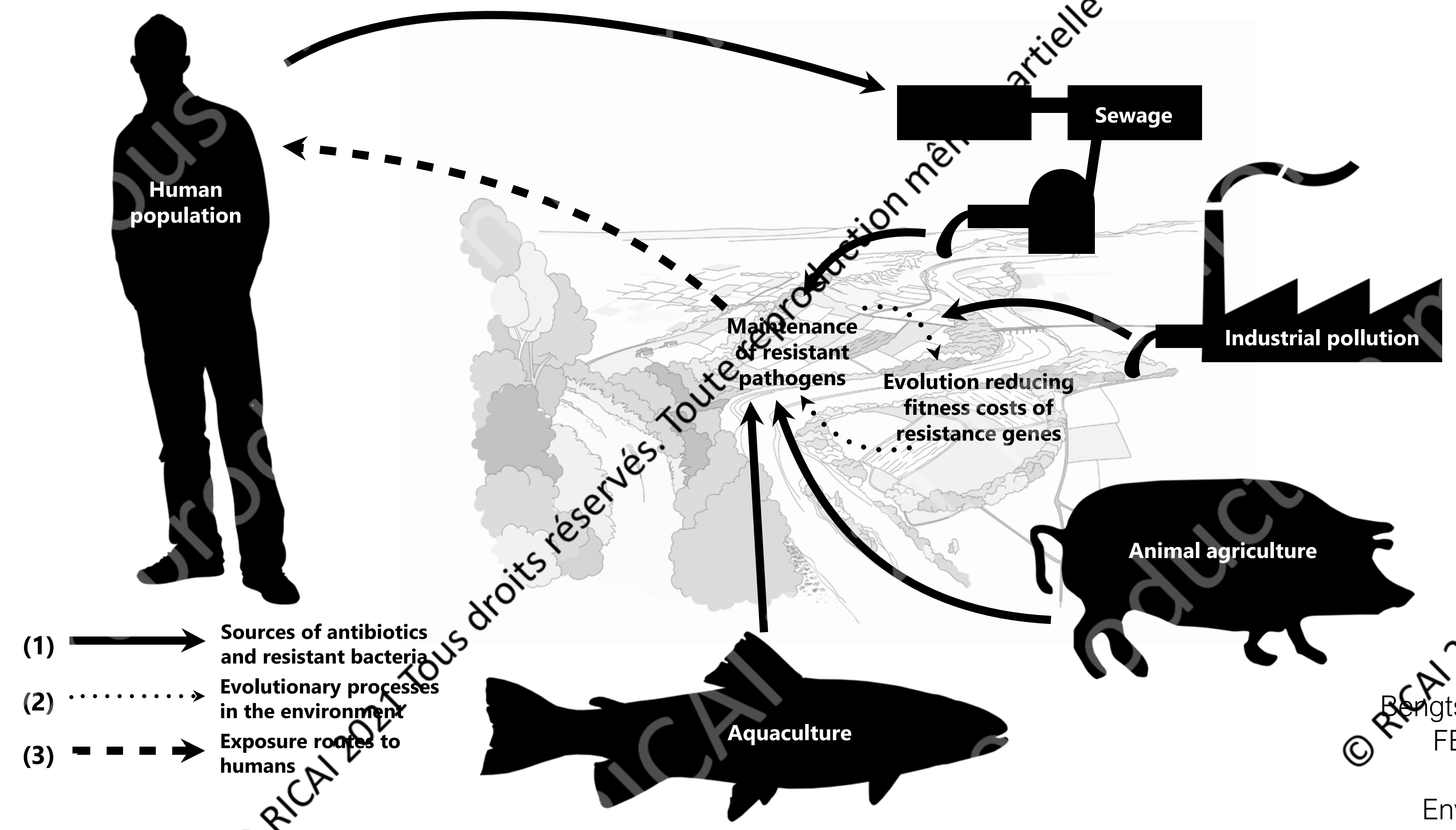
Exposure to AMR



- Resistant bacteria and resistance genes have been detected in all these settings
- It is yet unknown if exposure is sufficient to be a significant human health risk in relation to human-to-human transmission



Evolution of AMR



Bengtsson-Palme et al. 2018
FEMS Microbiol Reviews
Larsson et al. 2018
Environment International



Industrial AMR pollution

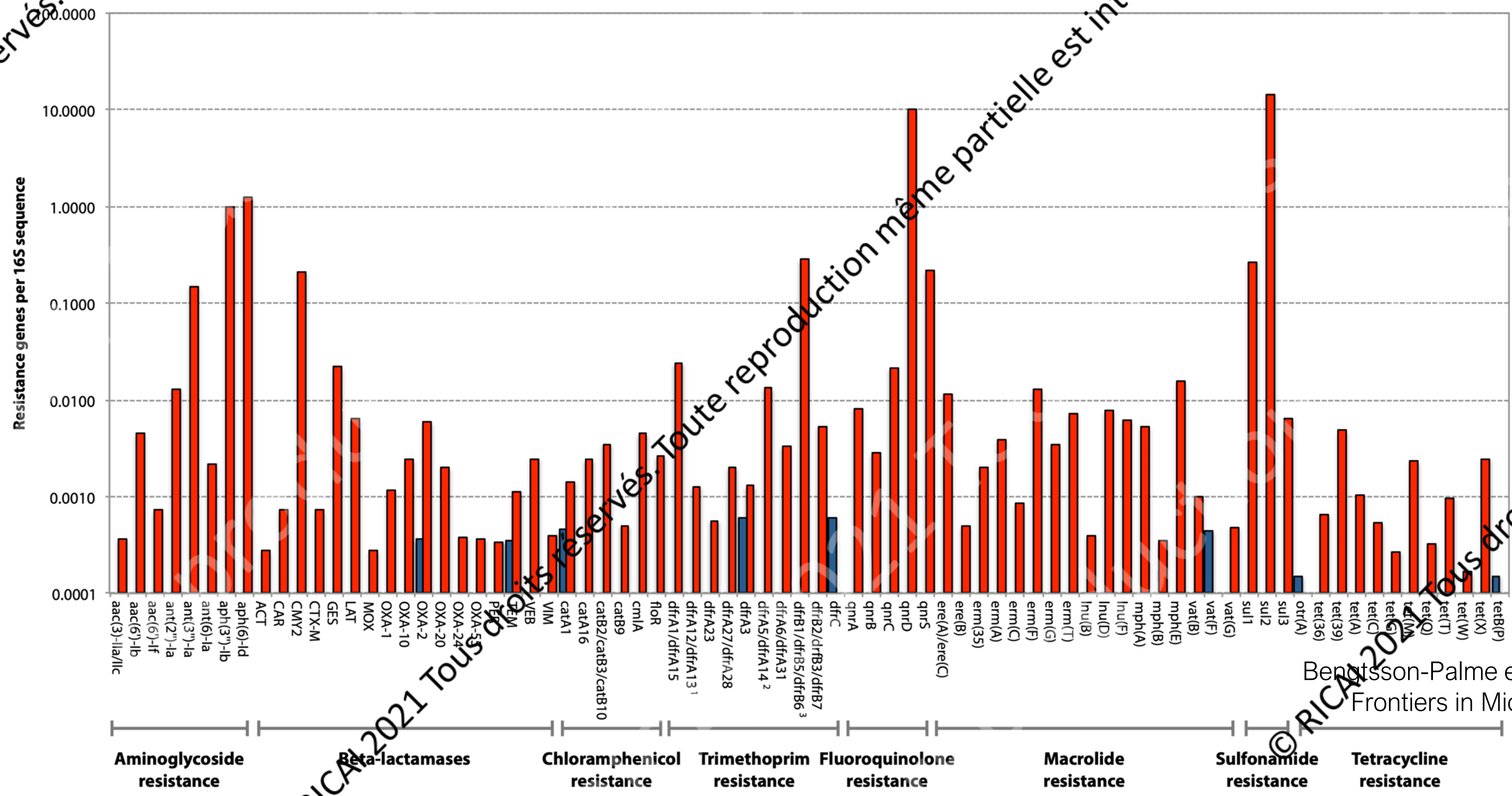


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Bengtsson-Palme et al. 2014
Frontiers in Microbiology

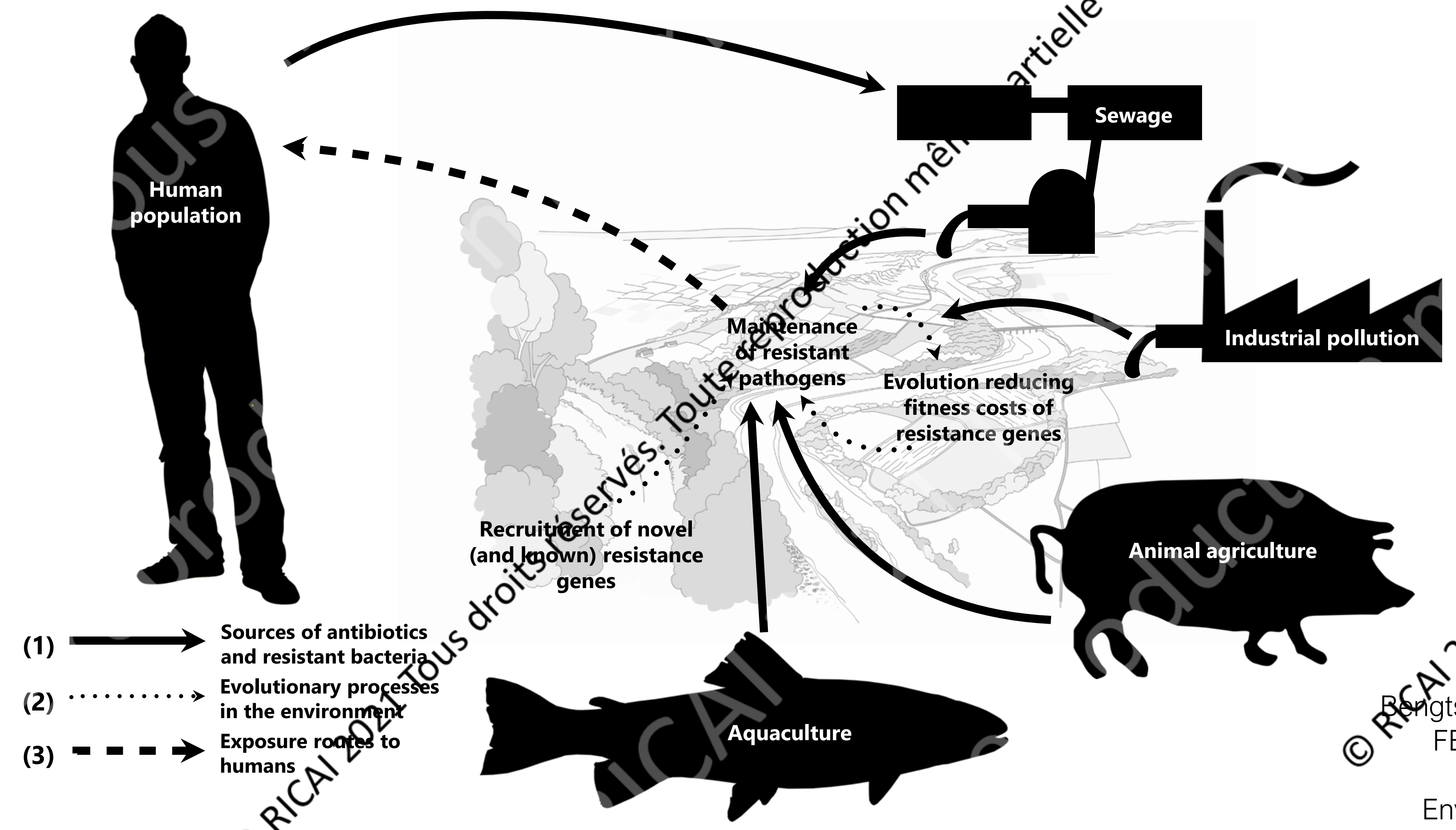
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Swedish Lake Indian Lake



Bengtsson-Palme et al. 2014
Frontiers in Microbiology

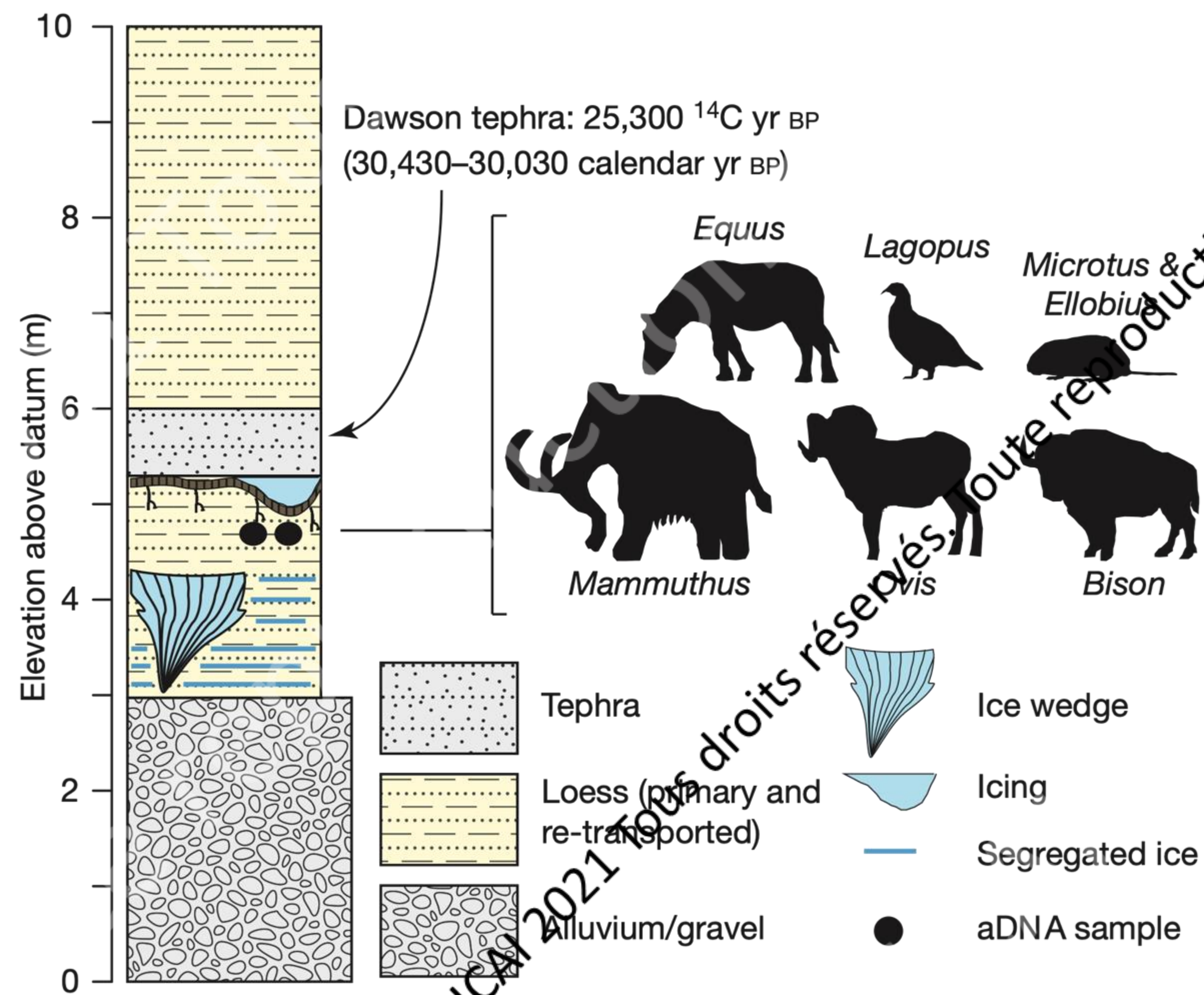
Evolution of AMR



- (1) —————> Sources of antibiotics and resistant bacteria
- (2)> Evolutionary processes in the environment
- (3) - - - -> Exposure routes to humans

Bengtsson-Palme et al. 2018
 FEMS Microbiol Reviews
 Larsson et al. 2018
 Environment International

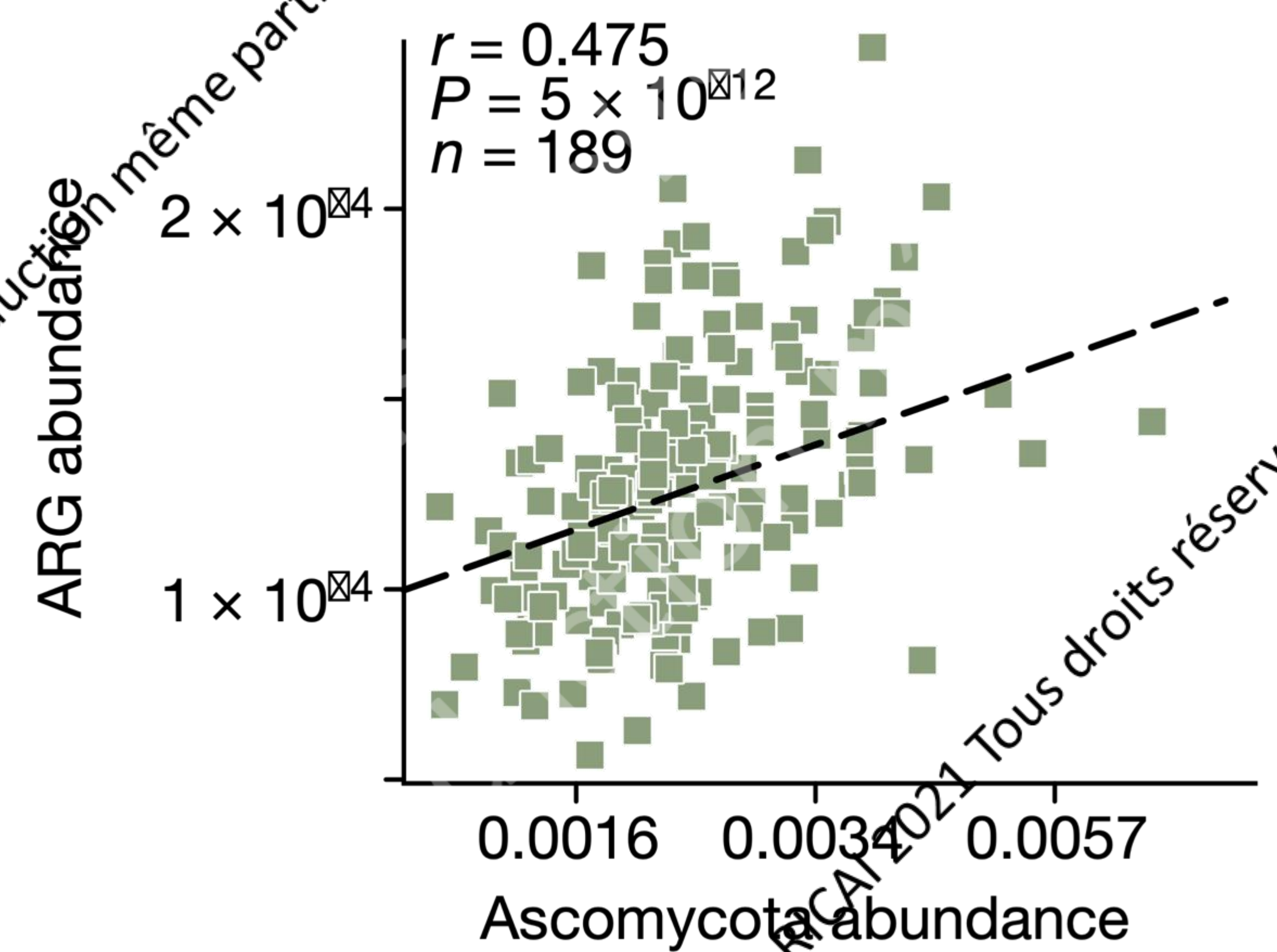
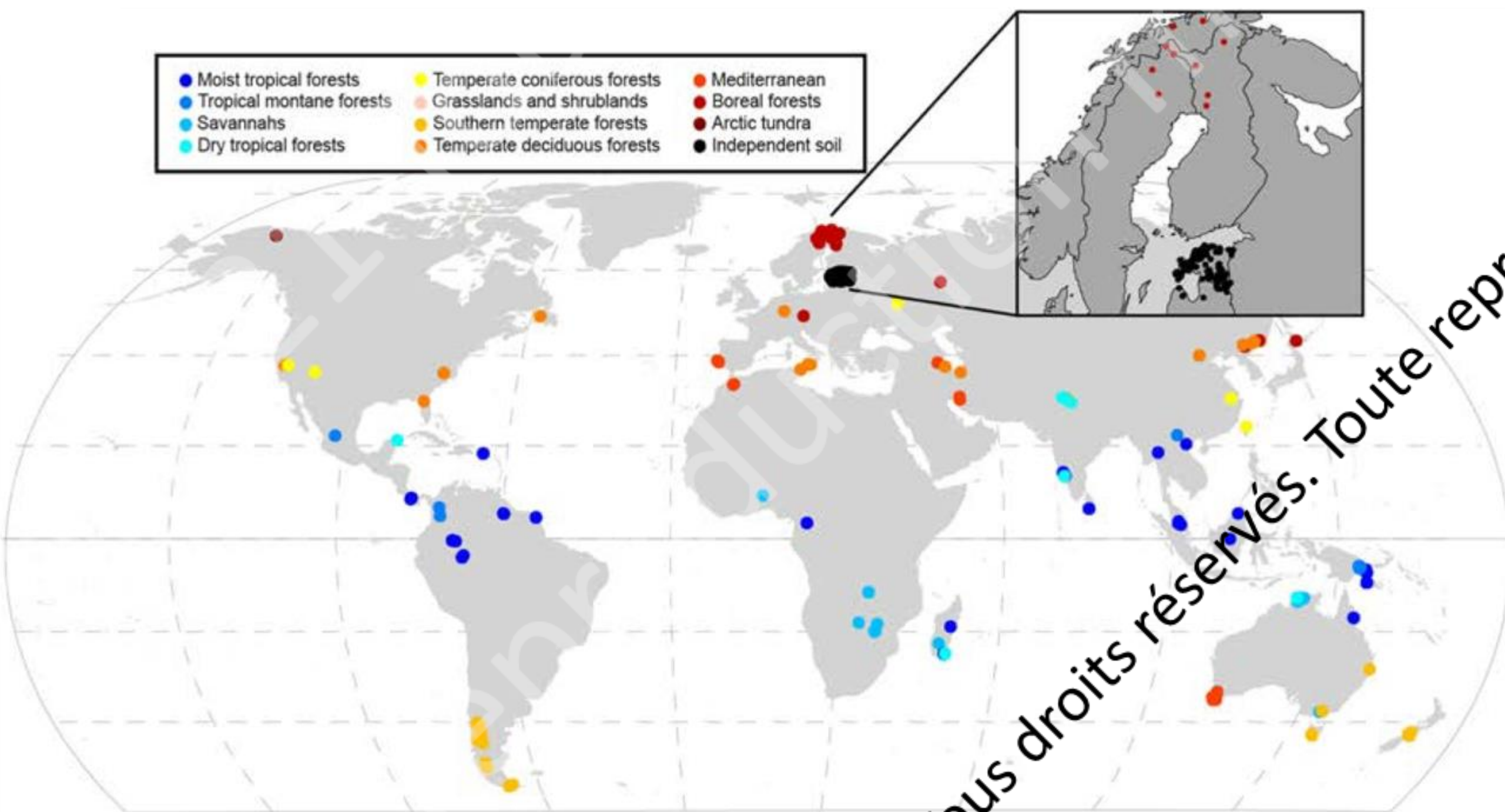
AMR is ancient



- Resistance genes in 30,000 years old samples
- 100% identical resistance genes in pathogens and soil bacteria

D'Costa et al. 2011
Nature
Forsberg et al. 2012
Science

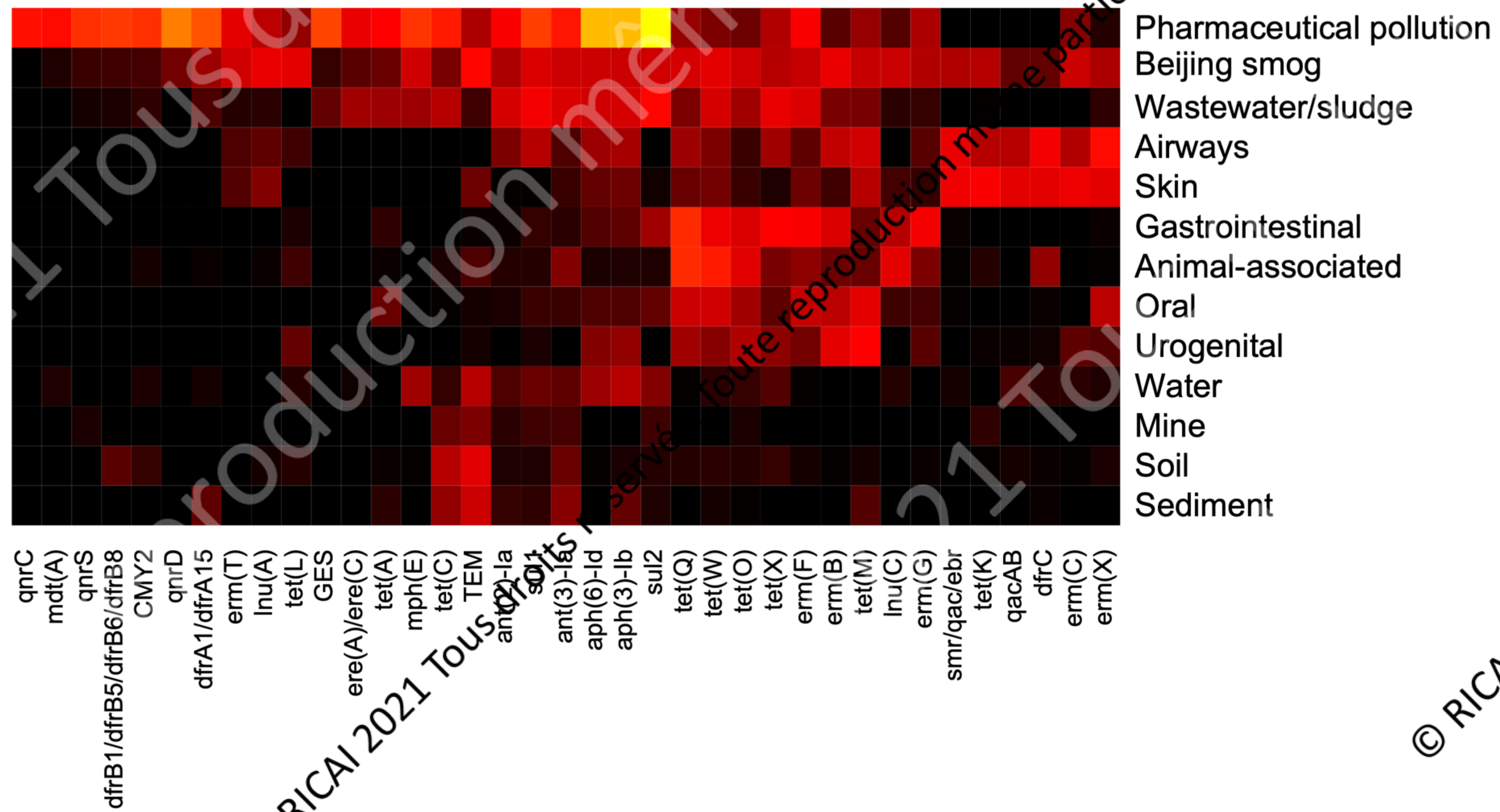
AMR as a response to natural antibiotics



Bahram et al. 2018 Nature



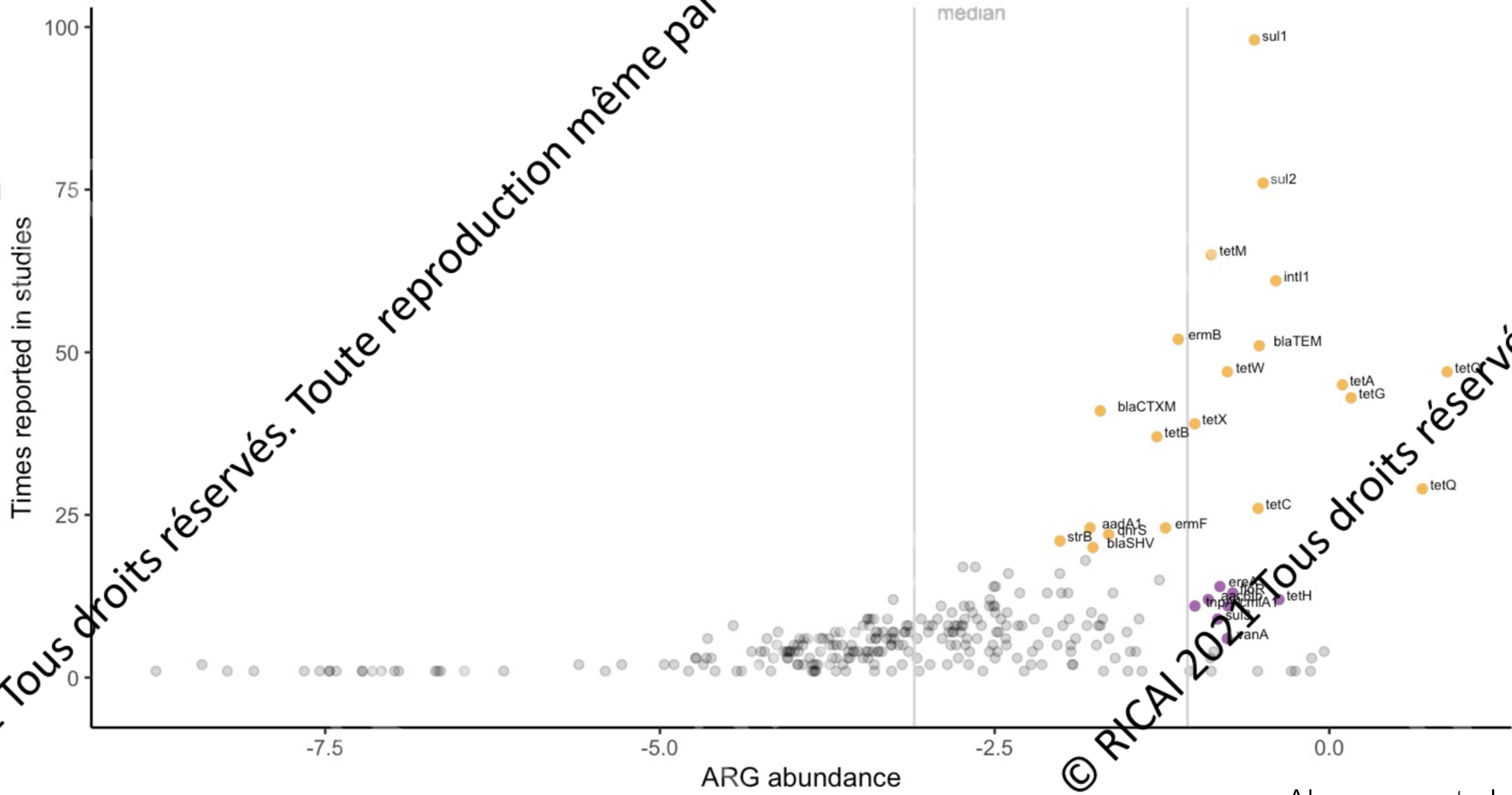
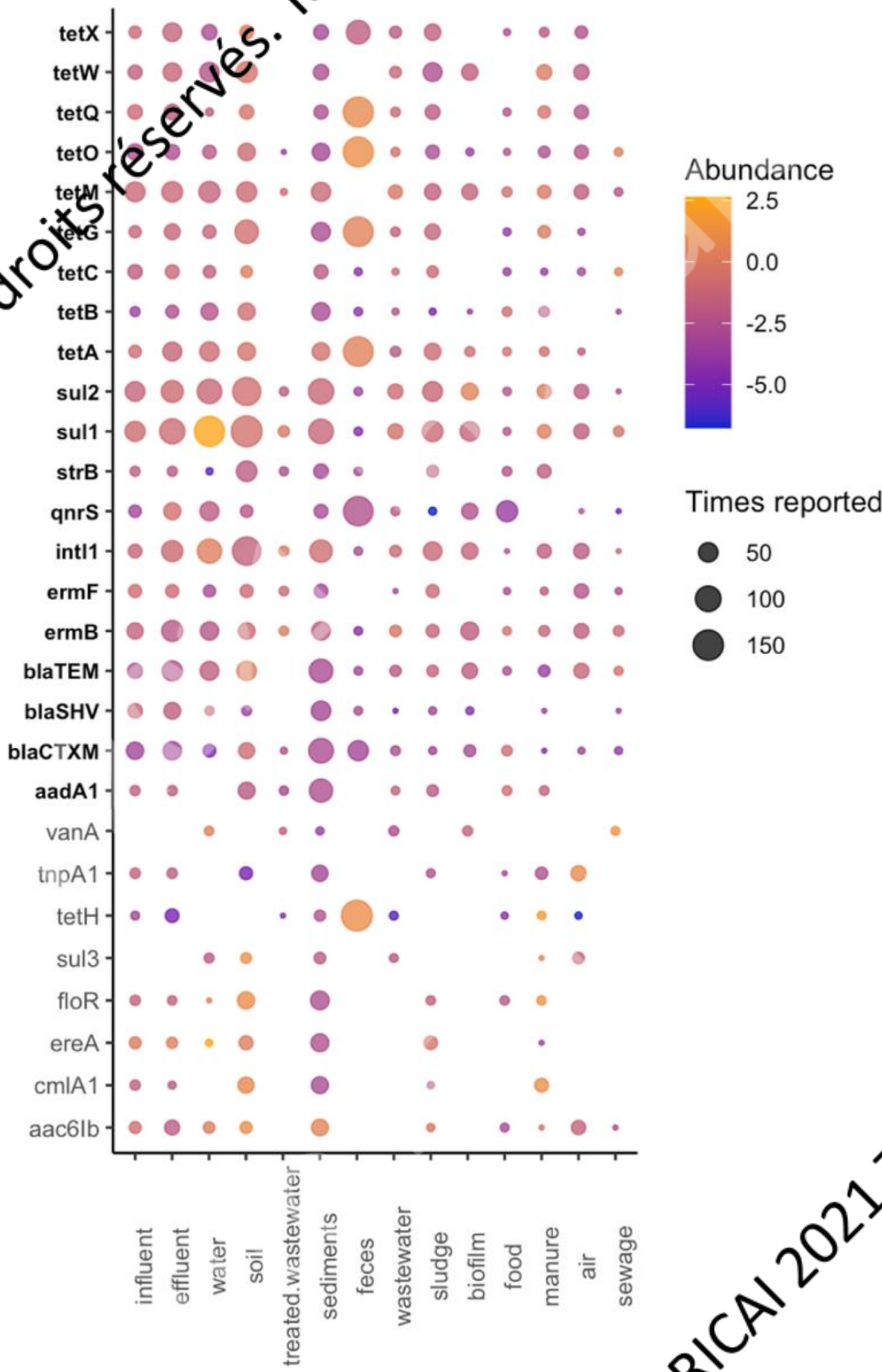
Global ARGs



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Pal et al. 2018
Microbiome

Global ARGs



Abramova et al. In prep.

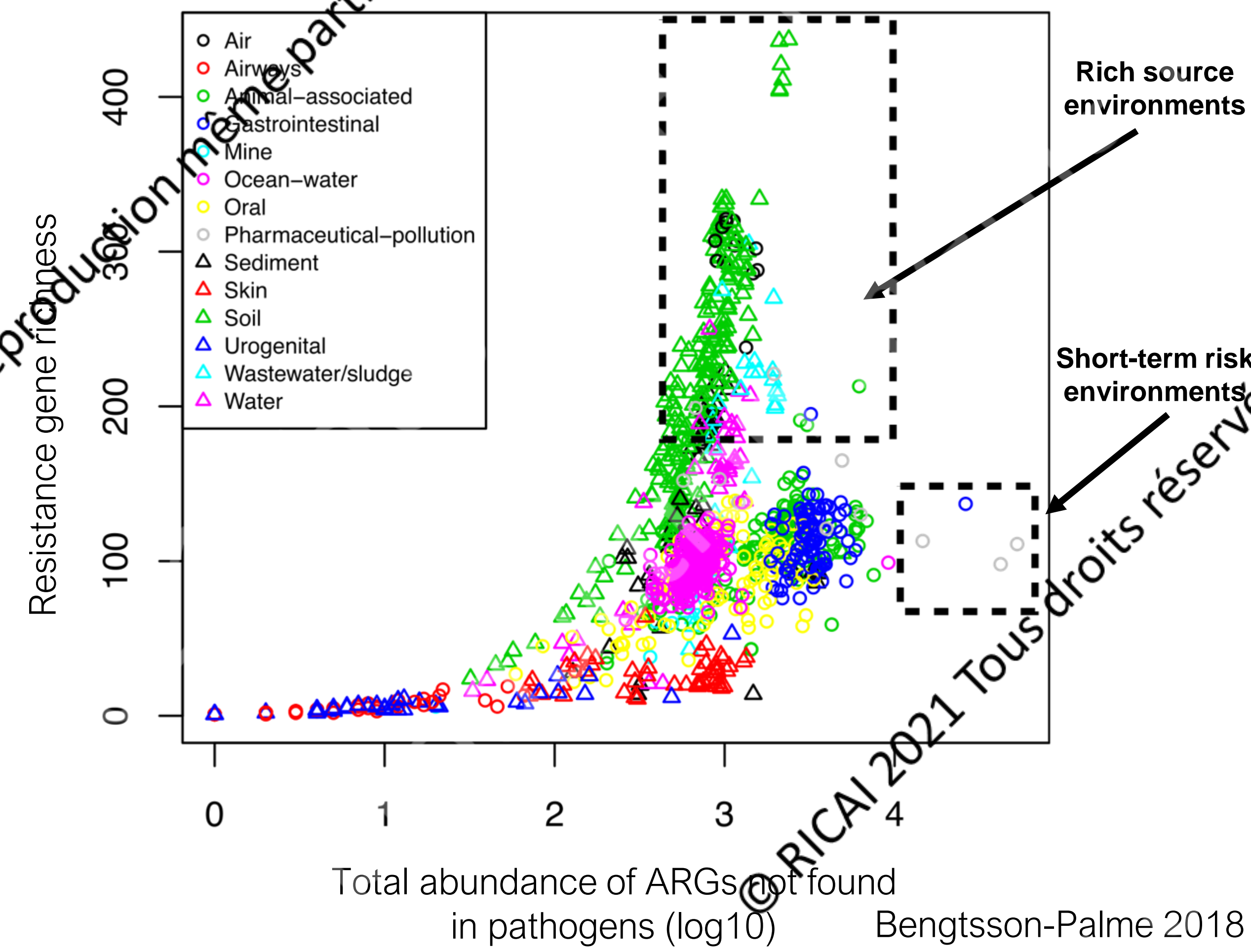
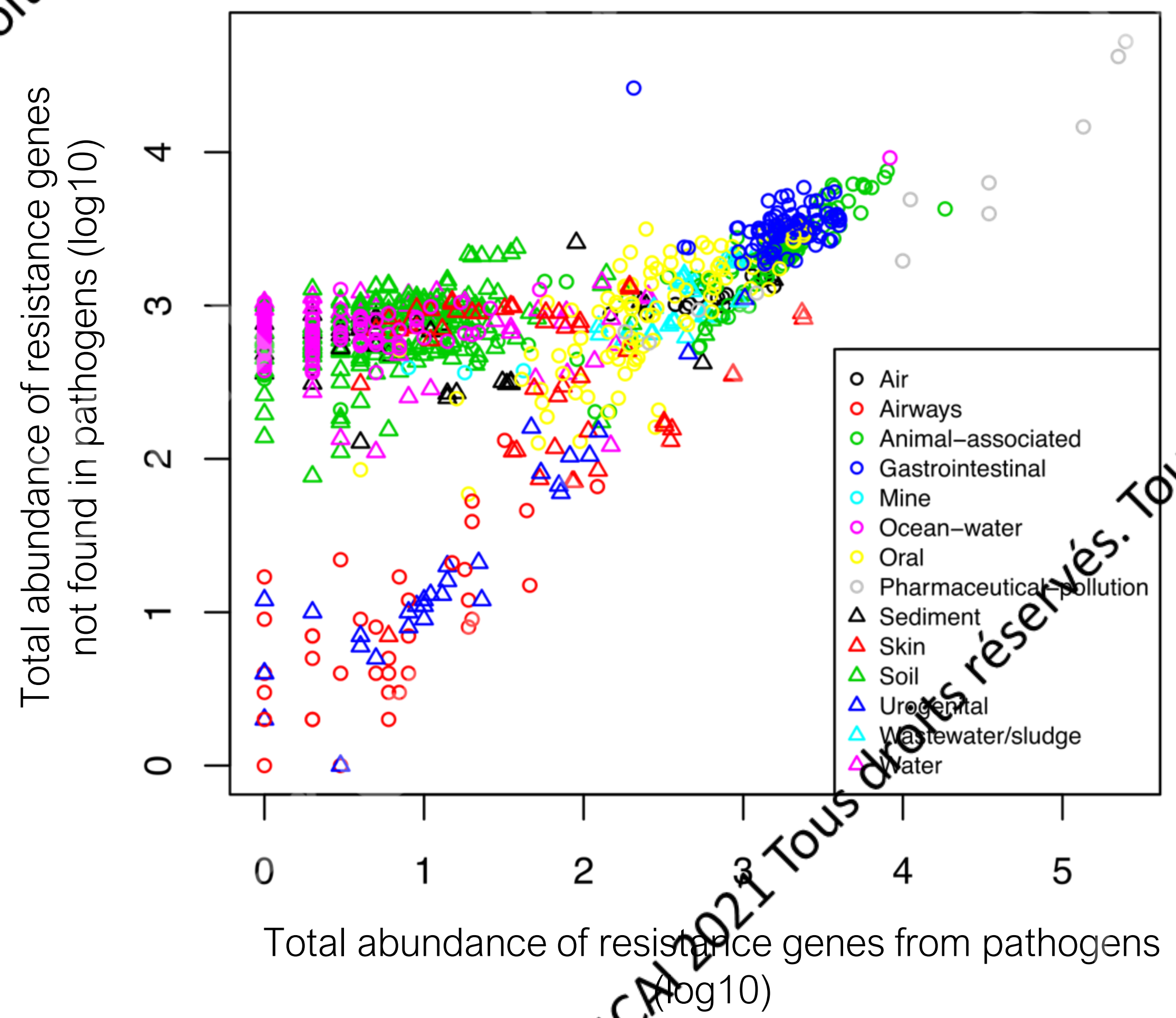


Some resistance genes are virtually everywhere

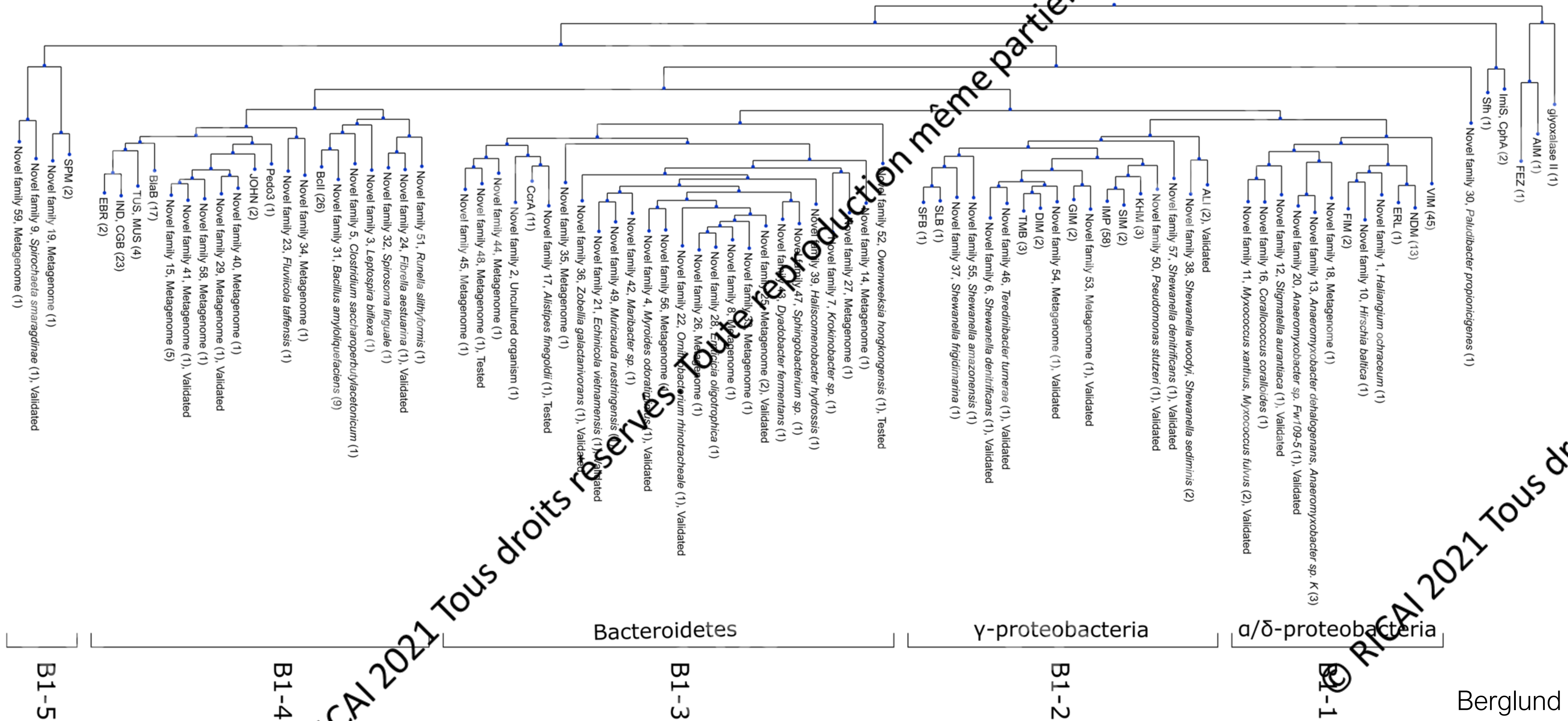
- *sul1*
- *sul2*
- *bla*_{TEM}
- *tet*(M)
- *aph*(3'')-Ib a.k.a. *strA*
- *aph*(6)-Id a.k.a. *strB*

All of these have been linked to integrons or other highly movable genetic elements that exist on a multitude of plasmids

Are there undiscovered ARGs?

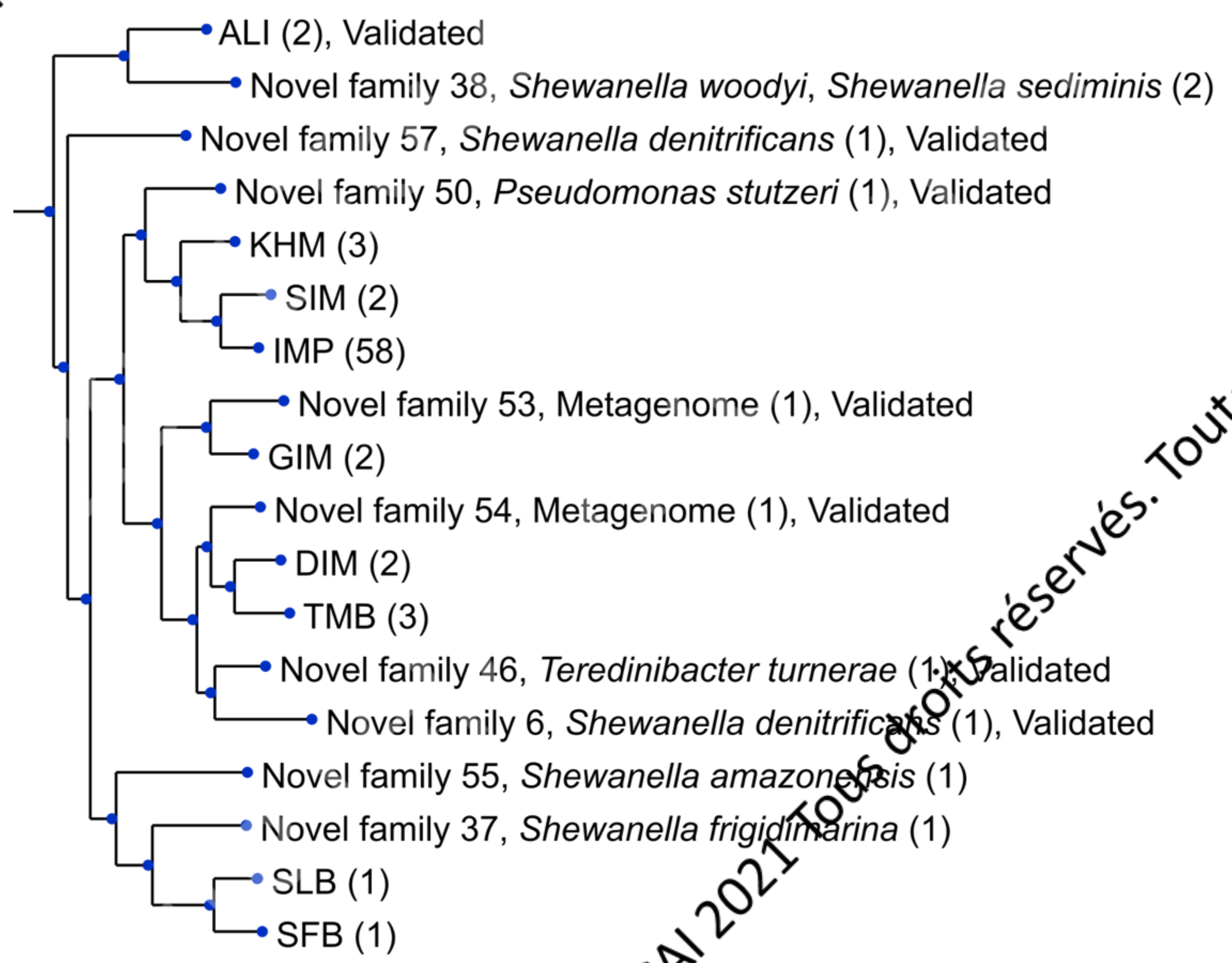


New metallo- β -lactamases



Berglund et al. 2017
Microbiome

New metallo- β -lactamases



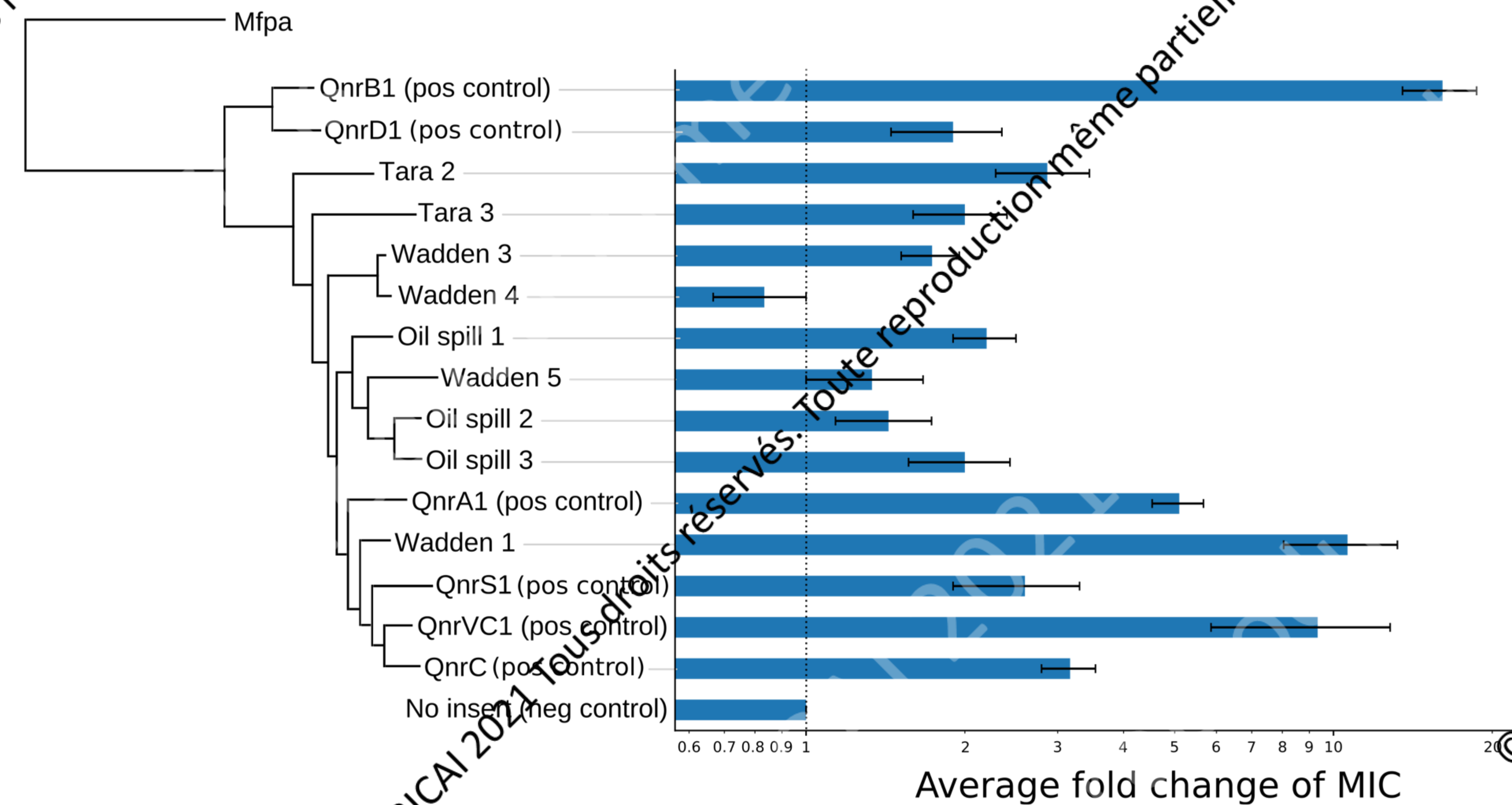
Y-proteobacteria

B1-2

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Berglund et al. 2017
Microbiome

New fluoroquinolone ARGs

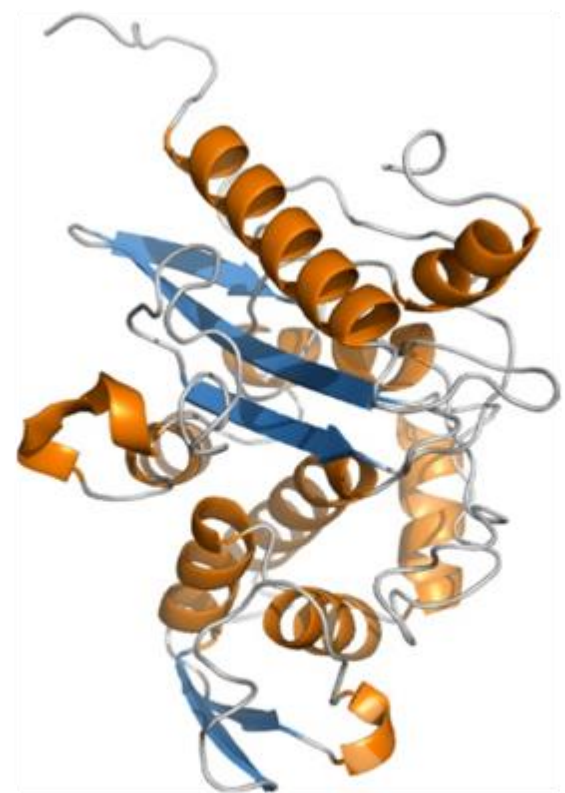


Boulund et al. 2017
BMC Genomics

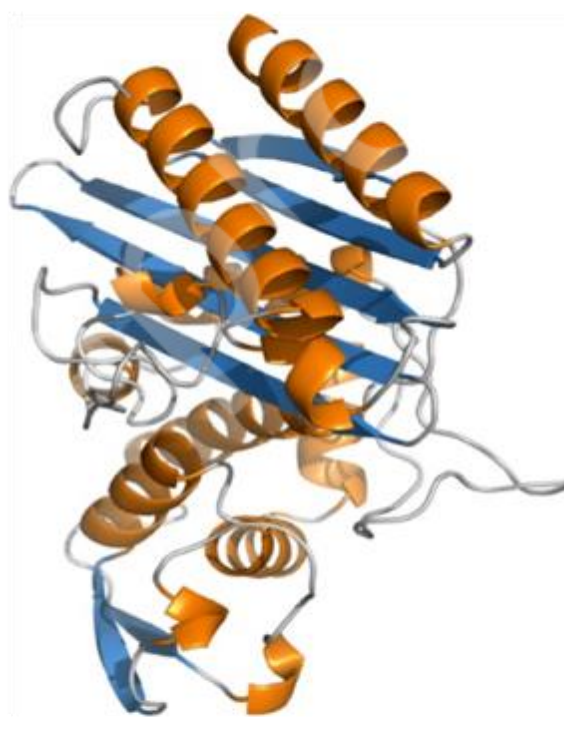
Structure modeling to find new ARGs



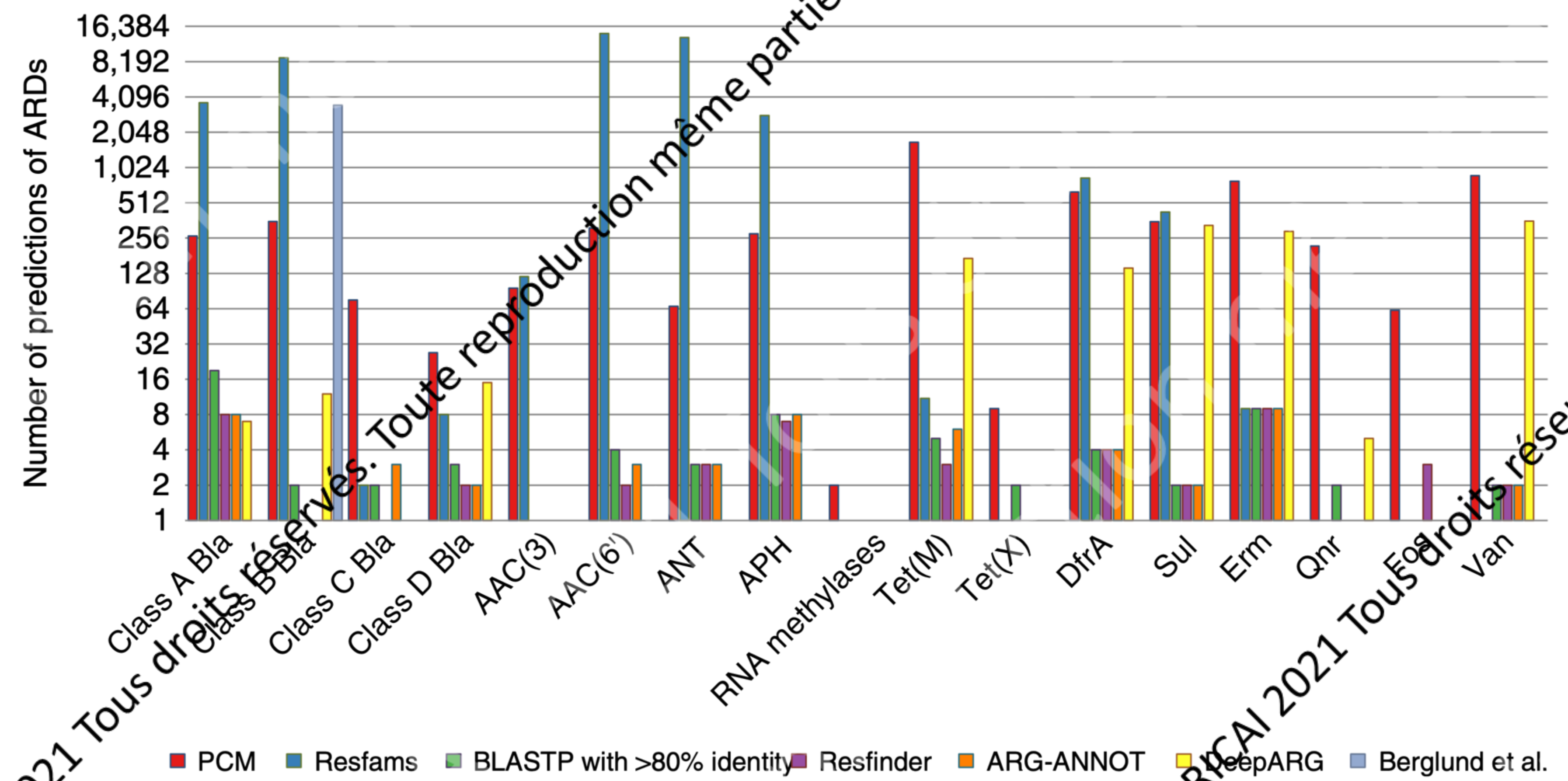
Reference template



Candidate modelled with negative template



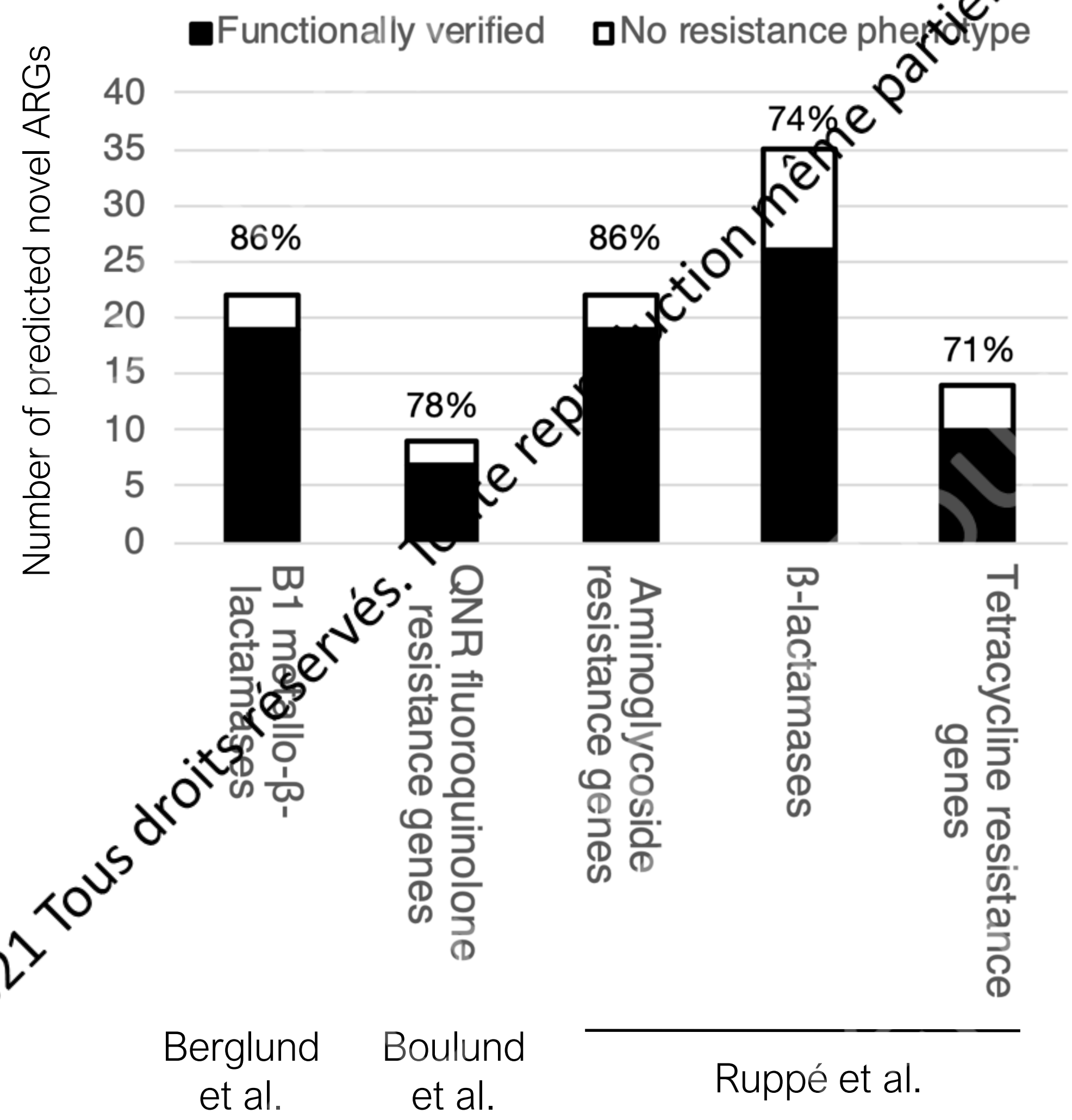
Candidate modelled with reference template



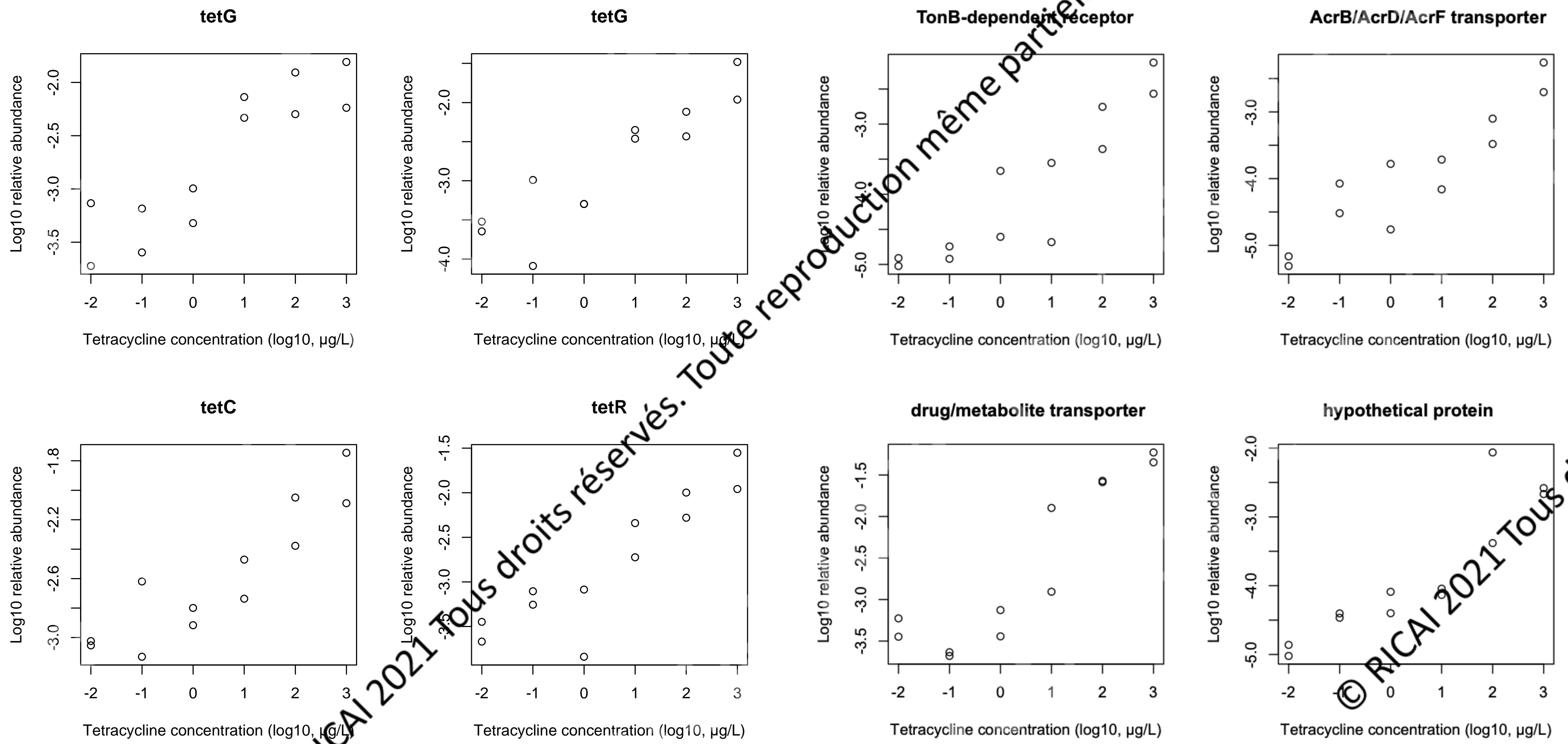
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Ruppé et al. 2018
Nature Microbiology

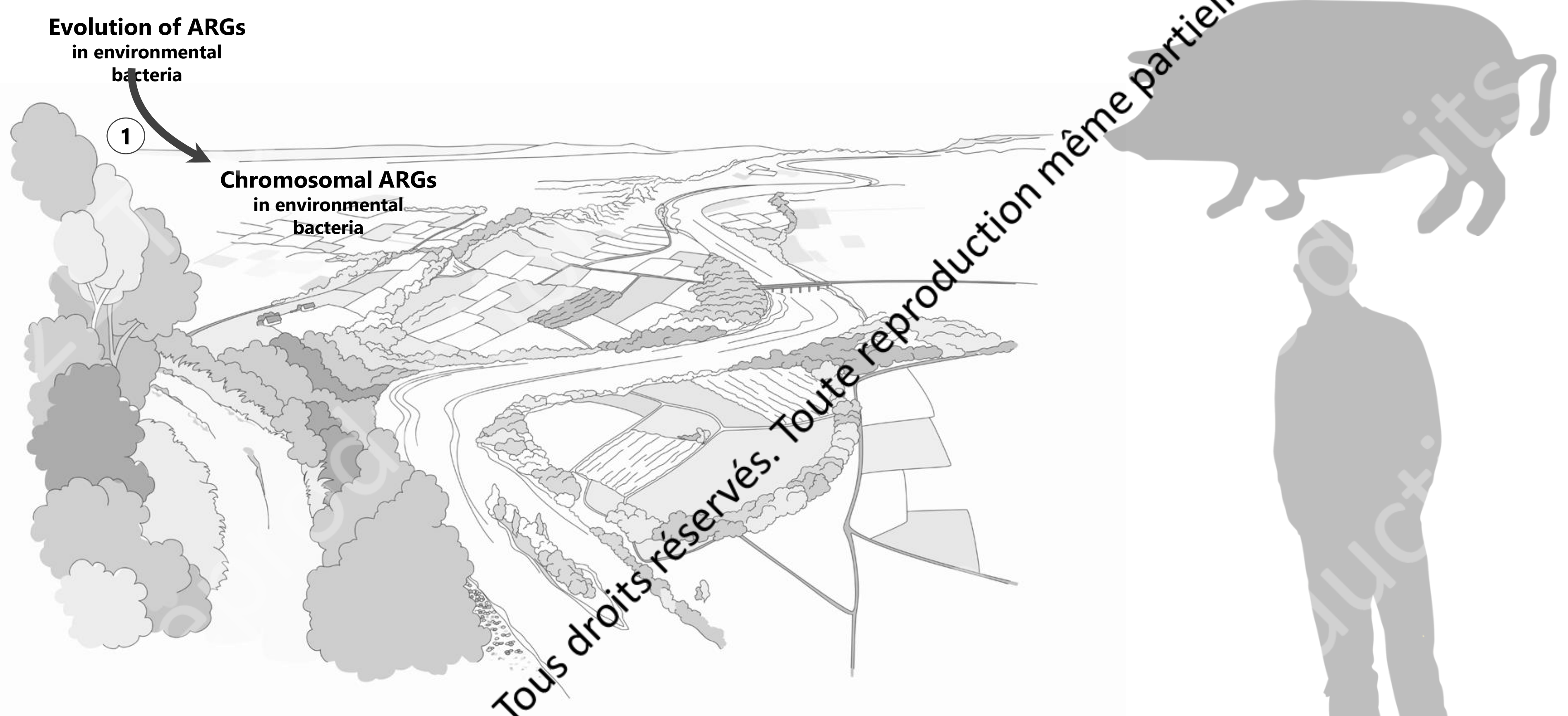
Are these genes functional?



Non-homologous ARGs



From the environment to pathogens

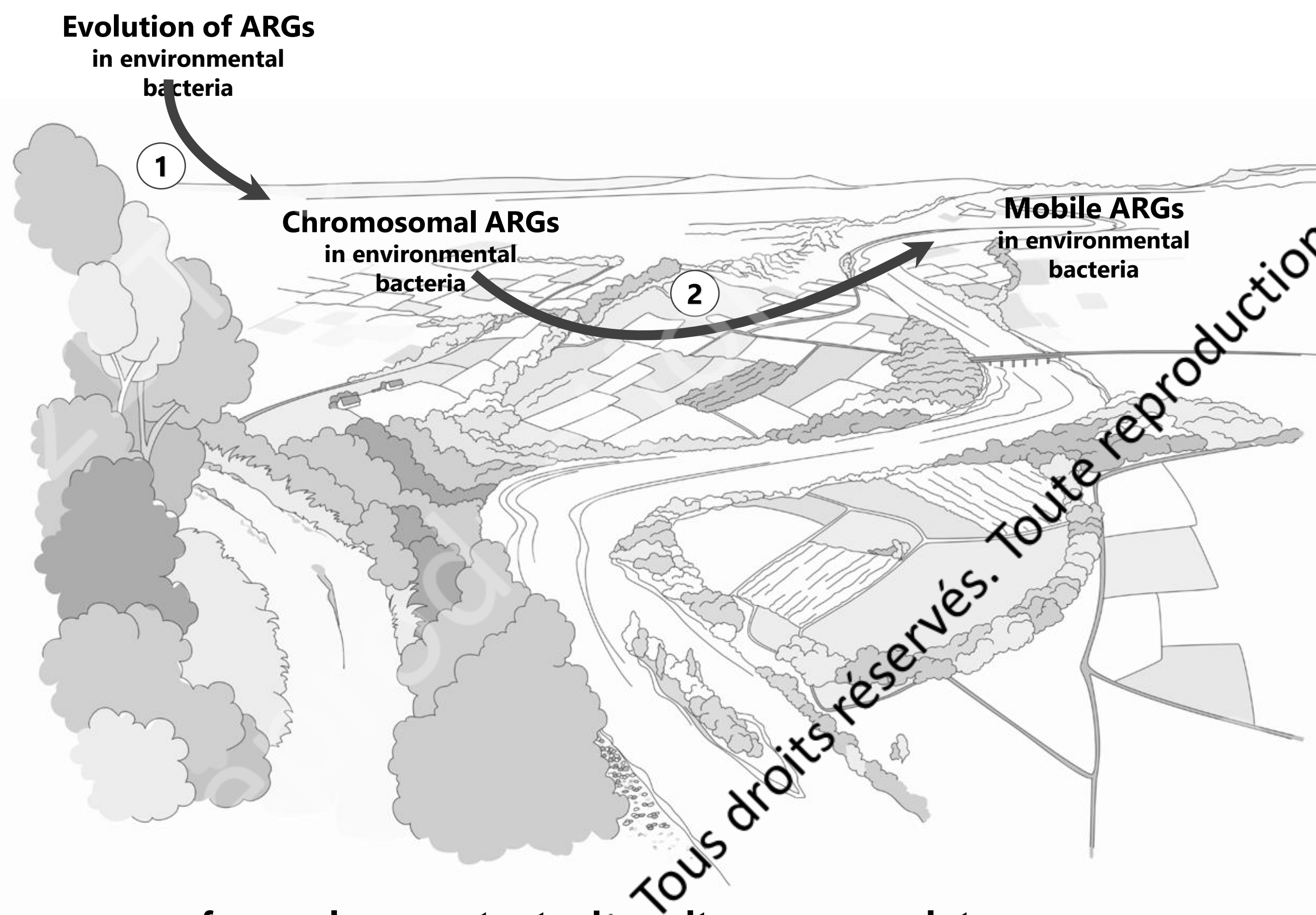


1. Emergence of gene in a context where it causes resistance

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Bengtsson-Palme et al. 2018
FEMS Microbiol Reviews

From the environment to pathogens



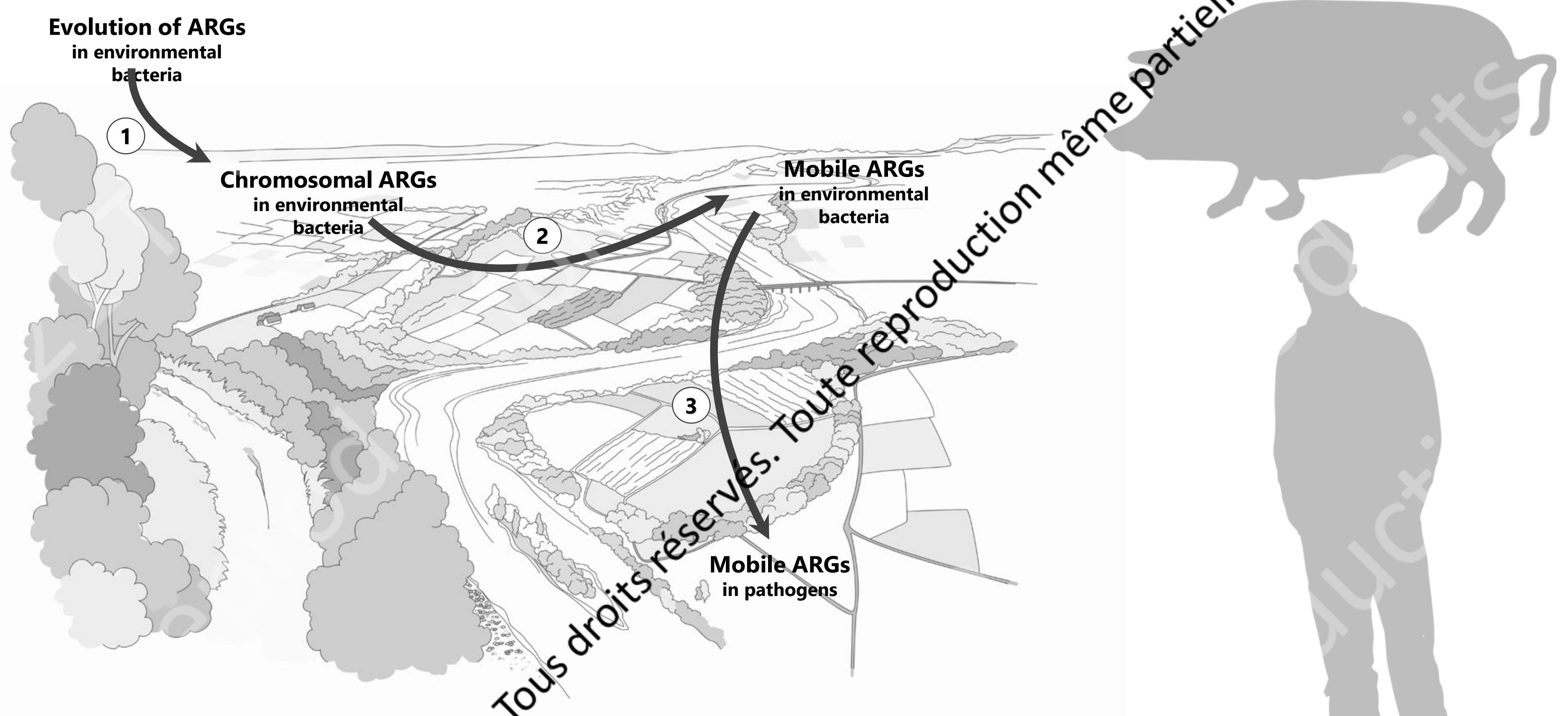
1. Emergence of gene in a context where it causes resistance
2. Mobilization of resistance gene to a mobile genetic element



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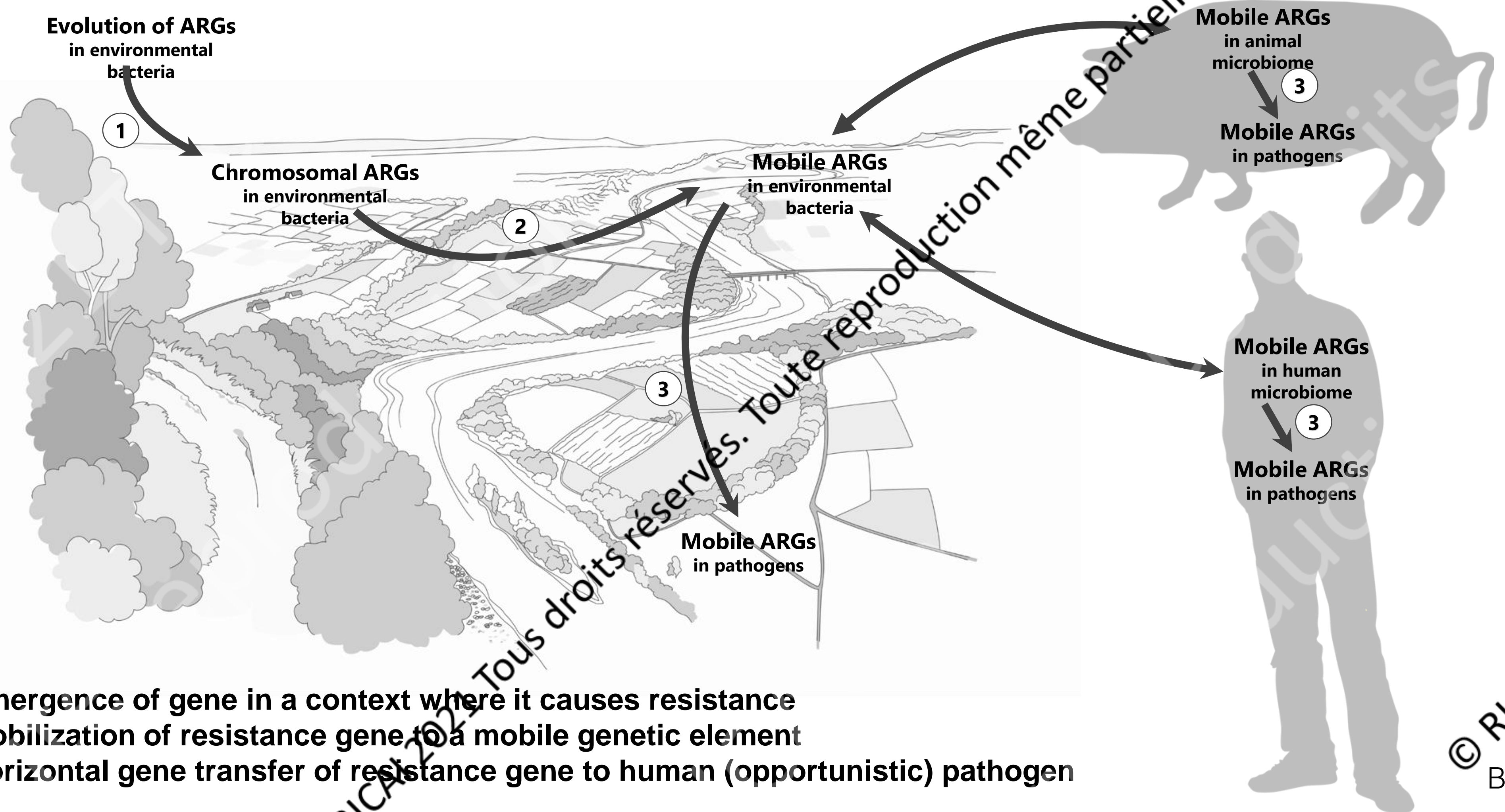
From the environment to pathogens



1. Emergence of gene in a context where it causes resistance
2. Mobilization of resistance gene to a mobile genetic element
3. Horizontal gene transfer of resistance gene to human (opportunistic) pathogen

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 Bengtsson-Palme et al. 2018
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From the environment to pathogens

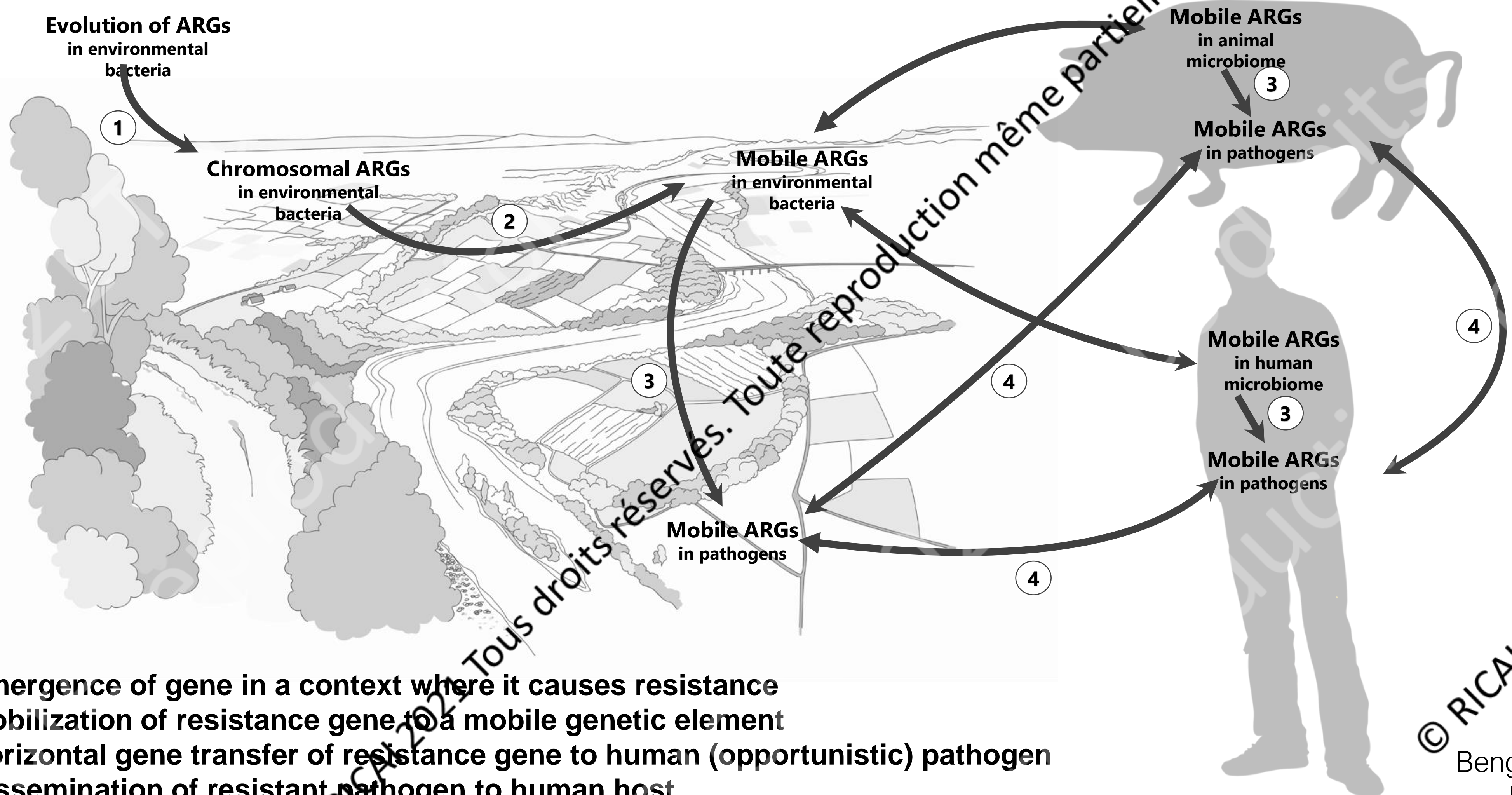


1. Emergence of gene in a context where it causes resistance
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From the environment to pathogens

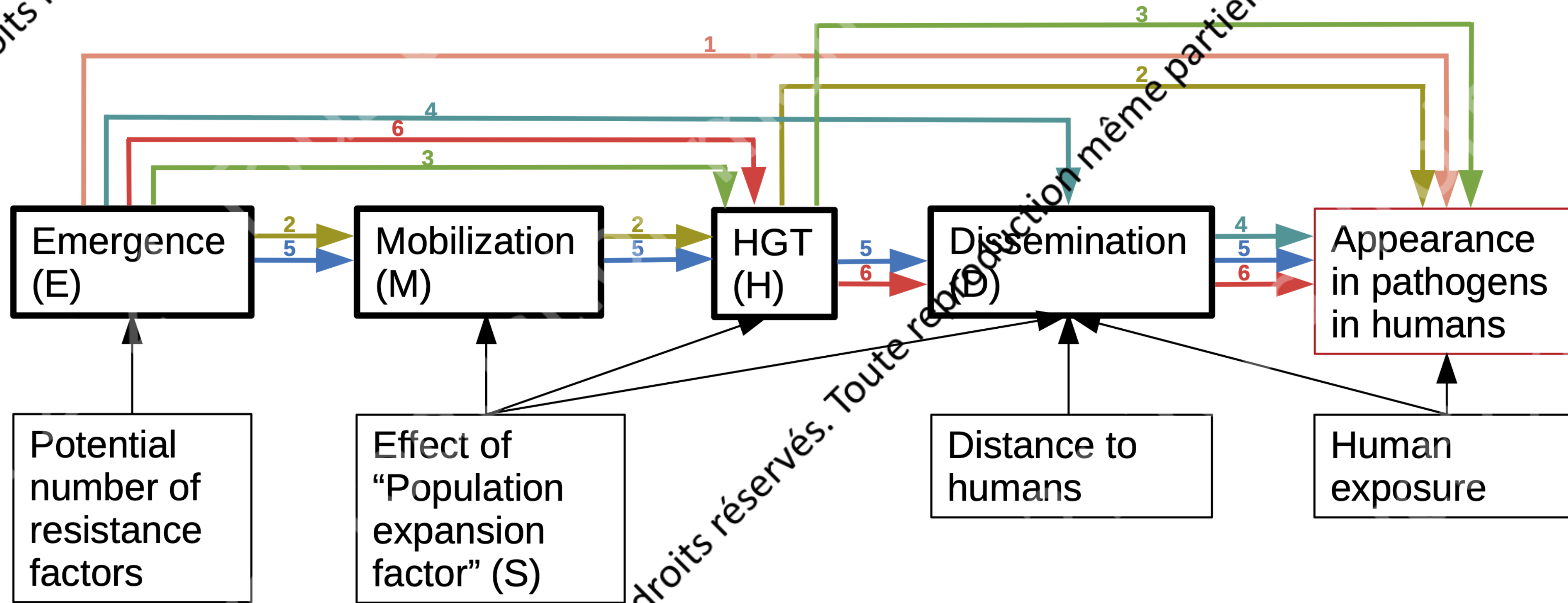


1. Emergence of gene in a context where it causes resistance
2. Mobilization of resistance gene to a mobile genetic element
3. Horizontal gene transfer of resistance gene to human (opportunistic) pathogen
4. Dissemination of resistant pathogen to human host

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Can we model this process?

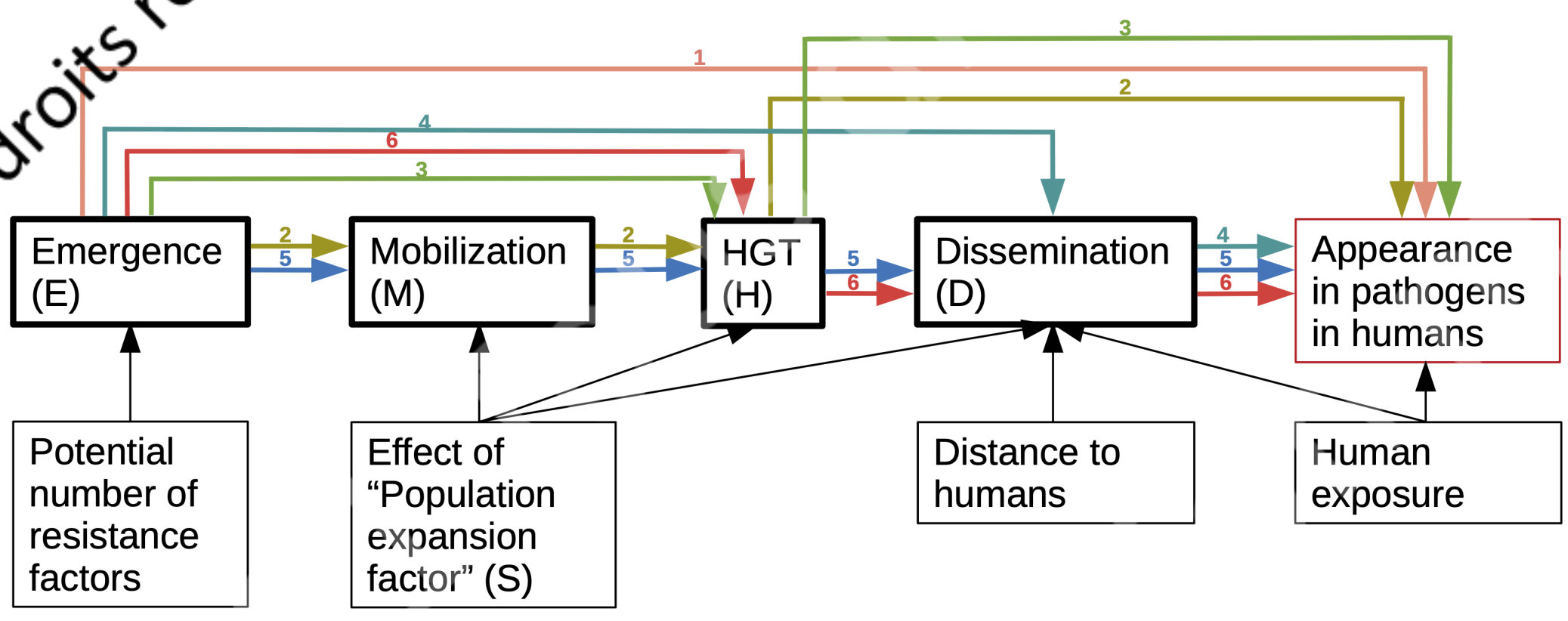


- (1) Pathogens in human microbiome
- (2) Non-pathogenic human-associated bacteria
- (3) MGEs in human-associated bacteria

- (4) Pathogens in the environment
- (5) Chromosomes of environmental bacteria
- (6) MGEs in environmental bacteria

Bengtsson-Palme et al. 2021
Environmental Science & Technology

Can we model this process?



- (1) Pathogens in human microbiome
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- (3) MGEs in human-associated bacteria
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- (6) MGEs in environmental bacteria

Description of pathway

Appearance directly on a mobile genetic element in a human pathogen

Equation

$$E1(t) = 10^{30} * P_{ph} * P_m * E * S^t$$

Appearance in non-pathogenic human bacteria, mobilized and transferred to human pathogens

$$E2(t) = 10^{30} * P_h * E * M_H * t * S^t$$

Appearance on a mobile genetic element in non-pathogenic human-associated bacteria

$$E3(t) = 10^{30} * P_h * P_m * E * H * t * S^t$$

Appearance in pathogens in environment and disseminated to humans

$$E4(t) = 10^{30} * P_p * P_m * E * S^t * D * t$$

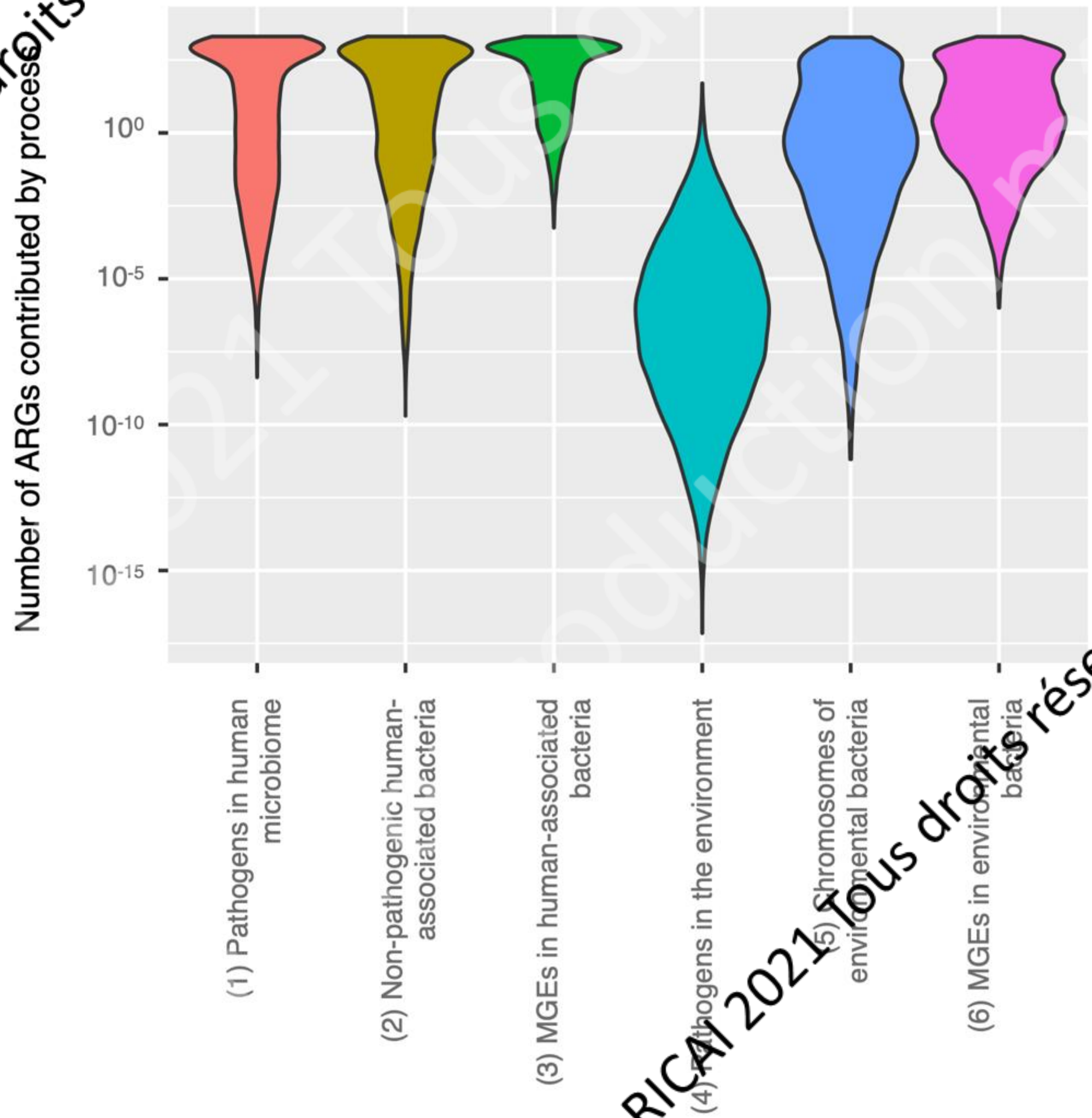
Appearance in environmental bacteria, mobilized, transferred to pathogens and disseminated to humans

$$E5(t) = 10^{30} * E * M_H * t * S^t * D * t/2$$

Appearance on a mobile genetic element in environmental bacteria, transferred to pathogens and disseminated to humans

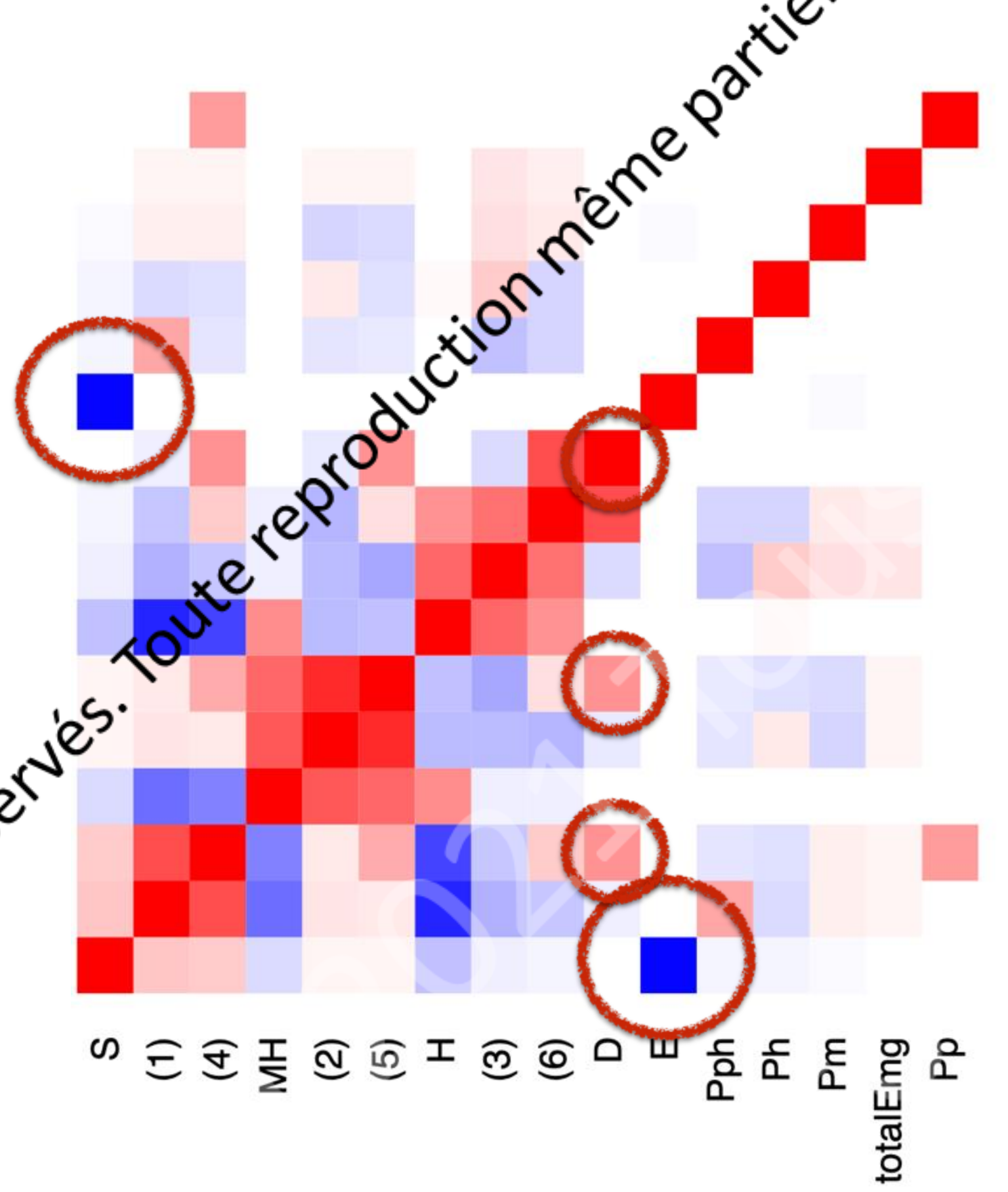
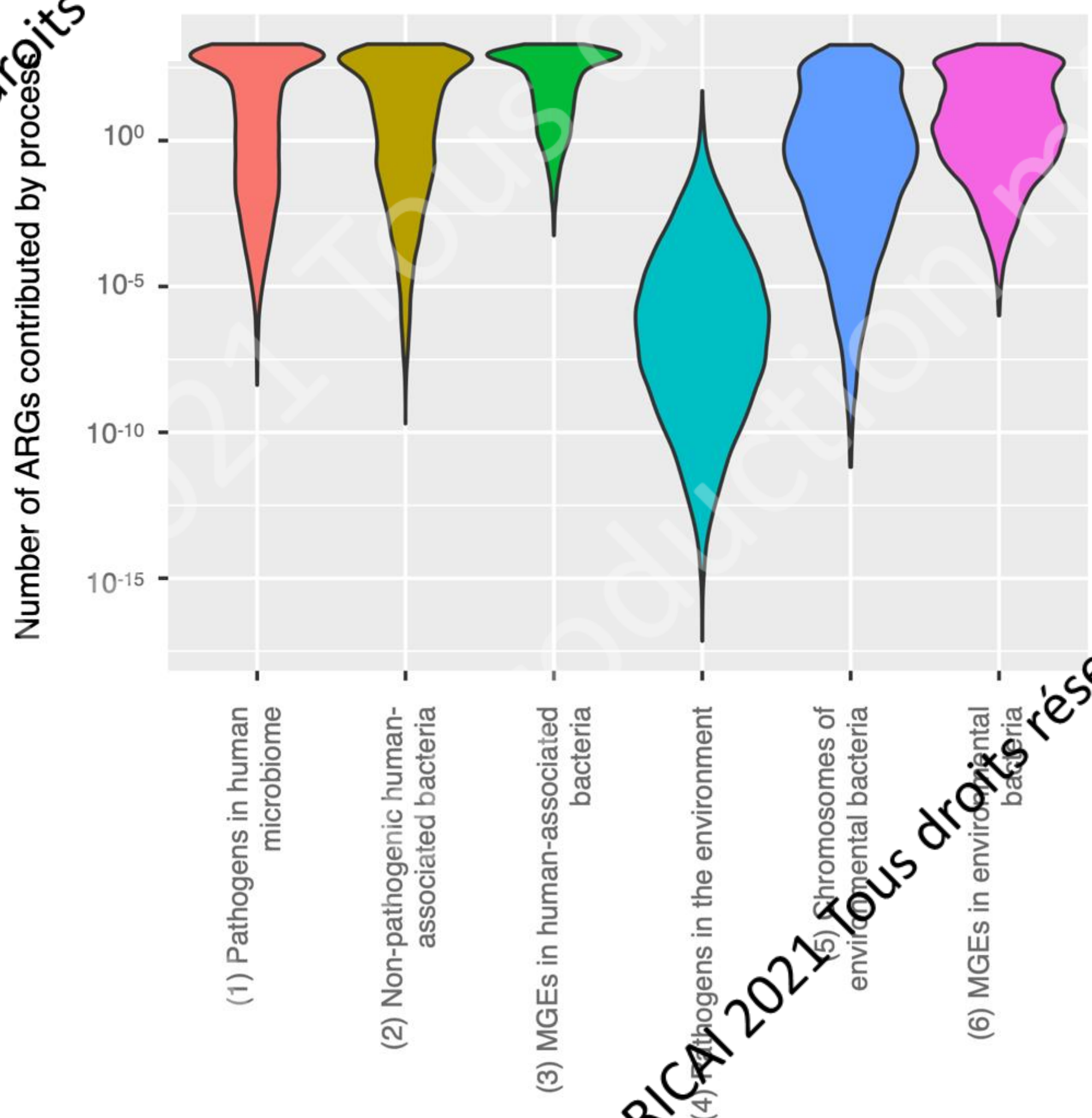
$$E6(t) = 10^{30} * P_m * E * H * t * S^t * D * t/2$$

Important processes



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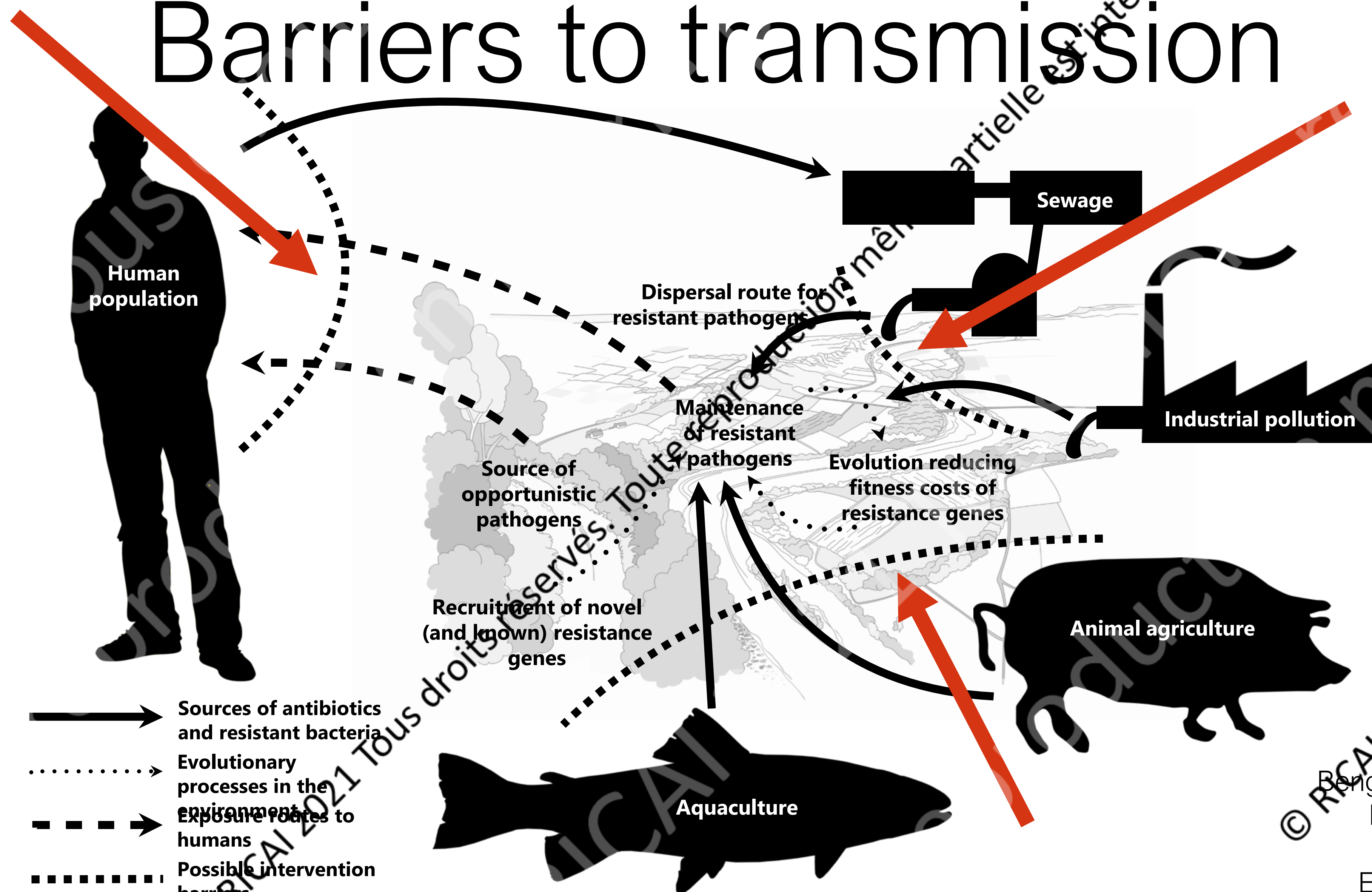
Important processes



- Fraction of all bacteria that are pathogenic (Pp)
 - Total number of ARGs in pathogens (totalEmg)
 - Proportion of mobile DNA in a bacterium (Pm)
 - Proportion of bacteria that lives in humans (Ph)
 - Proportion of pathogenic bacteria in humans (Pph)
 - Proportion of bacteria carrying a given ARG (E)
 - Dissemination rate to humans (D)
 - (6) MGEs in environmental bacteria
 - (3) MGEs in human-associated bacteria
 - Horizontal gene transfer rate (H)
 - (5) Chromosomes of environmental bacteria
 - (2) Non-pathogenic human-associated bacteria
 - Mobilization and transfer rate of ARGs (MH)
 - (4) Pathogens in the environment
 - (1) Pathogens in human microbiome
 - Population expansion rate (S)
- Pearson correlation
- 1 0 1

Bengtsson-Palme et al. 2021
 Environmental Science & Technology

Barriers to transmission



Bengtsson-Palme et al. 2018
FEMS Microbiol Reviews
Larsson et al. 2018
Environment International

Monitoring environmental resistance

Requires knowledge of background levels

- Determine important sources of resistance
- Determine important human exposure settings
- Identify changes over time
- Allow temporary interventions
- Early warning for emerging resistance threats

Requires time series data

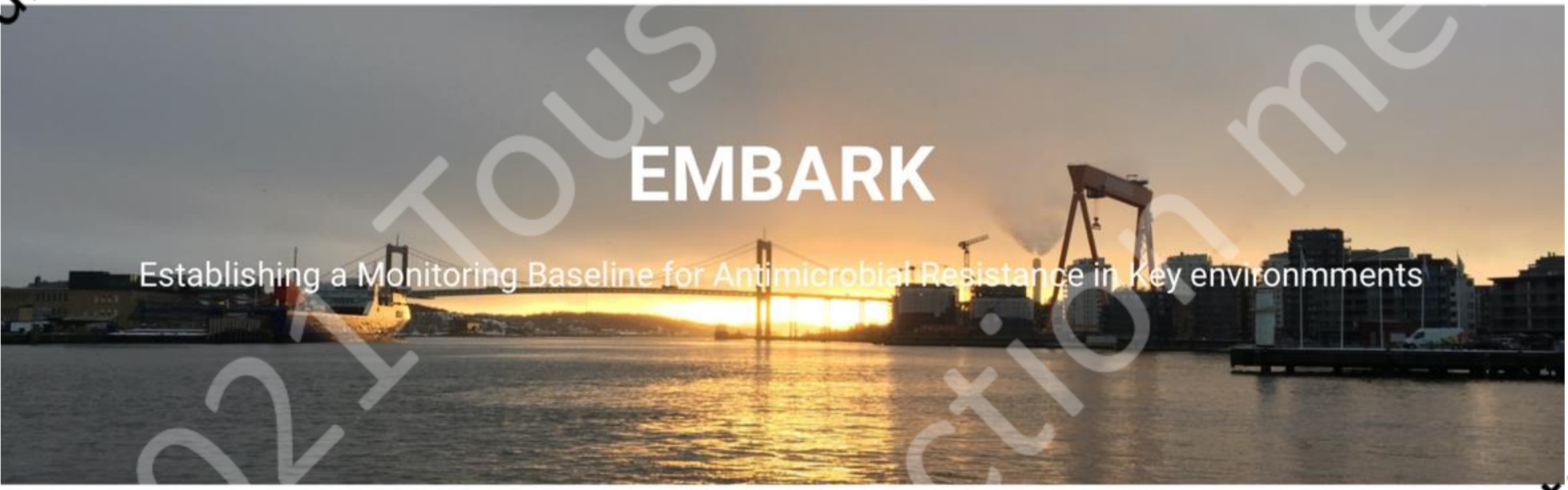
Requires methods to detect non-clinical resistance

EMBARK

- Establish a baseline for resistance in different environments
- Standardize and compare difference methods for environmental monitoring
- Develop methods to detect emerging resistance threats
- Develop a modular monitoring framework allowing comparison of data between agencies and countries

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<http://microbiology.se>

Mission
The aims and goals of the EMBARK program

Protocols
Find the protocol proposals made by the EMBARK program

The Team
Read more about the people involved in EMBARK

<http://antimicrobialresistance.eu>



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Microbiology Lab Pod

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