Interaction Between *Yersinia pestis* Ail Outer Membrane Protein and the C-Terminal Domain of Human Vitronectin

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Understanding the role and function of transmembrane proteins in bacteria is of paramount importance in microbiology and immunology research. Particularly, the investigation of transmembrane proteins in pathogenic bacteria is essential for elucidating mechanisms of virulence and immune evasion. Among the human diseases caused by bacteria, plague had a profound impacr throughout history, reshaping societies and leaving an indelible mark on the human experience. Despite advances in medicine and hygiene, the bacterium responsible for the plague remains a persistent and dangerous threat, underscoring the continuing importance of vigilance and research in the figth against this infectious disease.

Yersinia pestis, the causative agent of plague, evades the human immune system by using plasma vitronectin proteins to protect itself from lysis. This shielding effect is facilitated by the interaction between vitronectin and the bacterial transmembrane protein Ail, which protrudes from the outer membrane of the bacteria. Extensive all-atom long-scale molecular dynamics simulations conducted on Ail within a realistic bacterial membrane model, demonstrated the formation of a stable complex[1] which is driven by interactions involving the disordered regions of these two proteins.
Furthermore, the identification of the key amino acids responsible for mediating this complexation has shed light on specific mechanisms by which Y. pestis evades the immune system. These findings not only offer insights into bacterial evasion tactics but also have the potential to inform the development of novel antibacterial strategies.

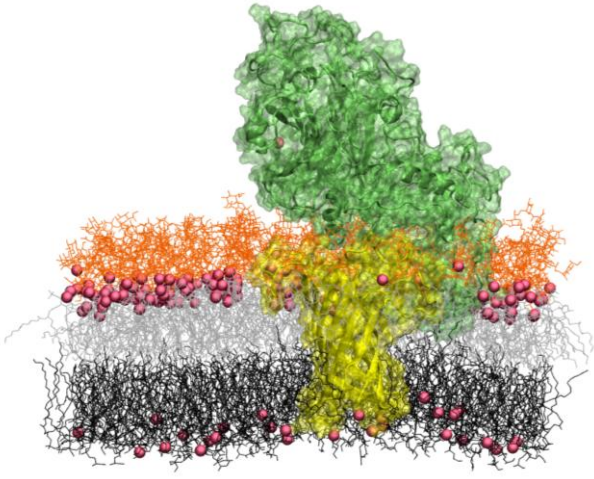

Figure 1. Representative snapshot of the Ail/Vitronectin complex embedded in the *Y. pestis* outer membrane environment. The bacterial protein is represented in yellow, while the human plasma protein is shown in cyan. Lipids and sugars are represented in lines and Ca^{2+} ions are shown in van der Waals

Keywords: molecular dynamics, protein-protein interaction, bacteria

[1] Vasseur, L.; Barbault, F.; Monari, A. Interaction Between *Yersinia Pestis* Ail Outer Membrane Protein and the C-Terminal Domain of Human Vitronectin. January 7, 2024. https://doi.org/10.1101/2024.01.07.574511.