Tuberculosis drug may also target visceral leishmaniasis

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A drug that has already been approved for treatment of tuberculosis could also be a powerful tool to combat another of the developing world's major diseases, researchers at the University of Dundee have found.

Visceral leishmaniasis is a disease which blights the developing world with 200,000 to 400,000 new cases and 48,000 deaths annually. The vast majority of cases are seen in six countries - Bangladesh, Brazil, Ethiopia, India, South Sudan and Sudan.

There are no vaccines available and current drug treatments all have serious limitations such as prolonged administration (mainly by injection), high cost, drug resistance, toxicity and potential for foetal malformations.

Researchers in the School of Life Sciences at Dundee have discovered that a drug called delamanid, which was recently approved for the treatment of tuberculosis, can cure a mouse model of visceral leishmaniasis at oral doses that may be achievable in patients.

Professor Alan Fairlamb, who led the research project, said, "There is an urgent requirement for safe, oral and cost-effective drugs for the treatment of visceral leishmaniasis.

"What we have found is that delamanid has the potential to be repurposed as a much-needed oral therapy for VL. The opportunity to

use an existing approved drug for a new indication is an exciting and cost-effective way to treat this neglected disease of poverty."

The research has been carried out at Dundee by Professor Fairlamb's research group, working with the team of Dr Kevin Read in the University's Drug Discovery Unit (DDU).

The DDU is the only fully operational, fully integrated drug discovery group working across multiple diseases based within a UK university, and one of only a handful worldwide. The Unit tackles unmet medical need through small molecule drug discovery, bridging the gap between academic scientific research and commercial drug discovery and development.

Professor Fairlamb said that delamanid was seen to be active against the parasites which cause visceral leishmaniasis. It is thought to kill the parasites through conversion by an unknown enzyme to form toxic products.

"The next steps now are to identify the primary target of delamanid and look at suitable drug combinations to improve efficacy and safety, as well as slowing the emergence of resistance," said Professor Fairlamb.

"We are already entering discussions with downstream partners to initiate Phase II clinical trials."

More information: Stephen Patterson et al. The anti-tubercular drug delamanid as a potential oral treatment for visceral leishmaniasis, *eLife* (2016). DOI: 10.7554/eLife.09744

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