MtbTransReg

**Project ID:** 637730
**Funded under:** H2020-EU.1.1. - EXCELLENT SCIENCE - European Research Council (ERC)

**Translational regulation in the persistence and drug susceptibility of Mycobacterium tuberculosis**

**From** 2015-06-01 **to** 2020-05-31, ongoing project | MtbTransReg Website

### Project details

<table>
<thead>
<tr>
<th><strong>Total cost:</strong></th>
<th><strong>EU contribution:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>EUR 1 495 625</td>
<td>EUR 1 495 625</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Topic(s):</strong></th>
<th><strong>Call for proposal:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>ERC-StG-2014 - ERC Starting Grant</td>
<td>ERC-2014-STG See other projects for this call</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Coordinated in:</strong></th>
<th><strong>Funding scheme:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>ERC-STG - Starting Grant</td>
</tr>
</tbody>
</table>

### Objective

Mycobacterium tuberculosis causes human tuberculosis but can also persist for decades as an asymptomatic latent infection. The mechanisms underlying persistence are poorly understood, and the emergence of drug-resistant tuberculosis makes the development of effective new treatments an urgent challenge. Understanding the ability of M. tuberculosis to switch between replicating and non-replicating states during infection and disease is central to the search for improved treatments. The number of copies of a protein produced by a cell is generally viewed as being determined by the number of mRNA transcripts, but recent findings suggest that ‘specialised ribosomes’ can modify proteome profiles by preferential translation of particular mRNA subsets, particularly in response to stress. mRNA molecules contain specific signals that optimise their interaction with ribosomes; known as leader sequences, these include the Shine-Dalgarno (SD) sequence required for canonical translation initiation in bacteria. I recently demonstrated that M. tuberculosis expresses an unexpected number of leaderless mRNA transcripts that lack the SD sequence. In Escherichia coli, only a few leaderless transcripts have been described and they are selectively translated by specialised ribosomes. I propose to test the hypothesis that differential translation of mRNA subsets contributes to M. tuberculosis persistence and drug susceptibility.

I will investigate the importance of selective translation of leaderless and SD mRNAs in the context of adaptation to stress and drug resistance in M. tuberculosis, using cutting-edge experimental techniques combined with bioinformatic analyses. The proposed project addresses the fundamental systems biology challenge of establishing quantitative correlations between transcriptome and proteome data, and beyond contributing to the rational design of novel treatments to cure tuberculosis, could help to re-shape classical paradigms of bacterial gene regulation.

### Related information

<table>
<thead>
<tr>
<th><strong>Report Summaries</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodic Reporting for period 2 - MtbTransReg (Translational regulation in the persistence and drug susceptibility of Mycobacterium tuberculosis)</td>
</tr>
</tbody>
</table>
Host Institution
LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE ROYAL CHARTER
KEPPEL STREET
WC1E 7HT LONDON
United Kingdom
EU contribution: EUR 1 495 625

Activity type: Higher or Secondary Education Establishments
Contact the organisation

Beneficiaries
LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE ROYAL CHARTER
KEPPEL STREET
WC1E 7HT LONDON
United Kingdom
EU contribution: EUR 1 495 625

Activity type: Higher or Secondary Education Establishments
Contact the organisation

To know more
http://erc.europa.eu/

Last updated on 2016-01-20
Retrieved on 2019-07-18

© European Union, 2019