REVEALING POTENTIAL ANTIMICROBIAL RESISTANCE GENE MOBILITY TRENDS USING >15000 REPLICONS

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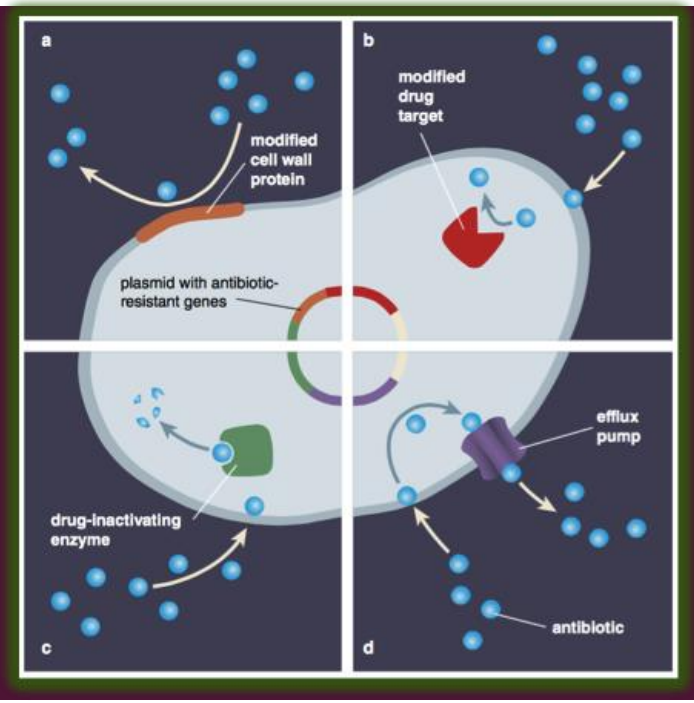
ODSI SEMINAR SERIES



https://antimicrobialresistance101.files.wordpress.com/2015/04/mechanisms-of-antibiotic-resistance.png

ANTIMICROBIAL RESISTANCE (AMR) IS ON THE RISE

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Government pledges more than £30m to fight superbugs

'Game-changing' antibiotic can kill off superbugs

By Ana Sandoiu | Published Tuesday 27 March 2018

Fact checked by Jasmin Collier

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A new study, published in the *Journal of Medicinal Chemistry*, offers the first proof that a new synthetic form of the antibiotic teixobactin can neutralize drug-resistant bacteria.

Drug resistant E.coli bacteria are already a significant problem in Europe

Antibiotic resistance is a growing problem around the world

By Anne Gulland, GLOBAL HEALTH SECURITY CORRESPONDENT

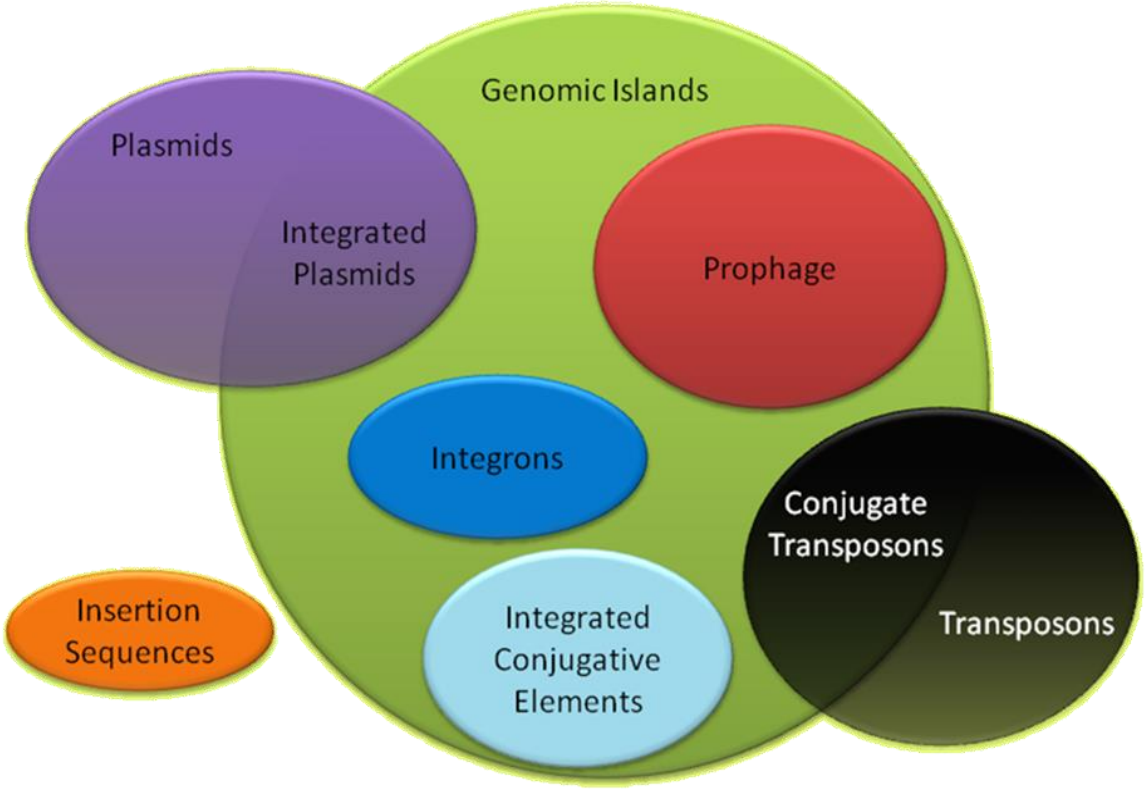
22 MAY 2018 • 11:30AM

The UK government has given the fight against deadly superbugs a boost with a pledge of £31m for the development of new drugs and diagnostics.

Need for research in understanding AMR mobility trends to improve public health AMR risk assessment and prevention

http://ww.greaterkashmir.com/cms/gall_content/2016/1/2016_1$largeimg212_Jan_2016_230832597.jpg

AMR Genes Can Be Transferred Horizontally Through Mobile Genetic Elements



(Langille et al. 2010; Nature Reviews)

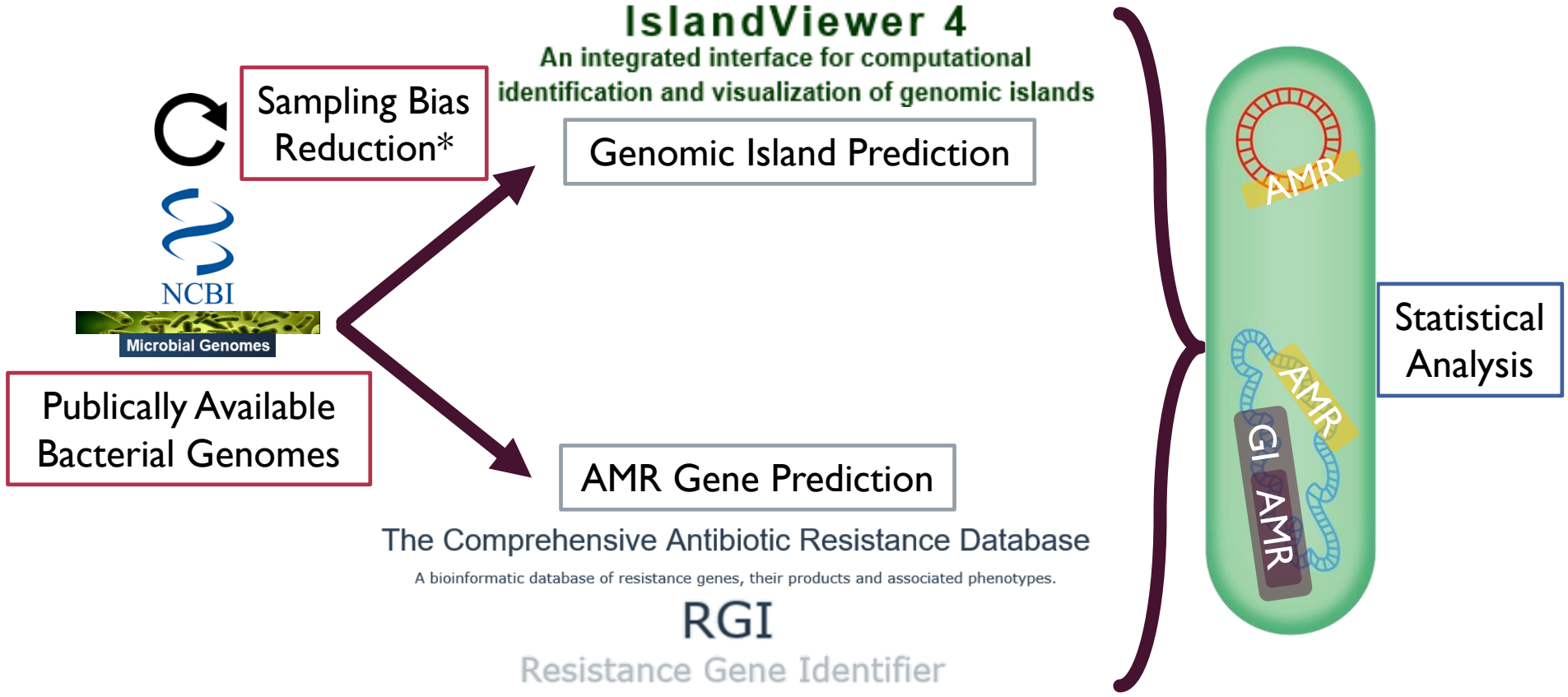
ARE THERE ANY AMR ASSOCIATIONS?

With increasing amount of genomic data, could we gain a more comprehensive understanding of AMR mobility trends that would be useful for public health AMR risk assessments?

Hypothesis:

AMR genes are disproportionally associated with mobile sequences but differences should exist for certain AMR gene classes.

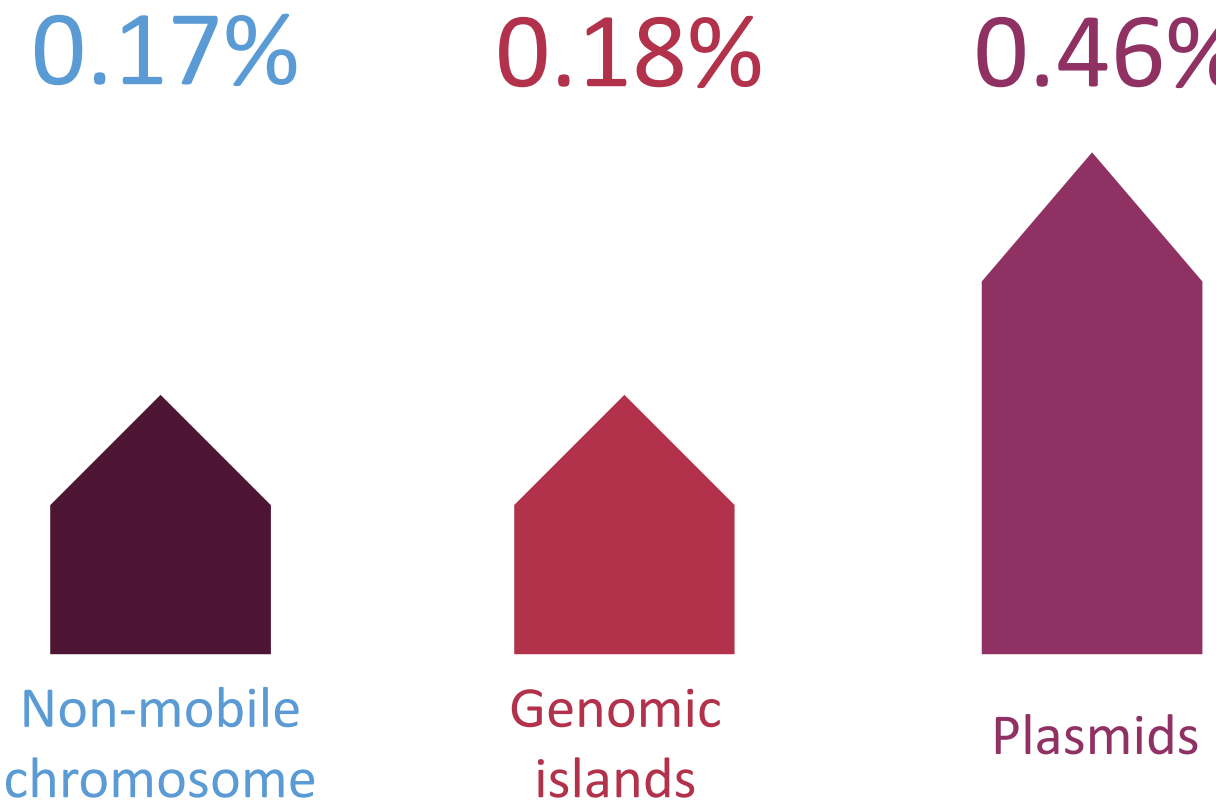
Methodology: Understanding AMR Association



*Analysis was done with and without dataset reduction

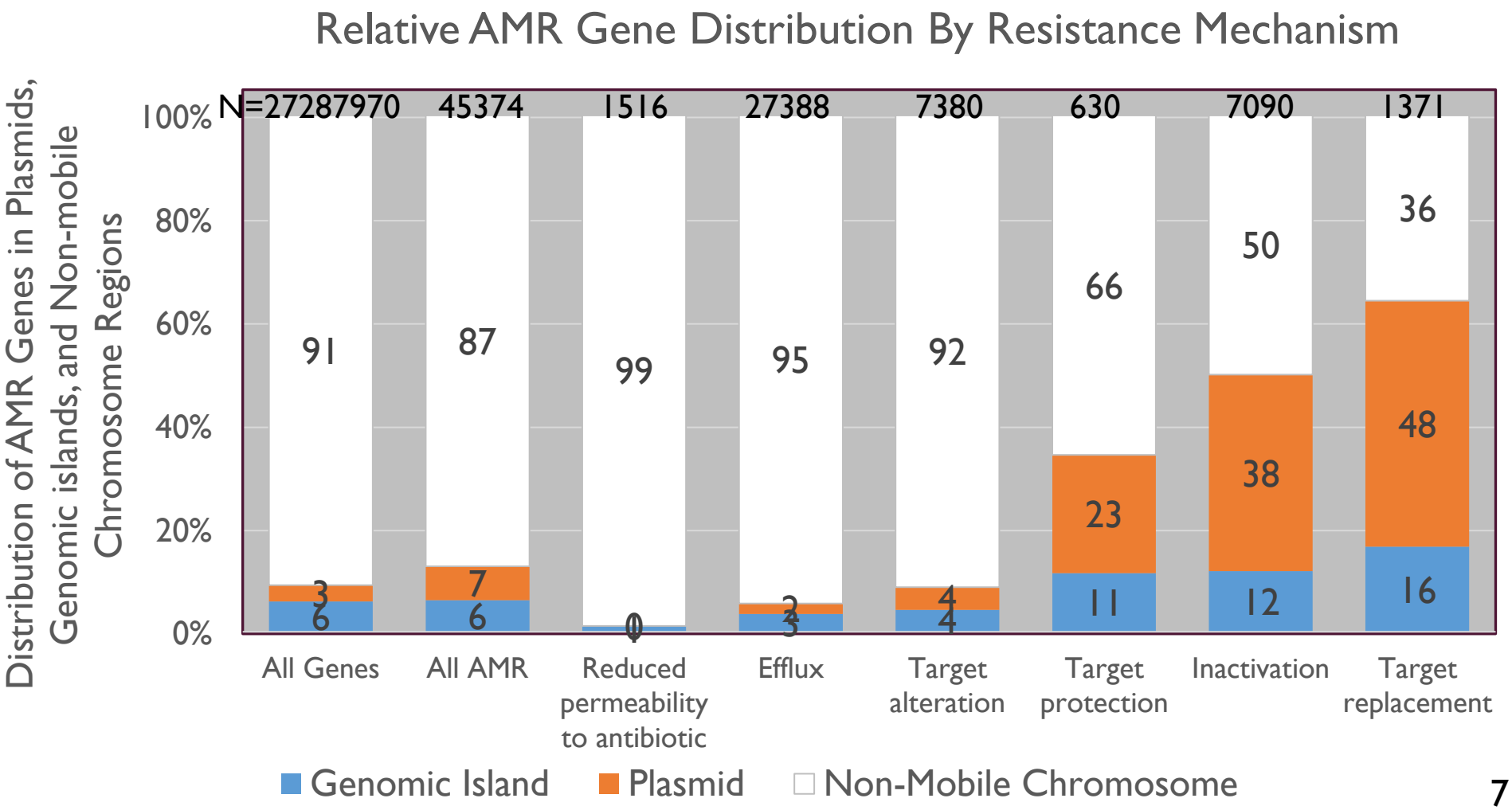
(Bertelli, C. et al. 2017, PMID:28472413)
(Jia, B. et al. 2017, PMID:27789705)

COLLECTIVELY, AMR GENES ARE DISPROPORTIONALLY FOUND IN MOBILE SEQUENCES, PARTICULARLY PLASMIDS

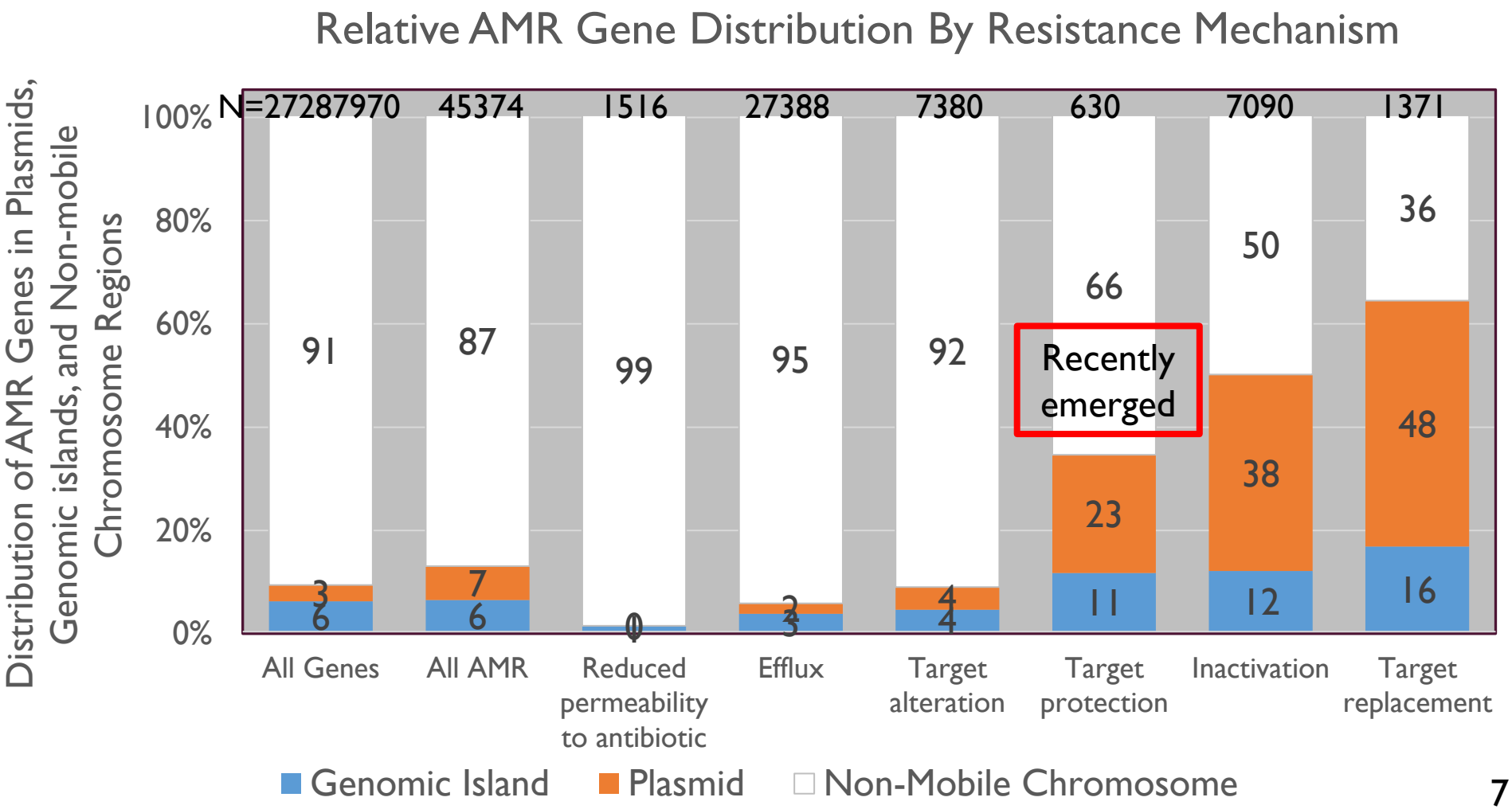


(p-value < 1e-200; note GIs are generally under predicted)

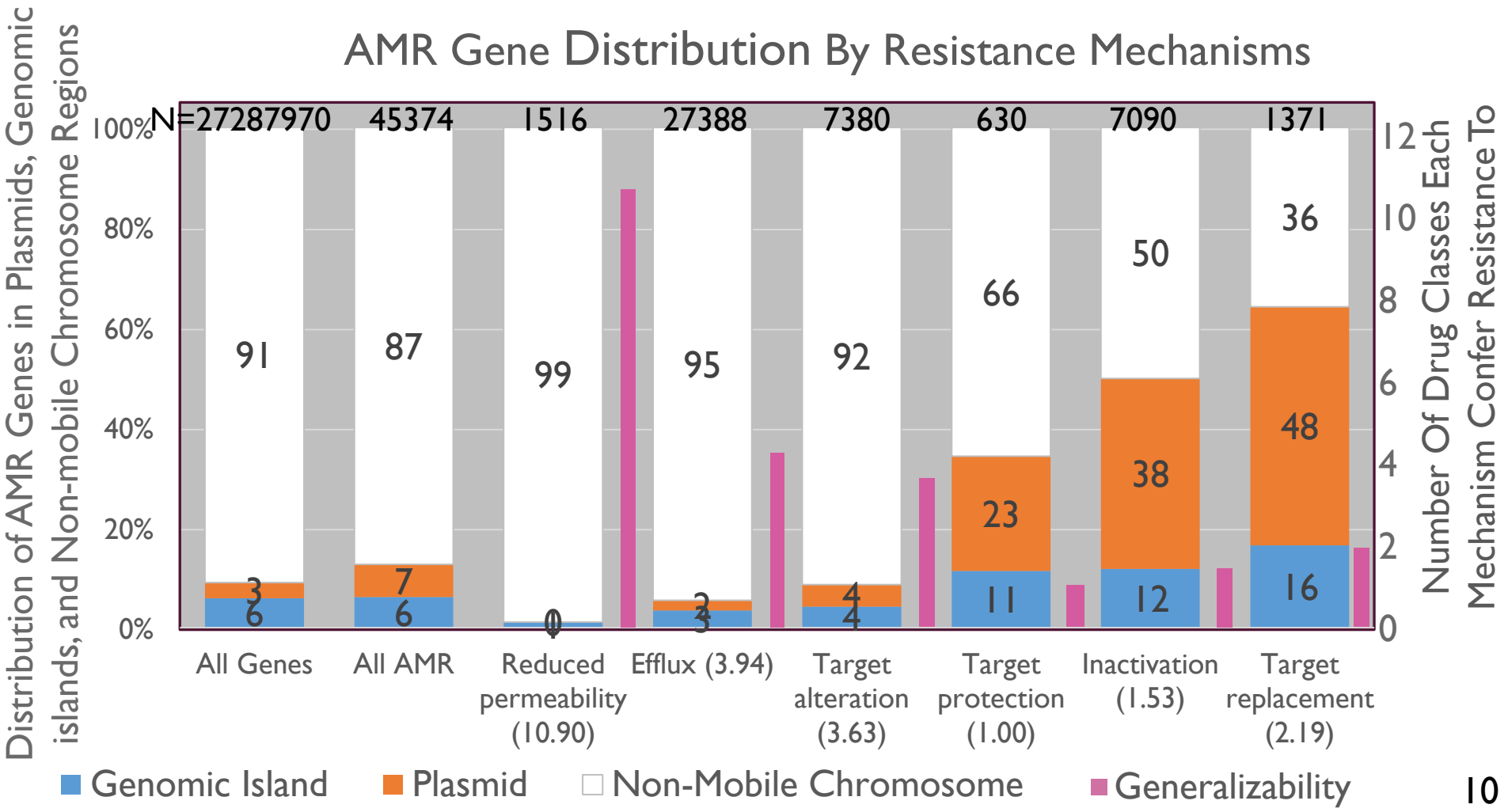
ASSOCIATIONS DEPEND ON THE AMR MECHANISM



ASSOCIATIONS DEPEND ON TIME SINCE MOBILIZATION



AMR GENES WITH LOW GENERALIZABILITY ARE ASSOCIATED WITH MOBILE ELEMENTS



SPECIALIZED AMR GENES MIGHT BE ECOLOGICAL PUBLIC GOODS

- Ecological “Public Goods” (1)
  - Specialized AMR genes are disproportionally found on mobile elements
  - Specialization requires a higher fitness cost for an individual (2)
  - AMR gene does not need to be present in all individuals in order to benefit all members of a community
  - HGT of public good traits enforces corporation in community – No cheaters!

(1. Olson M, 2009, ISBN: 97806745375 14; 2. Andersson DI, 2010, PMID: 20208551)

SUMMARY & FUTURE DIRECTIONS

AMR Mobility

{Mechanism of Action+ Time Since Acquisition + Specialization + Community Benefits + ???}

Identification of highly mobile AMR determinants and patterns of AMR mobility will provide a basis for improving metagenomics AMR prediction and for prioritizing AMR related risks in public health

THANK YOU!
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CRSNG

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