# 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
- Alpha D-Mannose sugar
- Glycosylinositol-phosphorylceramides (GIPC)

Pathogenic fungi have been reported as the major cause for decimation of people per year globally and threaten a serious damage to agricultural activities and food production. Thus, a novel pragmatic strategy is critically needed in combating the fungal growth and development(1). Germination of dormant spores is the most vital phase for disease initiation leading to the host-pathogen interaction and resulting in the outcome of fungal infections. Another emerging issue to be consider is the development of resistant strains during the past decades due to the overuse of fungicides. Therefore, identifying a new antifungal which selectively inhibits the spore germination of fungal pathogens without affecting humans and environment is of high importance (2,3).

The main objective of this project is to deploy a small antifungal protein (AFP of 6kDa) secreted by a group of filamentous Ascomycetes, having high inhibitory effect on fungal pathogens. In our studies, we broadly focused on AFPs from Aspergillus giganteus, Penicillium chrysogenum and Aspergillus niger. These parental AFPs are selective in precluding the spore germination via disruption of fungal membrane integrity without affecting mammals and plants. 1) To decipher the mode of action of AFP parental peptides (PAF from Penicillium chrysogenum and AnAFP from Aspergillus niger) and their interactions with the fungal cell membrane at the atomic level, we are performing Gaussian accelerated molecular dynamics simulation (GaMD). 2) This study is of crucial importance in aiding the structure-based rational peptide design with the three parental peptides (AFP, PAF and AnAFP), to generate a library of different chimeric AFPs (cAFPs). The designed cAFPs will be tested for their antifungal mode of action, specificity and effectiveness in binding to the build fungal cell membrane. **(Fig 1)**.

In addition, we extend our work by modelling two different membranes having a different acidic glycosphingolipids composition. One membrane composition with acidic glycosphingolipids alpha-D-Man$\alpha$3Man$\alpha$2InsPCer and another membrane composition with $\beta$-D-galactofuranose-2Man$\alpha$3Man$\alpha$2InsPCer. Besides, we want to model the fungal membrane having alpha-D-Man$\alpha$3Man$\alpha$2InsPCer acidic glycosphingolipids first, as it is most commonly found among the fungi belonging to the Phylum Ascomycota. We also strongly believe that this insilico comparative study of having two different sets of acidic glycosphingolipids membrane composition, might definitely help us in identifying the key moieties of AFPâs and cAFPâs contributing for more strong and selective non-bonded interactions with the fungal membrane. **(Fig 2)**.

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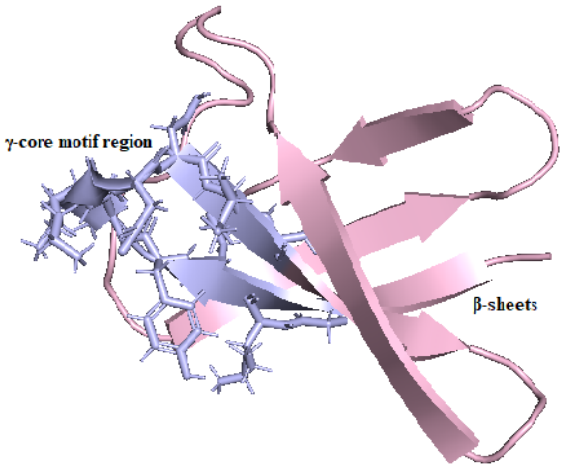


***Figure 1:*** *3D- Structure of AFP peptide with $\beta$-sheets and well conserved $\gamma$-core motif region of all AFP members from prokaryotes ans eukaryotes are reprsented in sticks.*

This insilico study will be performed 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 to identify which of the molecular moieties of the parental AFPs mediate species specificity and whether they can be combined in a single chimera without destroying the beta-barrel 3D structure and the $\gamma$-core motif. Thereby, this study helps in arriving

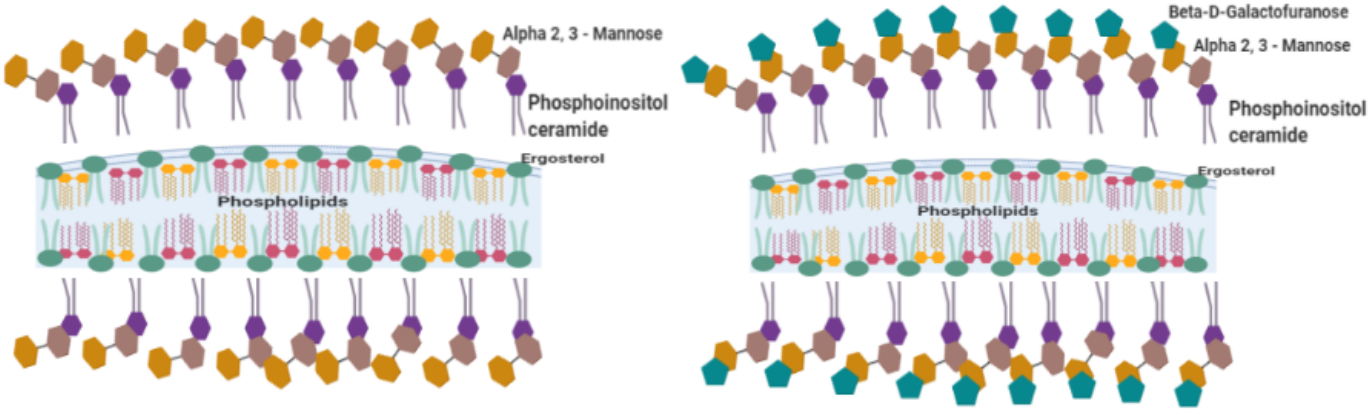


***Figure 2:*** *Models of heterogeneous fungal bilayer membrane having different Acidic glycosphingolipids composition (GuimarÃ£es et al.(2014) - Structural diversity and biological significance of glycosphingolipids in pathogenic and opportunistic fungi.).*

at the most potent antifungal peptide having a high efficacy for restraining the host-pathogen interaction without causing any harm to mammals or plants.

## WWW

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

## More Information

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## Project Partners

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