Colicin Evolution: Lessons from Billions of Years of Bacterial Warfare

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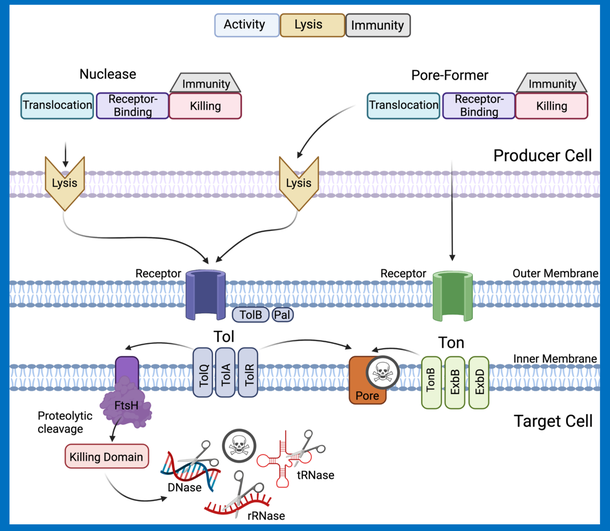
Introduction

Background:

- Antibiotic resistance is a major problem the world faces.
- Bacteriocins are antimicrobials produced by bacteria that kill other bacteria.
- Colicins are bacteriocins produced by *E. coli* and are a model system for bacteriocin evolution.
- Colicins can kill by pore formation or nuclease activity.

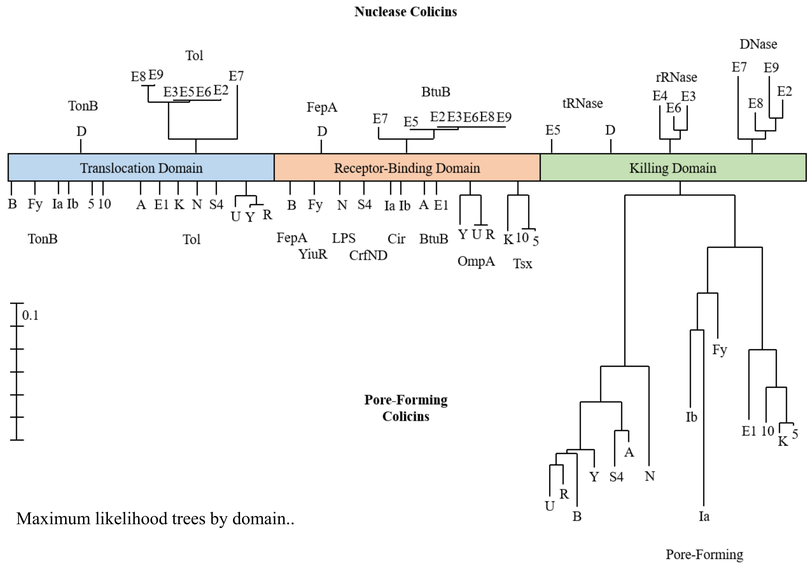
Objective/Goal: How do colicins evolve, and what does their evolution tell us about bacteriocins as a long-term solution to antibiotic resistance?



Methods

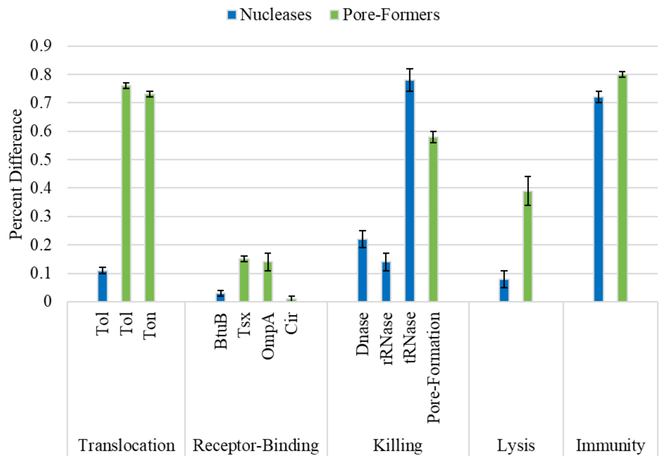
- Obtained protein sequences from online databases (NCBI and UniProt)
- Aligned protein sequences in each protein domain with MEGA-X
- Created and analyzed phylogenetic trees

Results



Maximum likelihood trees by domain..

- Differences in killing mechanism can explain this variation.
- Nucleases must cross both outer and inner membranes to access nucleic acids in the cytoplasm and kill the cell, so **nuclease cell entry options may be more limited.**
- Pore-formers kill by inserting themselves in the inner membrane, so this killing mechanism can stay the same but cell entry methods must change to avoid resistance.
- The least costly way to evolve resistance is receptor mutations, which drives pore-formers to use novel receptors.



Overall Mean Percent Difference in Amino Acid Sequence

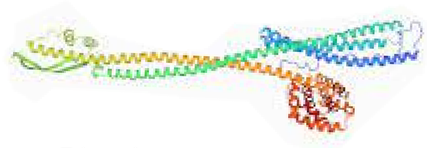
Alignment of nuclease colicins in C-terminus

- Pore-forming colicins can use more receptors and translocation systems and have more sequence dissimilarity, suggesting that **pore-formers are older than nuclease colicins**.
- Pore-formers and nucleases experience different selective pressures.
- Pore-formers have most differences in translocation and receptor-binding domains, whereas nucleases are most different in the killing domain.
- Nuclease colicins must be cleaved in order to enter the cytoplasm.
- **Proteolytic cleavage occurs at the region where high sequence dissimilarity starts to occur for nuclease colicins.**

Discussion

Conclusions:

- Understanding where selective pressure encourages evolution will help us best use colicins in the future
- Ex: we can predict potential receptors
- Resistance to any antimicrobial will evolve, but understanding how and when this resistance arise helps us better plan for the future.



Future Directions:

- Does this model of evolution apply to other bacteriocins, such as pyocins?
- How does colicin evolution affect killing ability?
- Using this information when genetically engineering bacteriocins or designing bacteriocin-based technologies

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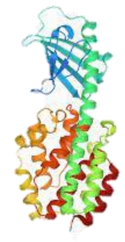

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