

**Title:** Evaluation of the SecA Inhibitors as Novel Anti-Microbial Agents

**Author:** Christina Cerovsky

**Faculty Sponsor:** Phang C Tai, Ph.D.

**Introduction:** Widespread use of conventional antibiotics accompanied by natural selection of the infectious bacteria has led to the emergence of drug resistance among the bacterial population. Thus, there is an increasing need for novel, more effective antibiotic compounds successful in treating bacterial infections resistant to available therapies. SecA, an indispensable ATPase of the protein translocation machinery, acts as a motor present in all bacteria; it couples ATP hydrolysis with pre-protein translocation through SecYEG channels<sup>1</sup> across the bacterial cytoplasmic membrane<sup>2</sup>. While bacterial SecYEG channels enhance the effectiveness as well as specificity of protein translocation within the bacteria, SecA is necessary for promoting both protein translocation as well as ion channel activity<sup>1</sup>.

**Methods:** SecA inhibitor, SCA-107 was used to perform EMS (0.5%) mutagenesis on *E. coli* NR698. Mutagenesis increased the frequency of mutations without unnecessary killing of cells. Along with isolating the mutant, DNA sequencing was completed.

**Results:** After EMS treatment and treatment with both 10 and 20  $\mu$ M SCA- 107, it appears that the EMS treated NR698 could have produced mutants resistant against 10 and 20  $\mu$ M SCA-107. Continued resistance appeared after the mutants were screened again on LB only agar plates treated with 20  $\mu$ M SCA-107.

**Conclusion:** It appears that the particular strain of *E. coli* NR698 used successfully developed mutants capable of withstanding treatment using 20  $\mu$ M SCA-107. The findings from the EMS (0.5%) mutagenesis treatment appear promising and further research is needed to confirm results obtained. Following additional testing with higher concentrations of SCA- 107, DNA extraction and PCR will be performed on the mutants. Verification is needed to confirm that the mutations are SecA mutations.

---

<sup>1</sup> Hsieh, Y., Zhang, H., Lin, B., Cui, N., Na, B., Yang, H., Jiang, C., Sui, S., & Tai, PC. (2011), SecA alone can promote protein translocation and ion channel activity: SecYEG increases efficiency and signal peptide specificity, *THE JOURNAL OF BIOLOGICAL CHEMISTRY*, 286(52), 44702-44709.

<sup>2</sup> Jang, M., De Jonghe, S., Segers, K., Anne, J., & Herdewijn, P. (2011), Synthesis of novel 5-amino-thiazolo[4,5-d] pyrimidines as *E. coli* and *S. aureus* SecA inhibitors, *Bioorganic & Medicinal Chemistry*, 19(1), 702-14.