Evaluation of the Seca Inhibitors as Novel Anti-Microbial Agents

Christina Cerovsky  
*Georgia State University*

Jinshan Jin  
*Georgia State University*

Hsiuchin Yang  
*Georgia State University*

Binghe Wang  
*Georgia State University*

Phang C. Tai  
*Georgia State University*

Follow this and additional works at: [https://scholarworks.gsu.edu/discovery](https://scholarworks.gsu.edu/discovery)

Part of the [Medicine and Health Sciences Commons](https://scholarworks.gsu.edu/discovery/vol1/iss1/12)

Recommended Citation  
DOI: [https://doi.org/10.31922/disc1.12](https://doi.org/10.31922/disc1.12)  
Available at: [https://scholarworks.gsu.edu/discovery/vol1/iss1/12](https://scholarworks.gsu.edu/discovery/vol1/iss1/12)

This Article is brought to you for free and open access by ScholarWorks @ Georgia State University. It has been accepted for inclusion in DISCOVERY: Georgia State Honors College Undergraduate Research Journal by an authorized editor of ScholarWorks @ Georgia State University. For more information, please contact scholarworks@gsu.edu.
Due to the misuse of conventional antibiotics and natural selection of the infectious bacterial population, drug resistance has emerged. Thus, there is an increasing need for novel, more effective antibiotic compounds that are successful in treating bacterial infections currently resistant to available therapies. SecA is an indispensable ATPase of the protein translocation machinery present in all bacteria. It is responsible for the secretion of many essential proteins, some toxins and virulence factors, and essential for bacterial survival. SecA has no developing antimicrobial agents. SCA-13 (HO) is a pyrimidine analog and was derived from Strains of (++) and deletion (-) of MepA and NorA efflux pumps. The compound HO was tested in samples with the overexpression (++) and deletion (-) of MepA and NorA efflux pumps. As HO increases, a new band is seen in the tryptic digest, indicating that the drug alters the SecA conformation. This could indicate that SecA is the target for HO.

One of the methods of resistance is for the compound/treatment to be pumped out of the cell via an efflux pump. We examined the effect of changes in the MepA and NorA efflux pumps on the HO compound. MepA and NorA efflux pumps are illustrated above. NorA is a member of the SMR family of efflux pumps.

The compound HO was tested in samples with the overexpression (++) and deletion (-) of MepA and NorA efflux pumps as shown by the IC50 values.

**Abstract**

Due to the misuse of conventional antibiotics and natural selection of the infectious bacterial population, drug resistance has emerged. Thus, there is an increasing need for novel, more effective antibiotic compounds that are successful in treating bacterial infections currently resistant to available therapies. SecA is an indispensable ATPase of the protein translocation machinery present in all bacteria. It is responsible for the secretion of many essential proteins, some toxins and virulence factors, and essential for bacterial survival. SecA has no developing antimicrobial agents. SCA-13 (HO) is a pyrimidine analog and was derived from Strains of (++) and deletion (-) of MepA and NorA efflux pumps. The compound HO was tested in samples with the overexpression (++) and deletion (-) of MepA and NorA efflux pumps.

**Results**

**Inhibitory effect of HO on SecA Translocation ATPase**

<table>
<thead>
<tr>
<th>Strain</th>
<th>IC50 (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT (83254)</td>
<td>48</td>
</tr>
<tr>
<td>K2068 (MepA++)</td>
<td>22</td>
</tr>
<tr>
<td>K2906 (MepA-)</td>
<td>47</td>
</tr>
<tr>
<td>K2361 (NorA++)</td>
<td>47</td>
</tr>
<tr>
<td>K1758 (NorA-)</td>
<td>27</td>
</tr>
<tr>
<td>S. aureus Mu50</td>
<td>15</td>
</tr>
<tr>
<td>B. anthracis</td>
<td>12.5</td>
</tr>
</tbody>
</table>

The compound HO was tested in samples with the overexpression (++) and deletion (-) of MepA and NorA efflux pumps.

**Conclusions**

HO is a potent inhibitor for SecA that seems to be unaffected by an efflux pump. This particular compound, when bound to SecA, alters the trypsin digest which indicates that HO changes the confirmation of SecA.

This work was supported by NIH Grant GM34676