Single Nucleotide and Amino Acid Substitutions - Small Alterations with Big Effects

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ABSTRACT

The consequences of single nucleotide polymorphisms leading to non-synonymous and synonymous non-silent mutations are challenging to predict without an associated phenotype. However, bacterial core genomes are characterized by single nucleotide polymorphisms whereby the consequences mainly remain to be explored. In this talk I describe the consequences of single nucleotide polymorphisms that occurred unintentionally or by natural selection in the genomes of *Salmonella typhimurium* and *Escherichia coli*. Rdar biofilm formation characterized by the expression of the extracellular matrix components amyloid curli fimbriae and the exopolysaccharide cellulose is controlled by the transcriptional regulator CsgD, a major regulatory hub. Rdar bioflm formation is an anti-virulence factor involved in the balance between environmental survival and acute virulence. However, already single nucleotide polymorphisms can shift this balance. For example, we and others identified single nucleotide alterations in the *csgD* promoter region that determine the expression pattern of a highly regulated versus a constitutive rdar morphotype (Romling *et al*., 1998; Xiang *et al*., 2024; Li *et al*., 2024). Cyclic di-GMP is a ubiquitous second messenger that positively regulates rdar biofilm formation and *csgD* expression. Single nucleotide polymorphisms in cyclic di-GMP turnover proteins can thereby shift the balance between rdar biofilm formation and acute virulence (Cimdins *et al.*, 2017*;* Sokaribo *et al*., 2021). Beyond *S. typhimurium* and *E. coli* is the cyclic di-GMP/cyclic di-nucleotide signaling network a major hotspot for synonymous mutations that can have far reaching effects (Romling *et al*., 2023; Cao *et al*., 2024; Li *et al*., 2022). Consequently, the plasticity of bacterial genomes remains mainly unexplored.

Keywords: Jensen Inequality, Concave Utility, Convex Analysis, Expected Utility, Risk Aversion.

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