Effectiveness of Antimicrobial Dark Therapy Utilizing Porphyrins Against Infections Caused by the Model Organism Mycobacterium smegmatis

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Effectiveness of a Novel Porphyrin Exhibiting Dark Toxicity Against the Model Organism *Mycobacterium smegmatis*

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Background
Antibiotic resistance is a growing problem in the US and around the world. Porphyrin technology is emerging as a promising alternative to antibiotics to work effectively against infections caused by a variety of bacteria. Alternative and ancillary treatments are being developed as antibiotics continue to fail to treat common infections. The organism *Mycobacterium smegmatis* is used as a model for the bacterium that causes the lung infection tuberculosis.

The ZnP Porphyrin
A novel, patented porphyrin which shows evidence of dark toxicity against bacteria while leaving eukaryotic tissue unharmed. Mechanism hypothesized to be perforation of the cell wall of bacteria and intercalation with DNA to inhibit bacterial cell growth.

ZnP Uptake
Texas Red Fluorescent Microscopy

<table>
<thead>
<tr>
<th>Concentration (log(CFUs/mL))</th>
<th>Time (Hr)</th>
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</thead>
<tbody>
<tr>
<td>Control</td>
<td>T0</td>
</tr>
<tr>
<td>25mM ZnP</td>
<td>T7</td>
</tr>
<tr>
<td>50mM ZnP</td>
<td>T24</td>
</tr>
</tbody>
</table>

25mM ZnP, 45 min post exposure, 100X

50mM ZnP, 60 min post exposure, 100X

50mM ZnP, 120 min post exposure, 100X

Bacterial Growth Inhibition

Anaerobic Killing Assay Results

Aerobic Killing Assay Results

Conclusions
- ZnP can be fairly rapidly uptaken (approx. 1 hour) and penetrate the cell wall of *M. smegmatis*
- ZnP serves as a plausible alternative or ancillary treatment to antibiotics in infections caused by the genus *Mycobacterium*.
- Evidence that ZnP halts aerobic cellular processes such as protein synthesis, metabolic reactions and energy production necessary for bacterial cell growth.

Future Directions
Refine the concentration of ZnP find the MIC, expose formerly antibiotic-resistant *M. smegmatis* to ZnP and treat with an antibiotic, as well as understand the impact of ZnP on *M. smegmatis* biofilm formation and disruption.

Acknowledgements
Dr. Jayne B. Robinson Ph.D., Mentor, the University of Dayton Honors Program, the College of Arts and Sciences Office of the Dean, Dr. Shawn Swavey Ph.D., Neha Patel