Dynamics of Chimeric AFP peptides

Insilico analysis of parental and chimeric AFP peptides

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In Short

- Modeling of Fungal membrane
- Deciphering mode of action of AFPs
- Gaussian accelerated Molecular Dynamics
- Investigation of interpeptide and intermolecular interactions

Pathogenic Fungi are of constant threat to major human death each year globally and also causing a serious damge to a vast amount of crop production. Thus creates an urge for developing a novel strategies for combating the fungal growth and development. Interestingly, the small antifungal protein (AFP) belonging to a group of filamentous Ascomycetes out turns to be an effective high potential inhibitor for fungal pathogens. AFP of Aspergillus giganteus is known as the founder molecule of the AFP family comprised of about more than 50 members.

In our current study, we are going to decipher the mode of action of the two commonly focused parental AFPs (i.e) PAF from Penicillium chrysogenum and AnAFP from Aspergillus niger. These small peptides of 6kDa having a potentially stable intramolecular disulfide bonds, predominant β-sheets and a net cationic charge found to play a crucial role in precluding the spore germination via disruption of the fungal membrane integrity without affecting mammals and plants.Thus, AFPs emerges as a most promising lead compound in the development of novel antifungal peptides.The results from previous studies also states that a well conserved γ-core motif region of all antimicrobial proteins belonging to AFP family to be interfering with integrity of the cytoplasmic plasma membranes **(Fig 1)**.

Thereby, In our study we will investigate the mode of action of AFP parental peptides (PAF and AnAFP) and their interactions with the modeled fungal membrane at the atomistic level by combining both Classical and Gaussian accelerated molecular dynamics simulations using CHARMM 36 force field. Gaussian accelerated molecular dynamics simulations helps to enhance the sampling size for studying large system by reducing the energy barriers between different minima, thereby enables in exploring different low-energy conformational states without an increase in the simulation timescale of milliseconds.This technique is well suited for studying the system of size of more than 150k atoms, by having isoforms of each AFP peptides understudy above the fungal membrane surface. Such a setup helps to investigate the occurrence of interpeptides interactions leading to a potential aggregation **(Fig 2)**.

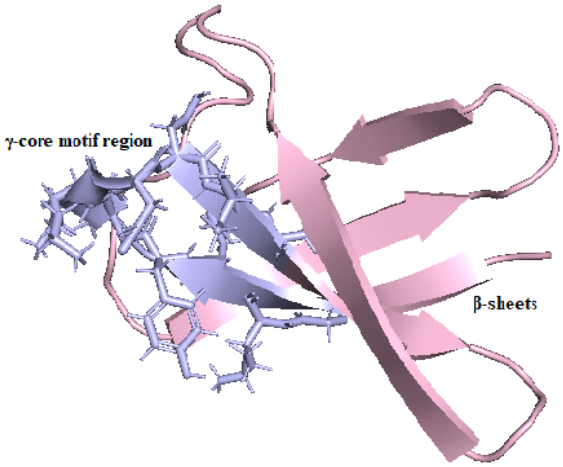

***Figure 1:** 3D- Structure of AFP peptide with β-sheets and well conserved γ-core motif region of all AFP members from prokaryotes ans eukaryotes are reprsented in sticks..*

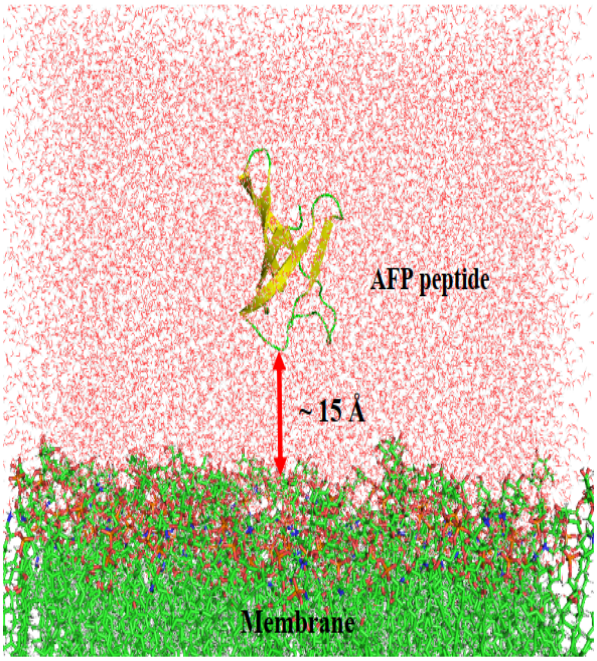

***Figure 2:** Insilico modeled AFP peptide placed at distance of 15Å above the modeled fungal membrane- CHARMM-GUI).*

This insilico study will be perfomed using well parallelized software package of NAMD 2.13 version on the HLRN server to identify the key moieties of AFPs favouring the intermolecular interactions with the fungal membrane. Besides, a subsequent study will also be performed for all chimeric AFPs (cAFPs) peptides designed by our experimental partners to identify the most potent antifungal peptide having an high efficacy for restraining the host-pathogen interaction.

WWW

https://www.biomodeling.tu-berlin.de

More Information

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Project Partners

Group of Prof. Dr. Vera Meyer, Institut für Biotechnologie, TU Berlin.

Funding

DFG RTG 2473/0