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The structure of bacterial Mfd dictates the pathogenicity in *Bacillus cereus*

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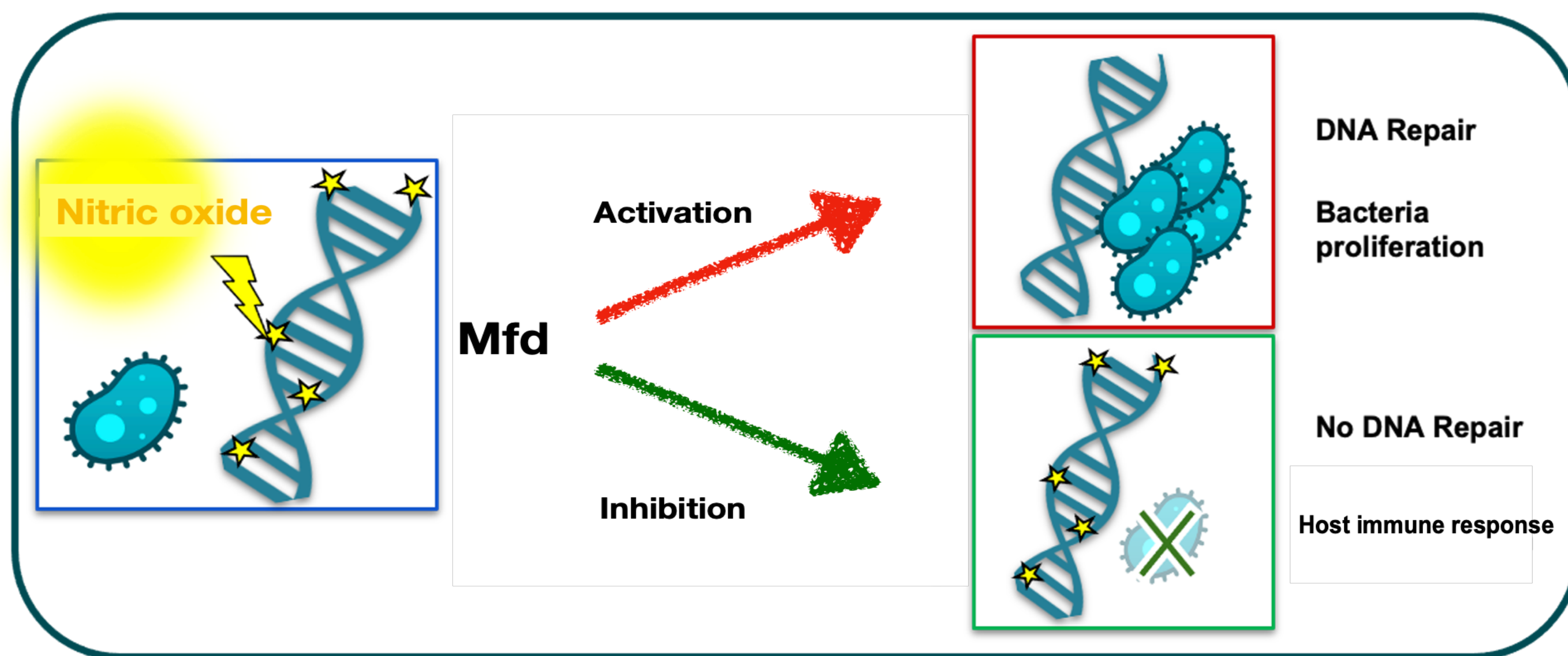
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Mfd -Mutation frequency decline- protein is ubiquitous and involved in bacterial DNA repair. Mfd confers bacterial protection against the nitric oxide immune response mounted by the host during infection¹⁻². Mfd preserves DNA integrity, helps to repair DNA damage. Reversely, its neutralization empowers the host immune system.

Issue: are there patterns in sequence, and 3D markers in structure of Mfd that could explain the clinic vs non-pathogenic phenotype of *Bacillus cereus*?

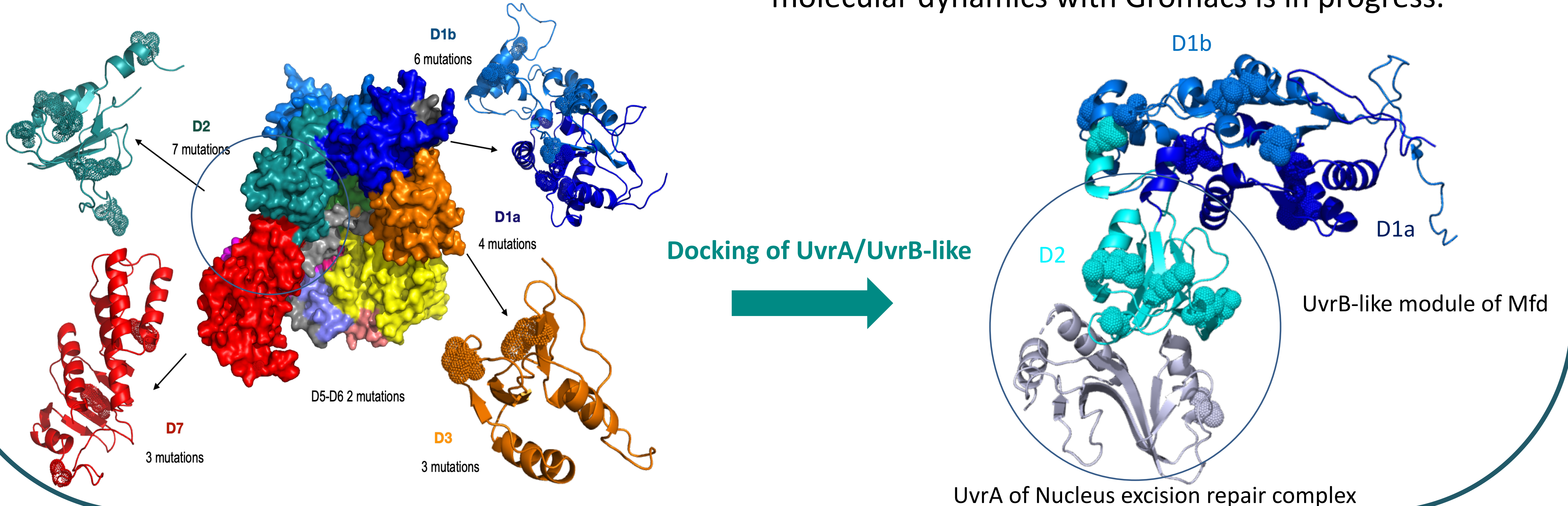
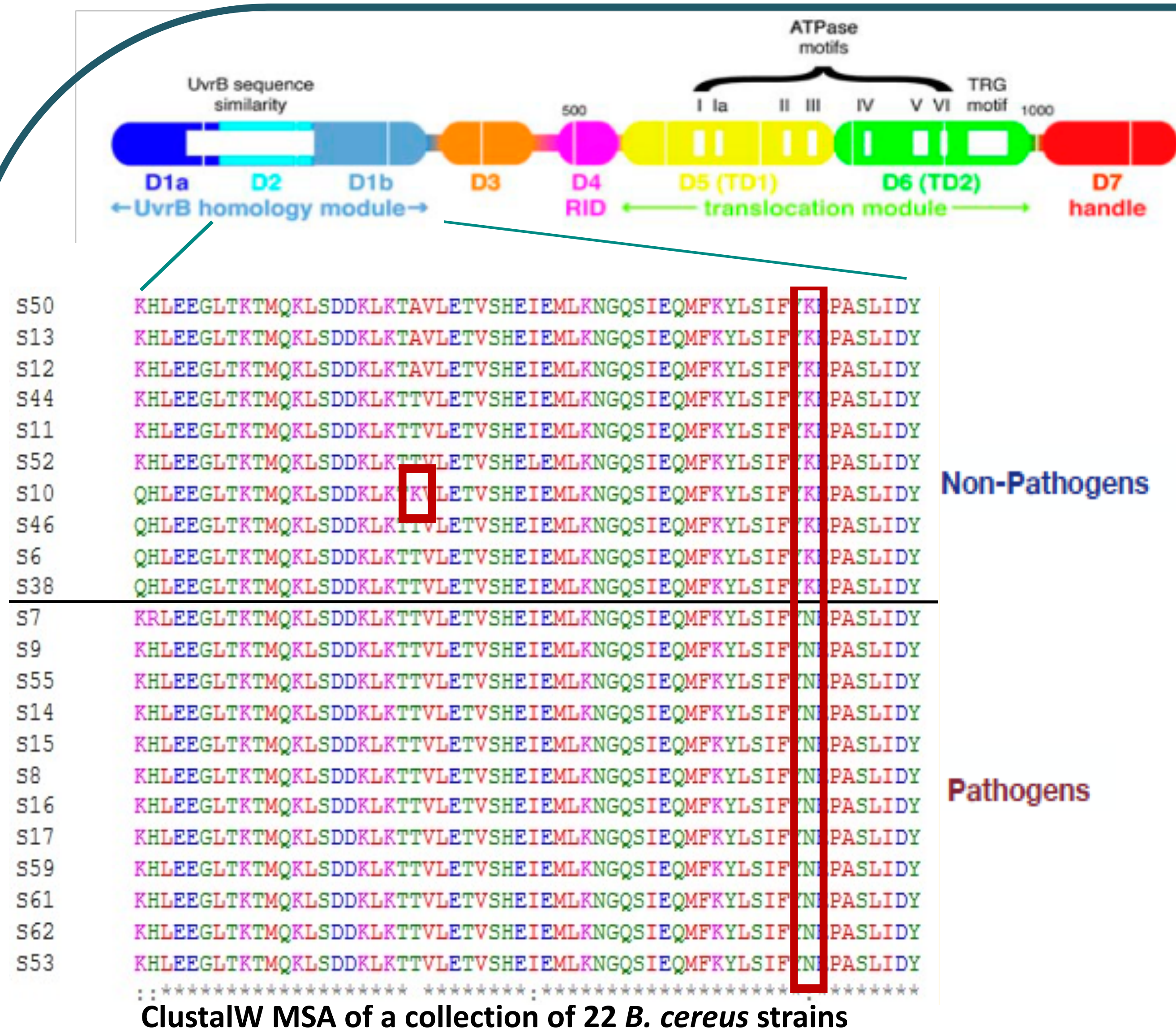


Method We did multiple sequence analysis (MSA) of a collection of *B. cereus* strains with conflicting pathogenicity signatures. The two most distant Mfd were homology modeled and analyzed with respect to solved structures of Mfd from *E. coli*³⁻⁴. To assess the relevance of the mutation ratio, we did MSA within the same collection for house-keeping genes with distinct expression level PykA and FtsZ.

Results

Based on Mfd sequences alignment, clinical and non pathogenic strains could be separated in two clusters. In total, 28/1176 residues are distinct between the most distant strains S50 and S53. They located on UvrB homology module. To infer on putative co-evolution, we performed a MSA for the protein partner UvrA. UvrA shows the same profile of pathogenic/non pathogenic as Mfd and a higher level of substitutions while PykA and FtsZ show hardly any mutations.

Interaction of UvrA/UvrB homology module has been modelled using solved complex from *E. coli*³⁻⁴. It requires the disruption of D2/D7 interaction but engages a conserved interface. Refinement through molecular dynamics with Gromacs is in progress.



Mfd alignment in *B. cereus* separates pathogenic vs non pathogenic strains. Using an *in vivo* insect model of infection, we are currently testing if *mfd* gene of a pathogenic strain complements a non-pathogenic strain and *vice-versa*, if Mfd gene of a non-pathogenic strain could complement the virulent phenotype of a pathogenic strain. Also, residues identified as substituted will be shortly site-directed mutated.

¹ C. Darrigo, *et al* 2016, doi: 10.1371/journal.pone.0163321.

² E. Guillemet, *et al*, "2016, doi: 10.1038/srep29349.

³ A. M. Deaconescu, *et al*, 2006, doi: 10.1016/j.cell.2005.11.045

⁴ A. M. Deaconescu, *et al*, 2012, doi:10.1073/pnas.1115105109