Scientists show that HIV drugs can also target tropical parasites

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Scientists have discovered that drugs used to treat HIV may also one day become lifesaving drugs targeted at parasitic diseases such as leishmaniasis and malaria. According to new research published in The *FASEB Journal*, scientists have identified the target of action for some anti-HIV drugs with known abilities to kill serious pathogenic parasites. While scientists have long known that these HIV drugs can kill parasites, exactly how they work was previously unknown. Researchers discovered that a particular protein called Ddi 1 from Leishmania parasites is sensitive to anti-HIV inhibitors. This research could one day significantly change the treatment of parasitic diseases.

"People in developing countries can be exposed to parasitic diseases such as malaria and leishmaniasis that can kill millions of people, so new and effective drugs are urgently needed to combat these infections," said Colin Berry, Ph.D., a researcher involved in the work from the Cardiff School of Biosciences at Cardiff University in Cardiff in the United Kingdom. "The use of existing anti-HIV agents has indicated that there is a potential target in some parasites and by identifying the protein responsible, we hope to exploit this weakness in the parasite to develop new and effective therapeutics to combat these devastating diseases."

Scientists studied yeast that lacked the Ddi 1 protein and found that high levels of proteins were secreted. The addition of the Leishmania Ddi 1 protein returned the yeast to normal low secretion levels until HIV proteinase inhibitors were added. These inhibitors blocked the ability of Leishmania Ddi 1 to reduce secretions and showed that the Ddi 1 protein

interacted with the drugs. Additionally, when researchers used human Ddi 1, they identified drugs that were good at blocking the activity of the Leishmania protein, but which were much weaker against the human equivalent, suggesting that possible side effects in a future drug could be reduced. Study data support the potential use of this class of compounds for leishmaniasis, but do not yet support the use of existing marketed compounds in a clinical context. The potency of the existing compounds indicates that they may be a useful start point for further exploratory chemistry.

"Like HIV, parasitic diseases have been and still are a serious threat to human health world-wide," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "Millions die each year from these maladies and we desperately need new drugs. How fortuitous that agents designed against one killer, HIV, may now be turned against parasitic diseases such as leishmaniasis and malaria."

More information: Rhian E. White, David J. Powell, and Colin Berry. HIV proteinase inhibitors target the Ddi1-like protein of Leishmania parasites. *FASEB J* May 2011 25:1729-1736; doi:10.1096/fj.10-178947

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