Discovering new drugs to fight TB

August 30 2011

(Medical Xpress) -- Research at Victoria University is targeting new drugs to fight drug-resistant and other forms of tuberculosis (TB).

In June this year the first case of extensively-drug resistant TB in New Zealand was reported. The strain of Mycobacterium tuberculosis isolated is the most drug-resistant strain recorded to date in Australasia.

Although TB has slipped under the radar in New Zealand, around 300 new cases are diagnosed here every year. Around the world there are a massive 9.4 million new cases annually and 1.7 million people die from the disease. TB takes about the same number of lives as HIV/AIDS —and more than malaria.

Ronan O'Toole, a senior lecturer in the School of Biological Sciences, leads a team of Victoria researchers looking for innovative new compounds to help eliminate Mycobacterium tuberculosis.

He says current clinical TB drugs have been around for more than 30 years and resistance has become a major problem.

"People with TB have to take antibiotics for six months, and that's the short course. Some patients may not stick with the treatment to the end, and when drugs are not used appropriately, you can eventually get resistance."

In 2009, there were a quarter of a million new cases of people with multi-drug resistant tuberculosis.

Dr O'Toole recently spent time studying multi- and extensively-drug resistant strains of M. tuberculosis in level 3 containment facilities at the Centre for TB Research at John Hopkins University in Baltimore.

"One of them was resistant to 10 of the available tuberculosis drugs. This leaves few drugs to treat such strains with."

With funding from the Health Research Council of New Zealand and the Wellington Medical Research Foundation, Dr O'Toole has been investigating techniques to speed up screening for new drugs to fight TB.

He and his students have developed novel procedures for identifying compounds that inhibit M. tuberculosis. These are then applied to libraries of synthetic compounds, and natural products isolated from native plants and marine organisms, to highlight promising treatments.

"Our techniques allow us to screen thousands of compounds much faster to see where possible new treatments might come from."

Using targeted screening protocols, they can also pre-select for compounds which have a new mode of action against the cell of M. tuberculosis.

One strand of the work has seen the researchers testing native plants to see if they can help in the fight against TB. Dr O'Toole's group has prepared extracts from a variety of New Zealand plants and found that a number of them inhibited the growth of M. tuberculosis.

The most promising extract came from the inner bark of the Pukatea tree (Laurelia novae-zelandiae). This is of interest, says Dr O'Toole, as Pukatea bark extract was reportedly used by Maori as a traditional treatment for tuberculosis ulcers. The findings indicate the potential that native plants and other organisms may have as sources of tuberculosis

drugs.

In a joint project with the TB research group at the Malaghan Institute, the researchers are also trying to find out more about latent forms of the bacteria.

Dr O'Toole says the World Health Organisation has estimated that up to one-third of the world's population carries M. tuberculosis in its latent form.

"People with latent TB are not infectious and most will not develop the symptoms of active TB but the WHO estimate highlights the extent of the reservoir that exists for the bacterium."

One goal of the project is to find out what signals drive the bacteria to enter and exit latency. A second objective is to find compounds that will kill the M. tuberculosis cells that are present in latent TB cases.

"Currently, we have few drugs that are effective against latent TB," says Dr O'Toole.

Despite the size of the problem, Irish-born Dr O'Toole is optimistic about the future.

"With continued investment in discovering and developing new treatments, I am confident it is a disease we will get on top of in my lifetime."

Provided by Victoria University