<table>
<thead>
<tr>
<th>Research Theme</th>
<th>Infection and Immunity</th>
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<tr>
<td>Research Project Title</td>
<td>How do Mycobacteria go to Sleep: Development of Latency Model for Mycobacterium Tuberculosis</td>
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<tr>
<td>Principal Investigator</td>
<td>Associate Professor Kevin Pethe, LKCMedicine</td>
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**Background**

The persistence of Mycobacterium tuberculosis despite prolonged chemotherapy represents a major obstacle for the control of tuberculosis. The mechanisms used by M. tuberculosis to persist in a quiescent, non-replicating state are poorly characterized. Hypoxia is believed to be a major cue inducing latent tuberculosis infection. However, a proper characterization of the physiology of quiescent mycobacteria is hampered by the lack of in vitro model allowing long-term survival of hypoxic non-replicating mycobacteria. We recently optimized a model in which persistent mycobacteria can survive for more than 60 days without a significant drop in viability (as opposed to 5-7 days with the current models). This model gives us an opportunity to study the mechanisms of long-term persistence in M. tuberculosis.

The objective of the project is to characterize the physiology of hypoxic non-replicating mycobacteria in order to discover novel targets or biomarkers for latent tuberculosis.

**Proposed work**

1. Characterization of the physiology of hypoxic non-replicating mycobacteria using a combination of chemical biology, transcriptomics (RNA-seq) and biochemistry approaches.
2. Profiling of various clinical isolates to determine if the mechanisms of persistence are conserved between distant lineages.
3. Genetic screen to determine the mycobacterial genes essential for long-term survival.
4. Testing the susceptibility of hypoxic non-replicating mycobacteria to chemical perturbation

**Contact Us**

If you have questions regarding this project, please email the Principal Investigator.

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