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In vivo, in vitro interaction of silver nanoparticles with leucine amino peptidase from human and *Plasmodium falciparum*

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Statement of the Problem: There is increasing requirement for the development of new drug protocols against malaria, a fatal disease caused by the lethal parasite *Plasmodium falciparum*. Leucine aminopeptidase (PfLAP) of *Plasmodium falciparum* is being pursued as a promising target for the discovery of novel antimalarials.

Methodology: *Pf*LAP and HsLAP were expressed in *Escherichia coli*, and AgNPs (3-10 nm) characterized by ultra-violet spectroscopy and transmission electron microscopy. The effects of silver nanoparticles (AgNPs) against *P. falciparum* leucine amino-peptidase (PfLAP) and the human homolog (HsLAP) were compared.

Findings: PfLAP indicated a K_m of 694 µM towards leucine-*p*-nitroanilide and a V_{max} of 57.9 µmol.ml^{-1}. min^{-1} while *Hs*LAP had a Km of 1.6 mM and V_{max} of 119.6 µmol.ml-1.min-1. On interaction with AgNPs (670 nM) PfLAP was selectively inhibited (57.1 %; K_i=610 nM) relative to HsLAP (10.8 %; K_i=5.22 µM). The viability of *P. falciparum* parasites was decreased when exposed to silver nanoparticles, with an IC_{50} value of 6.96 µM, compared to an IC_{50} value of 647.7 µM for human HeLa cells.

Conclusion & Significance: Structural differences between the enzyme variants, particularly the orientation and distance of surface Met^{349} in PfLAP and Met^{306} in HsLAP to the zinc binding sites were significant and may allow for selective targeting of *Pf*LAP by AgNPs.

Biography

Chris Whiteley is an Emeritus Professor of Biochemistry at Rhodes University, Grahamstown, South Africa and distinguished Research Professor at National Taiwan University Science & Technology, Visiting International Professor in Enzymology at School of Bioscience & BioEngineering of South China University Technology, Guangzhou, PRC. He served as Visiting Research Scientist at the Department of Chemical Engineering, National Taiwan University, Taipei, Taiwan in 2004 and as Visiting Professor of Biochemistry at Institute of Biomedical Technology, Veterans General Hospital, Yang Ming University, Taipei, Taiwan. He also worked as Visiting Professor of Enzymology & Organic Synthesis at Oregon State University, Corvallis, Oregon, USA and Visiting Professor of Organic Synthesis at University British Columbia, Vancouver, Canada. He is the Executive Member of Royal Chemical Society (London), MRSC (C. Chem), South African Chemical Institute (SACI). He has published 6 chapters in books and has 110 peer-reviewed papers on Biomedical Enzymology and Nanomaterials.

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