The structure of bacterial Mfd dictates the pathogenicity in Bacillus cereus

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

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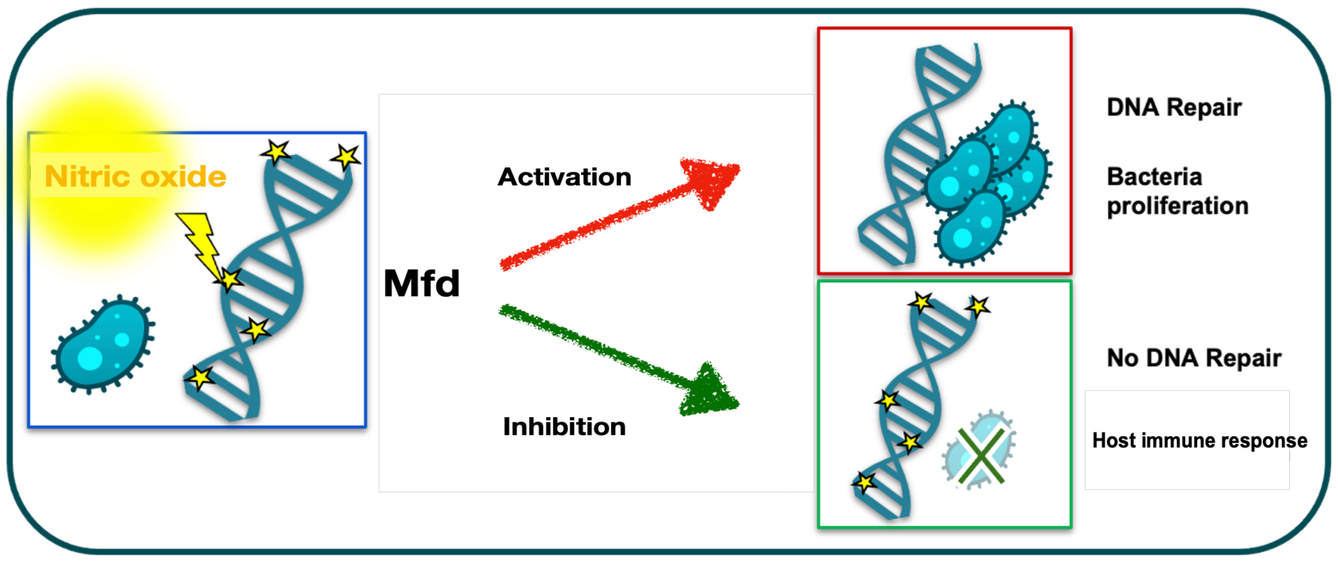
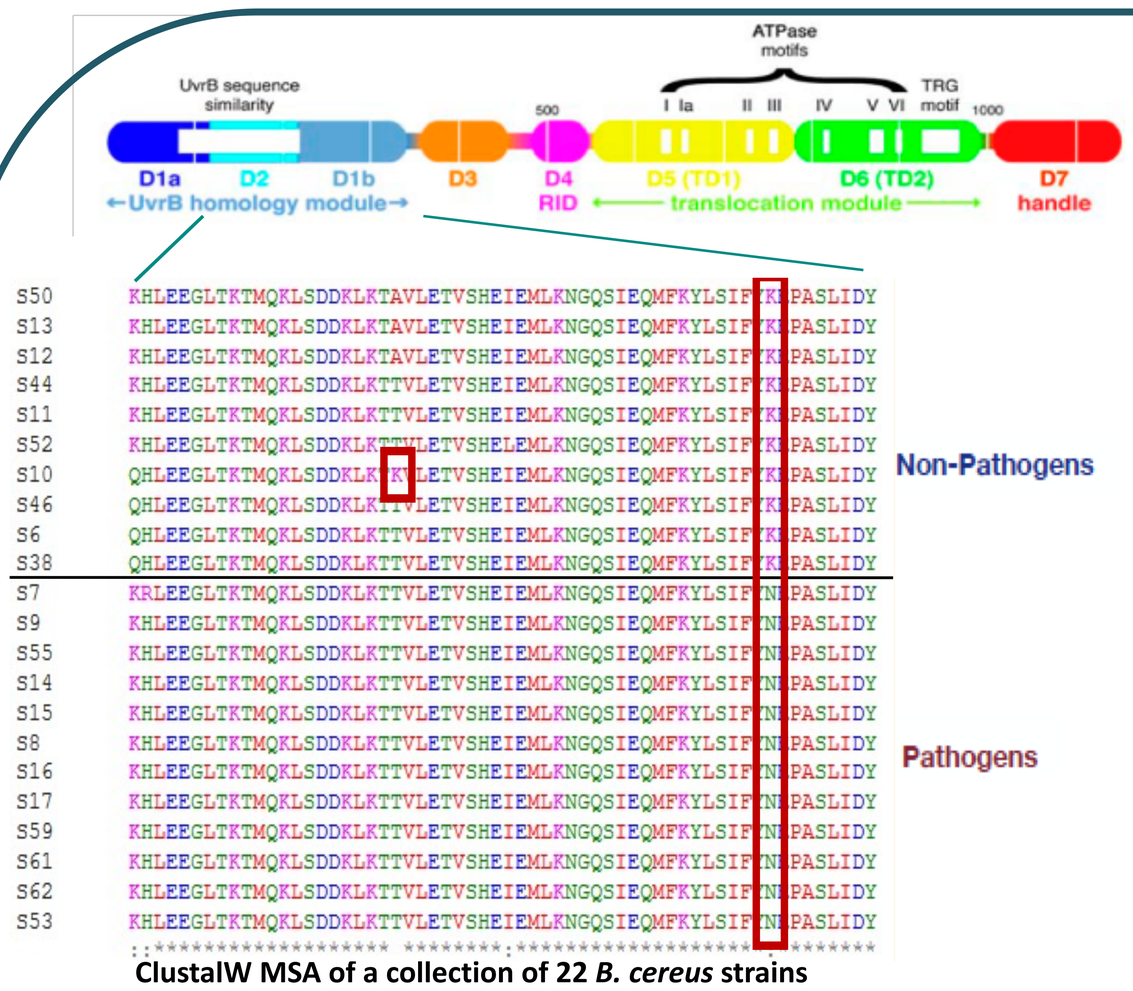
Mfd -Mutation frequency decline- protein is ubiquitous and involved in bacterial DNA repair. Mfd confers bacterial protection against the nitric oxid immune response mounted by the host during infection[1-2]. Mfd preserves DNA integrity, helps to repair DNA damage. Reversely, its neutralization empowers 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.

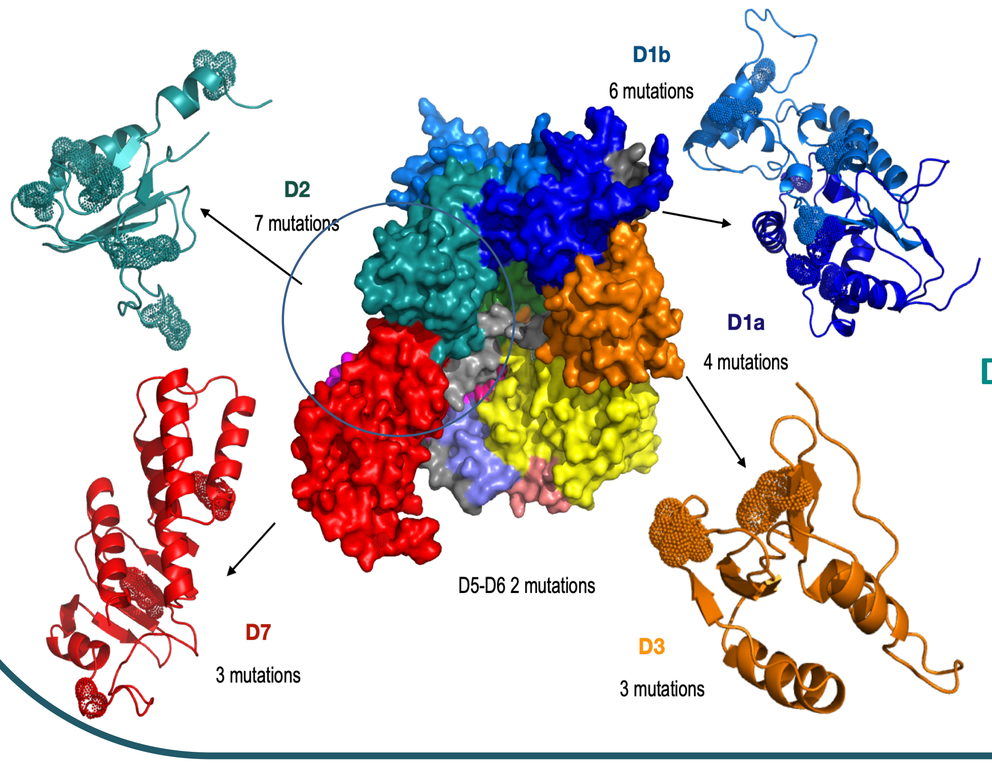


ClustalW MSA of a collection of 22 *B. cereus* strains

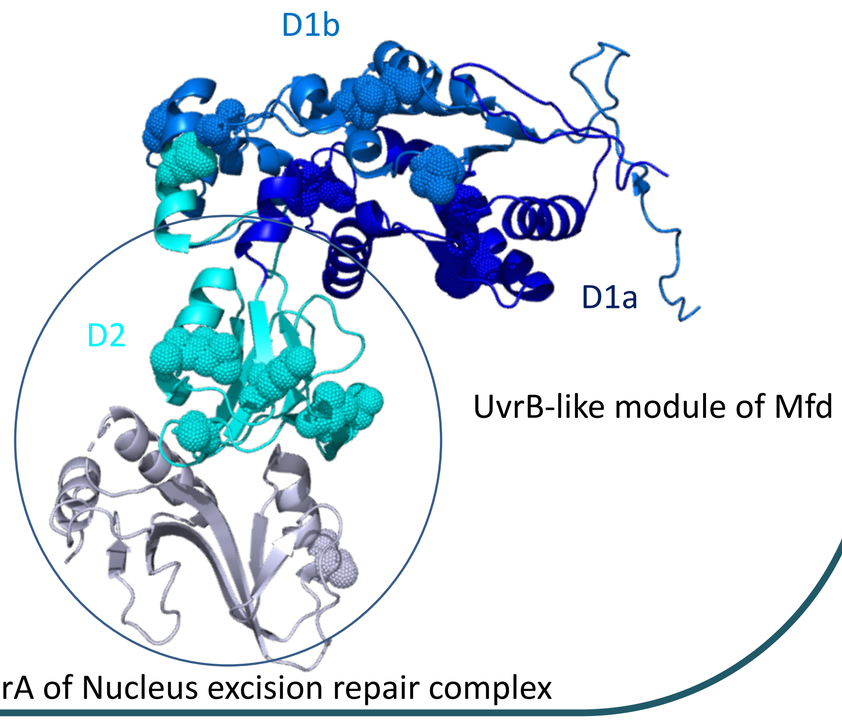
Results

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.



Docking of UvrA/UvrB-like



UvrB-like module of Mfd

UvrA of Nucleus excision repair complex

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.

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[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