Uploaded to the VFC Website

2017

This Document has been provided to you courtesy of Veterans-For-Change!

Feel free to pass to any veteran who might be able to use this information!

For thousands more files like this and hundreds of links to useful information, and hundreds of "Frequently Asked Questions, please go to:

Veterans-For-Change

If Veterans don't help Veterans, who will?

Note: VFC is not liable for source information in this document, it is merely provided as a courtesy to our members & subscribers.

New approach bolsters protein in blood vessels to protect against cerebral malaria

Published on September 30, 2016 at 12:56 AM

Boosting a protective protein to stabilize blood vessels weakened by malaria showed improved survival beyond that of antimalarial drugs alone in pre-clinical research.

Toronto General Research Institute (TGRI) and the Sandra Rotman Centre for Global Health, University of Toronto and University Health Network researchers describe in *Science Translational Medicine*, **28 September 2016** how their approach bolsters the body's own capabilities to protect itself against cerebral malaria, rather than solely targeting the malaria parasites in the blood.

Over 400,000 lives are lost each year to severe and cerebral malaria, mainly among children in sub-Saharan Africa. For children surviving cerebral malaria, up to one-third may develop long-term neurological injury including epilepsy, behavioural disorders and/or motor, sensory or language deficits.

Led by Dr. Sarah Higgins, now a Research Fellow at Harvard Medical School and Beth Israel Deaconess Medical Center, and Dr. Kevin Kain, Science Director, Tropical Disease Unit, Toronto General Hospital, University Health Network, the researchers demonstrate how giving mice angiopoietin-1 (Ang-1), a key protein which protects the lining in blood vessels in humans and mice, when combined with the best antimalarial drug artesunate, results in 100 per cent of mice surviving severe malaria, compared to about 60% of the mice infected with malaria who received artesunate alone.

Equally important, the research also showed that Ang-1 preserves the blood-brain barrier, a critical network of blood vessels that allows nutrients to cross over into the brain, while keeping out foreign substances that may harm it. An infection such as severe malaria causes changes in blood vessels, resulting in a breakdown of the blood-brain barrier and brain injury.

"To protect against this injury, we recreated what the body produces," explains Dr. Higgins, "Ang-1 enables blood vessels to maintain normal function and serves as a protective barrier for the brain." Dr. Higgins, who did the research while a graduate student in the lab of Dr. Kevin Kain, is the first author in the research paper entitled, "Dysregulation of angiopoietin-1 plays a critical mechanistic role in the pathogenesis of cerebral malaria."

In a series of elegantly designed experiments, the team first tested 180 children aged one to 10 years old, with severe cerebral malaria in Uganda, along with children who had no or mild malaria. They found that those with severe and cerebral malaria had significantly lower amounts of Ang-1.

The team then went on to test mice with malaria and found that, similar to humans, Ang-1 drops significantly in these mice. They also "knocked out" the gene for Ang-1 in mice, and found that its protective effects disappeared. In the final experiment, when the ill mice were injected with Ang-1, in addition to the antimalarial medication, they survived and had no brain injury.

The development of cerebral malaria is not well understood, but research has shown that how an individual responds to the illness is important in determining its severity and outcome. Strategies which target only the parasite are not enough to prevent complications and deaths in individuals with severe infection.

"Patients often die from their response to the infection, rather than directly from their infections," points out Dr. Kain, who is also the Director, SA Rotman Laboratories at the Sandra Rotman Centre for Global Health and Senior Scientist at TGRI.

"Our approach is about modifying 'us' rather than solely focusing on drugs to kill microbes, and for life-threatening infections like cerebral malaria, this strategy may improve outcome while decreasing drug resistance," he says.

"We want to change the paradigm. Our primary goal should be about improving survival and preventing brain injury, rather than a strict preoccupation with antimicrobial drugs to kill bugs. Our findings have broad implications for other life-threatening infections such as sepsis, toxic shock, for which we currently have no specific treatments."

Source:

University Health Network (UHN)