

COMSTECH-NTD NETWORK JOINT LECTURE SERIES

Identifying and Validating New Drug Targets for Neglected Tropical Diseases

27 September, 2021

2:30 PM Pak

10:30 AM UK

Register to attend:

<https://forms.gle/LaRnELNEZ9K9u6Ai8>

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The protozoan kinetoplastid parasites *Leishmania* spp, *Trypanosoma brucei* and *Trypanosoma cruzi* are responsible for potentially fatal diseases that affect over 22 million people worldwide, with an estimated 450 million people at risk. Current therapies are expensive and not widely accessible. In addition, drug toxicity and emerging resistance are major concerns and there is a major need for new tractable drug targets. In this presentation I will describe examples of phenotypic and target-based approaches towards the discovery of new leishmanial drug targets and the identification of tractable chemical starting points for future drug discovery programmes. For the former we have used a natural chalcone, with antileishmanial properties, as a starting point to develop and apply probes to identify the molecular target. In the second, target-based, strategy, we have identified the essential kinetoplastid sphingolipid synthase (SLS) as an attractive pharmaceutical target due to the divergence of function compared with the mammalian orthologous. We have developed screening assays to identify potential inhibitors against the *Leishmania major* enzyme. One assay identified the OTC antihistamine *clemastine fumarate* as a potential antileishmanial and I will discuss our efforts to validate and exploit this finding.



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