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Tuberculosis therapeutics and screening assay

Summary

Tuberculosis (TB) is one of the leading infectious causes of death worldwide. Among the most vulnerable are children and those with HIV/AIDS. Each year the disease is becoming more challenging to treat due to growing resistance to the currently available drugs.

To further reduce TB incidence, new approaches and interventions are required. Scientists from the MRC Unit The Gambia at the London School of Hygiene and Tropical Medicine have recently shown that protein kinase inhibitors can directly inhibit the growth of *Mycobacterium tuberculosis* complex (MTBC) species. This novel approach offers a therapeutic opportunity to target MTBC species. Furthermore, a screening assay has been developed for determining the anti-MTBC abilities of protein kinase inhibitors, which is faster and more robust than the existing methods.

Applications

- **Direct inhibition of MTBC species growth**
- **Method for investigating anti-MTBC abilities of protein kinase inhibitors**

Benefits

- Novel use of existing drugs that are effective at lower doses and can potentially be used in combination therapy and on immuno-compromised patients
- Selection of only the therapeutic agents that will be effective against MTBC species in as little as five days

Background

TB is a global disease caused by members of the MTBC species. The WHO reported that 10 million people were ill with TB, and TB caused 1.5 million deaths in 2020. TB is a treatable and curable disease but remains a severe threat to public health. Active, drug-susceptible TB is treated with a 6-month course of four antibiotics. This extensive treatment promotes the development of multi-drug resistant TB (MDR TB), where bacteria do not respond to two of the most effective first-line anti-TB drugs. Second-line drug options are limited and require extensive chemotherapy with expensive and toxic medicines. Therefore, a need remains for novel and effective methods to treat TB.

Technology and its advantages

Protein kinase inhibitors have previously been shown as host-directed therapeutics (HDTs). Still, researchers from the LSHTM MRC Gambia Unit have identified a new mode of action by which protein kinase inhibitors directly inhibit the growth of MTBC species. Specifically, the inhibitor Gefitinib can be used in broad spectrum TB treatment, which has particular advantages to MDR TB and does not require

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identification of the MTBC species. Whereas the inhibitors Erlotinib and Imatinib have direct inhibition of specific MTBC species.

Benefits of the novel use of protein kinase inhibitors include:

- Faster results and effective at lower doses than prior art uses as HDTs
- Effective at a lower concentration allowing for reduced chemotoxicity
- Can be used in combination treatments
- Can be used for patients not expected to benefit from HDT treatment, such as patients with HIV/AIDS or patients taking immunosuppressive drugs

The invention also includes a method for determining the ability of a protein kinase inhibitor to inhibit the growth of an MTBC species. The screening assay directly measures bacterial growth, allowing the user to identify a protein kinase inhibitor as potentially effective in treating TB by direct inhibition.

Benefits of the screening assay include:

- Increased sensitivity
- Allows for patient stratification in which the agent used for treatment can be tailored to meet the patient's specific needs
- Data can be generated in as little as five days compared to the prior art, which can take a few weeks

Market Opportunity

Coherent Market Insights valued the global TB drugs market at $1,146.50 million in 2019. This is expected to exhibit a CAGR of 5.3% over the forecast period (2019-2027) to surpass $1,651.20 million by 2027.

Team

Dr Leopold Tientcheu Djomkam is the lead inventor of this technology and Assistant Professor at the LSHTM MRC Unit, The Gambia. His research was the first to describe differences in treatment response between *Mycobacterium africanum* and *Mycobacterium tuberculosis*-infected patients with public health implications in West Africa. He investigates the development of HDTs for TB in populations infected with different MTBC species.

Dr Schadrac Agbla is a tenure track fellow at the University of Liverpool. His research focuses on medical statistics, using advanced epidemiology and multifactorial data analysis methods. He is interested in infectious diseases epidemiology and the development of tools for disease control.

Prof Daniel Kalman is a Professor in the Department of Pathology and Laboratory Medicine at Emory University School of Medicine. The general goal of his research is to understand how bacterial and viral pathogens interface with the host. He leads clinical trials of new HDTs for TB.

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Intellectual Property

A patent has been filed for the technology with a priority date of the 13th of June 2022 (Application No. UK2208654.0).

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