

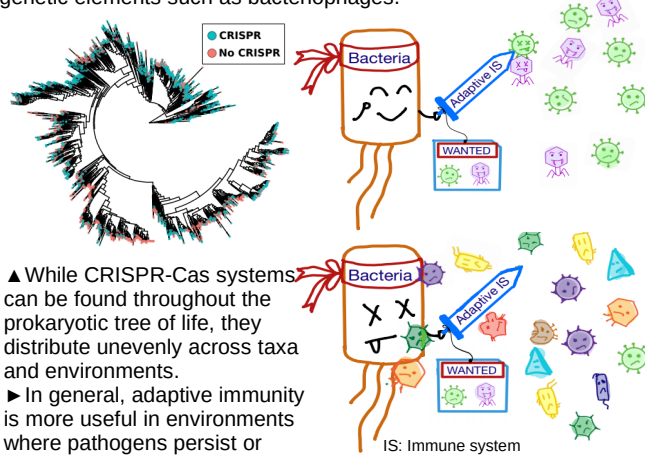
Ecological drivers of CRISPR immune systems

Wei Xiao, Jake L Weissman, Philip L F Johnson

College of Computer, Mathematical, and Natural Sciences, University of Maryland

Introduction

CRISPR-Cas is the only known adaptive immune system of prokaryotes. It is a powerful defense system against mobile genetic elements such as bacteriophages.



▲ While CRISPR-Cas systems can be found throughout the prokaryotic tree of life, they distribute unevenly across taxa and environments.

► In general, adaptive immunity is more useful in environments where pathogens persist or reoccur.

Theoretical models have predicted that CRISPR is ideal in low pathogen density environments,^[1] where the microbe density is likely to be low as well. A recent experiment showed that microbes were more likely to acquire CRISPR immunity in environments with more host diversity.^[2] Given this theory and experiment, we sought to test hypotheses connecting CRISPR incidence with prokaryotic density/diversity by analyzing 16S rRNA and metagenomic data from publicly available environmental sequencing projects.

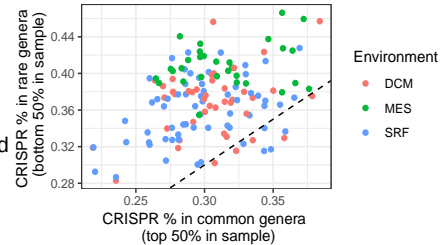
Methods

	Source	Pros & Cons	Microbe Density/Diversity Source	
			Density	Diversity
(1)	Identify CRISPR arrays with CRISPRCasFinder from Complete genomes in Refseq	Certain and complete but less accurate about environments	Reads of 16s rRNA	
(2)	Identify CRISPR arrays from metagenome-assembled genomes or cas2 gene from metagenomic samples	Less complete but more ecologically relevant	metagenome-assembled genomes	Metagenomic samples

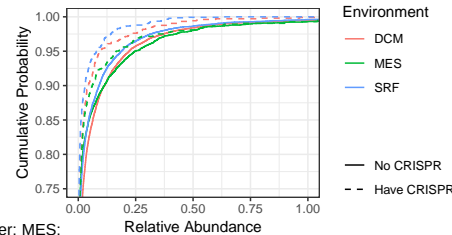
Results

CRISPR-Density (Compare within sample)

- Method (1): 139 samples from Tara Ocean Project.
- CRISPR systems are significantly favored in lower abundance (less dense) taxa and disfavored in higher abundance taxa.



- Method (2): 2631 Tara Ocean metagenome-assembled genomes.
- The probability of having CRISPR array as found by CRISPRCasFinder accumulates faster in lower relative abundance genomes.



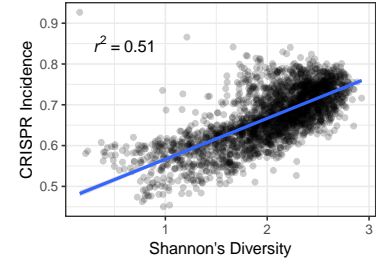
DCM: deep chlorophyll maximum layer; MES: mesopelagic Zone; SRF: upper layer zone

Conclusion

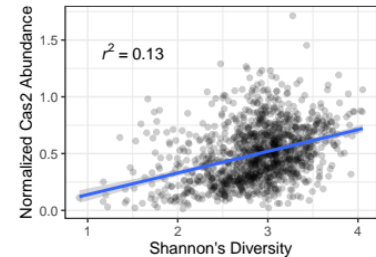
Our results show patterns consistent with previous modeling of density^[1] and previous experiment manipulates diversity^[2]. Together, these observations confirm that, at least in certain types of environments, the prokaryotic ecological context indeed plays a key role in selecting for CRISPR immunity, potentially due to correlations with pathogen dynamics.

CRISPR-Diversity (Compare between samples)

- Method (1): ~2000 oral 16s rRNA samples from Human Microbiome Project.
- CRISPR system incidence significantly correlated with diversity in human oral environments.



- Method (2): ~2000 metagenomic samples from Human Microbiome Project.
- The normalized cas2 abundance significantly correlated with diversity in human oral environments.



[1]. Mayer, Andreas, et al. "Diversity of immune strategies explained by adaptation to pathogen statistics." Proceedings of the National Academy of Sciences 113.31 (2016): 8630-8635. [2] Alseth, Ellinor O., et al. "Bacterial biodiversity drives the evolution of CRISPR-based phage resistance in *Pseudomonas aeruginosa*." bioRxiv (2019): 586115.