



Profile of a Leading Biomedical Scientist in Africa

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Pharmacogenetics and Genomics, 2008. 18:467–476

Prediction of sites under adaptive evolution in cytochrome P450 sequences and their relationship to substrate recognition sites

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We have used maximum-likelihood models of codon substitution to investigate the role of adaptive evolution in the evolution of cytochrome P450 (CYP) sequences.

Evidence for the operation of adaptive evolution in the evolution of rat CYP2C, rabbit CYP2C, rat CYP2D, human CYP3A and rabbit CYP4A was observed. The absence of signal in rat CYP2B, rat CYP3A, human CYP2C and monkey CYP2C suggests that the adaptive evolution did not operate in the evolution of these cytochromes. Our results show identical adaptive evolution patterns for



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2008 Research Grants for AiBST

The African Institute of Biomedical Science and Technology (AiBST), www.aibst.com, is a relatively young initiative founded in 2002. AiBST is an Educational, Research & Development and Entrepreneurships institute that aims to promote pharmaceutical and biomedical sciences and technology towards solving Africa's healthcare challenges. To achieve its objectives, it has regional centres and partnerships with established universities in Africa that focus on postgraduate education, training of professionals, carrying out biomedical R&D, and translating research findings into biomedical solutions and services.

In recognition of its novel approach to addressing Africa's healthcare challenges, sound research projects, and product oriented activities, various organizations have now granted the institute funding. This funding will go a long way in translating AiBST's vision into a reality that promises to reshape Africa's biomedical landscape.

Research grants for 2008 have been obtained from:

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Pharmacogenetics and Genomics, 2008. 18:467-476

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rabbit (lagomorpha) and rat (rodentia) CYP2C. The absence of signal for adaptive evolution in primate CYP2C suggests that the identical rat and rabbit CYP2C patterns arose in the last common ancestor of rodentia and lagomorpha. Furthermore, we have found statistically significant association of sites under adaptive evolution and Gotoh's substrate recognition sites in rat and rabbit CYP2C (5%), human CYP3A and rat CYP2D (10%). From these correlations, the given substrate-dependent nature of differences in CYP substrate-specificity profiles and differences in cytochrome active-site residues, we hypothesize that the most likely role of adaptive evolution in the evolution of cytochrome P450 substrate specificities was to fix mutations that permitted an increased number of binding modes (thereby expanding the substrate repertoire). The pattern of adaptive evolution observed in this work is consistent with results from microsomal studies in which CYP2C isoforms are responsible for most of the metabolism of foreign compounds in rat and rabbit, and CYP3A isoforms play the same role in humans.

Keywords: adaptive evolution, cytochrome P450, selection, positive darwinian selection, substrate recognition site ●

Collen Masimirembwa Foundation Reaching Out

In fulfilling one of Collen Masimirembwa Foundation's objectives of **'assisting some less privileged members of the community with particular focus on education at primary, secondary and tertiary levels'** the foundation pledged to pay the school fees of all orphans at the Mashambanhaka Primary School (Uzumba, Zimbabwe) from grade one to seven. It also



(b) Pupils at Mashambanhaka Primary School

pledged to pay the school fees for the subsequent year of the top three students in each of the grade 1 to 6 classes. The foundation has since paid the school fees for the 2008 1st and 2nd terms of the 200 orphans at the school and the fees of the 18 students who excelled in 2007.



(a) Mashambanhaka Primary School (Uzumba)

The selection of Mashambanhaka Primary School as the first beneficiary of the Foundation's pledge is based on the fact that the Founder, Dr. Collen Masimirembwa is a former pupil of this school where he did his grade 2 and 3 in 1975 and 1976 respectively. The targeting of orphans is in response to the devastating impact of the HIV/AIDS pandemic which has left up to 20% of most primary school pupils orphaned in Zimbabwe. Rewarding top

performance by some of the pupils is meant to foster a culture of high academic achievement at an early age ●

Swedish Workplace HIV& AIDS Program (SWHAP)

On the 10th of June 2008 the SWEDISH WORKPLACE HIV & AIDS PROGRAM (SWHAP) in collaboration with the AFRICAN INSTITUTE OF BIOMEDICAL SCIENCE & TECHNOLOGY conducted a breakfast seminar on Executive Sensitisation on HIV/AIDS Strategic Management funded by NIR.

Ms Edith Maziofa (National Coordinator SWHAP) introduced the presenters to the participants. She took the opportunity to highlight the objectives of SWHAP, major ones being to assist employees and employers combat the pandemic, make their workplaces the national spearheads of work related HIV/AIDS activities and to initiate a global corporate engagement.

Eighteen participants from eight companies attended. These were Million Chingombe, Fred Knott, Joseph Sithole, Sandi Zaranyika and Grace Nembaware from SANDVIK; Kedius Mphingo and Mike Derry from SKF/RESCO, Farai Masunda; Pax Cox and Tony Cox from ERICOM; M Baloyi, E Patel and M Matamba from ATLAS COPCO; M Ndlovu from SCANLINK; F. Munhuweyi and P. Mahachi from ZAPSO; Ngoni Chibukire from SAFAIDS; and K Shadmeu from RESCO.

Mr Mutambara (The Director of the Zimbabwe Business Council on Aids (ZBCA) made a presentation as to why HIV/AIDS is a strategic issue for business. Mr Fredrick Mandizvidza (The CEO of the African Institute of Biomedical Science and Technology (AiBST), made a presentation on the complex ways HIV/AIDS affects business and why it should become a Boardroom issue as it impacts on the viability and profitabilities of companies. Dr. Enock Mayida (AiBST Doctor) gave an overview of the HIV/AIDS

NIR

Näringslivets Internationella Råd
International Council
of Swedish Industry

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2008 Research Grants for AiBST

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1. WHO-TDR grant (76 000 USD) - Principal Investigator: Dr. Collen Masimirembwa



After successfully demonstrating AiBST's capacity to provide preclinical DMPK services of a quality and turn-around time comparable to that in leading pharmaceutical companies and international CRO (Contract Research Organisations), WHO-TDR granted AiBST funds to strengthen the DMPK/PD & Toxicology department so that it can support its drug discovery projects with *in silico* and *in vitro* ADMET services. The grant of 76 000 USD will go a long way in strengthening AiBST's department of DMPK/PD & Toxicology by the recruitment of post-docs and technicians, and purchase of reagents.

2. IPICS pilot grant (200 000 SEK) - Principal Investigator: Dr. Collen Masimirembwa.



The International Programme in Chemical Sciences at Uppsala University (IPICS) awarded AiBST a pilot grant to support its efforts to better understand the metabolism and pharmacokinetics (DMPK) of anti-parasitic drugs. Understanding the pharmacogenetics of the biotransformation of these drugs holds key to their safe and efficacious use. This is particularly important in light of the fact that few new drugs are being brought on the market to combat neglected diseases and that co-infections are predisposing patients to poly-pharmacy which can result in undesirable drug-drug interactions. This grant will fund AiBST's research into the metabolism and pharmacokinetics of anti-parasitic drugs. Success in this pilot project will make AiBST eligible for long term support by IPICS.

3. TWAS grant (10 000 USD) - Principal Investigator: Dr. Collen Masimirembwa.



The Academy of Sciences for the Developing World (TWAS) has granted AiBST funds to carry out studies on the Clinical effects of CYP2B6 polymorphism on the use of efavirenz in HIV/AIDS patients in Zimbabwe. This will enable AiBST to develop a clinical pharmacogenetic algorithm in the use of the anti-retroviral drug, efavirenz.

4. EU ((AntiMal) (680 000 Euro over 2.5 years)) - Principal Investigator: Dr. Collen Masimirembwa.



The AntiMal Consortium at the Liverpool School of Tropical medicine is an EU funded (under Framework 6) project led by Prof. Steve Ward. The goal of this initiative is to establish a portfolio of new anti-malarial drugs. It also aims to integrate and strengthen drug discovery capacity in African institutions. AiBST (Dr. Collen Masimirembwa) and UCT (Prof. Kelly Chibale) were jointly awarded a research grant of 680 000 Eur over 2.5 years to strengthen their expertise in pharmacology in the discovery of new drugs against malaria under this consortium. Dr. Collen Masimirembwa will work on upgrading the DMPK/PD Toxicology, training of scientists on Industrial DMPK and supporting some AntiMal projects with ADMET services. Prof. Kelly Chibale and Prof. Peter Smith at the UTC will explore new chemistries and test them on *in vitro* and *in vivo* malaria models for efficacy. This grant will strengthen the Pharmacology in the discovery and development of new drugs for the treatment of malaria.

5. CDC grant (150 000 USD/year for 3 years) - Principal Investigator: Dr. Collen Masimirembwa.



The Centres for Disease Control and Prevention, Department of Health and Human Services; National Center for HIV, VIRAL HEPATITIS; STDS and TB Prevention, awarded AiBST a research grant of 150 000 USD/year over three years to train private healthcare professionals in the diagnosis, treatment and monitoring of HIV/AIDS. This was based on AiBST's strength on advanced professional training and a cutting edge molecular diagnostic laboratory which provides healthcare providers with services such as CD4 counts, viral load determinations, therapeutic drug monitoring (TDM) and disease impact assessment modelling tools. This project will see AiBST train over 540 healthcare professionals annually in the 10 provinces of Zimbabwe. This grant will build capacity for training private healthcare professionals in the diagnosis, treatment and monitoring of HIV/AIDS ●

Profile of a Leading African Biomedical Scientist

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Selected Achievements:

1. Full professor since January 2004
2. Member of University Board of Trustees (Professors representative) since January 2004
3. Scientific Adviser of International Foundation for Science (IFS) since 2006
4. Deputy Director for the consortium for the Establishment of Drug Discovery, Development and Clinical Sciences and Technologies in Malaria, TB and HIV/AIDS in Africa at the African Institute of Biomedical Science and Technology.
5. Scientific Adviser to NAPRECA (Network of Natural Products Research in East and Central Africa)

Selected Publications:

1. Maurice Boda, Paul V. Tan, **Barthelemy Nyasse**. Rapid in vivo screening method for the evaluation of new antihelicobacter medicinal plants. *African Journal of Traditional, Complementary & Alternative Medicines* **3**(4), 102-114 (2006)
2. **B. Nyasse**, I. Ngantchou, E.M. Tchana, B. Sonké, C. Denier, C. Fontaine. Inhibition of both *Trypanosoma brucei* bloodstream form and related glycolytic enzymes by a new kolavic acid derivative isolated from *Entada abyssinica*: *Pharmazie* **59**, 873-875 (2004).
3. **B. Nyasse**, E. Nkwengoua, B. Sondengam, C. Denier and M. Willson: Modified berberine and protoberberines from *Enantia chlorantha* as potential inhibitors of *Trypanosoma brucei*. *Pharmazie* **57**, 358-361 (2002)
4. T. V. Tan and **B. Nyasse**: Anti-ulcer compound from *Voacanga africana* with possible histamine H₂ receptor blocking activity, *Phytotherapy*, **7**(6), 509-515 (2000)
5. **Barthélemy Nyasse**, Leif Grehn, Hernani L.S. Maia, Luis S. Monteiro and Ulf Ragnarsson: 2-Naphthalenesulfonyl as a Tosyl Substitute for Protection of Amino Functions. Cyclic Voltammetry Studies on Model Sulfonamides and their Preparative Cleavage by Reduction, *J. Org. Chem.*, **64**, 7135-7139 (1999).
6. L. Grehn, **B. Nyasse** and U. Ragnarsson: A practical Reagent for the Synthesis of Substituted Hydrazines, *Synthesis*, 1429-1432 (1997) ●

Swedish Workplace HIV& AIDS Program (SWHAP)

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pandemic in Zimbabwe and the clinical challenges the medical fraternity was facing in combating the disease. Dr. Collen Masimirembwa (The President and Chief Scientific Officer of AiBST) gave a presentation on the technology platforms available at AiBST for the diagnosis, treatment and monitoring of HIV/AIDS and how the companies could access these tools towards effective workplace HIV/AIDS policies (Fig 1a and b).

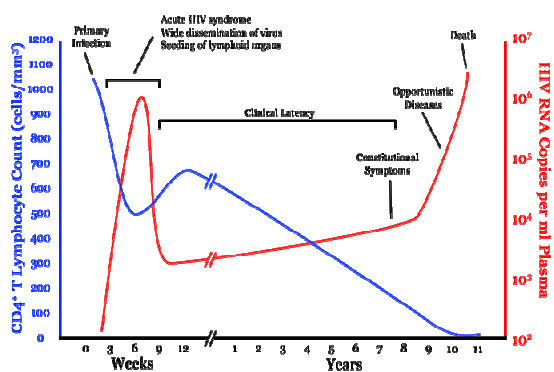


Fig 1(a)

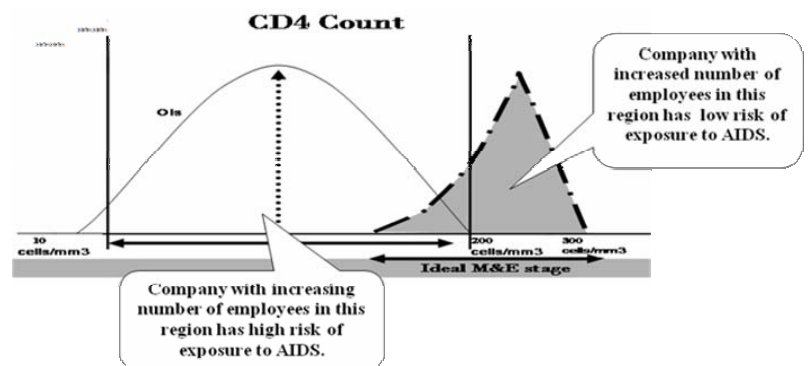


Fig 1(b)

Fig 1 (a) Summary of the pathogenesis of HIV/AIDS and (b) a snapshot model of a company's risk with respect to HIV/AIDS. Discussion of these aspects were made with respect to the opportunities for diagnosis, treatment, monitoring technology platforms that are available at the African Institute of Biomedical Science and Technology.

Active discussion followed the presentations with the attendees acknowledging that the seminar was worthwhile and provided them with concrete ways of addressing the HIV/AIDS pandemic in the workplace ●

1st Conference on African Network for Drugs/Diagnostics Discover & Innovation (ANDI)



Special Programme for Research & Training
in Tropical Diseases (TDR) sponsored by
UNICEF/UNDP/World Bank/WHO



World Health
Organization

"African Network for Drugs/Diagnostics Discovery & Innovation (ANDI)"

Dates: October 6 - 8, 2008

Venue: Transcorp Hilton Abuja, Nigeria

https://extranet.who.int/datacol/survey.asp?survey_id=904 (Username and Password: andi).

DEADLINE FOR ABSTRACTS: 15 July 2008

"Creating a sustainable platform for R&D innovation in Africa"

The objective of the African Network for Drug/Diagnostics Discovery and Innovation (ANDI) is to promote and sustain an African-led R&D innovation by building capacity, developing infrastructure, promoting collaborative efforts and delivering affordable new tools including those based on natural products and traditional medicines.

The meeting will bring together experts from Africa and overseas, African experts in Diaspora, policy makers, international agencies as well as donors, to discuss the rationale for the establishment of ANDI.

New Staff at AiBST



Dr. Milimo Maimbo joined AiBST on the 1st of June as a Postdoctoral fellow in the Department of Molecular Sciences. She studied for a Bachelor of Science (Hons) Biological Science, University of Zimbabwe from 1997 and graduated with a thesis titled: "Taxonomic characterization of the genus *Ganoderma* occurring in Zimbabwe by the analysis of total soluble mycelial proteins and Random Amplified Polymorphic DNAs (RFLPs).

Dr. Milimo Maimbo

She then joined the Master of Science in Biotechnology Programme at the University of Zimbabwe in 2001. In 2002 she went to Japan where she did a Master of Science degree in Agriculture at Kochi University, specializing in Biotechnology and Plant Pathology. Her thesis work was on "Isolation of genes involved in the development of bacterial wilt caused by *Ralstonia solanacearum*". In 2008 she graduated with a Phd in Agriculture from Ehime University also in Japan, specializing in Plant Pathology and biotechnology with a dissertation titled "Studies on mechanisms of development of bacterial wilt caused by *Ralstonia solanacearum*".

Dr. Milimo Maimbo, therefore, brings with her extensive experience in molecular biology which includes Real Time - PCR, sequencing, gene expression, and tissue culture. Her postdoctoral work will be on Biobanking and Pharmacogenetics of African populations and the development of clinical pharmacodiagnostic tools for use in the diagnosis and treatment of infectious diseases.



Ms Milcah Dhoro joined AiBST on the 1st of June as a Biomedical Laboratory Technologist. She completed a BSc Honours Degree in Biological Sciences at Midlands State University in 2004. Thereafter she joined the Tobacco Research Board as a Research Officer in the Molecular and Cell Biology Division for four years. Her work in the Diagnostic section involved the following activities; (i) screening tobacco and other commercial crops (maize, rice), for genetic modification using PCR, (ii) detection of viruses in plant material using dsRNA analysis and ELISA (iii) genetic fingerprinting of various plant species (grass, maize, tobacco) using molecular markers (ISSRs, RAPDs and RFLPs). She was also the Management Representative for the Quality Management System. This involved continuous monitoring and maintenance of the QMS compliance to ISO 17025:2005 requirements as well as updating management and SANAS on the status of the QMS. As

part of her continual personal development, she registered for an MPhil with the Department of Biochemistry, UZ, in 2006 under the supervision of Professor Chetsanga. She is now writing up her thesis on the identification and differentiation of *Fusarium* species.

Milcah Dhoro, therefore brings with her solid biomedical laboratory work experience and management skills that will be of great value to AiBST. She will be responsible for the development of standard operating procedures (SOPs), procurement of equipment and reagents, laboratory support for, and management of research projects, and ensure that AiBST laboratories attain ISO 17025 accreditation ●