

In silico investigation of MexBA-OprM efflux pump

Our team :

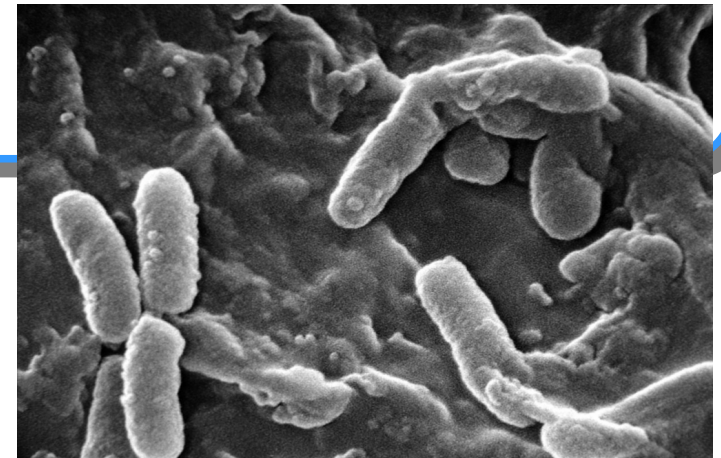
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- Clément Moroldo



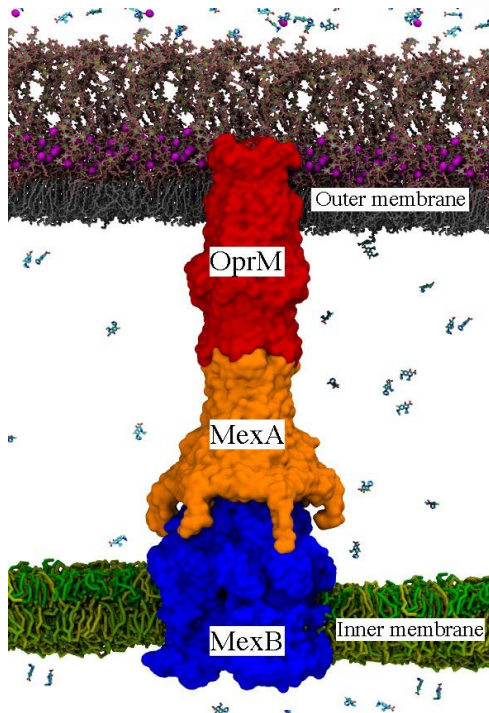
DSIMB DE-Assembly

- **Context**

- Pathogenous gram-negative bacterium: *Pseudomonas aeruginosa*
- Causes nosocomial diseases
- Antibiotics multi-resistant strains



Pseudomonas aeruginosa scanning microscopy

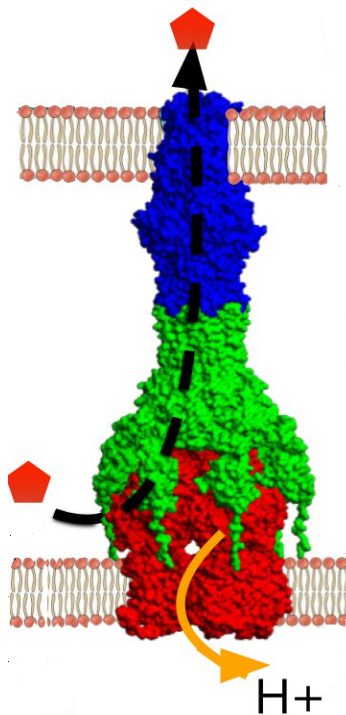


- Resistance mechanism is known
- Efflux pump overexpression : MexAB-OprM
- Tripartite pump

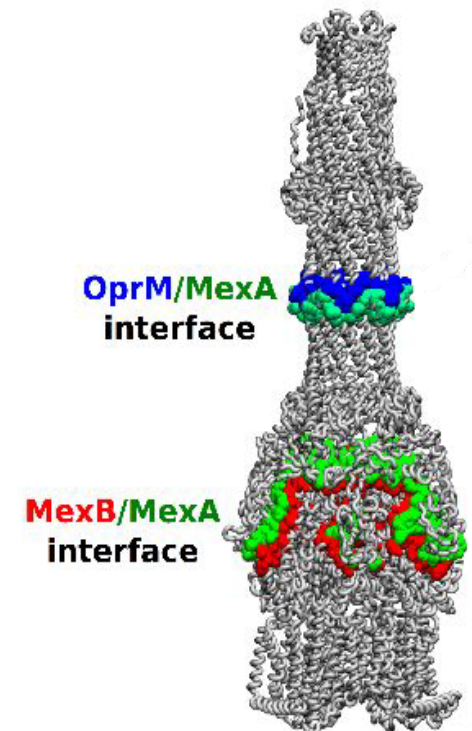
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Problematic

How to inhibit MexAB-OprM efflux pump to make antibiotic efficient against multi-resistant *Pseudomonas* strains?



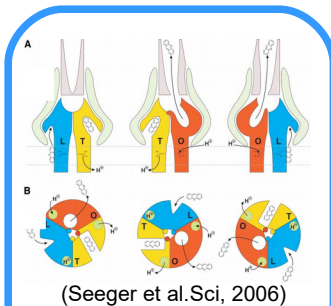
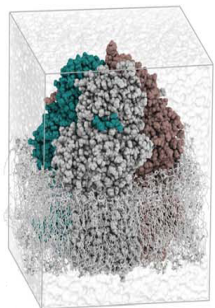
- Difficulty to obstruct the canal
- To target interfaces between partners
- To target assembling mechanism
- To target efflux mechanism



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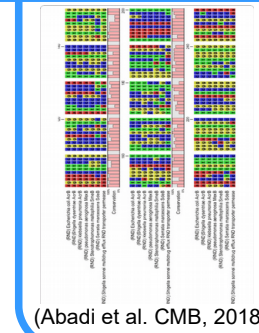
Investigations – To find a key region

Molecular Dynamics

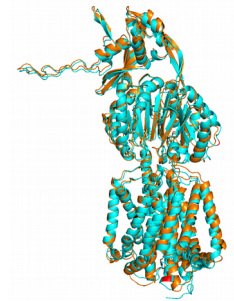


Structural analysis

Sequence analysis



(Abadi et al. CMB, 2018)



Comparison based study

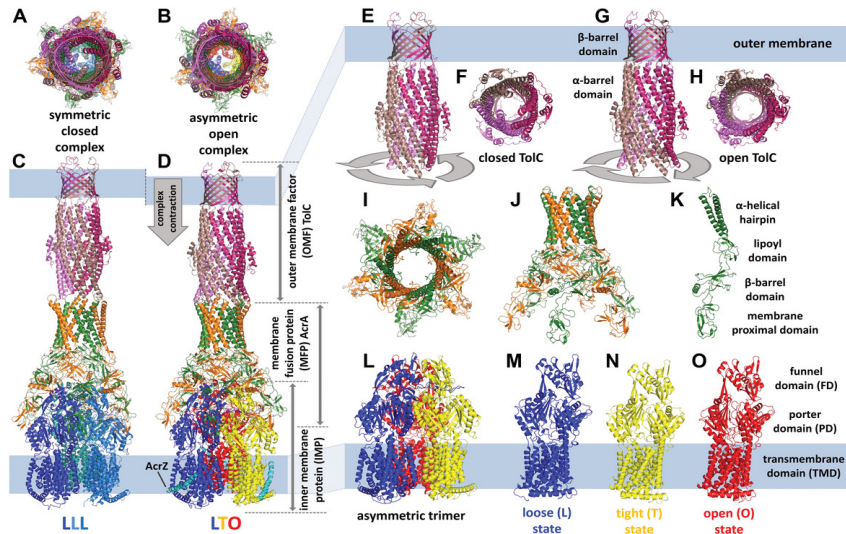
To inhibit
efflux function

To inhibit
assembling

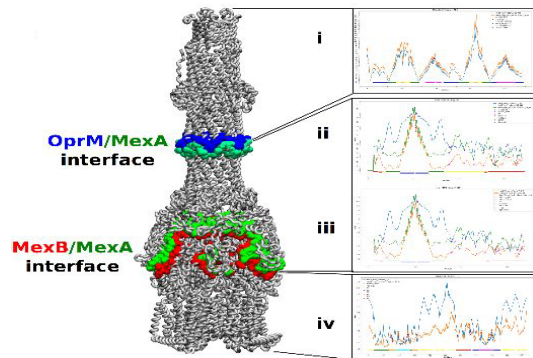
To find a ligand : virtual screening - small molecules and peptides

DSIMB DE-Assembly

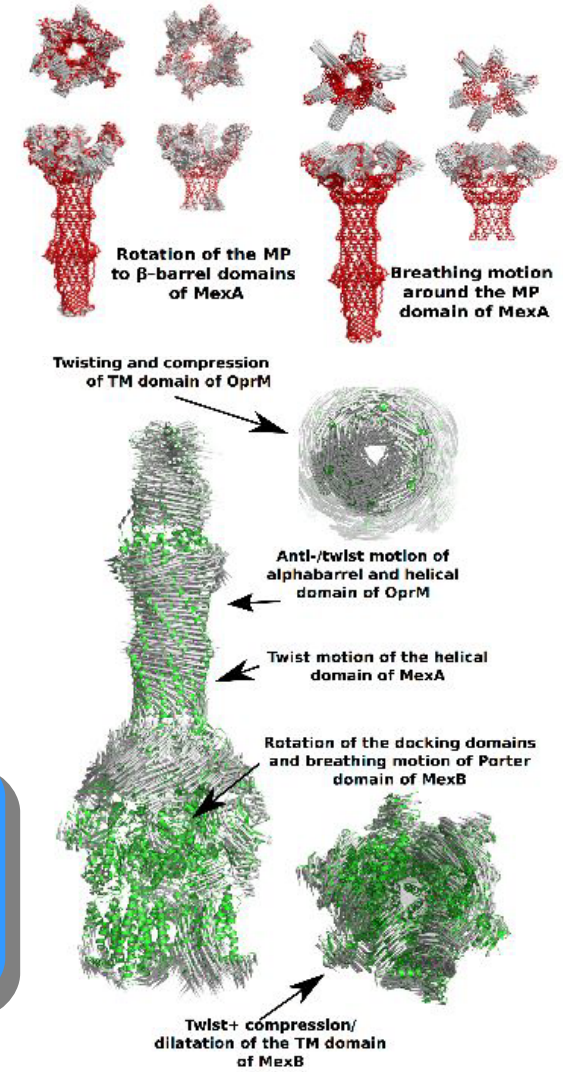
Results – To identify region of interest



Complex AcrAB-TolC (Kobylka et al, Ann N Y Acad Sci, 2019)



- Based on studies about an homolog
- Better insight about the pump mechanism



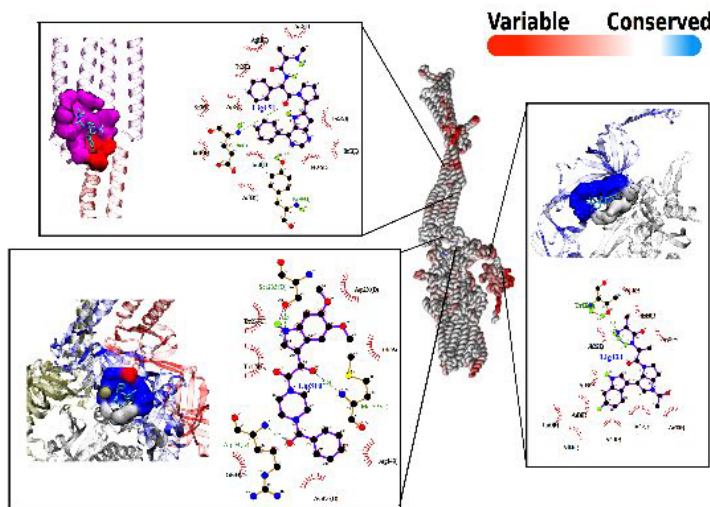
- Interfaces area stability
- Mecanism related motion observed through simulation

DSIMB DEAssembly

Results – Virtual Screening

Identification of drugs targeting the interfaces:

Virtual Screening & Molecular docking



Small molecules interacting with key regions for assembling mechanism



Peptides interactions with OprM interface region with MexA

Acknowledgments

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Ikram Lalaimia
Clément Moroldo

