EDCTP

European & Developing Countries Clinical Trials Partnership

PROJECT PORTFOLIO

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1 Career Development / Senior fellowships

1.1 HIV / AIDS Career Development and Senior Fellowships

Table 5-1: HIV/AIDS fellowship projects supported by EDCTP

Project Acronym (Coordinator)	Study classification / design	Product(s)	Manufacturer / Developer	Study population	Status
Alabi SF -HIV	Laboratory assay development	In-house viral load assays	In-house (based on Roche HIV version)	none	Completed
Ekouevi SF - HIV	Phase II multicentre open label trial	Truvada (Emtricitabine + Tenofivir), Niverapine and Zudovudine/Azidothymid	Gilead Sciences, Boehringer Ingelheim and Tübingen respectively	60 mother-child pairs per step (10 per site and per step in Abidjan, Côte d'Ivoire, Soweto, South Africa and Phnom Penh in Cambodia	Completed
Serwanga- CDF	Prospective cohort study on protective HIV immunity	none	Not applicable	200 HIV serodiscordant couples with particular interest in the seronegative partners at high risk for HIV-1 infection.	Completed
Sevene - CDF	Prospect cohort safety study	Sulphadoxine-Pyrimithamine + standard regimen (Stavudine, lamuvidine and niverapine)	WHO pre-qualified drugs	The pregnant women from first ante-natal visit to deliverly, and both mother and baby followed until the child is 12 months old	Completed
Njai- SF	Longitudinal study on HIV immunology	none	Not applicable	The proposed study will use the unique Rural Clinical Cohort established in 1990	Completed
Ndembi -SF	Prospective cohort study on determinants of dual infection with HIV strains	none	Not applicable	A rural clinical cohort (RCC) of over 500 individuals (HIV+ and HIV-) established in 1990	Completed
Mwinzi - SF	Prevalence study on IRIS in	standard regimen (Stavudine,	WHO pre-qualified drugs	HIV-schistosome co-infection patients undergoing HAART In western Kenya.	Completed

	schistomiasis on HAART	lamuvidine and niverapine)			
Kiepela - SF	Laboratory analyses of HIV mucosal immunity and KIR:HAL genes	none	Not applicable		Ongoing
Kityo -SF	Prospective cohort study on drug resistance in children	standard regimen (Stavudine, lamuvidine and niverapine)	WHO pre-qualified drugs	360 HIV-infected children under 12 years of age in three JCRC clinics already participating in the established PASER network monitoring HIVDR in adults	Ongoing
Burgers -SF	Laboratory study on the effect of HIV on lung immunity in TB patients	None	Not applicable	70 adult latent TB patients: 35 HIV+ with CD4 counts >400 and 35 HIV- persons	Completed
Mduluza –SF	Prospective cohort study on the evolution of neutrolising antibodies in HIV – C	None	Not applicable	Stored samples of 70 individuals aged between 15 - 55 years old with acute/recent stages of HIV-1C infection followed up to day 440 in Botswana	Completed
Kayondo –SF	Laboratory analyses for ART resistace in treatment naïve patients	Combivir + niverapine or tenofivir	?? prequalified formulations	Stored samples from structured treatment interrupted (STI) and continuous treatment (CT) arms of the DART of Combivir + Nevirapine or Tenofovir combination regimen	Ongoing
Kennedy -SF	Capacity building for HIV/STI prevention trials in a post-conflict Liberia	None	Not applicable	None	Completed
Kinyanda – SF	Prevalence study of mental health among clinical trials participants in HIV/AIDS	None	Not applicable	HIV patients on HAART in Uganda	Ongoing
Ndounga - SF	Establishment of a HIV positive cohort for site preparation	None	Not applicable	HIV infected individuals	Ongoing

	for HIV and malaria clinical trials in the Republic of Congo				
Delany Moretlwe - SF	Prospective cohort study on HPV and genital warts in HIV-1 negative and HIV-1 positive men taking ART in South Africa.	None	Not applicable	Men having sex with men	Completed
Nchinda - SF	Laboratory pre-clinical evaluation of dendritic cell antigens and HIV gag protein vaccines	None	Not applicable	In vitro studies (samples from chronically HIV infected patients in Cameroon)	Ongoing
Were - SF	Prospective cohort study on HIV incidence	None	Not applicable	Women in HIV serodiscordant stable relationships and sex workers in Eldoret	Completed
Orrell - SF	A randomised controlled Trial	None	Not applicable (treatment monitoring device)	Adherence-failure relationships in a South African antiretroviral delivery site using an electronic adherence device and sparse Pharmacokinetic sampling	Completed
Kiwanuka - SF	Randomised trial of mobile phone reminder vs physical contact tracing among HIV high risk persons in fishing communities in Uganda	None	Not applicable	HIV risk individuals in fishing communities around Lake Victoria	Ongoing
Ocama - SF	Prevalence survey of Hep B and vertical transmission	None	Not applicable	Mothers attending the postnatal/ immunization clinic in Gulu hospital	Ongoing

Jallow – SF	Cohort studies of sex workers and discordant couples	None	Not applicable	Study participants from WANETAM and WAPHIR cohorts (The Gambia, Guinea Bissau and Senegal)	Ongoing
Masimirembwa -SF	A phase IV prospective study to evaluate a pharmacogenetic-guided dosing algorithm based on patient CYP2B6 genotype	Efavirenz	DuPont Pharmaceuticals	Adult patients (>18 years) who are starting on an Efavirenz containing HAART regimen due to a reaction with Nevirapine or due to undergoing concurrent treatment for TB	Ongoing

1.1.1 Abraham Alabi

EDCTP Project Coordinator:	Abraham Alabi (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Development and evaluation of high throughput, cheap and reliable assays for monitoring HIV-1 and HIV-2 viral loads in ARV programmes and clinical trials in developing countries
EDCTP Project Code:	TA.2004.40200.001
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	28 September 2008
Collaborators:	• Steve Kaye (MRC Laboratories, The Gambia) • Samuel McConkey (MRC Laboratories, The Gambia)
Site Principal Investigator(s):	• Clayton Onyango (The Gambia) • Modou Camara (The Gambia) • Steve Kaye (The Gambia) • Samuel MacConkey (The Gambia) • Sarah Rowland Jones (The Gambia) • Simon Agwale (Nigeria)
Goal:	To develop robust and affordable in-house virus load assays for quantifying HIV-1 and HIV-2 RNA in the blood of an infected individual; with similar sensitivity, specificity, and reproducibility to currently available commercial HIV viral load assays. A secondary objective is to train scientists in the West Africa sub-region to encourage a wider use of the assay
Collaborating site(s):	Medical Research Council (UK)
Study design:	Laboratory assay development and validation
Product(s):	In-house viral load assay
Manufacturer/Developer:	Roche proto-type
Status:	Completed
Results and Outcomes:	The project produced a locally validated HIV viral load assay. 10 scientists from West Africa and 9 from Eastern Africa were trained in the course. Six publications resulted from the grant.
Publications:	

1.1.2 Didier Ekouevi

EDCTP Project Coordinator:	Didier Ekouevi (Centre Hospitalier Universitaire (CHU) de Treichville, Cote d'Ivoire)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Phase II multicentre open label trial to evaluate the pharmacokinetics and the safety and toxicity of the Tenofovir-Emtricitabine combination in pregnant women and infants in Africa and Asia
EDCTP Project Code:	TA.2004.40200.003
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	30 October 2007
Collaborators:	• Gerard Allou (Centre Hospitalier Universitaire (CHU) de Treichville, Cote d'Ivoire) • Patricia Fassinou (CHU de Treichville, Cote d'Ivoire) • Appolinaire Horo (CHU de Treichville, Cote d'Ivoire) • Hassan Toure (CHU de Treichville, Cote d'Ivoire) • Ida Viho (CHU de Treichville, Cote d'Ivoire)
Site Principal Investigator(s):	• Thérèse N'dri-Yoman (Côte d'ivoire) • Eric Nerrienet (Cambodia) • Leang Sim Kruy (Cambodia) • James Mcintyre (South Africa) • Marie-Laure Chaix (France) • Christine Rouzioux (France) • Jean-Marc Treluyer (France) • Elisabeth Rey (France) • Stéphane Blanche (France) • Elise Arrive (France)
Clinical Trial/Study Sponsor:	French National Research Agency (France)
Trial/Study title:	Phase II multicentre open label trial to evaluate the pharmacokinetics and the safety and toxicity of the Tenofovir-Emtricitabine combination in pregnant women and infants in Africa and Asia
Objective(s):	To assess safety, pharmacokinetics (PK) and resistance profile of Truvada® (tenofovir disporoxyl fumarate [TDF 300 mg] + Emtricitabine [FTC 200 mg]), an alternative ARV regimen for PMTCT in resource-limited settings in HIV-infected pregnant women and their infants
Clinical Trial/Study site(s):	Centre Hospitalier Universitaire (CHU) de Treichville (Cote d'Ivoire)
Study design and population:	Phase II trial; Pregnant women (HIV+, ≥18 years, 28-38 weeks gestation) and their infants N=72
Product:	• Truvada (Emtricitabine + Tenofivir) • Niverapine • Zudovudine/Azidothymid
Manufacturer/Developer:	• Gilead Sciences (USA) • Boehringer Ingelheim (Germany) • University of Tübingen (Germany)
Cofunders:	National Agency for AIDS Research (ANRS, France)
Trial Registration number(s):	NCT00334256
Status:	Completed
Results and Outcomes:	This study laid a foundation for collaboration in prevention of mother-to-child transmission trials between South Africa, Ivory

	Coast and Cambodia. The study showed that emtricitabine (FTC) achieves adequate blood levels in mothers and their neonates. Three publications have come out of the studies.
Publications:	1. The TEmAA ANRS 12109 Study group. Tolerance and viral resistance after single-dose nevirapine with tenofovir and emtricitabine to prevent vertical transmission of HIV-1. *AIDS.* 2009; 23(7):825-33 2. Hirt D, Urien S, Ekouévi DK, Rey E, Arrivé E, Blanche S, Amani-Bosse C, Nerrienet E, Gray G, Kone M, Leang SK, McIntyre J, Dabis F, Tréluyer JM. Population Pharmacokinetics of Tenofovir in HIV-1-Infected Pregnant Women and Their Neonates (ANRS 12109). *Clinical pharmacology & Therapeutics*. 2008 Nov 5; 1-5 3. Hirt D, Urien S, Rey E, Arrive E, Ekouevi DK, Coffie P, Leang SK, Lalsab S, Avit D, Nerrienet E, McIntyre J, Blanche S, Dabis F, Treluyer, JM. Population Pharmacokinetics of Emtricitabine in Human Immunodeficiency Virus Type 1-Infected Pregnant Women and Their Neonates. *Antimicrobial agents and chemotherapy*. 2009 March;53(3);1067-1073

1.1.3 Jenifer Serwanga

EDCTP Project Coordinator:	Jenifer Serwanga (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Career Development Fellowship
EDCTP Project Title:	Pattern of HIV-induced T-cell response influencing viral load course following HIV infection
EDCTP Project Code:	TA.2005.40203.003
EDCTP Project Start Date:	30 October 2006
EDCTP Project End Date:	23 May 2010
Collaborators:	• Jill Gilmour (International AIDS Vaccine Initiative, Netherlands) • Martin Grobusch (University of the Witwatersrand, South Africa) • Pontiano Kaleebu (MRC/UVRI, Uganda) • Andrew McMichael (University of Oxford, UK)
Site Principal Investigator(s):	• Heiner Grosskurth (Uganda) • Pontiano Kaleebu (Uganda) • Pietro Pala (Uganda) • Daniel Bugembe Lule (Uganda) • Andrew McMicheal (UK)
Trial/Study title:	Pattern of HIV-induced T-cell response influencing viral load course following HIV infection
Objective(s):	1. To determine the plasma viral load pVL trajectory from primary infection through viral set point and beyond 2. To evaluate the relationship between HLA class I polymorphisms and pVL trajectory 3. To evaluate the pattern and magnitude of HIV-1 specific CD8 T-cell response longitudinally following infection 4. To sequence the virus at specified intervals following HIV-1 infection to assess viral evolution and escape from HIV specific responses.
Study design:	Prospective cohort study on protective HIV immunity
Number of subjects:	200
Status:	Completed
Results and Outcomes:	The study investigated how T cell responses in the early phase of HIV-1 infection may influence the course of disease. The results showed that different persons have different levels of both conserved (sustained) and temporary responses to HIV infection. Six staff (Daniel Lule, Kenneth Musinguzi, Ekii Obuku, Samuel Okurut, Andrew Ekii and Pietro Pala) were trained in various short courses including good clinical practices.

1.1.4 Esperança Sevene

EDCTP Project Coordinator:	Esparanca Sevene (Eduardo Mondlane University, Mozambique)
EDCTP Project Call:	Career Development Fellowship
EDCTP Project Title:	Intensive safety monitoring of antimalarial and anti-retroviral drugs used during pregnancy in Manhiça
EDCTP Project Code:	TA.2005.40203.007
EDCTP Project Start Date:	23 April 2010
EDCTP Project End Date:	27 February 2010
Collaborators:	• Xavier Carne (Hospital Clinic of Barcelona, Spain) • Catarina David (Manhiça Health Research Center, Mozambique) • Alexander Dodoo (University of Ghana) • Sureia Hassamo (Mozambique) • Lidia Laço (Mozambique) • Sonia Machevo (Mozambique) • Alda Mariano (Eduardo Mondlane University, Mozambique) • Clara Menendez (University of Barcelona, Spain) • Ana Sofia Roberto (Mozambique) • Joaquina do Rosário (Mozambique)
Goal:	To describe potential adverse drug reactions to anti-malarial and anti-retroviral drugs in pregnant women including adverse pregnancy outcomes
Objective(s):	To measure the incidence of these adverse drug reactions and to determine risk factors that may contribute to the development of adverse drug reactions to anti-retroviral and antimalarial drugs in the pregnant women
Study design:	Prospect cohort safety study
Number of subjects:	2041
Product:	Sulphadoxine-Pyrimithamine + standard regimen (Stavudine, lamuvidine and niverapine)
Manufacturer/Developer:	WHO prequalified regimen drugs
Status:	Completed
Results and outcomes:	A total of 2041 pregnant woman were recruited in the study. Of these 1608 delivered at the hospital. After delivery, 1473 and 877 mothers presented their babies for assessment at second and twelfth month respectively. Fifteen pregnant women presented adverse drug reactions to drugs used during pregnancy but all recovered without sequelae. The study team attended four courses on pharmacovigilance and data management during the course of the projects.
Publications:	1. Sevene E, Bardají A, Mariano A, Machevo S, Ayala E, Sigaúque B, Alonso P, Carné X, Menendez C. Drug exposure and pregnancy outcomes in Mozambique. *Paediatr Drugs*. 2012 Feb 1;14(1):43-9. doi: 10.2165/11591270 2. Sevene E, González R, Menéndez C. Current knowledge and challenges of antimalarial drugs for treatment and prevention in pregnancy. *Expert Opin Pharmacother*. 2010 Jun;11(8):1277-93 3. Cliff J, Lewin S, Woelk G, Fernandes B, Mariano A, Sevene E; Daniels K; Matinhure S; Oxman A; Lavis J. Policy development in malaria vector management in Mozambique, South Africa and Zimbabwe. *Health Policy and Planning.* 2010; doi: 10.1093/heapol/czq008 4. Woelk G, Daniels K, Cliff J, Lewin S, Sevene E, Fernandes B, Mariano A, Matinhure S, Oxman AD, Lavis JN, Stålsby Lundborg C. Translating research into policy: Lessons

learned from eclampsia treatment and malaria control in three southern African countries. *Health Research Policy and Systems.* 2009; 7:31. doi:10.1186/1478-4505-7-31
5. Aponte JJ, Schellenberg D, Egan A, Breckenridge A, Carneiro I, Critchley J, Danquah I, Dodoo A, Kobbe R, Lell R, May J, Premji Z, Sanz S, Sevene E, Soulaymani-Becheikh R, Winstanley P, Adjei S, Anemana S, Chandramohan D, Issifou S, Mockenhaupt F, Owusu-Agyei S, Greenwood B, Grobusch MP, Kremsner PG, Macete E, Mshinda H, Newman RD, Slutsker L, Tanner M, Alonso P, Menendez C. Efficacy and safety of intermittent preventive treatment with sulfadoxine-pyrimethamine for malaria in African infants: a pooled analysis of six randomised, placebo-controlled trials. *The Lancet*. 2009 Oct 31;374(9700):1533-42. doi: 10.1016/S0140-6736(09)61258-7
6. Daniels K, Lewin S, Practihc Policy Group (Sevene E, Mariano A). Translating research into maternal health care policy: a qualitative case study of the use of evidence in policies for the treatment of eclampsia and pre-eclampsia in South Africa. *Health Res Policy Syst*. 2008 Dec 17;6:12. doi: 10.1186/1478-4505-6-12
7. Sevene E, Mariano A, Mehta U, Machai M, Dodoo A, Vilardell D, Patel S, Barnes K, Carné X. Spontaneous Adverse Drug Reaction Reporting in Rural Districts of Mozambique. *Drug Safety.* 2008; 31(10): 867-876
8. Bardagí A, Sigaúque B, Bruni L, Romagosa C, Sanz S, Mabunda S, Mandomando I, Aponte J, Sevene E, Alonso PL, Menendez C. Clinical malaria in African pregnant women. *Malar J.* 2008; 7(27):1-7
9. Ward SA, Sevene EJP, Hastings IM, Nosten F, Mcgready R. Antimalarial drugs and pregnancy: safety, pharmacokinetics, and pharmacovigilance. *The Lancet Infect Dis.* 2007;7:136-44.

1.1.5 Harr Freeya Njai

EDCTP Project Coordinator:	Harr Freeya Njai (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Characterisation of neutralizing antibody responses in Chronic clades A and D Human Immunodeficiency Virus Type 1 (HIV-1) infections and the relationship with established markers of disease progression – A longitudinal study in rural Uganda
EDCTP Project Code:	TA.2007.40200.001
EDCTP Project Start Date:	13 August 2008
EDCTP Project End Date:	12 August 2010
Collaborators:	• Sunita Balla (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Heiner Grosskurth (MRC/UVRI, Uganda) • Pontiano Kaleebu (MRC/UVRI, Uganda) • Anatoli Kamali (MRC/UVRI, Uganda) • David Montefiori (Duke University, USA)
Site Principal Investigator(s):	• Heiner Grosskurth (Uganda) • Pontiano Kaleebu (Uganda) • Anatoli Kamali (Uganda)
Objective(s):	To identify and assess the prevalence and potency of broadly neutralising antibodies in a cohort of non-B HIV chronically infected individuals in rural Uganda.
Collaborating site(s):	• Helen Donners (Belgium) • David Montefiori (Duke University, USA)
Study design:	Longitudinal study on HIV immunology
Cofunders:	• Duke University Medical Center (Uganda) • ITM (Belgium) • MRC/UVRI (Uganda)
Status:	Completed
Results and Outcomes:	Magnitude of the NAb response against SF162.LS (subtype B) and MW965.26 (subtype C) varied but was relatively potent in most cases (ID50 titers >1,000, range 20->43740). Between 5-10 years of infection, samples neutralized MW965.26 more than SF162 with a median of 6,243 at T2; at infections more than 10 years the same neutralization profile is seen (i.e. MW965 is more neutralized than SF162). In infections between 5-10 years median neutralization property was significantly higher at T1 than at T2 among those aged between 5-10 years, p values 0.0048 (MW965.26) and 0.012 (SF162.LS). One publication has come out of this work.
MSc study:	Topic: PCR and sequencing assays Candidate: Juma Magambo (MRC/UVRI, Uganda)
Publications:	1. Njai HF, Tomusange K, Sokolik-Wolak B, Montefiori D, Balla S, Vanham G, Levin J, Maher D, Kamali A, Grosskurth H, Pala P, Kaleebu P. Prevalence of neutralizing antibody responses in chronic clades A and D human immunodeficiency virus type 1 (HIV-1) infections. *Retrovirology.* 2009; 6(3):39.

1.1.6 Nicaise Ndembi

EDCTP Project Coordinator:	Nicaise Ndembi (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Frequency and determinants of dual infection with different strains of HIV-1 in low- and high-risk populations in Uganda
EDCTP Project Code:	TA.2007.40200.011
EDCTP Project Start Date:	31 July 2008
EDCTP Project End Date:	30 July 2010
Collaborators:	• Eric Arts (ase Western Reserve University, USA) • Frances Gotch (Imperial College London, UK) • Heiner Grosskurth (MRC/UVRI, Uganda) • Pontiano Kaleebu (MRC/UVRI, Uganda) • Philippe Lemey (Katholieke Universiteit Leuven, Belgium) • Pietro Pala (MRC/UVRI, Uganda) • Deogratius Ssemwanga • Annemie Vandamme (Katholieke Universiteit Leuven, Belgium) • Carolyn Williamson (University of Cape Town, South Africa)
Site Principal Investigator(s):	Pontiano Kaleebu (Uganda)
Primary Objective(s):	To evaluate the frequency and determinants of dual infection with different strains of HIV-1 in low- and high- risk populations in Uganda. This study had four major objectives and 1 minor: • Implement and validate novel sequence analysis methods developed at the Rega Institute (Belgium) for the detection of instances of co-infection and superinfection in longitudinally collected samples • Determine the clinical consequences of dual infection by comparing disease progression (viral loads and CD4+ counts) between those with and without dual infection • Determine the course of virologic recombination that occurs after dual infection • Determine the immunologic correlates of dual infection • Determine the prevalence of HIV-1 drug resistance among recently infected commercial sex workers.
Collaborating site(s):	George Shaw (UK)
Study design:	Prospective cohort study on determinants of dual infection with HIV strains
Number of subjects:	500
Status:	Completed
Results and Outcomes:	Various methodologies have been optimised and used for the detection and confirmation of dual infection. The study was unable to determine the incidence of co-infection and superinfection but was able to show HIV-1 subtype distribution, multiple infections, sexual networks and partnership histories in Commercial Sex Workers in Kampala. The prevalence of transmitted drug resistance among newly infected commercial sex workers was done among 42 women that seroconverted in the high risk population. DNA sequencing work is in progress.

Publications:	1. Ssemwanga D, Lyagoba F, Ndembi N, Mayanja BN, Larke N, Wang S, Baalwa J, Williamson C, Grosskurth H, Kaleebu P. Multiple HIV-1 infections with evidence of recombination in heterosexual partnerships in a low risk Rural Clinical Cohort in Uganda. *Virology*. 2011 Mar 1;411(1):113-31. Epub 2011 Jan 15. 2. Ndembi N, Hamers RL, Sigaloff KC, Lyagoba F, Magambo B, Nanteza B, Watera C, Kaleebu P, Rinke de Wit TF. Transmitted antiretroviral drug resistance among newly HIV-1 diagnosed young individuals in Kampala. *AIDS*. 2011 Apr 24;25(7):905-10 3. Ssemwanga D, Ndembi N, Lyagoba F, Bukenya J, Seeley J, Vandepitte J, Grosskurth H, Kaleebu P. HIV-1 subtype distribution, multiple infections, sexual networks and partnership histories in Commercial Sex Workers in Kampala, Uganda. *AIDS Res Hum Retroviruses*. 2012 Apr;28(4):357-65 4. Ssemwanga D, Ndembi N, Lyagoba F, Magambo B, Kapaata A, Bukenya J, Lubega GW, Bertagnolio S, Vandepitte J, Grosskurth H, Kaleebu P. Transmitted Antiretroviral Drug Resistance among drug-naïve Commercial Sex Workers with recent infection in Kampala, Uganda. *Clin Infect Dis*. 2012 May;54 Suppl 4:S339-42.

1.1.7 Pauline Mwinzi

EDCTP Project Coordinator:	Pauline Mwinzi (Kenya Medical Research Institute (KEMRI), Kenya)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Immune reconstitution inflammatory syndrome (IRIS) in schistosomiasis patients undergoing HAART
EDCTP Project Code:	TA.2008.40200.007
EDCTP Project Start Date:	24 November 2009
EDCTP Project End Date:	24 November 2011
Collaborators:	• Robert Colebunders (Prince Leopold Institute of Tropical Medicine (ITM), Belgium) • Diana Karanja (KEMRI, Kenya) • Luc Kestens (ITM, Belgium) • Erick Muok (KEMRI, Belgium) • Katja Polman (ITM, Belgium)
Site Principal Investigator(s):	• Diana Karanja (Kenya) • Erick Muok (Kenya)
Objective(s):	To study the Immunopathogenesls, clinical aspects and management of manifestation of IRIS in HIV-schistosome co-infection patients undergoing HAART In western Kenya. Schistosome infections are common in the same areas where HIV prevalence is also high.
Collaborating site(s):	Bob Colebunders (Belgium), Luc Kestens (Belgium), Katja Polman(Belgium)
Study design:	Prevalence study on IRIS in schistomiasis on HAART
Product:	Standard regimen (Stavudine, lamuvidine and niverapine) and anti-schtistosmes
Status:	Completed
Results and Outcomes:	622 HIV-positive patients were followed. In the first year of follow up 12 patients expressed signs and symptoms of IRIS of whom two met the case definition of IRIS. As a requirement for all staff participants on this project, GCP/GCLP training was provided online from the EDCTP-sponsored AMANET online courses.
PhD study	Title: Immunology of Schistosoma associated IRIS Candidate: Eric Muok (Kenya)
MSc studies:	Title: Pathogenesis of Schistosomiasis/HIV Co-Infection: Polymorphisms in IL-23 Receptor in Schistosomiasis Patients Undergoing Highly Active Antiretroviral Therapy (HAART)" Candidate: George Ogola
	Title: Role of vitaminD3 (1-ALPHA, 25-Dihydroxyvitamin D3) in Schistosoma -IRIS Candidate: Elses Simuyu
Publications:	1. Ogola GO, Ouma C, Jura WG, Muok EO, Colebunders R, Mwinzi PN. A non-synonymous polymorphism in IL-23R Gene (rs1884444) is associated with reduced risk to schistosomiasis-associated Immune Reconstitution Inflammatory Syndrome in a Kenyan population. *BMC Infect Dis*. 2014 Jun 10;14(1):316. doi:10.1186/1471-2334-14-316.

1.1.8 Photini Kiepela

EDCTP Project Coordinator:	Photini Kiepela (Medical Research Council South Africa (MRC), South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Training in mucosal immunity and the evaluation of KIR:nHLA genes in HIV-1 clade c infection: key components to HIV vaccine design
EDCTP Project Code:	TA.2008.40200.015
EDCTP Project Start Date:	25 March 2010
EDCTP Project End Date:	31 December 2014
Collaborators:	• S. Ganesh (MRC, South Africa) • Sharika Gappoo (MRC, South Africa) • R. Govinden (MRC, South Africa) • Thumbi Ndungu'U (University of KwaZulu-Natal, South Africa) • Thesla Palanee (MRC, South Africa) • Jo-Ann Passmore (University of Cape Town, South Africa) • Gita Ramjee (MRC, South Africa)
Site Principal Investigator(s):	• S Ganesh (South Africa) • Sharika Gappoo (South Africa) • R Govinden (South Africa) • Thumbi Ndung'U (South Africa) • Thesla Palanee (South Africa)
Objective(s):	To answer questions relating to the role of host HLA and KIR genotype as HLA class I contributes to both the innate and adaptive immune responses
Study design:	Laboratory analyses of HIV mucosal immunity and KIR:HAL genes
Status:	Completed
Results and outcomes:	KIR: HLA genotyping was performed on a total of 557 HIV-1 exposed individuals, 142 of whom acquired HIV-1 infection and 415 remained HIV-1 negative over a 2 year period. Figure 1 depicts the frequency of each KIR and HLA ligand gene n HIV-1 infected individuals compared to exposed HIV-1 seronegative. There was a significantly higher representation of 2DS2 in HIV-infected compared to HIV-1 negative individuals (62%vs 51% p=0.025), and a significantly lower representation of B80TA and Bw6 (25%vs39% (p=002); 21%vs 31% (p=0.23) respectively. The overall median ratio was 1 (IQR 0.75-2) in the 418 participants (309 HIV negatives and 109 positives) for whom a ratio was computed. The median number of inhibitory genes was 2 (IQR 1-3) and the median number of activating genes was 2 (IQR 1-2). The median ratio in HIV negative and HIV positive individuals was 1.5 and 1, respectively. HIV-1 infected individuals had a lower proportion (26%vs33%) of ≤3 inhibitory KIR genes and higher proportion (25%vs20%) of ≥3 activating KIR genes compared to HIV-1 negative, this was not significant (p=0.136; p=0.217). However the proportion with a ratio of ≤1.5 inhibitory: activating KIR genes was significantly lower (37%vs 47% p=0.036) in HIV-1 infected compared to HIV-exposed seronegative individuals. In other words individuals with an inhibitory: activating KIR gene ratio of ≤1.5 had a 34% reduced risk of acquiring HIV-1 infection compared to those with inhibitory:activating KIR gene ratio of ≥1.5. There was a higher frequency of 2DS2+C1 gene combination in

	HIV-1 infected individuals compared to HIV-1 exposed seronegative (59%vs48%) and those individuals harbouring this KIR: HLA ligand combination were 1.5 times more likely to acquire HIV-1 infection. Certain KIR: HLA ligand associations (2DS2+C1) are significantly linked with susceptibility to HIV-1 infection. Four successful e-learning workshops where we trained 74 postgraduate students. These e-learning workshops were: Mucosal Immunity Workshop 10-11th August 2010, Durban, South Africa; Mucosal Immunity HIV/HPV Workshop 17-18th February 2011, Cape Town, South Africa; Statistical Methods in HIV Vaccine Trial Design and Evaluation 28-30 March 2012, Durban, South Africa; and Vaccine Strategies against Tuberculosis, 17-19 September 2012, Durban, South Africa. A “HDI” (Host Defense Interactions http://hdi.bio-med.ch) portal was established in collaboration with Prof JP Kreahenbuhl from HSeT.

1.1.9 Cissy Kityo Mutuuluza

EDCTP Project Coordinator:	Cissy Kityo (Joint Clinical Research Center (JCRC), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Evaluating antiretroviral drug resistance in HIV infected children in Africa
EDCTP Project Code:	TA.2008.40200.022
EDCTP Project Start Date:	23 November 2009
EDCTP Project End Date:	23 November 2012
Collaborators:	• Diana Gibb (Medical Research Council (MRC), UK) • Joshua Kayiwa (JCRC, Uganda) • Peter Mugyenyi (JCRC, Uganda) • Victor Musiime (JCRC, Uganda) • Lillian Nakatudde (JCRC, Uganda) • Tobias Rinke de Wit (International Centre of Reproductive Health (ICRH), Netherlands)
Site Principal Investigator(s):	• Joshua Kiyiwa (Uganda) • Peter Mugyenyi (Uganda) • Victor Musiime (Uganda) • Lillian Nakatudda (Uganda)
Objective(s):	To determine what proportion of a paediatric cohort prevent HIV drug resistance (HIVDR) as measured by viral load suppression, and what HIVDR mutations and mutational patterns are observed in patients not achieving undetectable viral load.
Collaborating site(s):	MRC (UK)
Study design:	Prospective cohort study on drug resistance in children
Number of subjects:	360
Product:	Standard regimen (Stavudine, lamuvidine and niverapine)
Manufacturer/Developer:	Prequalified regimens
Status:	Completed
Results and outcomes:	
Publications:	

1.1.10 Wendy Burgers

EDCTP Project Coordinator:	Wendy Burgers (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	The effect of HIV co-infection on the immune response to *Mycobacterium tuberculosis* (*M.tb*) in the lung
EDCTP Project Code:	TA.2008.40200.020
EDCTP Project Start Date:	9 October 2009
EDCTP Project End Date:	9 October 2011
Collaborators:	• Willem Hanekom (University of Cape Town, South Africa) • Barbara Kalsdorf (Research Center Borstel, Germany) • Gerhard Walzl (Stellenbosch University, South Africa) • Robert Wilkinson (University of Cape Town, South Africa)
Site Principal Investigator(s):	• Willem Hanekom (South Africa) • Barbara Karlsdof (Germany) • Gerhard Walzl (South Africa) • Robert Wilkinson (South Africa)
Objective(s):	To examine the effect of HIV co-infection on the immune response to *Mycobacterium tuberculosis*. The proposed research aims to identify aspects of the immune response to *M.tb* which differ in persons latently infected with TB in the presence or absence of HIV co-infection.
Study design:	Laboratory study on the effect of HIV on lung immunity in TB patients
Number of subjects:	70
Status:	Completed
Results and outcomes:	By the end of the project 75% of the intended study volunteers were recruited, all samples stored and all planned analyses done. The project has also been successful in being awarded funds (R90,000 for 1 year) from a local South African source, the NHLS Trust, with the Senior Fellow Wendy Burgers as PI (Principal Investigator). This grant will allow completion of the remaining sample collection and analysis on this project, and perform (limited) additional analyses focusing on innate immune dysfunction, in particular alveolar macrophage function in the lungs, as well as establish links with TB researchers at UKZN and Harvard Medical School, Boston, USA.
PhD study:	Rubina Bunjun
MSc study	Narjis Khatoon Thawer
PostDoc study:	Zekerias Ginbot, Andreia Soares
Publications:	

1.1.11 Takafira Mduluza

EDCTP Project Coordinator:	Takafira Mduluza (University of Zimbabwe, Zimbabwe)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Evolution of neutralizing antibodies among acute to early HIV Subtype C infected individuals in Botswana: one year longitudinal study.
EDCTP Project Code:	TA.2009.40200.005
EDCTP Project Start Date:	14 May 2010
EDCTP Project End Date:	14 May 2012
Collaborato(s):	• Joseph Makhema (Botswana Harvard Partnership (BHP), Botswana) • Keikantse Matlhagela (BHP, Botswana) • Rosemary Musonda (BHP, Botswana)
Site Principal Investigator(s):	• Joseph Makhema (Botswana) • Keikantse Mathlagela (Botswana) • Sikhulile Moyo • Rosemary Musonda (Botswana) • Vladmir Novitsky
Objective(s):	To characterise the evolution of neutralising antibodies against HIV-1 subtype C gp 120 molecular envelope clones from acute/and early heterosexual acquired HIV-1 subtype C infections in Botswana
Study design:	Prospective cohort study on the evolution of neutrolising antibodies in HIV –C
Number of subjects:	72
Status:	Completed
Results and outcomes:	Using stored samples collected from 72 HIV-infected patients in 2005-2008, 50 plasma samples were analysed. Results so far show that broadly neutralizing antibodies are indeed present during pregnancy and at selected time points during the course of infection in the case of acute and recently infected individuals. Most plasmas have 50% neutralizing capacity, but the majority fail to exhibit 90% neutralisation. There was no strong inhibition of IN93, an HIV-1C strain similar to the predominant subtype C in the region. There is potential of identifying samples that show broad inhibition of various virus strains; with some samples showing high inhibition of subtype B (BR92).
MSc studies:	Candidate: Keabetswe Bedi
	Candidate: Sheron Dzoro

1.1.12 Jonathan Kayondo

EDCTP Project Coordinator:	Jonathan Kayondo (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Evolution of HIV-1 ARV drug resistance mutations in ART naïve individuals during therapy; threshold frequency levels and linkage context associated with treatment failure in Uganda
EDCTP Project Code:	TA.2009.40200.011
EDCTP Project Start Date:	30 March 2010
EDCTP Project End Date:	31 December 2012
Collaborators:	• Pontiano Kaleebu (MRC/UVRI, Uganda) • Jean Mbisa (Health Protection Agency (HPA), UK) • Chris Parry (MRC/UVRI, Uganda) • Deenan Pillay (University College London/HPA, UK)
Objective(s):	To complement the just commenced Wellcome Trust-funded Uganda Virus Research Institute postdoctoral research, which looks at issues related to Nevirapine induced HIV-1 drug resistance, by including in-depth investigations on the evolution of drug resistance mutations in ART-naïve individuals.
Collaborating site(s):	HPA (UK)
Study design:	Laboratory analyses for ART resistance in treatment naïve patients
Number of subjects:	Unspecified stored samples
Product:	Combivir plus niverapine or tenofivir
Manufacturer/Developer:	Prequalified formulations
Status:	Completed
Results and Outcomes:	Single genome sequencing has been established by the Principal Investigator at the UVRI laboratory. The Institute has also acquired phylogenetic and sequence analysis software packages. Four patients that had persistent viraemia during combivir/nevirapine therapy are being followed in the study. Samples collected during a previous trial were retrospectively used for an in-depth analysis of 3 cases infected with subtype D virus. All three were enrolled on Combivir/NVP regimen. One case was a patient on continuous therapy (CT-F), the second was failing on structures treatment interruption (STI-F) and the third was suppressing on the STI protocol (STI-S). Single genomes from three to five different points (wks-2, or baseline, 60, 72, 84, 108 and 120 across 2 years) in each patient were sequenced and analysed for various virus evolutionary dynamics. About 30 to 40 single genomes per time-point were sequenced. The results showed linked multi-RTI resistance mutations regardless of treatment structure although the evolution was different between treatment arms. A manuscript has been prepared for publication. An added positive outcome of the projects is that the work has enabled UVRI to apply for the H3 Africa Bioinformatics network of excellence as a development node. Thus the bioinformatics capacity that started during course of this fellowship will be propelled further and will be a key resource for the host institution's genetics proposal.

1.1.13 Stephen Kennedy

EDCTP Project Coordinator:	Steven Kennedy (University of Liberia)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Building Research Infrastructure and Capacity to Implement an HIV/STD Prevention Trial in Post-Conflict Liberia
EDCTP Project Code:	TA.2009.40200.023
EDCTP Project Start Date:	7 May 2010
EDCTP Project End Date:	7 May 2012
Collaborators:	
Objective(s):	To support research infrastructure, training and partnerships to prevent HIV/AIDS in rural Liberia and to implement and evaluate an HIV/AIDS programme for high risk rural youth in post-conflict Liberia.
Study design:	Capacity building for HIV/STI prevention trials in a post-conflict Liberia
Number of subjects:	250
Status:	Completed
Results and Outcomes:	HIV and STI baseline data have been collected in post-conflict Liberia. A total of 118 males and 132 females (n=250) were initially enrolled into the programs. The 3-month follow-up survey was administered to 115 males and 126 females (n=241) in both programs from the four communities, thus constituting an overall retention rate of 96% (i.e. attrition rate 4%). The 9-month follow-up survey was administered to 111 males and 113 female (n=224), constituting an overall retention rate of 90% (i.e. attrition rate 10%), respectively.
Publications:	1. Atwood KA, Kennedy SB, Shamblen S, Tegli J, Garber S, Fahnbulleh PW, Korvah PM, Kolubah M, Mulbah-Kamara C, Fulton S. Impact of school-based hiv prevention program in post-conflict Liberia. *AIDS Education and Prevention.* 2012;24(1): 68–77 2. Atwood KA, Kennedy SB, Shamblen S, Taylor CH, Quaqua M, Bee EM, Gobeh ME, Woods DV, Dennis B. Reducing sexual risk taking behaviors among adolescents who engage in transactional sex in post-conflict Liberia. *Vulnerable Children and Youth Studies*. 2012 Mar;7(1):55–65

1.1.14 Eugene Kinyanda

EDCTP Project Coordinator:	Eugene Kinyanda (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Clinical trials in HIV/AIDS in Africa: Should they routinely control for mental health factors?
EDCTP Project Code:	TA.2010.40200.011
EDCTP Project Start Date:	12 April 2011
EDCTP Project End Date:	30 July 2014
Collaborators:	• Heiner Grosskurth (LSHTM, UK/Mwanza Intervention Trials Unit (MITU), Tanzania) • Jonathan Levin (MRC/UVRI Uganda Research Unit on AIDS, Uganda) • Vikram Patel (London School of Hygiene and Tropical Medicine (LSHTM), UK/Sangath Centre Porvorim, India)
Objective(s):	The study aims to answer the following questions: 1. What is the prevalence of mental health problems associated with major depressive disorders (MDD) and maladaptive coping style (MACS) among HIV-infected patients in Uganda, and what is the incidence of MDD in HIV/AIDS? 2. Do mental health problems associated with MDD and MACS significantly impact on HIV disease progression in an Ugandian socio-cultural environment including through non-adherence to ART? 3. What would be the potential impact of MDD and MACS mental health covariates on HIV disease progression on the DART trial results under a range of possible differential treatment effects in the subgroups of patients with and without psychological problems?
Study design:	Prevalence study of mental health among clinical trials participants in HIV/AIDS
Number of subjects:	230
Status:	Completed
Results and Outcomes:	So far 230 subjects (Entebbe: 140; Masaka: 90) have been recruited. The rate of major depressive disorder in Masaka site (N= 25) is 4%. An MSc student (Alan Kalungi) has completed his masters project and submitted his report to the university awaiting defence of his masters. A manuscript entitled, 'Association between serotonin transporter gene 5-HTTLPR/rs 25531 and STin2. VNTRs polymorphisms and suicidality among people living with HIV I AIDS in a Ugandan population' has been submitted to the journal BMC Genetics. The fellow has developed an extensive network within and outside Uganda. Three publications are in development: • Psychiatric morbidity in early HIV infection and its association with risk factors and negative outcomes as seen in urban and rural Uganda • Incidence and persistence of major depressive disorders among people living with HIV in Uganda • Effect of depression on HIV-disease progression and associated outcomes: a longitudinal analysis from Uganda
MSc study	Title: Association between serotonin transporter gene polymorphisms and suicidality in HIV/AIDS in a Ugandan population

	Candidate: Alan Kalungi (Makerere University, Uganda)
Publications:	1. Kinyanda E, Hoskins S, Nakku J, Nawaz S, Patel V. Prevalence and risk factors of major depressive disorder in HIV/AIDS as seen in semi-urban Entebbe district, Uganda. *BMC Psychiatry.* 2011;11:205

1.1.15 Mathieu Ndounga

EDCTP Project Coordinator:	Mathieu Ndounga (Centre d'Etudes sur les Ressources Végétales (CERVE), Congo)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Establishment of a HIV positive cohort for site preparation for HIV and malaria clinical trials in the Republic of Congo
EDCTP Project Code:	TA.2010.40200.011
EDCTP Project Start Date:	29 April 2011
EDCTP Project End Date:	29 April 2013
Collaborators:	• Roth Cecile Laure Mapapa Miakassissa (CERVE, Congo) • Rock Fabien Niama (Laboratoire Nationale de Sante Publique, Congo) • Francine Ntoumi (Organization for the Coordination of Endemic Disease Control in Central (OCEAC), Cameroon) • Mayengue Issamou Pembe (University Marien Ngouabi of Brazzaville, Congo) • Celine Samba Louka (CERVE, Congo)
Goal:	This project aims at developing capacities for the conduct of clinical trials on HIV/AIDS, malaria and tuberculosis in Central Africa as part of CANTAM
Objective(s):	• To investigate the effect of HIV infection on clinical malaria infections • To evaluate the impact of clinical malaria on HIV infection • To develop human capacities in the conduct of clinical research for future HIV clinical trials in Brazzaville
Study design:	Clinical site development
Number of subjects:	101 children aged from 9 months to 10 years
Status:	Closed
Results and outcomes:	By end of 2012 a cohort of 101 HIV-infected children has been established in Brazzaville. Preliminary results show that all the HIV-infected children did not present with positive blood smear after 4 months of follow up.
PhD study:	Topic: Investigate viral load through the Laboratoire national de santé Publique in Brazzaville Candidate: Laure Ghoma Linguissi (Fondation Congolaise Pour La Recherche Médicale, Congo)

1.1.16 Sinead Delany Moretlwe

EDCTP Project Coordinator:	Sinead Delany Moretlwe (University of the Witwatersrand, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	HPV in Men (HIM): Natural history of human papillomavirus (HPV) infection and genital warts in HIV-1 negative men, HIV-1 positive men not yet taking ART, and HIV-1 positive men taking ART in South Africa.
EDCTP Project Code:	TA.2010.40200.034
EDCTP Project Start Date:	8 June 2011
EDCTP Project End Date:	31 March 2014
Collaborators:	• David Lewis (National Institute for Communicable Diseases, South Africa) • Philippe Mayaud (London School of Hygiene and Tropical Medicine (LSHTM), UK)
Goal:	To show the epidemiology of HPV infection in men by HIV status and to provide data to inform mathematical models that predict the impact of HPV vaccination (e.g. using Gardasil) in various African settings, including South Africa.
Objective(s):	**Primary objective** To determine the prevalence of HPV disease (anogenital and oropharyngeal), type distribution of low risk (LR)- and high risk (HR)-HPV DNA, and HPV seroprevalence in men in South Africa over a 12 -18 month period. **Secondary objectives** To determine: 1. The incidence of HPV disease and infection in this cohort over a maximum of 18 months 2. The persistence of HPV disease and infection (presence of HPV DNA) in this cohort followed for a maximum of 18 months 3. Socio-demographic, behavioural and clinical factors associated with HPV infection and disease in this cohort 4. Acceptability of anal swabbing in this population of presumed predominantly heterosexual African young men; and knowledge and acceptability of vaccine and factors associated with vaccine acceptability in this cohort.
Study design:	Cohort study on HPV and genital warts in HIV-1 negative and HIV-1 positive men taking ART in South Africa
Number of subjects:	150
Status:	Completed
Results and outcomes:	Clinical trial: b • The study enrolled 150 HIV negative men and 304 enrolled HIV positive men, 107 not yet eligible for ART and 197 on ART. Enrolment was completed on 12 August 2013. • All laboratory testing was completed, apart from serology testing. A total of 1300 HPV DNA samples were tested. • In terms of the primary outcome, anogenital HPV prevalence was 81% among the HIV positive cohort compared to 55 % in the HIV negative cohort. The prevalence of high risk HPV (HR-HPV) was 10% in the HIV positive group compared to 13% in the negative cohorts. Similarly, the prevalence of low risk HPV was 38% in the HIV positive and 24% in negative cohorts respectively. • In terms of factors associated with HPV infection,

	preliminary analyses stratified by HIV status showed that in the HIV cohort: smoking cigarettes and a CD4+ less than 200 at enrolment was associated with higher prevalence of HPV infection. For the HIV negative cohort, only alcohol use was significantly associated with prevalent HPV infection. All the other factors including history of smoking, life time number of sexual partners, circumcision were not significantly associated with prevalent HPV infection. • The prevalence of Anal genital Warts was significantly higher in the HIV positive cohort 11.84% compared to the HIV negative cohort 1.33% Surprisingly, anogenital swab collection was acceptable and based on assessment of 282 swabs, the prevalence of anal HPV infection in the HIV positive cohort was 31.79%. • Genital ulceration on examination ,history of an STI and WHO clinical stage OR 23.9 were significant predictors of prevalent AGWs in univariate analysis. • Qualitative interviews with 30 male HIV positive participants revealed that the overall men found the study acceptable however the collection of anal swabs was not acceptable to all. • One publication has been released and they are anticipating at least two additional publications in peer-reviewed journals on: Prevalence, type distribution, persistence and incidence of HPV DNA and AGW Knowledge and psychosocial aspects of HPV infection, acceptability of anal swabbing and acceptability of a HPV vaccine. Capacity building: • One Msc student was involved in the development of the protocol and graduated in 2011 • A pHD student has been recruited to undertake a PhD based on data collected from the study. The student was awarded the CARTA (Consortium for Advanced Research Training in Africa) PhD fellowship and was involved in exchange visits to two institutions in Europe. • 13 people have been trained in total. They received training in e.g. laboratory training, GCP training.
MSc study:	Candidate: Jo Gibbs (LSHTM, UK) Supervisor: Sinead Delany Moretlwe and Philippe Mayaud

1.1.17 Godwin Nchinda

EDCTP Project Coordinator:	Godwin Nchinda (International Reference Centre Chantal Biya (CIRCB), Cameroon)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Pre-clinical evaluation of dendritic cell targeted consensus B, C, CRFO2_AG and MOSAIC HIV gag protein vaccines in PBMC from chronically infected patients in Central Africa
EDCTP Project Code:	TA.2010.40200.016
EDCTP Project Start Date:	10 March 2011
EDCTP Project End Date:	10 March 2013
Collaborators:	• Vittorio Colizzi, (CIRCB, Cameroon) • Ralph Steinman (The Rockefeller University, USA) • Klaus Uerberla (Ruhr University Bochum, Germany)
Goal:	This project will verify if a consensus B based HIV gagP24 vaccine targeted to dendritic cells would be able to recall *in vitro* similar gag specific T cell responses in peripheral blood mononuclear cells (PBMCs) from people chronically infected with the prevalent strains of HIV-1 in Africa.
Objective(s):	1. To examine if a DC targeted consensus B HIV gag p24 protein vaccine could recall in vitro pre-existing gag specific T cells in PBMCs of subjects chronically infected with unrelated HIV-1 strains prevalent in Africa 2. To compare in terms of magnitude, breadth, and depth T cell responses recalled in vitro in PBMCs of subjects chronically infected with HIV-1 in central Africa by 4 four different DC targeted HIV gag p24 protein vaccines based on CRFO2_AG, C, B and MOSAIC HIV gag sequences, which are designed to address the problems associated with HIV-1 diversity.
Collaborating site(s):	• Rokerfeller University (USA) • Ruhr University (Germany)
Study design:	Laboratory pre-clinical evaluation of dendritic cell antigens and HIV gag protein vaccines
Status:	Closed
Results and outcomes:	The project contributed to training of 4 PhD students, 2 MSc and 1 nurse. The EDCTP funds have been used to purchase a number of equipment. The project has established links with University of Yaounde 1, Institut Pasteur Cameroon, Case Western Reserve University and Tromsø Science Park of Norway.
PhD studies	Candidate: Georgia Ambada
	Candidate: Carol Ngaye
	Candidate: Tchaji Colin
	Candidate: Benson Nyachongi
MSc studies	Candidate: Nja Nadesh
	Candidate: Archille Nague

1.1.18 Edwin Were

EDCTP Project Coordinator:	Edwin Were (Moi University, Kenya)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Enhancing HIV prevention trial capacity in Eldoret, Kenya through a baseline HIV incidence study on two HIV prevention priority populations
EDCTP Project Code:	TA.2011.40200.012
EDCTP Project Start Date:	29 February 2012
EDCTP Project End Date:	30 June 2014
Objective(s):	The primary objective is to determine the HIV incidence in women in HIV serodiscordant stable relationships and sex workers in Eldoret, Kenya. The secondary objectives are to: 1. Evaluate the acceptability of a model of service provision strategy offering targeted reproductive health services (including STI treatment and condom uptake) to a cohort of HIV serodiscordant couples and commercial sex workers in Eldoret MTRH catchment area 2. Collaborate with established centres such as South African Research Ethics Training Initiative (SARETI) to develop and teach short courses under the existing MUSOM program in Eldoret on good clinical practice and ethical issues in HIV prevention trials. Furthermore, two Masters level training will be supported in the existing MUSOM program
Collaborating site(s):	Family Health Options Kenya (FHOK), Eldoret, Kenya
Study design:	Prospective cohort study on HIV incidence
Number of subjects:	Cohort of 500 to 700 HIV negative women, with approximately 250 to 350 HIV negative female partners of HIV positive men and same number of HIV negative sex workers.
Status:	Completed
Results and Outcomes:	The study opened enrolment in April 2012. The project aimed at recruiting 700 uninfected women and by the end of the study they had enrolled 670 women of which 113 were from Discordant Couples and 557 from Female Sex Workers. The participants were followed-up for 12 to 18 months. During the follow-up period, 12 incident HIV infections occurred, 11 among the sex works and 1 in women in discordant relationships. The rate of retention recorded for the study is 88.4% and 81.7% for discordant couples and female sex workers respectively. The studies secondary aims were to : • Estimate the acceptance of a model of service provision strategy for targeted reproductive health services • Offer update training on good clinical practice, basics of international research ethics and aspects of research methodology to research teams working on HIV prevention trials in Eldoret. To meet its first secondary aim, 16 focus group discussions were successfully carried out with members of the two priority populations (HIV uninfected women in discordant couples and HIV uninfected women from sex worker population). The data was transcribed, translated into English and the thematic analysis completed. To meet its second secondary aim, a research methods and ethics curriculum was developed at the university and is currently undergoing University vetting.

	Throughout the project period the following reproductive health services were provided to women from both cohorts: • Syndromic management of genital tract • infection • Non-condom Contraception • Condoms • Lubricants • Cervical cancer screening • Risk reduction counselling These services are on-going with support from the Ministry of Health however the group intends to apply for more support to continue with these services as well as other research studies. Two manuscripts on the primary study results and the development of a research menthods and ethics curriculum are currently under the institutions internal review. Two graduate students in the Masters of International Research Ethics programme in the Moi University were supported through this study.
MSc study:	Masters in International Research Ethics Course Candidate: Margaret Anyango Gogo (Moi University, Kenya)
	Masters in International Research Ethics Course Candidate: Henry K. Lodea (Moi University, Kenya)

1.1.19 Catherine Orrell

EDCTP Project Coordinator:	Catherine Orrell (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	A randomised controlled trial to explore the adherence-failure relationships in a South African antiretroviral delivery site using an electronic adherence device and sparse pharmacokinetic sampling (The TAP study)
EDCTP Project Code:	TA.2011.40200.015
EDCTP Project Start Date:	29 February 2012
EDCTP Project End Date:	30 June 2014
Collaborators:	• David Bangsberg (Harvard University, USA) • Karen Cohen (University of Cape Town (UCT), South Africa) • Gary Maartens (UCT, South Africa) • Catherine Orrell, Karen Cohen (UCT) • Robin Wood (UCT, South Africa)
Goal:	1. To determine whether an adherence monitoring device (EAMD) with text message and dosing feedback improves adherence, retention in care and virological outcomes among individuals receiving new antiretroviral therapy (ARM 1: EAMD alone, used as a pill box; ARM 2: EAMD with reminder message for late dosing and feedback on dosing patterns at clinical visits) 2. To determine whether population pharmacokinetic data explain the discordance between adherence and virological response.
Objective(s):	This study will use a locally developed real time adherence monitoring tool to explore and improve adherence in ART-naïve individuals commencing treatment in an established ART cohort. The study will use adherence, virological and pharmacokinetic data to examine adherence failure discordance. The questions to be answered by the study are: 1. Does a real-time electronic adherence monitoring tool with text message feedback improve adherence, retention in care and virological outcomes among ART-naïve individuals receiving first-line therapy? 2. Does population pharmacokinetic data explain discordance between adherence and virological response?
Collaborating site(s):	Harvard University (USA)
Study design:	A randomised controlled trial with two arms, as follows: **Control arm:** Standard of care at ART clinic with use of an electronic adherence monitoring device (EAMD or Wisepill) to monitor adherence only (i.e., without any feedback). **Experimental group:** Control arm with the addition of the use of the EAMD text message service when dosing late, and EAMD dosing feedback at 4-monthly visits.
Study population:	ADULTS and ADOLESCENTS (12-80 years); HIV+, ART-naïve individuals N=230
Trial Registration number(s):	PACTR201311000641402
Status:	Completed
Results and outcomes:	. Research activities: • Study recruitment and follow-up was completed with 186 participants completing the study, 19 lost to follow-up, 16 transferred elsewhere , 1 withdrawing consent and 8 dying. • Cytochrome 2B6 genotyping and PK sample analysis have been

	completed and results received. • Data analysis is on-going for the primary study outcome. Three manuscripts are underway (one on the primary outcome, namely adherence according to the Wisepill device by randomised arm; one covering the pharmacokinetic and pharmacogenetic results; and one comparing the impact of the different adherence measures used during the study on virological suppression. An abstract for the Conference on Retroviruses and Opportunistic Infections (CROI) has been drafted is to be submitted for presentation in February 2015. • Analysis of baseline data was completed and will be presented at the 2014 EDCTP forum (Berlin) Capacity Building: • The PI, Dr Catherine Orrell, completed three semesters of training in Biostatistics through the School of Public Health at the University of Cape Town (UCT) in 2012 and 2013. She is also registered for a PhD in the Department of Medicine at UCT. • Three counsellors have been trained in in good clinical practice (GCP) and are receiving advanced counselling training in 2014/15. This will enable them become research assistants which will greatly improve their future employment prospects. • Several study results or outcomes meetings have been held with clinical site staff Networking: New collaborations have been developed with : • Prof Nick Holford from University of Auckland who will provide expertise on efavirenz population pharmacokinectic modelling. • Prof David Haas at van der Bilt University, USA, whose expertise will be used to explore the use of genotypes to better understand individual ART levels. Funding: • The fellow received a discovery foundation academic fellowship award in 2012.

1.1.20 Noah Kiwanuka

EDCTP Project Coordinator:	Noah Kiwanuka (Medical Research Council Programme on AIDS - Uganda Virus Research Institute (MRC/UVRI), Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	A randomised trial to assess retention rates using mobile phones versus contact tracing, andto characterize trends in HIV-1 prevalence and incidence in a potential HIV vaccine efficacy population of fishing communities around Lake Victoria, Uganda
EDCTP Project Code:	TA.2011.40200.035
EDCTP Project Start Date:	13 April 2012
EDCTP Project End Date:	31 August 2014
Collaborators:	• Francis Bajunirwe (MRC/UVRI, Uganda) • Anatoli Kamali (MRC/UVRI, Uganda) • Juliet Mpendo (MRC/UVRI, Uganda)
Trial/Study title:	A randomized trial to assess retention rates using mobile phones versus contact tracing, and characterize trends in HIV-1 prevalence and incidence in a potential HIV vaccine efficacy population of fishing communities around Lake Victoria, Uganda
Goal:	The aim of the project is to perform an assessment of the suitability of HIV risk individuals in fishing communities around Lake Victoria for HIV vaccine efficacy trials through characterization of recruitment, retention, willingness to participate (WTP), and trends in HIV prevalence and incidence, and to build statistical and data management capacity for clinical trials research. The research questions are: (1) does mobile phone reminder yield significantly higher retention rate than physical contact tracing among HIV high risk persons in fishing communities in Uganda?; (2) what are the trends in HIV-1 incidence and prevalence among HIV risk individuals in fishing communities around Lake Victoria?; (3) what is the level of determinants of willingness to participate in HIV vaccine efficacy studies among HIV-1 risk individuals in fishing communities around Lake Victoria
Objective(s):	**Primary Objective:** 1. To determine whether retention in the study will be significantly different among persons followed up using mobile telephones (calls and text messages) compared to physical contact tracing. **Secondary Objectives:** 1. To characterize trends in HIV-1 incidence and prevalence among HIV risk individuals in fishing communities around Lake Victoria 2. To determine the level and determinants of willingness to participate in HIV vaccine efficacy studies among HIV-1 risk individuals in fishing communities around Lake Victoria 3. To build clinical trials-specific statistical and data management capacity to provide support and skills to clinical trial investigators, faculty and students.
Clinical Trial/Study site(s):	Lambu and Kasenyi (Uganda)
Study design:	A randomised controlled trial with two arms, as follows: **Experimental group:** Participants called or sent SMS reminder prior to every scheduled visit (1, 3, 6, 12, 18 months). **Control group:** Physical contact reminders prior to every

	scheduled visit (1, 3, 6, 12, 18 months).
Study population:	ADULTS and ADOLESCENTS (15-49 years); Individuals at high-risk for HIV infection. N=662
Clinical Trial Registration(s):	PACTR201311000696101
Status:	Completed
Results and outcomes:	

1.1.21 Ponsiano Ocama

EDCTP Project Coordinator:	Ponsiano Ocama (Makerere University, Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Early childhood transmission of viral hepatitis B among HIV and non-HIV infected mothers attending postnatal and immunization clinic at Gulu Hospital, Northern Uganda
EDCTP Project Code:	TA.2011.40200.004
EDCTP Project Start Date:	16 February 2012
EDCTP Project End Date:	30 October 2014
Collaborators:	• Robert Colebunders (University of Antwerp, Belgium) • Felix Kaducu (Gulu University, Uganda) • Kenneth Opio Christopher (Makerere University College of Health Sciences, Uganda) • Joseph Sempa (Infectious Diseases Institute, Makerere University College of Health Sciences, Uganda)
Goal:	The primary purpose of this proposed study is to investigate the prevalence and factors that may lead to reduction of transmission of hepatitis B virus (HBV) among babies born in Northern Uganda.
Objective(s):	1. To determine the prevalence of hepatitis B surface antigen (HBsAg) in mothers attending the postnatal/immunization clinic in Gulu regional referral hospital 2. To determine the incidence of HBV infection among babies born to HBsAg-positive and HBsAg negative mothers with or without HIV infection attending postnatal/immunization clinic in Gulu regional referral hospital and aged over 9 months 3. To assess factors associated with early transmission of HBV to babies born to HBsAg-positive and HBsAg-negative mothers attending postnatal/immunization clinic in Gulu regional referral hospital.
Collaborating site(s):	University of Antwerp (Belgium) Gulu University (Uganda)
Study design:	Prevalence survey of Hep B and vertical transmission
Number of subjects:	619
Status:	Completed
Results and outcomes:	• Recruitment was completed however the recruitment target in the infected arms was not achieved due to low prevalence of mothers with at least one infection (HIV/HBV). • 410 babies were followed up and reviewed at 9 months. All babies tested negative for HBsAg as they were at the very beginning (6 weeks). • The estimated prevalence of HBsAg was 20% however this study found that the prevalence in the area was about 10%. • Preliminarily, 12% of the mothers were HIV positive, almost similar to HBsAg. Exposure rate (positive anti-HBcAb was 57.7%). Of all patients who tested positive for HBeAg, positivity rate was 17%, which means most of the chronic hepatitis B is basically of the HBeAg negative type also conforming to the fact that hepatitis B viral loads were relatively low- median HBV DNA of 6,805 IU/mL (IQR 39,22333). In this circumstance it is expected that perinatal transmission would be low and as has been seen in this

	study, there was no transmission in the patient population as majority of the mothers were in the inactive carrier phase of the infection. In a way therefore the 6 week vaccination is adequate in preventing transmission since most transmissions seem to occur by horizontal transmission in early childhood rather than in the perinatal period. The group hopes that if vaccination programs are adequate in the North of Uganda (and probably in the rest of the country as well), there should be a demonstrable reduction in the prevalence and incidence of HBV in the country over several years of successful vaccination program. • Dr Jackie Zirabamuzule was trained on this grant and has graduated with an MMed Internal Medicine. She conducted research on genotypes of hepatitis B in Uganda and found that Hepatitis B genotype A and D as the most predominant. • A consortium focusing on Hepatitis B has been formed to carry out further studies and assist in implementations of findings in the country. • A new collaboration has been developed John Hopkins university to study HIV and Hepatocellular carcinoma in Uganda where the grantee is the PI at the Uganda site.

1.1.22 Sabelle Jallow

EDCTP Project Coordinator:	Sabelle Jallow (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Functional characteristics of effector and memory NK cellular responses and their comparison with adaptive T cell responses in HIV-vaccinated subjects and risk populations
EDCTP Project Code:	TA.2011.40200.053
EDCTP Project Start Date:	1 December 2012
EDCTP Project End Date:	30 May 2015
Collaborators:	• Anders Fomsgaard (Statens Serum Institut, (SSI), Denmark) • Assan Jaye (MRC Laboratories, The Gambia) • Souleymane Mboup (University Cheikh Anta DIOP de Dakar (UCAD), Senegal) • Eleanor Mary Riley (London School of Hygiene and Tropical Medicine (LSHTM), UK)
Clinical Trial/Study Sponsor:	Medical Research Council (The Gambia)
Goal:	To explore the existence of effector and re-call NK responses and their comparative functional characteristics with adaptive responses on the available HIV study platforms developed within the network
Objective(s):	1. To determine if NK cell recall responses are elicited in HIV uninfected infants and infected adults who received HIV vaccine candidates 2. To determine if NK cell recall responses are present in HIV-exposed but uninfected adults and in HIV sero-discordant couples. If present, we will characterise these responses (both the effector recall NK responses) 3. To determine the relationship between NK cell responses and the frequency and quality of CD4+ and CD8+ T cell responses in at-risk populations
Clinical Trial/Study site(s):	The Gambia, Guinea Bissau and Dakar
Collaborating site(s):	• LSHTM (UK) • SSI (Denmark)
Study design:	Laboratory
Number of subjects:	Objective 1: 24 uninfected infants (vaccinated); 24 sex-matched controls (unvaccinated) Objective 2: 25 HIV-infected adults Objective 3: 20 sero-negative subjects, 20 HIV negative individuals (discordant partners) matched with 20 HIV positive partners (discordant); 30 sero-negative sex workers and 30 age matched HIV positive subjects
Status:	Ongoing
Results and Outcomes:	A preliminary analysis or a pilot study has been performed on some of the samples from the discordant couples cohort in Senegal. This data shows that HIV peptides can activate NK functional responses in HIV-positive individuals; and that HIV exposed but uninfected subjects elicit higher NK functional responses (as measured by higher degranulation and higher interferon –gamma production); and less NK activation (lower CD25) as compared to those who are HIV-infected. These results have been presented nationally, regionally and internationally. In a recent international scientific meeting, the 17th Annual meeting of the International Conference on AIDS and STIs in Africa (ICASA), in Cape town, South Africa, the

	abstract on results from this preliminary study won one of the five best abstract awards; the “Best Young Investigators award for basic science.

1.1.23 Collen Masimirembwa

EDCTP Project Coordinator:	Collen Masimirembwa (African Institute of Biomedical Science & Technology (AIBST), Zimbabwe)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	A prospective study to evaluate a pharmacogenetic-guided dosing algorithm based on patient CYP2B6 genotype compared to the empirical standard dose in the safe and efficacious use of efavirenz in HIV/AIDS patients in Zimbabwe
EDCTP Project Code:	TA.2011.40200.052
EDCTP Project Start Date:	1 November 2012
EDCTP Project End Date:	31 December 2014
Collaborators:	• Florence Chingwena (Harare City Health Department, Zimbabwe) • Prosper Chonzi (Harare City Health Department, Zimbabwe) • Milcah Dhoro (AIBST, Zimbabwe) • Gerard Kadzirange (University of Zimbabwe) • Tafireyi Nemaura (AIBST, Zimbabwe) • Charles Nhachi (University of Zimbabwe) • Roslyn Thelingwani (AIBST, Zimbabwe)
Clinical Trial/Study Sponsor:	AIBST (Zimbabwe)
Goal:	To evaluate the impact of an efavirenz pharmacogenetic-guided dosing algorithm with respect to safety and efficacy and comparing it to the empirical standard dosing of efavirenz
Objective(s):	Primary Objectives: 1. To compare efavirenz exposure levels in patients in whom the initiation dose is based on a pharmacogenetic algorithm with those in patients given the standard dose 2. To compare HIV viral load suppression and CD4 counts in patients in whom efavirenz dose is based on a pharmacogenetic algorithm with those in patients given the standard dose 3. To compare the incidences and severity of efavirenz associated adverse drug reactions; liver function, skin hypersensitivity reactions and central nervous system (CNS) effects in patients in whom the efavirenz dose is based on a pharmacogenetic algorithm with those given the standard dose 4. To validate the CYP2D6 genotyping method for use in the clinical study Secondary Objective: 1. To assess the cost-effectiveness of applying the pharmacogenetics dosing algorithm in the use of efavirenz
Clinical Trial/Study site(s):	• Wilkins Infectious Disease Hospital (Harare) • Chitugwiza Hospital, Opportunistic Infections Unit (Chitugwiza)
Study design:	Prospective randomised controlled trial
Number of subjects:	250
Product(s):	Efavirenz
Manufacturer:	Bristol-Myers Squibb
Trial registration number(s):	MRCZ/A/1561
Status:	Completed
Results and Outcomes:	1.

	(a) Recruitment of sufficient number of patients on ARVs from which a subset of patients specifically on efavirenz containing HAART has been completed. A total of 430 patients on ART and/or TB treatment have been recruited. Of these 190 patients are on efavirenz containing regimens. The mixing of HIV/AIDS and TB patients is because efavirenz is mostly used in HIV/AIDS patients who are also being treated for TB. (b) Mapping the ADRs profiles of the patients and dividing them into Cases and Controls for major ADRs associated with ARVs (skin hypersensitivity reactions, lipodystrophy, central nervous system and peripheral neuropathy) has been completed. The data clearly shows the significant role of efavirenz in predisposing patients to CNS side effects, thus provide a clinical link between efavirenz use and CNS side effects in our population. (c) The experimental validation of the CYP2B6 genotyping protocol which was then subsequently applied in genotyping the patients. Three approaches were evaluated, PCR-RFLP, allele specific PCR, RT-PCR and DNA sequencing and they all showed 100% concordance in determining the CYP2B6 genotype in 20 samples of GG, GT and TT genotypes (Dhoro et al., 2013a). A strong CYP2B6*6 genotype-CNS side effects association was observed (Dhoro et al. 2013b). This was in agreement with studies in other populations but the first time demonstrated in the Zimbabwean population. (d) Determination of the CD4 and viral load in the patients on efavirenz containing highly active antiretroviral therapy (HAART). This data will be important in relating efficacy of treatment in both TDM adjusted dose patients and those without adjustments, and latter with the plasma concentration for the drug, thus integrate the data in pharmacokinetic and pharmacodynamic (PK/PD) modelling (e) Experimental validation of the HPLC method for the determination of efavirenz and its major metabolite, 8-hydroxy efavirenz. The lower limit of quantitation (LLOQ) was 0.2 uM, the recovery from plasma was 95-103% with a coefficient of variation (CV) of <15%. The linearity was in the range 0.2 to 50 uM. This is very important in establishing the link between drug concentrations, CYP2B6 genotype and the occurrence and severity of ADRs. This triple link has only been demonstrated in a few case studies in Japan and will be for the first time in Africa and at population level. f) As indicated in our first report, the last part of our study was to establish the triple link of CYP2B6 genotype, efavirenz plasma concentrations and CNS side effects and the feasibility of using a pharmacogenetic based algorithm to individualise treatment with efavirenz. We have completed the sample collection and analysis of this study and are working on a manuscript on this data (M. Dhoro, S. Zvada, B. Ngara, C. Nhachi, G. Kadzirange, P. Chonzi, C. Final Technical Report Page 4 of 12 Masimirembwa. CYP2B6*6, CYP2B6*18, Body weight and sex are predictors of Efavirenz Pharmacokinetics and Treatment Response: Population pharmacokinetic modeling in an HIV/AIDS and TB cohort in Zimbabwe)

	HIV/AIDS and TB cohort in Zimbabwe. We have conclusively shown that the CYP2B6*6 genotype is predictive of high concentrations of efavirenz and predisposition to CNS sides effects and require only 200 mg of the drug instead of the standard 600 mg a day. We have also shown that for the other patients heterozygous, that those carrying one defect CYP2B6 allele and those without a defect should only be given 400 mg of efavirenz a day. Our findings are supported by a recent major study, ENCORE, which demonstrated the non-inferiority of 400 mg to the 600 mg efavirenz dose. This therefore represents the climax of our study which medicines control regulatory authorities should now consider towards revising the use of this drug. We have now engaged the Medicines Control Authority of Zimbabwe (MCAZ) and the National AIDS Council (NAC). We have also been on radio stations explaining our results to the public, an outreach that has been well received and patients phoned in expressing their appreciation of having the reason for their ADRs explained based on our study. 8. The work done so has also resulted in secondary of achievements such as: (1) Establishment of a Clinical Trial Research Group whose purpose is to critically discuss the design and execution of clinical studies in African settings. (2) Publication of 3 manuscripts and a manuscript in preparation (3) Initiation of a Clinical Trial Unit (CTC) at one of the major hospitals in Zimbabwe, Chitungwiza General Hospital, for the conduct of Phase I Clinical Studies. (4) The completion of PhD studies and successful defence of the thesis in December 2014, by Milcah Dhoro on Pharmacogenetics of Efavirenz
PhD study	Title: Determination of drug absorption, distribution, metabolism, excretion and toxicity (ADMET) biomarkers for drug safety and efficacy in the treatment of HIV/AIDS and TB in Zimbabwe Candidate: Milcah Dhoro (University of Zimbabwe)
Publications:	1. Dhoro M, Nhachi C , Masimirembwa C. Technological and cost comparison of cytochrome P450 2B6 (516G>T) genotyping methods in routine clinical practice*. African Journal of Biotechnology*. 2013.12(19): 2706-2710 (DOI: 10.5897/AJB2013.12043) 2. Nemaura T, Dhoro T, Nhachi C, Kadzirange G, Chonzi C, Masimirembwa C. Evaluation of the Prevalence, Progression and Severity of Common Adverse Reactions (Lipodystrophy, CNS, Peripheral Neuropathy, and Hypersensitivity Reactions) Associated with Anti-Retroviral Therapy (ART) and Anti-Tuberculosis Treatment in Outpatients in Zimbabwe. *AIDS and Clinical Research*. 2013; 4(4). 3. Dhoro M, Ngara B, Kadzirange G, Nhachi C, Masimirembwa C. Genetic variants of drug metabolizing enzymes and drug transporter (ABCB1) as possible

	biomarkers for adverse drug reactions in an HIV/AIDS cohort in Zimbabwe. *Curr HIV Res*. 2013 Sep;11(6):481-90. 4. Dhoro et al. CYP2B6*6, CYP2B6*18, Body weight and sex are predictors of efavirenz pharmacokinetics and treatment response: population pharmacokinetic modeling in an HIV/AIDS and TB cohort in Zimbabwe *BMC Pharmacology and Toxicology* (2015) 16:4

1.2 Tuberculosis Career Development and Senior fellowships

Table 4-2: Tuberculosis fellowship projects supported by EDCTP

Project Acronym (Coordinator)	Type of studyPhase of trial	Product(s)	Manufacturer / Developer	Study population	Status
Mukhtar – SF	Epidemiology of TB	None	Not applicable	100 villages randomly selected from five geographical regions in eastern Sudan, 100 households from each village resulting in recruitment of about 70,000 individuals	Closed
Hanekom – SF	Prospective cohort analyses	None	Not applicable	5,675 neonates	Closed
Rangaka – CDF	Immunology of TB reconstitution in HIV	None	Not applicable	Over 200 patients with HIV and TB	Closed
Adetifa –CDF	Comparison of immunological and molecular TB diagnostics techniques	None	Not applicable	188 stored samples (73 smear positive, 93 smear negative, 22 progressors)	Completed
Dheda – SF	Immunology of TB Lung innate immunity pathways	None	Not applicable	74 TB patients and health contacts	Completed
Nicol – SF	Point of care genotypic diagnosis of TB and drug resistance	GeneXpert	Cepheid, Sunnyvale, CA, USA	2522 patients	Completed
Nachega –SF	Phase II: Randomised placebo control trial for prevention of TB-IRIS with non-steroidal anti-inflammatory drugs	Meloxicam and omeprazole	Not applicable – generic formulations	TB patients on HAART	Ongoing
Oyakhirome – SF	TB, TB-HIV and MDR prevalence in preparation for future trials	None	Not applicable	General population	Completed
Hatherill –SF	Epidemiology of TB and intestinal helminthes infection	None	Not applicable	800 children in South Africa and Kenya	Ongoing
Worodria –SF	Monitoring treatment outcomes of TB patients on ART	None	Not applicable	230 TB patient on HAART in Kampala	Ongoing
Scriba –SF	Cohort studies on immunological determinants of TB	None	Not applicable	4 to 12 year old pre-adolescent children, at risk of progression to TB	Ongoing
Kouanda –SF	Phase II: PK studies for minimum	Rifabutin;	Not applicable	TB-HIV coinfected patients in	On going

	dosage	Lopinavir/ritonavir	(generic)	Burkina Faso	
Lamorde – SF	Phase IIIb: Evaulation of pharmacokinetic interactions between artemisinin-based therapies and rifampicin-based tuberculosis treatment in African patients	Dihydroartemisinin-Piperaquine/ Rifampicin	Sigma-Tau Pharmaceuticals Tubingen	TB patients (18-65 years) in their last month of Rifampicin treatment (Kampala, Uganda)	Ongoing
Padayatchi – SF	Phase IV study: Evaluation of efficacy and safety of 24 weeks moxifloxacin-containing regimen [isoniazid (H), rifampin I, pyrazinamide (Z), moxifloxacin (M)] with a 32 weeks control regimen [isoniazid (H), rifampiI(R), pyrazinamide (Z), ethamIol (E)] in TB retreatment.	Moxifloxacin Isoniazid/Rifampicin /Pyrazinamide	Bayer HeathCare Tubingen	Adults with a smear positive pulmonary TB with a past history of TB	Ongoing

1.2.1 Maowia Mukhtar

EDCTP Project Coordinator:	Maowia Mukhtar (University of Khartoum, Sudan)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	The burden of tuberculosis in eastern Sudan: epidemiology and drug resistance patterns of *Mycobacterium tuberculosis* isolates
EDCTP Project Code:	TA.2004.40200.005
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	30 June 2007
Collaborators:	• Greet Dieltiens Prince Leopold Institute of Tropical Medicine (ITM), Belgium • Nageed Saeed (Federal Ministry of Health, Sudan) • Patrick van der Stuyft (ITM, Belgium)
Goal:	To conduct epidemiological studies to identify suitable sites for future diagnostic, treatment and vaccine trials on tuberculosis in Sudan
Primary Objective(s):	• To study and map the burden of tuberculosis in Eastern Sudan • To undestand the epidemiology of pulmonary TB • To determine the drug resistance pattern of *Mycobacterium tuberculosis* isolates.
Study design:	Epidemiological survey
Number of subjects:	100 villages randomly selected from five geographical regions in eastern Sudan, 100 households from each village resulting in recruitment of about 70,000 individuals
Status:	Completed
Results and outcomes:	The project has produced epidemiological understanding of TB in Sudan which provides a foundation for future trials in TB

1.2.2 Willem Hanekom

EDCTP Project Coordinator:	Willem Hanekom (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	The BCG-induced immune correlates of protection against tuberculosis
EDCTP Project Code:	TA.2004.40200.004
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	6 October 2008
Collaborators:	• Adrian Hill (University of Oxford, UK) • Gregory Hussey (University of Cape Town, South Africa) • Gilla Kaplan (New Jersey Medical School, USA)
Goal:	To identify BCG immune correlates of protection against TB in children whose understanding is critical for TB vaccine development
Objective(s):	1. To determine whether the post-vaccination number, function and/or antigenic repertoire of specific conventional CD4+ and CD8+ T cells correlate with protection against TB 2. To determine whether the post-vaccination number and/or function of specific regulatory CD4+ T cells correlate with protection against TB 3. To determine whether the post-vaccination gene expression and cytokine secretion profiles of whole blood, and of PBMC, correlate with protection against TB.
Clinical Trial/Study site(s):	South African Tuberculosis Vaccine Initiative (SATVI, South Africa)
Collaborating site(s):	• New Jersey Medical School (USA) • University of Oxford (UK)
Study design:	Prospective cohort analyses
Number of subjects:	5662 children
Status:	Completed
Results and outcomes:	There were no differences in plasma levels of interferon-gamma, a cytokine commonly used to measure vaccination outcome, or any other cytokine, between the TB protected and TB non-protected children. However, when combinations of cytokines were evaluated, a model that included fractalkine, interleukin 12p40 and epidermal growth factor, correct discrimination in 82% of “protected” and “unprotected” infants was possible. Combinations of cytokines from plasma from blood incubated for 7 hours without antigen also allowed correct discrimination between the 2 groups. The studies on correlates of protective immunity from BCG have strengthened laboratories at SATVI which has since been awarded several EDCTP grants for TB vaccine studies and trials. This fellowship supported the return of Willem Hanekom to the country to re-establish his research career in South Africa.
Publications:	1. Hatherill M, Hawkridge T, Whitelaw A, Tameris M, Mahomed H, Moyo S, Hanekom W, Hussey G. Isolation of Non-Tuberculous Mycobacteria in Children Investigated for Pulmonary Tuberculosis. *PLoS ONE.* 2006 Dec;1:e21 2. Hanekom WA. The immune response to BCG vaccination of newborns. *Ann N Y Acad Sci*. 2005 Dec;1062:69-78 3. Murray RA, Mansoor N, Harbacheuski R, Soler J, Davids V, Soares A, Hawkridge A, Hussey GD, Maecker H, Kaplan G, Hanekom WA. Bacillus Calmette Guerin vaccination of human newborns induces a specific, functional CD8+ T cell response. *J Immunol*. 2006 Oct 15;177(8):5647-51

4. Hanekom WA, Abel B, Scriba TJ. Immunological protection against tuberculosis. *S Afr Med J*. 2007 Oct;97(10 Pt 2):973-7
5. Hussey G, Hawkridge T, Hanekom W. Childhood tuberculosis: old and new vaccines. *Paediatr Respir Rev*. 2007 Jun;8(2):148-54
6. Scriba TJ, Kalsdorf B, Abrahams D-A, Isaacs F, Hofmeister J, Black G, Hassan HY, Wilkinson RJ, Walzl G, Gelderbloem SG, Mahomed H, Hussey GD, Hanekom WA. Distinct, specific IL-17 and IL-22-producing CD4+ T cell subsets contribute to the human anti-mycobacterial immune response. *J Immunol*. 2008; 180:1962-1970
7. Beveridge NER, Fletcher HA, Hughes J, Pathan AA, Scriba TJ, Minassian A, Sander CR, Whelan KT, Dockrell HM, Hill A, Hanekom WA, McShane H. A comparison of IFNy detection methods used in tuberculosis vaccine trials. *Tuberculos*. November 2008;88(6):631-640.
8. Hatherill M, Hawkridge T, Zar HJ, Whitelaw A, Tameris M, Workman L, Geiter L, Hanekom WA, Hussey G. Induced sputum or gastric lavage for community-based diagnosis of childhood pulmonary tuberculosis? *Arch. Dis. Child*. 2009;94;195-201; originally published online 1 Oct 2008.
9. Soares AP, Scriba TJ, Joseph S, Harbacheuski R, Murray RA, Gelderbloem SJ, Hawkridge A, Hussey GD, Maecker H, Kaplan G, Hanekom WA. Bacille Calmette Guerin vaccination of human newborns induces T cells with complex cytokine and phenotypic profiles. *J Immunol*. 2008 Mar 1;180(5):3569-77.

1.2.3 Molebogang Rangaka

EDCTP Project Coordinator:	Molebogang Rangaka (University of Cape Town, South Africa)
EDCTP Project Call:	Career Development Fellowship
EDCTP Project Title:	Immunological investigation of the HIV-tuberculosis associated immune reconstitution
EDCTP Project Code:	TA.2005.40203.005
EDCTP Project Start Date:	15 December 2006
EDCTP Project End Date:	31 January 2009
Collaborators:	• Gary Maartens (University of Cape Town, South Africa) • Graeme Ayton Meintjes (University of Cape Town, South Africa) • Katalin Andrea Wilkinson (University of Cape Town, South Africa) • Robert Wilkinson (University of Cape Town, South Africa)
Goal:	To determine the frequency of *M.tb* specific T cells and serum cytokine agonist/antagonist ratios amongst IRIS cases compared to controls. The effect of steroid or placebo therapy on these variables was also studied.
Objective(s):	To understand the immune dysregulation that underlies HIV-Tuberculosis associated immune reconstitution inflammatory syndrome (TB IRIS).
Study design:	Laboratory investigations in a cohort of TB-HIV patients
Number of subjects:	>200 patients with HIV-TB co-infection
Status:	Completed
Results and outcomes:	The study has contributed to the establishment of well characterised cohorts of TB/HIV co-infected individuals in parts of Cape Town. Dr Rangaka competed for and was awarded a Wellcome Trust Training Fellowship at the end of the EDCTP award.
Publications:	1. Meintjes G, Rangaka M.X et al. Novel Relationship between Tuberculosis Immune Reconstitution Inflammatory Syndrome and Antitubercular Drug Resistance. *Clin Infect Dis*. 2009 Mar1;48(5):667-76. doi: 10.1086/596764 2. Meintjes G, Wilkinson KA, Rangaka MX, Skolimowska K, van Veen K, Abrahams M, Seldon R, Pepper DJ, Rebe K, Mouton P, van Cutsem G, Nicol MP, Maartens G, Wilkinson RJ. Type 1 Helper T Cells and FoxP3-positive T Cells in HIV–Tuberculosis-associated Immune Reconstitution Inflammatory Syndrome. *Am J Respir Crit Care Med*. 2008 Nov 15;178(10):1083-9. doi: 10.1164/rccm.200806-858OC. Epub 2008 Aug 28 3. Pepper DJ, Marais S, Maartens G, Rebe K, Morroni C, Rangaka MX, Oni T, Wilkinson RJ, Meintjes G. Neurologic Manifestations of Paradoxical Tuberculosis-Associated Immune Reconstitution Inflammatory Syndrome: A Case Series. *Clinical Infectious Diseases.* 2009 Jun 1;48(11):e96-107. doi: 10.1086/598988 4. Wilkinson KA, Seldon R, Meintjes G, Rangaka MX, Hanekom WA, Maartens G, Wilkinson RJ. Dissection of Regenerating T-Cell Responses against Tuberculosis in HIV-infected Adults Sensitized by *Mycobacterium tuberculosis*. *American Journal of Respiratory and Critical Care Medicine.* 2009 Oct 1;180(7):674-83. doi: 10.1164/rccm.200904-0568OC 5. Meintjes G, Wilkinson RJ, Morroni C, Pepper DJ, Rebe K, Rangaka MX, Oni T, Maartens G. Randomized placebo-

	controlled trial of prednisone for paradoxical TB-associated immune reconstitution inflammatory syndrome. *AIDS*. 2010 Sep 24;24(15):2381-90. doi: 10.1097/QAD.0b013e32833dfc68 6. Tadokera R, Meintjes G, Skolimowska KH, Wilkinson KA, Matthews K, Seldon R, Chegou NN, Maartens G, Rangaka MX, Rebe K, Walzl G, Wilkinson RJ. Hypercytokinaemia accompanies HIV-tuberculosis immune reconstitution inflammatory syndrome. *Eur Respir J*. 2011 May;37(5):1248-59. doi: 10.1183/09031936.00091010. Epub 2010 Sep 3.

1.2.4 Ifedayo Adetifa

EDCTP Project Coordinator:	Ifedayo Adetifa (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Project Call:	Career Development Fellowship
EDCTP Project Title:	A double blind, placebo controlled randomized trial of vitamin A supplementation for modulation of *Mycobacterium tuberculosis* immune responses in children aged 5-14 years with latent Tuberculosis
EDCTP Project Code:	TA.2005.40203.001
EDCTP Project Start Date:	15 March 2007
EDCTP Project End Date:	1 July 2010
Collaborators:	• Richard Adegbola (MRC Laboratories, The Gambia) • Martin Antonio (MRC Laboratories, The Gambia) • Philip Hill (MRC Laboratories, The Gambia)
Objective(s):	To provide additional evidence for the performance of novel diagnostics for latent tuberculosis and TB case detection in adults and children especially those with paucibacillary disease in a TB endemic country; and to identify differences in immune responses may improve our understanding of what constitutes protection against progression to TB in those latently infected
Study design:	Immunological studies in TB immunity
Number of samples:	188 stored samples (73 smear positive, 93 smear negative, 22 progressors)
Product:	
Manufacturer/Developer:	
Status:	Completed
Results and Outcomes:	In a cross sectional study, the ELISPOT test was more sensitive than the QFT-GIT for diagnosing TB disease, but both tests performed similarly in the diagnosis of LTBI in TB contacts. In an extension of this study to two newly licensed commercial IGRAs, it was found that both IGRAs and the TST responded in a similar manner to a gradient of exposure to TB. In addition, each IGRA in combination with TST increased sensitivity for diagnosis of LTBI but was also associated with a loss of specificity. Also tested as Hain Sciences Line probe assay, MTBDRplus® in a 2 step-procedure. On 93 smear negative culture positive samples, the LPA had a sensitivity of 45.2% (42 of 93) and over half of the results were blank. There was no relationship between the results from post decontamination ZN concentration staining and failed LPA results. In assessing gene expression for cytokines protective against TB disease progression IFN-γ was significantly lower in progressors compared to both non-progressors and TB cases ($p=0.0328$ and $p=0.0062$ respectively). For other cytokines-IL-10 and IL-12 similar levels were seen between the groups. IL-18 was significantly higher in progressors compared to non-progressors and confirmed TB cases ($p<0.001$ for both).
Publications:	1. Adetifa IM, Lugos MD, Hammond A, et al. Comparison of two interferon gamma release assays in the diagnosis of Mycobacterium tuberculosis infection and disease in The Gambia. *BMC Infect Dis*. 2007 Oct 25;7:122. 2. Lugos MD, Adetifa IM, Donkor S, Hill PC, Adegbola RA, Ota MO. Evaluation of the contribution of major T cell subsets to IFN-gamma production in TB infection by ELISPOT. *Immunol Invest*. 2009; 38:341-9. 3. Adetifa IM, Ota MO, Jeffries DJ, Hammond A, Lugos MD, Donkor S, Patrick O, Adegbola RA, Hill PC. Commercial

	interferon gamma release assays compared to the tuberculin skin test for diagnosis of latent *Mycobacterium tuberculosis* infection in childhood contacts in the Gambia. *Pediatr Infect Dis J*. 2010 May;29(5):439-43. doi: 10.1097/INF.0b013e3181cb45da. 4. Adetifa IM, Ota MO, Walther B, et al, Hill PC. Decay kinetics of an interferon gamma release assay with anti-tuberculosis therapy in newly diagnosed tuberculosis cases. *PLoS One*. 2010. Sep 1;5(9). pii:e12502.

1.2.5 Keertan Dheda

EDCTP Project Coordinator:	Keertan Dheda (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Human lung innate immune pathways regulating the stasis and killing of *M. tuberculosis* in a high burden setting
EDCTP Project Code:	TA.2007.40200.010
EDCTP Project Start Date:	28 July 2008
EDCTP Project End Date:	27 July 2010
Collaborators:	• Gregory Hussey (University of Cape Town, South Africa) • Graham Rook (University College London, UK) • Alimuddin Zumla (University College London, UK)
Objective(s):	1. To compare compartment-specific IFN- antigen-specific responses in TB versus non-TB patients 2. To procure and bank biological material (alveolar lavage fluid and cells) from HIV negative close contacts (of sputum smear positive patients) that have laboratory evidence of LTBI (TST+, IGRA+ i.e. converters) versus those that do not (TST-, IGRA- i.e. non-converters) 3. To compare expression and function of innate markers of protective immunity (pathogen recognition molecules/ receptors, cytokines, humoral factors and cell phenotypes) in converters and non-converters.
Collaborating site(s):	University College London (UK)
Study design:	Immunological studies
Status:	Completed
Results and outcomes:	Rapid diagnosis of TB meningitis by smear microscopy and PCR is problematic and the diagnostic delay can often translate into increased morbidity and mortality due to the poor sensitivity of these assays. The TB-specific quantitative T cell ELISPOT assay, when using CSF mononuclear cells and in conjunction with other rapid confirmatory tests (Gram stain and cryptococcal latex-agglutination) is an accurate and rapid rule-in test for TBM in a TB and HIV endemic setting. The RD-1, but not the purified-protein-derivative, cerebrospinal fluid-lymphocyte IFN-γ ELISPOT response is a useful rapid immunodiagnostic test for TBM. Further studies are continuing from the work described above.
Publications:	1. Patel VB, Singh R, Connolly C, ,Coovadia Y, Peer A, Parag P, Kasprowicz V, Zumla A, Ndung'u T, Dheda K. Cerebrospinal T cell responses aid the diagnosis of tuberculous meningitis in a HIV and TB endemic population. *Am J Respir Crit Care Med.* 2010 Aug 15;182(4):569-77. doi: 10.1164/rccm.200912-1931OC. Epub 2010 May 4. 2. Patel VB, Bhigjee AI, Paruk HF, Singh R, Meldau R, Connolly C, Ndung'u T, Dheda K. Utility of a novel lipoarabinomannan assay for the diagnosis of tuberculous meningitis in a resource-poor high-HIV prevalence setting. *Cerebrospinal Fluid Research.* 2009 November,2;6:13. PMID: 19878608 3. Cashmore TJ , Peter GJ, van Zyl-Smit RN, Semple PL, Maredza A, Meldau R, Zumla A, Nurse B, Dheda K. Feasibility and diagnostic utility of antigen-specific interferon-gamma responses for rapid immunodiagnosis of tuberculosis using induced sputum. *PLoS One*. 2010 Apr 28;5(4):e10389. PMID: 20442850? 4. Dheda K, van Zyl-Smit RN, Sechi LA, Badri M, Meldau R,

Meldau S, Symons G, Semple L, Maredza A, Dawson R, Wainright H, Whitelaw A, Vallie Y, Raubenheimer P, Bateman ED, Zumla A. Utility of quantitative T cell responses versus unstimulated IFN-{gamma} for the diagnosis of pleural tuberculosis. *Respir J*. 2009 Nov;34(5):1118-26. Epub 2009 Apr 22. PMID: 19386693

5. Dheda K, Van-Zyl Smit RN, Sechi LA, Badri M, Meldau R, Symons G, Khalfey H, Carr I, Maredza A, Dawson R, Wainright H, Whitelaw A, Bateman ED, Zumla A. Clinical diagnostic utility of IP-10 and LAM antigen levels for the diagnosis of tuberculous pleural effusions in a high burden setting. *PLoS One*. 2009;4(3):e4689. Epub 2009 Mar 11. PMID: 19277111
6. Dheda K, Smit RZ, Badri M, Pai M. T-cell interferon-gamma release assays for the rapid immunodiagnosis of tuberculosis: clinical utility in high-burden vs. low-burden settings. *Curr Opin Pulm Med*. 2009 May;15(3):188-200. Review. PMID: 19387262
7. Dheda K, van Zyl-Smit RN, Meldau R, Meldau S, Symons G, Khalfey H, Govender N, Rosu V, Sechi LA, Maredza A, Semple PL, Whitelaw A, Wainright H, Badri M, Dawson R, Bateman ED, Zumla A. Quantitative lung T cell responses aid the rapid diagnosis of pulmonary tuberculosis. *Thorax*. 2009 Oct;64(10):847-53. Epub 2009 Jul 9. PMID: 19592392
8. van Zyl-Smit RN, Dheda K, Meldau R. Quantitative Pulmonary T-Cell Responses for the Diagnosis of Active Tuberculosis. *Am J Respir Crit Care Med*. 2010 Feb 1;181(3):289; author reply 289-90. PMID: 20093656
9. van Zyl-Smit RN, Pai M, Peprah K, Meldau R, Kieck J, Juritz J, Badri M, Zumla A, Sechi LA, Bateman ED, Dheda K (senior and corresponding author). Within-subject variability and boosting of T-cell interferon-gamma responses after tuberculin skin testing. *Am J Respir Crit Care Med*. 2009 Jul 1;180(1):49-58. Epub 2009 Apr 2. PMID: 19342414
10. van Zyl-Smit RN, Zwerling A, Dheda K, Pai M. Within-subject variability of interferon-gamma assay results for tuberculosis and boosting effect of tuberculin skin testing: a systematic review. *PLoS One*. 2009 Dec 30;4(12):e8517. Review. PMID: 20041113
11. Dheda K, Schwander SK, Zhu B, Van Zyl-Smit RN, Zhang Y. The immunology of tuberculosis: From bench to bedside. *Respirology*. 2010 Apr;15(3):433-50. PMID: 20415982.

1.2.6 Mark Nicol

EDCTP Project Coordinator:	Mark Nicol (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	The impact of rapid genotypic detection of multi-drug resistant tuberculosis on treatment outcome in a semi-rural region of South Africa
EDCTP Project Code:	TA.2007.40200.009
EDCTP Project Start Date:	29 August 2008
EDCTP Project End Date:	20 September 2011
Collaborators:	• Willem Hanekom (University of Cape Town, South Africa) • Gregory Hussey (University of Cape Town, South Africa) • Lizette Phillips (Brewelskloof Hospital, South Africa) • Danie Theron (Brewelskloof Hospital, South Africa) • Tommie Victor (Stellenbosch University, South Africa) • Robert Wilkinson (University of Cape Town, South Africa)
Goal:	To assess the impact of a novel rapid molecular diagnostic test for tuberculosis and the presence of rifampicin resistance (Xpert MTB/RIF) on patient and health services outcomes.
Objective(s):	To determine whether the detection of tuberculosis by GeneXpert MTB/Rif testing in place of the routine diagnostic algorithm will lead to a reduction in: number of clinic visits prior to appropriate TB treatment; time to appropriate treatment for TB and reduced morbidity and mortality due to undiagnosed TB; number of TB cultures requested per patient; TB-related clinic workload and TB-related laboratory workload
Clinical Trial/Study site(s):	Blewelskloof Hospital, Khayelitsa, Worcester (South Africa)
Study design:	TB point of care diagnosis
Number of subjects:	1577
Product:	GeneXpert
Manufacturer/Developer:	Cepheid, Sunnyvale (USA)
Status:	Completed
Results and outcomes:	1577 patients with suspected TB were recruited. GeneXpert improves accuracy and shortens duration of diagnosis to treatment. The preliminary results of this study formed a substantial component of a report submitted to the WHO Strategic and Technical Advisory Group for Tuberculosis which in September 2010 issued a recommendation that Xpert MTB/RIF replace smear microscopy as the first line diagnostic test for TB in areas with high prevalence of MDR-TB or HIV. South-North networking in the project was well established working with the Foundation for Innovative New diagnostics (FIND) and TB Clinical Diagnostics Research Consortium of Johns Hopkins University and Boston Medical Centre. Other collaborative projects included development of a novel point-of-care diagnostics for TB with Northwestern University, USA. In the south the project links with EDCTP funded TB-NEAT consortium (PI Keertan Dheda), Wellcome Trust project in Malawi and Zimbabwe.
Publications:	1. Boehme CC, Nicol MP, Nabeta P, Michael JS, Gotuzzo, Tahirli R, Gler MT, Blakemore R, Worodria W, Gray C, Huang L, Caceres T, Mehdiyev R, Raymond L, Whitelaw A, Sagadevan K, Alexander H, Albert H, Cobelens F, Cox H, Alland D, Perkins MD. Feasibility, diagnostic accuracy, and effectiveness of decentralised use of the Xpert MTB/RIF test for diagnosis of tuberculosis and multidrug resis55ulticentrelticenter implementation study. *Lancet.* 2011 Apr 30;377(9776):1495-505

1.2.7 Jean Nachega

EDCTP Project Coordinator:	Jean Nachega (Stellenbosch University, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	A Multi-Site Double-Blind Placebo Controlled Randomised Clinical Trial to Prevent Immune Reconstitution Inflammatory Syndrome with Non-Steroid Anti-Inflammatory Drugs
EDCTP Project Code:	TA.2008.40200.021
EDCTP Project Start Date:	9 February 2010
EDCTP Project End Date:	31 December 2014
Collaborators:	• Robert Colebunders (University of Antwerp, Belgium) • Ingrid Wilson (Stellenbosch University, South Africa) • Gary Simon (Geroge Washinton University, USA)
Goal:	To investigate immune-modulation of non-steroidal anti-inflammatory treatment in TB IRIS among HIV infected patients
Objective(s):	1. Evaluate the impact of NSAIDs compared to placebo on preventing TB-IRIS in a TB-HIV infected South African Adults 2. Evaluate the impact of NSAIDs compared to placebo on CD4+ T-cell count recovery following initiation of ART in TB-HIV infected South African Adults 3. Evaluate the impact of NSAIDs compared to placebo on HIV-1 RNA response following initiation of ART in TB-HIV infected South African Adults 4. Evaluate the impact of NSAIDs compared to placebo on adherence of both TB and HIV medication following initiation of ART in TB-HIV infected South African Adults 5. Assess the impact of NSAIDs compared to placebo on quality of life following initiation of ART in TB-HIV infected South African Adults
Collaborating site(s):	• University of Antwerp (Belgium) • George Washington University • University of Western Cape
Study design:	Phase II: Randomised placebo control trial for prevention of TB-IRIS with non-steroidal ant-inflammatory drugs on TB patients on HAART
Trial registration	NCT02060006 (www.ClinicalTrials.gov) 2014RP034 (Western Cape Government, Department of Health)
Product:	Meloxicam and omeprazole
Manufacturer/Developer:	Generic formulations
Cofunders:	• Stellenbosch University (South Africa)
Status:	Completed
Results and outcomes:	Enrolment into the study started on 1 April 2014 . A GMP manufacturing facility for preparation of the double-blind (double-dummy capsules) formulation of Meloxicam (Mobic®) and placebo has been finalized; this work has been managed by the University of the Western Cape (Dr R Bapoo) under supervision of the Division of Pharmacology, Stellenbosch University (Professor Rosenkranz, co-investigator on this project and head of Division of Clinical Pharmacology at Stellenbosch University).

1.2.8 Sunny Oyakhirome

EDCTP Project Coordinator:	Sunny Oyakhirome (Albert Schweitzer Hospital, Gabon)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Career development and strengthening institutional capacity for clinical research in TB at the Faculty of Health Sciences in Brazzaville
EDCTP Project Code:	TA.2009.40200.010
EDCTP Project Start Date:	13 April 2010
EDCTP Project End Date:	13 April 2012
Collaborators:	• Michel Bitemo (CERVE) • Vladimir Malonga (Fondation Congolaise pour al Recherche Médicale (FCRM)/Faculté des sciences de la santé (FSSA), Congo) • Pembe Issamou Mayengue (FCRM/FSSA, Congo) • Mitawa Missontsa (FCRM/FSSA, Congo) • Benjamin Mordmüller (Albert Schweitzer Hospital, Gabon) • Francine Ntoumi (FCRM/FSSA, Congo) • Veronique Penlap Beng (University of Yaounde, Cameroon)
Objective(s):	To determine the prevalence of TB, TB/HIV co-infection and multi drug resistant TB (MDR) infections in the Congolese population and identify groups most at risk for recent TB transmission in urban areas of Brazzaville in the Republic of Congo. A follow up will be set up for evaluating TB transmission in Congo; quantify the problem of recent transmission and characterized circumstances and settings for transmission
Clinical Trial/Study site(s):	
Collaborating site(s):	• University of Yaounde (Cameroon) • Albert Schweitzer Hospital (Gabon)
Study design:	Trial site development
Status:	Completed
Results and outcomes:	Preliminary reports show that the EDCTP grant in Congo supported personnel, maintenance of laboratory equipment with their consumables and reagents. A TB research team formed as the result of the grant included a molecular biologist (Dr Pembe), a biostatistician (Mr Bitemo) and a local physician (Dr Mitawa). In the project period the newly formed team devoted time to the preparation of standards operating procedures necessary for handing TB and TB-HIV samples (from recruitment of patients to data analysis). The TB project has established collaboration with the TB CANTAM site at University Yaounde1 in Cameroon, University of Tübingen and the Medical Research Unit of Albert Schweitzer Hospital in Lambarene, Gabon.

1.2.9 Mark Hatherill

EDCTP Project Coordinator:	Mark Hatherill (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	The risk of pulmonary tuberculosis associated with intestinal helminth infection among children at two tuberculosis vaccine trial sites in sub-Saharan Africa
EDCTP Project Code:	TA.2009.40200.015
EDCTP Project Start Date:	20 April 2010
EDCTP Project End Date:	30 June 2014
Collaborators:	• Willem Hanekom (University of Cape Town, South Africa) • Gregory Hussey (University of Cape Town, South Africa) • Pauline Mwinzi (Kenya Medical Research Institute (KEMRI), Kenya) • Videlis Nduba (KEMRI, Kenya)
Objective(s):	Primary objectives: 1. To determine whether prevalent infection with intestinal helminths is associated with increased risk of pulmonary tuberculosis disease in children 2. To determine whether maternal infection with intestinal helminths is associated with increased risk of pulmonary tuberculosis disease in children 3. To compare the risk of pulmonary tuberculosis disease associated with prevalent infection with intestinal helminths between the research site in Breede Valley, South Africa, and the research site in Siaya District, Kenya. Secondary specific aims: 1. To determine whether prevalent infection with intestinal helminths is associated with increased risk of LTBI in children 2. To determine whether maternal infection with intestinal helminths is associated with increased risk of LTBI in children.
Collaborating site(s):	KEMRI (Kenya)
Study design:	Epidemiology of TB
Number of subjects:	800 (target) in both Kenya and South Africa
Status:	Completed
Results and outcomes:	Research activities: The study was critically dependent on a separate TB vaccine trial recruitment platform; however, recruitment in this trial was stopped and this affected recruitment rates at both the KEMRI and UCT site. A total of 326 participants (50% of the original 650 enrolment target) were enrolled in the absence of the TB vaccine trial recruitment platform. Therefore, in order to mitigate the risk of being underpowered to address the primary aims, focus shifted to the secondary aim research outputs, and analysis of the relationship between infant and maternal helminth exposure, measured by species specific antibody (IgG4), and mycobacterial immune responses. Results: UCT Site: Of the 209 participants enrolled, 177 participants had one TB Investigation and 32 participants had 2 admissions. Among the 177 children with one TB investigation, 19 cases of TB disease (10.7%) and 41 cases of TB Infection (23.1%) were observed. Only one child (0.8%) with helminth infection was

	observed. KEMRI Site: All of the 117 participants enrolled at the KEMRI site were 1st TB investigations, amongst whom only 5 children were diagnosed with TB disease (4.3%), less than half the rate at the UCT site. However, by contrast to the UCT site, 11 children (9.4%) had helminth Infection, a rate more than ten- fold greater. The findings of this study indicate that the childhood helminth co-Infection rate at the SATVI/UCT site has fallen dramatically from pre-study levels, perhaps due to public health Interventions such as mass deworming. Nevertheless, the incidence rate of childhood TB remains high. By contrast, the high prevalence of helminth Infection among children at the KEMRI/CDC site Indicate that helminth co-infection should be considered as a potential confounder un TB vaccine trails and other studies at the site. Capacity Building: Post-graduate PhD student E. Muok (KEMRI) visited UCT in 2012 and was trained on the intracellular Cytokine Staining (ICS) Whole blood Assay (WBA), a key measure of TB vaccine take, at the SATVI laboratories in Worcester and Cape Town. Post-graduate PhD student Erin Gray (funded by the Horsnell Laboratory) visited KEMRI/CDC in 2013 to learn about the field site and plan helminth Immunology asays in conjunction with Drs Horsnell, Hatherill, Nduba, and Mwinzi. Networking: Networking between the KEMRI and UCT sites led to Dr Horsnell (UCT) and Dr Mwinzi (KEMRI/CDC) developing an ongoing helminth research collaboration, including an invited presentation at a KEMRI workshop (Dr Horsnell), and an invitation to contribute a chapter for a book (Dr Mwinzi; Dr Horsnell Editor). The first participant was enrolled at the UCT site on 7 March 2011. By the end of 2011, a total of 135 infants had been enrolled (42% of the 325 target for Year 1). Health system strengthening has resulted in increased use of anthelmintic treatment in the community, with the result that 198 (32%) of 610 screened infants were excluded for this reason.

1.2.10 William Worodria

EDCTP Project Coordinator:	William Worodria (Makerere University, Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Short- and long-term clinical and immunological outcomes of patients with HIV/TB coinfections on ART
EDCTP Project Code:	jallow
EDCTP Project Start Date:	11 April 2011
EDCTP Project End Date:	11 April 2014
Collaborators:	• Robert Colebunders (University of Antwerp Belgium) • Yukari Manabe (Makerere University, Uganda)
Clinical Trial/Study Sponsor:	University of Amsterdam (The Netherlands)
Objective(s):	To study short-term effects of TB and ART treatment (the incidence, predictors and clinical characteristics of TB-IRIS, side effects of the therapy, causes of early mortality) and long term effects of ART after completing TB treatment (clinical events such as infections, late-onset IRIS, adverse effects of therapy or immunological and virological events such as changes in CD4 counts, CD4 %; viral load, viral resistance). Also to study possible factors influencing these outcomes such as adherence and factors affecting them, TB relapse and mycobacteriological factors, immunological defects and social factors that are associated with a recurrent TB episode and causes of mortality
Collaborating site(s):	• University of Antwerp (Belgium)
Study design:	Treatment monitoring
Number of subjects:	280 (target)
Product:	Prequalified TB regimens and HAART
Status:	Completed
Results and outcomes:	By 30 July 2012 the project had enrolled 79 study participants of which 44 were enrolled in the study. 29 of those enrolled in the study are on both HAART and TB treatment. Patient follow-up is continuing. Research activities: Despite a delay in enrolment, 189 out of 280 targeted patients were enrolled for the study. 126 patients completed study follow-up. All clinical activities were completed by 31 December 2013. Data analysis is still ongoing due to data issues therefore research results have not been reported for this project. An abstract for the International Union Against TB and Lung Disease Meeting in Barcelona has been accepted and is awaiting finalization. Capacity Building: Dr Jabo Christian who is enrolled on Masters of Medicine in Radiology at Makerere University successfully defended his thesis in May 2014. Ms Justine Nakiwala, the PhD student at the Institute of Tropical Medicine, Antwerp who was studying the role of neutrophils in the pathogenesis of TB-IRIS opted to carry out her research from another site in South Africa.

1.2.11 Thomas Scriba

EDCTP Project Coordinator:	Thomas Scriba (University of Cape Town, South Africa)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Inflammatory determinants of risk of tuberculosis disease
EDCTP Project Code:	TA.2011.40200.010
EDCTP Project Start Date:	5 March 2012
EDCTP Project End Date:	5 March 2014
Collaborators:	• Willem Hanekom (University of Cape Town, South Africa) • Martin Ota, (Medical Research Council Laboratories (MRC), The Gambia) • Suzanne Verver (KNCV Tuberculosis Foundation, Netherlands) • Robin Wood (University of Cape Town, South Africa)
Goal:	The hypothesis is that the innate response to *M.tb* in pre-adolescent children, with low-risk of progression to TB, is characterised by an appropriate and advantageous inflammatory response and this inflammatory response mediates better control of intracellular bacterial growth, compared with innate responses in adolescents, with high risk of progression, who have excessive inflammatory responses.
Objective(s):	The research questions are: 1. Do children between 4 and 12 years of age (low-risk of progression to TB) have less pronounced, or more regulated, inflammatory responses to mycobacteria, compared with adolescents (high-risk of progression)? 2. Do innate immune cells of children between 4 and 12 years of age have greater capacity to control intracellular bacterial growth, compared with innate immune cells of adolescents? 3. How do mycobacteria-specific T cells modulate the innate immune responses in these two age groups?
Collaborating site(s):	KNCV (The Netherlands)
Study design and population:	Cohort studies; 4 to 12 year-old pre-adolescent children, at risk of progression to TB
Number of subjects:	103
Status:	Completed
Results and outcomes:	Research Outcomes: • Completed enrolment of 117 study participants in April 2013; 64 adolescents aged 18 years (39 M.tb infected and 25 not M.tb infected) and 53 children aged 8 years (25 M.tb infected and 18 not M.tb infected). • Blood processing was successfully completed for the enrolled participants. Samples were collected and processed at a single time point from these study participants and since blood processing and mycobacterial growth inhibition assays had to be done in real time, these were successfully completed by mid-May 2013. • Completed selection of primer/probe sets that would measure mRNA expression of gene(s) involved in inflammation, regulation of inflammation and immunopathology. • Optimization of RNA extraction was completed although this was delayed by 8 months due to testing a large number of methods. • Only the whole blood mycobacterial growth inhibition assay was completed. The other assays are still being

	completed. Results from the growth inhibition assay revealed no significant differences between the different age groups, nor between M.tb infected and uninfected children. The data suggested that these whole blood growth inhibition assays do not provide a useful measure of age-associated differential host control of M.tb infection, or that no real biological differences exist between 8 and 18 year olds. The results obtained were unexpected given previous evidence of greater growth inhibition in infected persons from settings not endemic for TB. Capacity development: An MSc student, Jonathan Day, Postdoctoral fellow Adam Penn-Nicholson and PhD student Richard Baguma were trained in various clinical and laboratory research skills (details in report). A BSc Honours student, Tamlyn Mac Quene is performing the flow cytometry analysis as part of her research project. The study team personnel from SATVI received training in several soft skills and specific training in HIV counselling and Phelebotomy. Networking: The PhD student presented the preliminary results at several forums in South Africa and USA. Two new collaborations with Robin Wood at the University of Cape Town and Robert Wallis at The Aurum Institute, have been developed. Additionally, the research group at SATVI is now part of the new mycobacterial growth inhibition assay (MGIA) development group, a consortium of international scientists and organisations funded by the United States Food & Drug Administration (FDA). The group also managed to attract co-funding for the clinical activities required to enrol participants.

1.2.12 Riflopi

EDCTP Project Coordinator:	Seni Kouanda (Institut de Recherche en Sciences de la Santé, Burkina Faso)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Rifabutin with lopinavir/ritonavir in patients coinfected with tuberculosis and HIV in Burkina Faso: Pilot study of pharmacokinetics to define the minimum effective dose
EDCTP Project Code:	TA.2011.40200.026
EDCTP Project Start Date:	20 March 2012
EDCTP Project End Date:	20 March 2014
Collaborators:	• Potiandi Serge Diagbouga (Centre Muraz, Burkina Faso) • Regazzi Marrio (University of Pavia, Italy) • Alberto Matteelli (University of Brescia, Italy) • Gautier Ouédraogo (Institut de Recherche en Sciences de la Santé, Burkina Faso)
Objective(s):	1. To assess the pharmacokinetic profile of rifabutin (RFB) and its active metabolite 25-O-desacetyl-rifabutin on the two dosing regimens (RFB 150 mg or 300 mg 3 times a week) in TB-HIV coinfected patients in Burkina Faso, a resources-limited country with high prevalence of tuberculosis and HIV 2. To determine the pharmacokinetics parameters of RFB in combination with Lopinavir/ritonavir in Burkinabe HIV infected patients with tuberculosis, in order, to define optimal doses that will be further tested in a larger phase III trial comparing safety, tolerability and efficacy of RBT and RMP regimens in West Africa.
Collaborating site(s):	University of Brescia (Italy)
Study design and population:	Phase II: Pharmacokinectics for dosing; TB-HIV co-infected patients in Burkina Faso
Number of subjects:	ADULTS (≥18 years); HIV+ individuals; N=30
Product:	Rifabutin; Lopinavir/ritonavir
Manufacturer/Developer:	Generic formulations
Trial No:	PACTR201310000629390
Status:	Completed
Results and outcomes:	Capacity Building and networking: The fellow and co-investigator attended several training courses over the duration of the project to enhance their ability to develop and implement a clinical trial. In addition, the co-investigator had an opportunity to intern at the LBV in Aristide le Dantec University in Senegal. The fellow managed to develop collaborations with several research institutions and a pharmaceutical company to assist with acquisition of the investigational drugs, protocol development and skill transfer in the field of drug interactions and clinical research. In addition, the grantee managed to obtain funding to build and equip a new biomedical laboratory. Research: The target sample size was 30, but recruitment was delayed due to the drug acquisition process and delayed approval from the national regulatory committee. Only 11 patients had been enrolled at the time of reporting. 10 patients have undergone pharmacokinetic tests and data analysis is currently underway.

1.2.13 Mohammed Lamorde

EDCTP Project Coordinator:	Mohammed Lamorde (Makerere University, Uganda)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Evaluating pharmacokinetic interactions between artemisinin-based therapies and rifampicin-based tuberculosis treatment in African patients
EDCTP Project Code:	TA.2011.40200.047
EDCTP Project Start Date:	1 November 2012
EDCTP Project End Date:	30 April 2015
Collaborators:	• Abdulrazaq Habib (Bayero University, Nigeria) • Saye Khoo (University of Liverpool, UK) • Concepta Merry (University of Dublin, Ireland) • Pauline Byakika-Kibwika (Makerere University, Uganda) • Robert Balikuddembe (Makerere University, Uganda) • Andrew Kambugu (Makerere University, Uganda) • Lydia Nakiyingi (Makerere University, Uganda) • Alphonse Okwera (Makerere University, Uganda) • Joel Tarning (Mahidol University, Thailand)
Clinical Trial/Study Sponsor:	IDI, Makerere University College of Health Sciences, Kampala
Goal:	To investigate drug interactions between antimalarial and anti TB drugs with the overall goal of developing co-treatment strategies for malaria and TB co-infection
Objective(s):	Primary • Group 1: To investigate the single-dose PK of dihydroartemisinin (DHA) and piperaquine following oral administration of dihydroartemisinin-piperaquine to patients receiving rifampicin and to the same patients after completing rifampicin regimen • Group 2: To investigate the single-dose PK of artesunate, DHA, amodiaquine and DEAQ following oral administration of artesunate-amodiaquine to patients receiving rifampicin and to the same patients after completing rifampicin regimen • Group 3: To investigate the single-dose PK of artesunate and DHA following intravenous administration of artesunate to patients receiving rifampicin and to the same patients after completing rifampicin regimen. Secondary • To assess the short-term safety of the study drugs during rifampicin intake and after completing rifampicin regimen.
Clinical Trial/Study site(s):	Mulago National Teaching and Referral Hospital, Kampala (Uganda)
Collaborating site(s):	Bayero University Kano (Nigeria)
Study design:	Pharmacokinetic study
Number of subjects:	36
Product(s):	• Dihydroartemisinin-piperaquine (tablets) • Amodiaquine-artesunate (tablets) • Artesunate for injection
Trial registration number(s):	Pan African Clinical Trial Registry (PACTR201302000483287).
Status:	Ongoing
Results and Outcomes:	The initiation meeting for the clinical trial was held on 19/08/2013. Patient screening commenced on 09/09/13. The first subject was enrolled on 26/09/13. By October 31, nine (9) subjects had been screened and 5 subjects had been enrolled and commenced phase 1 intensive PK sampling.

Publications:	1. Seden K, Khoo S, Back D, Prevatt N, Lamorde M, Byakika-Kibwika P, Mayito J,Ryan M, Merry C. Drug-drug interactions between antiretrovirals and drugs used in the management of neglected tropical diseases: important considerations in the WHO 2020 Roadmap and London Declaration on Neglected Tropical Diseases. *AIDS*. 2013 Mar 13;27(5):675-86. 2. Lamorde M, Byakika-Kibwika P, Mayito J, Nabukeera L, Ryan M, Hanpithakpong W, Lefèvre G, Back DJ, Khoo SH, Merry C. Lower artemether, dihydroartemisinin and lumefantrine concentrations during rifampicin-based tuberculosis treatment. *AIDS*. 2013 Mar 27;27(6):961-5.

1.2.14 Nesri Padayatchi

EDCTP Project Coordinator:	Nesri Padayatchi (University of KwaZulu-Natal, South Africa)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Improving retreatment success of tuberculosis
EDCTP Project Code:	TA.2011.40200.044
EDCTP Project Start Date:	1 January 2013
EDCTP Project End Date:	31 December 2014
Collaborators:	• Gavin John Churchyard (Aurum Institute for Health Research, South Africa) • Wafaa El-Sadr (Columbia University, USA) Sarah Fortune (Harvard School of Public Health, USA) • Gerald Friedland (Yale University, USA) • William Jacobs (Albert Einstein College of Medicine, USA) • Salim S. Abdool Karim (University of KwaZulu-Natal, South Africa)
Clinical Trial/Study Sponsor:	CAPRISA
Goal:	To define an effective, shortened TB retreatment regimen that aims to improve retreatment TB outcomes and reduce TB treatment interruption and failure
Objective(s):	1. To determine if a moxifloxacin-containing regimen [isoniazid (H), rifampin (R), pyrazinamide (Z), moxifloxacin (M)] of 24 weeks duration is superior to a control regimen [isoniazid (H), rifampicin(R), pyrazinamide(Z), ethambutol(E)] of 32 weeks duration in improving treatment outcomes in patients with recurrent TB Secondary objectives: 1. To compare TB Treatment outcomes in the 2 arms 2. Proportion of patients who are culture negative at 8 weeks 3. Time to first culture negative sputum 4. Safety: Comparison of patients with Grade 3 and 4 adverse events 5. Efficacy: Failure of bacteriological cure and relapse within 1 year of completion of therapy as defines by culture using solid media
Clinical Trial/Study site(s):	CAPRISA eThekwini Clinical Research Site (eCRS), adjoining the largest government outpatient TB facilities, the Prince Cyril Zulu Communicable Disease Centre (PCZCDC)
Study design:	Randomised controlled trial
Number of subjects:	362
Product(s):	Moxifloxacin
Manufacturer/Developer:	Bayer
Cofunders:	CAPRISA
Trial registration number(s):	Pending
Status:	Completed
Results and Outcomes:	The site successfully opened participant recruitment and screening on 22 November 2013, with the first participant being randomized into the study on 25 November 2013.
PhD study:	Title: Improving Retreatment Success in TB Candidate: Nesri Padayatchi (South Africa)
Other/Sub-studies:	PK study on interaction of Moxifloxacin with Tenofivir

1.3 Malaria Career Development and Senior fellowships

Table 5-3: Malaria fellowship projects supported by EDCTP

Project Acronym (Coordinator)	Study classification /design	Product(s)	Manufacturer / Developer	Study population	Status
Djimde - SF	Phase IV randomised trial Mali	AS/AQ, AS/SP and AR-L	Pre-qualified drugs	780 subjects in which 2463 malaria episodes studied	Completed
Nzila - SF	Laboratory study to investigate the mechanism of piperaquine resistance	DHA-piperaquine and artemether-lumefantrine	Not applicable (used samples from completed clinical trials)	In-vitro cultures of Plasmdium falciparum	Completed
Talisuna - SF	Phase IV: Pharmacovigilance of anti-malarial drugs in Uganda	None	Not applicable	None (training of health staff and comparison by health facility/region)	Completed
Nebie -SF	Immunological studies on the role of T cells in malaria endemicity	None	Not applicable	219 adults and children in Burkina Faso	Completed
Moukoko -CDF	Malaria virulence markers	None	Not applicable	In vitro assays	Completed
Nwakanma - SF	PCR diagnosis of malaria	None	Not applicable	Out patients with malaria symptoms in Gambia	Completed
Cisse - SF	Phase III: IPT with community participation	Pyrimethamine/Sulphamethopyrazine (Dualkin); DHA and Piperaquine; and	Pre-qualified drugs	1893 children	Completed

		AS and AQ			
Dodoo - SF	In-vitro assessment of malaria antibodies	None	Not applicable	In vitro assays	Completed
Happi - SF	Biomarkers of artemesinin resistance	None	Not applicable	In vitro and in vivo assays	Completed
Phiri - SF	Phase II trial of oral iron therapy for treatment of post-malaria iron-deficiency anaemia in children	Iron and iron isotopes	International Atomic Energy Agency	Children under 3 with malaria	Completed
Achidi - SF	Baseline studies for clinical trials site develpment	None	Not applicable	General population in Cameroon	Completed
Tiono - SF	Phase IV: Cluster randomised trial: Impact of nets, home management and rapid diagnosis on malaria mortality in children	?	?	40 clusters of 40 children each and followed for 2 years	Completed
Byakika Kibwika - SF	Phase II: Safety, efficacy, PK and interaction with ART of iv artesunate and iv quinine	IV artsunate and (Quinine, ACT (Artemether-Lumefantrine or Dihydroartemisinin-piperaquine)	Gilead (for iv artesunate only). And prequalified for oral ACT (Artemether-Lumefantrine or Dihydroartemisinin-piperaquine) and Quinine	330 adult patients	Completed
Kouriba - SF	Immunological cohort studies: Role of monocytes in protection	None	Not applicable	In vitro assays	Completed

	against malaria in Mali				
Toure - SF	In-vitro studies: Evaluation of malaria immunity and merozoite vaccine candidates	None	Not applicable	In vitro assays	Completed
Ndiaye - SF	Cluster randomised Trial: IPT and home management of malaria in Senegal	None	Not applicable	24 clusters of villages randomised to each intervention	Completed
Adegnika -SF	Immunology studies of schisto/malaria co-infection	None	Not applicable	School children residing in two communities in the vicinity of Lambaréné	Completed
Obonyo – SF	Phase IV: Clindamycin and quinine for treating uncomplicated falciparum malaria: an open-labelled randomized trial	Clindaquine (Cleocine ®) Quinine Artemether-Lumerfantrine	Pfizer Tubingen Novartis International AG	Children (<5 years)	Completed
Beavogui - SF	Baseline study of epidemiological and sociological aspects of malaria in the four natural regions of Guinea	None	Not applicable	Children (6-10 years) in the four natural regions of Guinea	Completed

1.3.1 Abdoulaye Djimde

EDCTP Project Coordinator:	Abdoulaye Djimde (Malaria Research & Training Center, Malaria)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Assessment of the Public Health Benefit of artemisinin based combination therapies for uncomplicated malaria treatment in Mali
EDCTP Project Code:	TA.2004.40200.003
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	8 February 2009
Collaborators:	• Demba Dembele (Malaria Research & Training Center, Mali) • Bakary Fofana (Malaria Research & Training Center, Mali) • Bakari Sidibe (Malaria Research & Training Center, Mali) • Sekou Toure (Malaria Research & Training Center, Mali)
Objective(s):	1. To test hypothesis that repeated administration of artesunate/amodiquine (AS/AQ), artesunate pyrimethamine (AS/SP) and coartem (AR-L) for treatment of consecutive episodes of uncomplicated malaria reduces the incidence of uncomplicated malaria and attributable malaria 2. To measure the impact of repeated administration of the drugs on malarial immunity and malaria transmission
Study design:	Phase IV randomised trial
Number of subjects:	780
Product:	AS/AQ, AS/SP and AR-L
Manufacturer/Developer:	Prequalified drugs
Status:	Completed
Results and outcomes:	A total of 780 subjects were recruited with 260 per treatment arm. Collectively, they experienced 2463 episodes of malaria. Combined therapy of Arsucam or Arsumax reduced malaria incidence more than Coartem.
Publications:	1. Kaddouri H, Djimdé AA, Dama S, Kodio A, Tekete M, Hubert V, Koné A, Maiga H, Yattara O, Fofana B, Sidibe B, Sangaré CPO, Doumbo OK, Le Bras J. Baseline *in vitro* efficacy of ACT component drugs on *Plasmodium falciparum* clinical isolates of Mali. *Int J Parasitol*. 2008 Jun;38(7):791-8. Epub 2008 Jan 3 2. Djimdé AA, Fofana B, Sagara I, Sidibe B, Toure S, Dembele D, Dama S, Ouologuem D, Dicko A, Doumbo OK. Efficacy, Safety, and Selection of Molecular Markers of Drug Resistance by two ACTs in Mali. *Am. J. Trop. Med. Hyg*. 2008;78(3): 455–461 3. Tekete M, Djimde AA, Beavogui AH, Maiga H, Sagara I, Fofana B, Ouologuem D, Dama S, Kone A, Dembele D, Wele M, Dicko A, Doumbo OK. Efficacy of chloroquine, amodiaquine and sulphadoxine-pyrimethamine for the treatment of uncomplicated falciparum malaria: revisiting molecular markers in an area of emerging AQ and SP resistance in Mali. *Malar J*. 2009 Feb 26;8:34 4. Barger B, Maiga H, Traore OB, Tekete M, Timbine A, Dara A, Traore ZI, Gantt S, Doumbo OK, Djimde AA. Intermittent preventive treatment using artemisinin-based combination therapy reduces malaria morbidity among school-aged children in Mali. *Trop Med Int Health*. 2009 Jul;14(7):784-91. doi: 10.1111/j.1365-3156.2009.02294.x. Epub 2009 May 26.

1.3.2 Alexis Nzila

EDCTP Project Coordinator:	Alexis Nzila (Kenya Medical Research Institute (KEMRI), Kenya)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Understanding the mechanism of piperaquine PQ) resistance
EDCTP Project Code:	TA.2004.40200.003
EDCTP Project Start Date:	1 January 2005
EDCTP Project End Date:	25 November 2008
Collaborators:	• Xin-zhuan Su (National Institute of Health (NIH), USA) • Steve Ward (University of Liverpool, UK)
Goal:	To understand the mechanisms of PQ-resistance, with the overall goal to identify molecular markers that could be used to predict PQ resistance
Objective(s):	1. Assess the selective pressure of the PQ following the use of ArtekinTM 2. Select PQ resistance in vitro: by continuously culturing of parasites in presence of increasing concentrations of PQ 3. Identify molecular markers associated with piperaquine resistance.
Collaborating site(s):	• NIH (USA) • University of Liverpool (UK)
Study design:	Laboratory based investigations: In-vitro drug resistance studies
Product:	• PQ, Lumofantrine (LM) • Dihydroxyartemisin (DHA)
Status:	Completed
Results and outcomes:	The study collected baseline information on the activity of several antimalarials, PQ, Lumofantrine (LM) and Dihydroxyartemisin (DHA) in *P.falciparum* isolates in Kilifi, Kenya. 10 to 20% of isolates had reduced susceptibility to LM, yet this drug has just been introduced in the country; The use of PQ (as part of the use of Artekin®) selected for isolates with higher IC50s to LM, implying that the use of Artekin® may be associated with reduced Coartem® susceptibility. Wild type pfcrt-76 and pfmdr1-86 are associated with increasef LM IC50s. These genes could contribute to LM-resistance, although it is likely that other genes are also involved. Dr Nzila has been the recipient 2006 Royal Society Pfizer Award and 2009 EDCTP Senior Outstanding Scientist Award. He also successfully mentored Dr Leah Mwai who completed her EDCTP funded PhD in 2011.
Publications:	1. Certain LK, Briceño MR, Kiara SM, Nzila AM, Watkins WM, Sibley CH. Limited genetic diversity in pyrimethamine resistant strains of *Plasmodium falciparum* from Kenya. *J Infect Dis*. 2008;197(12):1743-51 2. Nduati E, Diriye A, Sheila O, Mwai L, Kiara S, Masseno V, Kokwaro G, Nzila A. Effect of folate derivatives on the activity of antifolate drugs used against malaria and cancer. *Parasitology Research.* 2008;102(6):1227-1234. 3. Mwai L, Ochong E, Abdi A, Murithi S, Ward S, Marsh K, Kokwaro G, Sassy P, Boormann S, Nzila A. Chloroquine resistance before and after its withdrawal in Kenya. *Malar J.* 2009 May 18;8:106. doi:10.1186/1475-2875-8-106. 4. Kiboi DM, Irungu BN, Langat B, Wittlin S, Brun R, Chollet J, Abiodun O, Nganga JK, Nyambati VCS, Rukunga GM, Bell A, Nzila A. Plasmodium berghei ANKA: Selection of resistance to piperaquine and lumefantrine in a mouse model. *Exp Parasitol*. 2009 Jul;122(3):196-202. doi:

	10.1016/j.exppara.2009.03.010. Epub 2009 Mar 24 5. Sasi P, Abdulrahaman A, Mwai L, Straimer J, Schieck E, Rippert A, Bashraheil M, Salim A, Peshu J, Awuondo K, Lowe B, Pirmohamed M, Winstanley P, Ward S, Nzila A, Borrmann S. *In vivo* and *in vitro* efficacy of amodiaquine against *Plasmodium falciparum* in an area of continued use of 4-aminoquinolines in East Africa. *J Infect Dis*. 2009 Jun 1;199(11):1575-82. doi: 10.1086/598862.

1.3.3 Ambrose Talisuna

EDCTP Project Coordinator:	Ambrose Talisuna (Ministry of Health, Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Safety of artemisinin derivatives-based combination therapy in children with uncomplicated malaria and population-based pharmacovigilance (PV): a capacity strengthening proposal for pharmacovigilance of antimalarial drugs in Africa
EDCTP Project Code:	TA.2005.40200.001
EDCTP Project Start Date:	25 May 2007
EDCTP Project End Date:	1 June 2010
Collaborators:	• Umberto D'Alessandro (Prince Leopold Institute of Tropical Medicine-ITM, Belgium) • Moses Kamya (Makerere University, Uganda) • Fred Wabwire (Makerere University, Uganda)
Site Principal Investigator(s):	• Moses Kamya (Uganda) • Fred Wabwire-Mangen (Uganda)
Objective(s):	1. The objective was to develop a PV system for monitoring the safety of antimalarial treatment at health facilities and within communities 2. A mixed model of a large multicentre trial at 12 sites (EDCTP funded) and a population based cohort at 2 Ugandan sentinel sites were used to detect signals and test hypotheses on the causal relationship between treatments and AEs.
Collaborating site(s):	ITM (Belgium)
Study design:	Phase IV (Pharmacovigilance)
Status:	Completed
Results and outcomes:	A total of 973 antimalarial treatments given either individually or in combination were followed-up. The highest prescriptions were for AL (59 %) followed by quinine (25%), SP (7%), AQ (4%), CQ (3%), AS monotherapy (0.7%) and DHAPQP (0.1%). In total, 443 AEs were documented in the active surveillance. Pregnancy registration was implemented between January and December 2009. A total of 808 pregnant women were followed with 568 completing follow up. The key success factors were firstly the availability of focal personnel to collect and distribute the forms as well as provide feedback on a monthly basis, Secondly, linkage to existing schemes such as the health management information system and sentinel surveillance.

1.3.4 Issa Nebie

EDCTP Project Coordinator:	Issa Nebie (Centre national de recherche de Formation sur le Paludisme (CNRFP), Burkina Faso)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Understanding the mechanisms underlying the difference in susceptibility to malaria in an area of hyperendemic malaria in Burkina Faso: The potential role of regulatory T cells
EDCTP Project Code:	TA.2005.40200.008
EDCTP Project Start Date:	30 October 2006
EDCTP Project End Date:	31 May 2010
Collaborators;	• Diadier Diallo (CNRFP, Burkina Faso) • Amidou Diarra (CNRFP, Burkina Faso) • David Modiano (University of Rome La Sapienza, Italy) • Sodiomon Sirima (CNRFP, Burkina Faso) • Maria Gabriella Torcia (University of Florence, Italy)
Goal:	To contribute to the understanding of the role of T cell in susceptibility/resistance to malaria that might help improving or designing new malaria control tools such as malaria vaccine
Objective(s):	• To compare the proportion of regulatory T cells in population living in malaria endemic areas • To estimate the number of Foxp3 and GITR expressing cells as indicators of functional activities of T-reg in populations living in malaria endemic areas • To estimate the number of cells producing regulatory cytokine (IFN-gamma, IL-10 and TGF-β) in populations living in malaria endemic areas • To strengthen research capacity of CNRFP (Burkina Faso) through equipment of laboratories and training of young scientists in cellular immunology.
Collaborating site(s):	• University of Rome La Sapienza (Italy) • University of Florence (Italy)
Status:	Completed
Results and outcomes:	CD4+CD25+high subpopulations which contain the majority of T-reg cells were predominant in Fulani ethnic group (statistical significance (P=0.045)). The proportion of CD4+ subsets and CD4+CD25+IL10+ among CD25+ subpopulation which produced the Th2 type cytokine IL10 were more prevalent in Mossi ethnic group compared to Fulani ethnic group (P=0.05 and P=0.03 respectively). The proportion of CD127low and Foxp3+ subpopulations were similar in both ethnic groups. In sub-cohort 2, CD4+CD25+high and Cd4+CD25+IL10+ among CD4+IL10+ were predominant in children with severe malaria compare to asymptomatic children and the observed differences were statistically significant (P=0.01 and P<0.001 respectively). Mr Sanou Guillaume Sylvestre (CNRFP PhD student) received training on flow in the labs at the University of Florence (Italy) and University of Bordeaux II (France). Three workshops were organised to standardise the assays and to analyse the data. Personnel were recruited (one lab technician, five nurses), two physicians were appointed for the project and two students (one PhD and one Master's) were registered to complete their training.
Publications:	1. Cherif MK1, Sanou GS, Maiga B, Israelsson E, Ouédraogo AL, Bougouma EC, Diarra A, Ouédraogo A, Ouattara AS, Troye-Blomberg M, Dolo A, Cavanagh DR, Theisen M, Modiano D, Sirima SB, Nebié I. FcγRIIa polymorphism and anti-malaria-specific IgG and IgG

	subclass responses in populations differing in susceptibility to malaria in Burkina Faso. Scand J Immunol. 2012 Jun;75(6):606-13. doi: 10.1111/j.1365-3083.2012.02690.x. 2. Sanou GS1, Tiendrebeogo RW, Ouédraogo AL, Diarra A, Ouédraogo A, Yaro JB, Ouédraogo E, Verra F, Behr C, Troye-Blomberg M, Modiano D, Dolo A, Torcia MG, Traoré Y, Sirima SB, Nébié I. Haematological parameters, natural regulatory CD4 + CD25 + FOXP3+ T cells and γδ T cells among two sympatric ethnic groups having different susceptibility to malaria in Burkina Faso. BMC Res Notes. 2012 Jan 27;5:76. doi: 10.1186/1756-0500-5-76.

1.3.5 Emboumbou Moukoko

EDCTP Project Coordinator:	Emboumbou Moukoko (University of Buea, Cameroon)
EDCTP Project Call:	Career Development Fellowship
EDCTP Project Title:	Identification of *Plasmodium falciparum* parasite virulence markers for the evaluation of the impact of malaria control intervention according to the local parasite populations
EDCTP Project Code:	TA.2005.40203.006
EDCTP Project Start Date:	21 November 2006
EDCTP Project End Date:	20 November 2008
Collaborators:	• Eric Akum Achidi (University of Buea, Cameroon) • Ogobara Doumbo (University of Bamako, Mali) • Albert Same Ekobo (University of Yaoundé, Cameroon) • Peter Kremsner (University of Tübingen, Germany) • Christophe Rogier (Research Unit in Parasite Biology and Epidemiology, France)
Goal:	To strengthen previous evidences, to determine more accurately the location of loci associated with pathogenicity, and to identify the *P. falciparum* gene(s) and genotypes that affect(s) the susceptibility to severe malaria (SM).
Objective(s):	To perform the combined epidemiological, clinical and genetic analysis (gene mapping of several loci of *P. falciparum* whole-genome and genotyping human haemoglobin) to identify parasite and human genetic markers associated with higher risk of severe disease (including cerebral malaria, severe malaria related anaemia, convulsion and hyperparasitaemia) compared to uncomplicated malaria (UCM) Secondary objectives: 1. To identify *P. falciparum* gene(s) and genotypes that affect(s) the pathogenicity (i.e. to severe malaria) using a genome wide gene mapping approach 2. To identify and control in the statistical the human genetic factors of malaria susceptibility to SM (i.e. haemoglobin and G6PD abnomalies) 3. To identify parasite genotypes associated with drug resistance.
Collaborating site(s):	• University of Bamako (Mali) • Research Unit in Parasite Biology and Epidemiology (France) • University of Tübingen (Germany)
Number of subjects:	956
Status:	Completed
Results and outcomes:	956 malaria patients were recruited from September 2007 to January 2009. Most of the data concerning the age, the sex, the clinical phenotype, the biological data and the clinical outcome was collected. The verification of the data bases was completed in the participating countries of Cameroon, Gabon and Mali. .The project enabled the grantee to set up molecular epidemiology expertise in the institution's laboratory. and he consequently got a lecturer position at University of Douala in Cameroon.

1.3.6 Davis Nwakanma

EDCTP Project Coordinator:	Davis Nwakanma (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Evaluation and implementation of high throughput PCR-based method for diagnosis and measurement of *P. falciparum* parasitaemia in clinical trials
EDCTP Project Code:	TA.2005.40200.006
EDCTP Project Start Date:	27 November 2006
EDCTP Project End Date:	27 May 2009
Collaborators:	• David Conway (MRC, The Gambia) • Natalia Escobar-Gomez (MRC, The Gambia) • Michael Walther (MRC, The Gambia)
Goal:	To evaluate a number of different quantitative real-time PCR (qPCR) methods to determine and establish a suitable protocol for routine application in malaria diagnosis and measurement of parasite density
Objective(s):	• To establish the application of qPCR determination of malaria parasitaemia for clinical trials • To evaluate parasite density estimates obtained from qPCR amplification of parasite DNA in blood sample for agreement with blood film slide microscopy • To conduct a cost comparison of qPCR with slide microcopy for the determination of malaria parasitaemia.
Study design:	Point of care diagnostics
Status:	Completed
Results and outcomes:	qPCR detected more infections than microscopy (22% vs 18%), but overall the coefficient of agreement between both methods was very high (κ = 0.86). Parasite density estimates by the two methods were very similar with near-perfect concordance (rho_c = 0.968). At 72h post-treatment it was possible to detected parasites by qPCR in ~20% of patients in whom microscopy failed to detect any infection. Median parasite clearance time was 16h by microscopy and 24h by qPCR. Parasite survival curves estimated by the two methods were significantly different (X2. =34.43; p=<.0001). Eleven PhD and MSc students were trained on short courses in the project.
Publications:	1. Nwakanma D, Gomez-Escobar N, Walther M, Crozier S, Dubovsky F, Malkin E, Locke E, Conway D. Quantitative detection of Plasmodium falciparum DNA in saliva, blood and urine. *J Infect Dis.* 2009;99: 1567-1574.

1.3.7 Badara Cisse

EDCTP Project Coordinator:	Badara Cisse (University Cheikh Anta Diop, Senegal)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	A pilot study of the Implementation of Seasonal Intermittent Preventive Treatment with Community Participation in Senegal
EDCTP Project Code:	TA.2005.40200.004
EDCTP Project Start Date:	14 May 2007
EDCTP Project End Date:	8 August 2010
Collaborators:	• Pierre Gazin (Institut de Recherche pour le Développement, Senegal) • Omar Gaye (University of Dakar, Senegal) • Brian Greenwood (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Paul Milligan (LSHTM, UK) • Pape Moussa Thior (Ministry of Health and Medical Prevention, Senegal) • Jean-François Trape (Institut de Recherche pour le Développement, Senegal)
Clinical Trial/Study Sponsor:	University Cheikh Anta Diop (Senegal)
Primary Objective(s):	To compare the effectiveness of Dualkin (cure rate at 28 and 42 days) compared to amodiaquine plus artesunate (e.g. Falcimon*) which is the used ACT for the treatment of uncomplicated Plasmodium falciparum. Falcimon* is a combination of amodiaquine plus artesunate. The secondary objectives of this study were to compare delay to fever and parasitemia clearance and to determine the prevalence of gametocyte carriage at day 14, 28 and 42. Other objectives included to assess the clinical efficacy (delay to fever and parasite clearance and prevalence of gametocytes carriage after treatment).
Collaborating site(s):	• LSHTM (UK) • Institut de Recherche pour le Développement (Senegal)
Study design:	Phase III
Study population:	CHILDREN (2 months-5 years) N=1833
Product:	Dualkin to amodiaquine plus artesunate
Trial Registration number(s):	NCT00529620
Status:	Completed
Results and outcomes:	This study provided evidence that seasonal IPTc with SP+PQ among children is highly effective and well tolerated. The combination of two long-acting drugs is optimal for malaria prevention and is most effective in the face of an emergence of resistant parasite genotypes. It was also demonstrated that amendments to age-based dosing of SP-Amodiaquine had the potential of increasing dosing accuracy and improve tolerability of the IPTc. The work has been an important reference for the WHO scientific advisory group. One junior physician, two nurses and 45 community volunteers were trained. The grantee also recruited an MSc student in parasitology and he was also a recipient of second Senior Fellowship grant from Malaria Capacity Development Consortium. Two more EDCTP-funded projects are now linked to the ground work of this project. These are a Senior Fellowship to Jean Louis Ndiaye and the Malaria Vectored Vaccines Consortium (IP.2008.31100.001), which were both awarded in 2010.

Publications:	1. Cisse B, Cairns M, Faye E, NDiaye O, Faye B, Cames C, Cheng Y, NDiaye M, Lô AC, Simondon K, Trape JF, Faye O, NDiaye JL, Gaye O, Greenwood B, Milligan P. Randomised Trial of Piperaquine with Sulfadoxine-Pyrimethamine or Dihydroartemisinin for Malaria Intermittent Preventive Treatment in Children. *PloS ONE.* 2009;4(9):e7164 2. Cairns M, Cisse B, Sokhna C, Cames C, Simondon K, Ba EH, Trape J-F, Gaye O, Greenwood BM, Milligan PJM. Amodiaquine dosage and tolerability for intermittent preventive treatment to prevent malaria in children. *Antimicrobial Agents and Chemotherapy*. March 2010;54(3):1265-1274.

1.3.8 Daniel Dodoo

EDCTP Project Coordinator:	Daniel Dodoo (Noguchi Memorial Institute for Medical Research, Ghana)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Assessment of functionality of antibodies that associate with protection from clinical malaria using the *in vitro P.falciparum* growth inhibition assay
EDCTP Project Code:	TA.2007.40200.012
EDCTP Project Start Date:	24 July 2008
EDCTP Project End Date:	30 March 2011
Collaborators:	• Klavs Berzins (Stockholm University, Sweden) • Michael Theisen (Statens Serum Institut (SSI), Denmark) • David Cavanagh (Edinburgh) • Bright Adu (Ghana) • Selorme Adukpo (Ghana) • Emimanuel Kakra Dickson (Ghana) • Edem Badji (Ghana) • Judith Antwi (Ghana) • Anna Mills (Ghana)
Goal:	To measure GLURP and MSP3 isotype and IgG subclass antibodies by ELISA in relation to susceptibility or protection from clinical malaria; establishment and field validation of the in vitro parasite growth inhibition assays using purified GLURP specific antibodies from selected individuals whose ELISA antibody responses to GLURP associate with protection against or susceptibility to clinical malaria after correcting for potential confounders.
Objective(s):	1. To establish in the field, the *in vitro* parasite growth inhibition assays with or without the presence of monocytes, using microscopy and flowcytometric readouts to assess parasite growth inhibition 2. To assess by ELISA, antibody responses to GLURP and MSP3 in relation to protection against or susceptibility to clinical malaria correcting for potential confounders such as age, socio-economic status, area of residence in study area, duration of residence in study area among others 3. To determine the functionality of purified antibodies in individuals who had malaria and those who did not have malaria during the study period by the *in vitro* parasite growth inhibition assay with or without the presence of monocytes.
Collaborating site(s):	• Stockholm University (Sweden) • SSI (Denmark)
Study design:	Laboratory based immunological and molecular biology investigations: *in vitro* assays
Status:	Completed
Results and outcomes:	The acquired Growth Inhibition Assay technique by the project staff has been established at the Immunology laboratory of Noguchi Memorial Institute and used in assessing the functionality of antibodies that correlate with protection from clinical malaria in the ELISA procedure. Eight individuals at the centre have been trained in GIA.

1.3.9 Christian Happi

EDCTP Project Coordinator:	Christian Happi (University of Ibadan, Nigeria)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Validation of New Biomarkers for Monitoring *Plasmodium falciparum* Reduced susceptibility/Tolerance or Resistance to Artemisinin Derivatives and Partner Drugs in Nigeria
EDCTP Project Code:	TA.2007.40200.016
EDCTP Project Start Date:	13 December 2008
EDCTP Project End Date:	12 December 2010
Goal:	To identify and validate new biomarkers/molecular determinants of parasites response to artemisinin derivatives (ARTs) and partner drugs *in vitro* and *in vivo.*
Objective(s):	1. Evaluate clinical treatment response parameters, *in vitro* and *in vivo* efficacy and drug blood levels of artemether-lumefantrine (AL) and artesunate-amodiaquine (AS-AQ) combinations in patients' infected with *P. falciparum* in Ibadan, Southwest Nigeria 2. Use the PCR, DNA sequencing approaches to identify new biomarkers/ molecular determinants of P. falciparum response to ARTs and Partner drugs *in vitro* and *in vivo* 3. Validate the role of new biomarkers/molecular determinants of *P. falciparum* response to ARTs and partner drugs by collating SNPs/SNPs patterns in parasite genes with clinical treatment response parameters, patients' treatment outcome, blood drug levels and in vitro quantitative responses (phenotypes).
Study design:	*In vitro* and *in vivo* bio-markers studies
Status:	Completed
Results and Outcomes:	Five major sub-studies were completed.. The capacity building programme at the grantee's laboratory at the College of Medicine, University of Ibadan, in Nigeria has been improved and has been used to train Dr Obaro Michael (a clinician) a former Master's Degree Programme student for his fellowship; Dr Onikepe Folarin a post doctoral Fellow to attend the Genome Epidemiology Meeting in Hinxton, UK and Miss Titilola Okuboyejo a PhD student partly being supported by this project to undergo a 3 months training on quantitative qPCR for gametocyte sex ratio determination.
Publications:	1. Sowunmi A, Adewoye EO, Gbotosho GO, Happi CT, Sijuade A, Folarin OA, Okuboyejo TM, Michael OS. Factors contributing to delay in parasite clearance in uncomplicated *falciparum* malaria in children. *Malaria Journal.* 2010;9(1):53 2. Gbotosho GO, Happi C, Folarin O, Keyamo O, Sowunmi A, Oduola AMJ. Rapid Detection of Lactate Dehydrogenase and Genotyping of *Plasmodium falciparum* in Saliva of Children with Acute Uncomplicated Malaria. *Am. J. Trop. Med. Hyg*. 2010;83(3):496-501 3. Michael OS, Gbotosho GO, Folarin OA, Okuboyejo T, Sowunmi A, Oduola, AMJ, Happi CT. Early variations in *Plasmodium falciparum* dynamics in Nigerian children after treatment with two artemisinin-based combinations: implications on delayed parasite clearance. *Malaria Journal*. 2010;9:335. 4. Van Tyne D, Park DJ, Schaffner SF, Neafsey DE, Angelino E, Cortese JF, Barnes KG, Rosen DM, Lukens AK, Daniels RF, Milner, Jr DA, Johnson, Shlyakhter I, Grossman SR,

	Becker JS, Yamins D, Karlsson EK, Ndiaye D, Sarr O, Mboup S, Happi C, Furlotte NA, Eskin E, Kang HM, Hartl DL, Birren BW, Wiegand RC, Lander ES, Wirth DF, Volkman SK, Sabeti PC. Identification and Functional Validation of the Novel Antimalarial Resistance Locus PF10_0355 in *Plasmodium falciparum*. *PLoS Genet*. 2011; 7(4): e1001383. doi:10.1371/journal.pgen.1001383.

1.3.10 Kamija Phiri

EDCTP Project Coordinator:	Kamija Phiri (University of Malawi, Malawi)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	A randomised controlled trial of oral iron therapy for treatment of post-malaria iron-deficiency anaemia in Malawian children com paring immediate post-discharge versus delayed treatment on iron uptake and haematological response
EDCTP Project Code:	TA.2008.40200.016
EDCTP Project Start Date:	29 September 2009
EDCTP Project End Date:	29 September 2011
Collaborators:	• Patrick van Rheenen (University Medical Center Groningen, Netherlands) • Feiko ter Kuile (University of Liverpool, UK) • Sarah White (Malawi-Liverpool-Wellcome Trust Research Programme, Malawi)
Clinical Trial/Study Sponsor:	College of Medicine, University of Malawi
Objective(s):	To determine whether delaying oral iron therapy in post-malaria iron deficiency anaemia for at least two weeks improves iron absorption and reduces the risk of iron-induced intestinal inflammation
Clinical Trial/Study site(s):	
Collaborating site(s):	• University Medical Center Groningen (The Netherlands) • University of Liverpool (UK)
Study design:	Phase II trial: Evaluation of different forms of oral iron for treatment of post malaria iron deficiency anaemia
Number of subjects:	CHILDREN (4-24 months) N=245
Product:	Iron tonic/iron isotopes
Manufacturer/Developer:	International Atomic Energy Agency
Trial Registration number(s):	PACTR2010050002141682
Status:	Completed
Results and Outcomes:	In 2010 protocol changes increased the sample size from 400 to 600. Due to slow recruitment at the original study site (Ndirande Health Centre in Blantyre) the study was moved to another district (Zomba) with a reported higher rate of potential participants. Between September 2011 and end of February 2012, a total of 148 participants had been recruited bringing the total to 245 participants (41% of required sample). The fellow had also successfully managed to source funds ($100,000) from Malaria Capacity development Consortium (MCDC) of the London School of Hygiene and Tropical Medicine to establish a Tropical Haematology Research Unit (THRU) in the Haematology Department, College of Medicine. A sub-study investigating iron absorption and incorporation into the blood cells is planned to be carried out in collaboration with partners at the Swiss Federal Institute of Technology (ETH) Institute of Food in Switzerland (Prof Richard Hurrell and team).
PhD study	Nyanyiwe Mbeye

1.3.11 Eric Achidi

EDCTP Project Coordinator:	Eric Achidi (University of Buea, Cameroon)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Malaria baseline studies towards characterising and establishing a clinical trial site at Mutengene, South West Region of Cameroon
EDCTP Project Code:	TA.2009.40200.008
EDCTP Project Start Date:	22 March 2010
EDCTP Project End Date:	22 March 2012
Collaborators:	• Julius Atashili (University of Buea, Cameroon) • Samuel Wanji • Njua Yafi • Judith Anchang
Objective(s):	The epidemiological study is designed to provide data on baseline malariometric parameters valuable for future intervention studies aimed at validating disease control tools. The specific objectives include conducting a population census of the study area, determining the malaria prevalence rates and density in cross sectional surveys, helminth and malaria co-infection rates and densities, number of episodes per year in cohort longitudinal studies, vectors transmitting parasites, their dynamics and inoculation rates, natural immune responses to malaria parasite exposure and prevalence of some genetic traits that protect against malaria.
Clinical Trial/Study site(s):	Mutengene, Fako Division (Cameroon)
Study design:	Epidemiological studies for clinical trials site develpment
Number of subjects:	15,344
Status:	Completed
Results and Outcomes:	At the end of the project a total of 15,344 individuals had been included and a series of baseline studies were conducted. These included studies household mosquito net ownership, prevalence of fever, prevalence of malaria parasitaemia by season, prevalence of intestinal helminthes by season, prevalence of anaemia, the prevalence of the sickle cell trait (HbAS) in the study group and levels of *Plasmodium falciparum* specific IgE/IgG2 antibodies in study participants. The project is well integrated within the EDCTP-funded central African network of excellence, CANTAM, and also received additional funding from the European Virtual Institute for Malaria Research (EVIMalaR). Eight members of the study team received various short term trainings.
PhD study:	Candidate: Njua Clarisse Yafi
Publications:	1. Achidi EA, Apinjoh TO, Anchang-Kimbi JK, Yafi CN, Besingi R, Awah NW, Troye-Blomberg M. *Plasmodium falciparum* Specific IgE, IgG and Anti-GPI IgG Antibodies in Cameroonian Children with Severe and Uncomplicated Malaria. *International Journal of Tropical Disease and Health*. 2012 Jun; 2(3): 157-172 2. Achidi EA, Apinjoh TO, Anchang-Kimbi JK, Mugri RN, Ngwai AN, Yafi CN. Severe and uncomplicated falciparum malaria in children from three regions and three ethnic groups in Cameroon: prospective study. *Malar J*. 2012 Jun 24;11:215. 3. Tchinda GG, Atashili J, Achidi EA, Kamga HL, Njunda AL, Ndumbe PM. Impact of malaria on hematological parameters in people living with HIV/AIDS attending the

	Laquintinie Hospital in Douala, Cameroon. *PLoS One*. 2012;7(7):e40553. doi: 10.1371/journal.pone.0040553. Epub 2012 Jul 10

1.3.12 Alfred Tiono

EDCTP Project Coordinator:	Alfred Tiono (Centre National de Recherche et de Formation sur le Paludisme (CNRFP), Burkina Faso)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Phase IV: A cluster-randomised controlled trial to assess the impact of combined strategies (impregnated bed nets + Home management of malaria oriented by Rapid Diagnosis Test) on severe malaria morbidity in children aged 6 to 59 months in Burkina Faso
EDCTP Project Code:	TA.2009.40200.019
EDCTP Project Start Date:	29 April 2010
EDCTP Project End Date:	28 February 2013
Collaborators:	• Issa Ouedraogo Nebie (CNRFP, Burkina Faso) • Sodiomon Bienvenu Sirima (CNRFP, Burkina Faso) • Alphonse Ouedraogo (CNRFP, Burkina Faso) • Abdoulaye Traore (CNRFP, Burkina Faso)
Objective(s):	To show the additional benefit in terms of reduction of severe malaria morbidity by adding the HMM to bed nets for children aged 6-59 months living in a seasonal malaria transmission area and to estimate the incidence of severe malaria in children aged 6-59 months living under insecticides impregnated bed nets with access to home based management of malaria strategy in a seasonal malaria transmission area
Clinical Trial/Study site(s):	CNRFP (Burkina Faso)
Study design:	Cluster randomised trial of bed nets and home management
Study population:	CHILDREN (6-59 months) N=6191 (40 clusters)
Status:	Ongoing
Results and outcomes:	At the end of first year ,the following was achieved: • Approval of the study by the community and ethics review board • Definition of study clusters • Purchase and distribution of bed nets • Training of staff • Conduct two of the planned four cross sectional studies •

1.3.13 Pauline Byakika Kibwika

EDCTP Project Coordinator:	Pauline Byakika Kibwika (Infectious Diseases Institute, Makerere University College Of Health Sciences, Uganda)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Comparison of efficacy, safety and pharmacokinetics of intravenous artesunate and intravenous quinine followed by oral artemisinin combination therapy for severe malaria treatment in Uganda AND evaluation of pharmacokinetic drug interactions of artesunate, quinine, lumefantrine and piperaquine with antiretroviral drugs
EDCTP Project Code:	TA.2009.40200.020
EDCTP Project Start Date:	14 March 2011
EDCTP Project End Date:	30 September 2013
Collaborators:	• Jane Achan (Makerere University, Uganda) • Moses R. Kamya (Makerere University (Uganda) • Elly Katabira (Makerere University, Uganda) • Noah Kiwanuka (Makerere University, Uganda) • Mohammed Lamorde (Makerere University, Uganda) • Harriet Mayanja-Kizza (Makerere University, Uganda) • Concepta Merry (Makerere University, Uganda/Trinity College, Ireland)
Clinical Trial/Study Sponsor:	Institute of Infectious Diseases (Uganda)
Goal:	To evaluate the effectiveness of IV artesunate plus ACT and IV quinine plus ACT as well as to study the pharmacokinetics of artemether-lumefantrine (AL) and dihydroartemisinin-piperaquine (DP) for treatment of severe malaria in adults and children in Tororo district hospital, Uganda.
Objective(s):	1. To compare treatment outcome (measured as risk of recurrent parasitaemia and risk of recurrent symptomatic malaria) following treatment with IV quinine followed by oral ACT (Artemether-Lumefantrine or Dihydroartemisinin-piperaquine) and IV artesunate followed by oral ACT (AL or DP) for treatment of severe malaria in Ugandan patients 2. To compare parasite clearance time following treatment with IV quinine followed by oral ACT (AL or DP) and IV artesunate followed by oral ACT (AL or DP) for treatment of severe malaria in Ugandan patients 3. To investigate the pharmacokinetic parameters of IV quinine, IV artesunate, oral AL and oral DP during severe malaria treatment in Ugandan patients and correlate these with treatment outcome 4. To investigate the pharmacokinetic drug interactions of quinine, artesunate, lumefantrine and piperaquine with the antiretroviral drugs (Nevirapine, Efavirenz, Lopinavir/ritonavir) in Ugandan patients.
Collaborating site(s):	University of Liverpool (UK)
Study design:	PK and drug interaction studies
Number of subjects:	400
Product:	Quinine, ACT (Artemether-Lumefantrine or Dihydroartemisinin-piperaquine) and IV artesunate
Manufacturer/Developer:	Gilead (for iv artesunate only)
Cofunders:	• International Society of Infectious Diseases
Trial Registration number(s):	PACTR201110000321348

Status:	Completed
Results and Outcomes:	Follow-up of 274 study participants sucessfully completed. Samples for genotyping successfully analysed at the Mulago Molecular Biology laboratory. Samples for drug assays shipped to Mahidol Clinical Pharmacology Laboratory, Thailand.

1.3.14 Bourema Kouriba

EDCTP Project Coordinator:	Bourema Kouriba (University of Bamako, Mali)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Role of functionally distinct monocyte subpopulations in protection against clinical Plasmodium falciparum malaria in people living in endemic area of Mali
EDCTP Project Code:	TA.2010.40200.007
EDCTP Project Start Date:	13 May 2011
EDCTP Project End Date:	13 May 2013
Collaborators:	• Charles Aarama (Malaria Research & Training Center, Mali) • Issa Diarra (Malaria Research & Training Center, Mali) • Abdoulaye Kone (Malaria Research & Training Center, Mali) • Amadou Niangaly (Malaria Research & Training Center, Mali) • Mahamadou S. Sissoko (Malaria Research & Training Center, Mali) • Kourane Sissoko (Malaria Research & Training Center, Mali)
Objective(s):	To assess the role of monocytes activation by infected red blood cell in the protection against clinical falciparum malaria in endemic area and determine the frequency of monocytes subpopulations according to the clinical outcome (asymptomatic, mild and severe) of malaria infection
Study design:	Immunological cohort studies
Study population:	CHILDREN (1-15 years old); N=210
Status:	Completed
Results and outcomes:	A cohort of 210 children aged 1-15 years was established in May 2011.

1.3.15 Aissatou Toure

EDCTP Project Coordinator:	Aissatou Toure (Pasteur Institute of Dakar, Senegal)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Optimization and standardization of the new functional antibody dependant respiratory burst (ADRB) assay to evaluate anti-malarial immunity in endemic populations and merozoite based vaccine candidates
EDCTP Project Code:	TA.2010.40200.027
EDCTP Project Start Date:	26 April 2011
EDCTP Project End Date:	31 December 2013
Collaborators:	• Sylvie Bay (Institut Pasteur, France) • Shirley Longacre (Institut Pasteur, France) • Adama Tall (Institut Pasteur de Madagascar)
Objective(s):	1. To optimize and standardize a "new" functional assay developed recently in our research unit, the Antibody Dependant Respiratory Burst (ADRB) assay detected by chemiluminescence, which has been correlated with clinical protection against malaria 2. To compare ADRB results with those of other commonly used functional assays such as the growth inhibition assay (GIA) 3. To use the ADRB assay as a tool to evaluate the level of malaria immunity in different endemic populations and to validate merozoite surface antigen vaccine candidates
Study design:	Laboratory based investigations: *in vitro* immunological and molecular biological assays
Status:	Completed
Results and outcomes:	In the first year of the project the team studied mononuclear cells in comparison with polymorphonuclear neutrophils but concluded that using freshly isolated polymorphonuclear neutrophils give better results. Conditions of Ph for optimising the ADRB assay were also studied and the conclusion is that better results are obtained with alkaline Ph. The team finished by studying different strains of *P. falciparum* in the ADRB using the Palo Alto strain of *P. falciparum* as reference in comparison with local adapted *P. falciparum* strain. They observed that the ADRB is significantly higher when the merozoites originated from local *P. falciparum* strains. After comparing optimized ADRB the results showed a correlation between high level of ADRB and a lower risk of malaria attack that confirm previous results. In summary the optimization of parameters resulted in an increase in signal intensity and sensitivity and ensured minimal variation and good reproducibility (CV<10%) of the ADRB assay. The assay validation with serum samples showed that antibodies that were not protective in vivo had no effect on neutrophils respiratory burst activity in the ADRB assay. ADRB activity was found age-dependent and a high ADRB response was positively correlated with in vivo clinical protection from P. falciparum malaria. The ADRB assay was more reliable as a standard assay in a holoendemic area than a mesoendemic area and that it was age-dependent.
PostDoc study	Charlotte Joos Ndiaye
Publications:	

1.3.16 Jean Louis Ndiaye

EDCTP Project Coordinator:	Jean Louis Ndiaye (University Cheikh Anta Diop of Dakar, Senegal)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Intermittent preventive treatment in children combined with malaria home management in an area with persisting high malaria prevalence in Senegal
EDCTP Project Code:	TA.2010.40200.032
EDCTP Project Start Date:	11 April 2011
EDCTP Project End Date:	11 April 2013
Collaborators:	• Badara Cisse (University Cheikh Anta DIOP de Dakar (UCAD), Senegal) • Oumar Gaye ((UCAD, Senegal) • Paul Milligan (London School of Hygiene and Tropical Medicine (LSHTM), UK) • Youssoupha Ndiaye (Ministere de la sante et de la prevention medicale, Senegal) • Pape Moussa Thior (Ministere de la sante et de la prevention medicale, Senegal)
Clinical Trial/Study Sponsor:	University Cheik Anta Diop de Dakar (Senegal)
Objective(s):	To determine whether seasonal IPTc with sulfadoxine-pyrimethamine plus amodiaquine provide added benefit in populations with access to prompt effective treatment through home–based management; whether IPTc has previously been shown effective when give for three months in areas with a short transmission season and whether seasonal IPTc is safe and acceptable when given for a longer period in areas with a longer transmission season. To also show the cost-effectiveness of adding seasonal IPTc to home management of malaria (HMM)
Collaborating site(s):	London School of Hygiene and Tropical Medicine (LSHTM, UK)
Study design:	Phase IV: Cluster randomised trial
Study population:	CHILDREN (3 months-10 years) N=4554
Product:	Sulfadoxine-pyrimethamine, Amodiaquine, Artemether-lumefantrine
Trial Registration number(s):	NCT01449045
Status:	Completed
Results and outcomes:	Twenty four community health workers and malaria volunteers were trained by the Department of Parasitology to do thick and thin blood smear to confirm all malaria cases in the 24 villages involved in the EDCTP research project. Out of 4554 chldren enrolled in the study, approximately 2000 children have received IPTc at fifth month (97% of intended sample of intervention group).
MSc studies	Candidate: Dr Mamadou Sarifou
	Candidate: Mr Cheikh Tidiane Ba

1.3.17 Akim Ayola Adegnika

EDCTP Project Coordinator:	Akim Adegnika (Medical Research Unit Albert Schweitzer Hospital, Gabon)
EDCTP Project Call:	Senior Fellowship
EDCTP Project Title:	Impact of schistosoma hematobium infection on immunological and clinical aspects of *P. falciparum* malaria in children
EDCTP Project Code:	TA.2011.40200.025
EDCTP Project Start Date:	9 February 2012
EDCTP Project End Date:	9 December 2014
Collaborators:	• Abraham Alabi (Albert Schweitzer Hospital, Gabon) • Maria Yazdanbakhsh (Leiden University, The Netherlands)
Objective(s):	This project aims to study the impact of *S. haematobium* infection on *P. falciparum* malaria induced immune response and clinical features in school children residing in two communities in the vicinity of Lambaréné (PK15 and PK17), where the malaria incidence rate is 1.3 person-years. The research questions to be answered by the project are: 1. How are plasmodia-specific pro-inflammatory Th1 and Th17 immune responses affected by coinfection with *S. haematobium*? 2. How does *S. haematobium* infection influence the clinical and parasitological profile of *P.falciparum* malaria?
Collaborating site(s):	Leiden University (The Netherlands)
Study design:	Immunology studies of schisto/malaria co-infection
Status:	Completed
Results and outcomes:	Research findings: • 754 school aged children were screened and 601 were included for follow-up. At baseline 141(19%) of the participants were positive for P. falciparum, 225/741(30%) were positive for Schistosoma hematobium, and 225/642(33%) for soil-transmitted helminthes infestation: 128(20.0%) for A. lumbricoides; 139(22.0%) for T. trichiura; and 43(7.0%) for hookworm. All infected children were treated accordingly and followed-up. • Preliminary results show that that the presence of P. falciparum infection was marked by an increase in innate and adaptive immune responsiveness while S. haematobium infection was characterized by an increased chemokine profile, with at the same time, lower pro inflammatory markers. When the study subjects were split into single infected and co-infected groups no effect of S. haematobium on the immune response of P. falciparum infected subjects was observed, neither for the innate nor for the adaptive component of the immune response. Therefore there no is effect of S. haematobium on the cytokine profile of subjects co-infected with P. falciparum. • Three scientific publications have resulted from this project Capacity Building: • GCP, GCLP and bio-ethics training of the study investigators and field workers • 4 MSc students were enrolled at various institutions and supervised by the Senior Fellow. 3 MSc students have completed their courses. • 1 PhD student has been registered and is being co-supervised by the Senior Fellow.

	• Training in laboratory techniques e.g., flow cytometry and in vitro culture techniques and equipment service e.g. training on the BD Accuri flow cytometry platform was undertaken by the PhD student and the CERMEL Head of Research Laboratory.
Publications:	1. Ayola A. Adegnika et al. Randomized, Controlled, Assessor-Blind Clinical Trial To Assess the Efficacy of Single- versus Repeated-Dose Albendazole To Treat Ascaris lumbricoides, Trichuris trichiura, and Hookworm Infection. *Antimicrob. Agents Chemother.* 2014, 58(5):2535. 2. Hilaire M. Kenguele,et al. Short Report: Impact of Short-Time Urine Freezing on the Sensitivity of an Established Schistosoma Real-Time PCR Assay. *Am. J. Trop. Med. Hyg.*, 90(6), 2014, pp. 1153–1155 3. Ateba-Ngoa et al. Cytokine and chemokine profile of the innate and adaptive immune response of schistosoma haematobium and plasmodium falciparum single and co-infected school-aged children from an endemic area of Lambaréné, Gabon. *Malaria Journal* (2015) 14:94

1.3.18 Charles Obonyo

EDCTP Project Coordinator:	Charles Obonyo (Kenya Medical Research Institute (KEMRI), Kenya)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Clindamycin plus quinine for treating uncomplicated *falciparum* malaria: an open-label randomized trial
EDCTP Project Code:	TA.2011.40200.059
EDCTP Project Start Date:	1 November 2012
EDCTP Project End Date:	31 January 2015
Collaborators:	• Charles Obonyo (Kenya Medical Research Institute (KEMRI), Kenya) • Elizabeth Juma (KEMRI, Kenya) • Bernhards Ogutu (KEMRI, Kenya) • John Logedi (MOH, Kenya) • Kevin Omondi (KEMRI, Kenya)
Clinical Trial/Study Sponsor:	KEMRI (Kenya)
Goal:	To evaluate the efficacy and safety of clindamycin plus quinine compared with artemether-lumefantrine among children less than 5 years of age diagnosed with uncomplicated *falciparum* malaria in western Kenya
Primary Objective(s):	1. To measure the clinical and parasitological efficacy of Clindamycin plus quinine and Artemether-Lumefantrine (current recommended regimen) among patients between 6-59 months of age suffering from uncomplicated P falciparum malaria, by determining the proportion of patients with Early Treatment Failures (ETF), Late Clinical Failures (LCF), Late Parasitological Failures (LPF), or with Adequate Clinical and Parasitological Response (ACPR) during a 28 day follow-up period.
Secondary Objective(s):	1. To differentiate recrudescence from new infections through Polymerase Chain Reaction (PCR) analysis 2. To determine fever and parasite clearance rates 3. To determine gametocyte carriage rates 4. To determine the change in mean haemoglobin by day 28 5. To determine the frequency of molecular markers for drug resistance.
Clinical Trial/Study site(s):	Homa Bay District Hospital, Western Kenya
Collaborating site(s):	Ahero District Hospital
Study design:	Phase IV open-label randomised trial
Number of subjects:	384 children
Product(s):	Clindamycin quinine Control product: Oral Artemether-lumefantrine (Novartis)
Manufacturer/Developer:	Pfizer
Trial registration number(s):	PACTR20129000419241
Status:	Completed
Results and Outcomes:	A study team of twelve members were recruited and trained on the study protocol. Study was initiated on 13 February 2014. So far 108 participants have been recruited. A second study site has been added to increase recruitment.

1.3.19 Abdoul Habib Beavogui

EDCTP Project Coordinator:	Abdoul Habib Beavogui (Centre National de Formation et de Recherche en Santé Rurale (CNFRSR) Jean SENECAL de Mafèrinyah, Guinea)
EDCTP Call Title:	Senior Fellowship
EDCTP Project Title:	Baseline Study of Epidemiological and Sociological aspects of Malaria in the four Natural Regions of Guinea
EDCTP Project Code:	TA.2011.40200.062
EDCTP Project Start Date:	1 November 2012
EDCTP Project End Date:	31 January 2015
Collaborators:	• Alexandre Delamou (Centre National de Formation et de Recherche en Santé Rurale (CNFRSR) Jean SENECAL de Mafèrinyah, Guinea) • Mohamed Diaby (University of General Lansana Conte, Guinea) • Abdoulaye Djimde (Malaria Research & Training Center, Mali) • Abdoulaye Doumbouyah (Centre National de Formation et de Recherche en Santé Rurale (CNFRSR) Jean SENECAL de Mafèrinyah, Guinea) • Issaka Sagara (University of Bamako, Mali)
Clinical Trial/Study Sponsor:	Ministry of Public Health and Hygiene (Guinea)
Goal:	The aim of this study is to characterise at the national level malaria epidemiological patterns and malaria indicators in children aged between six months and 10 years, depending on the season for two consecutive years.
Primary Objective(s):	1. Estimate malaria infection prevalence and disease prevalence in children aged between 6 months and 10 years in Guinea in dry and raining seasons 2. Evaluate haemoglobin levels in children aged between 6 months and 10 years in Guinea 3. Measure the genotype of the main resistance genes namely Pfcrt (P. falciparum chloroquine resistance transport), pfmdr1 (P. falciparum multidrug resistance 1); pfatp6 4. Determine impregnated or treated mosquito nets use in Guinea 5. Assess knowledge, attitudes and practices of mothers and legal parents of children aged between 6 months 10 years towards malaria in the first year of study and during the high malaria transmission season 6. Estimate entomological parameters of malaria transmission for two consecutive years and seasons withinthe four natural regions of Guinea.
Clinical Trial/Study site(s):	The study will be conducted in the four natural regions of Guinea: Lower Guinea, Middle Guinea, Upper Guinea and Forest Guinea
Study design:	Observational, cross-sectional survey
Study population:	400 children aged 6 months to 10 years and their mothers/legal guardians
Status:	Completed
Results and Outcomes:	25 investigators have been recruited and managed to complete the first and second cross sectional studies. A total of 2137 children aged between 6 months to 9 years were investigated in all four national regions.
PhD study:	Title: Malaria Epidemiology in Republic of Guinea Candidate: Dr Sidikiba Sidibe

MSc study:	Master in Epidemiology of the University of Bamako Candidate: Dr Malick Minkael Sylla

2 PhD and MSc scholarships

Table 6-1: Stand-alone (individual) PhD and MSc scholarships in HIV/AIDS, tuberculosis and malaria supported by EDCTP. Other PhD and MSc grants are included under their respective integrated/clinical trial projects

Project Acronym (Coordinator)	Disease area	Project details	Study population	Status of project
Jobe - MSc	HIV	Master of Science in Reproductive and Sexual Health Research	TBD	Completed
Oyakhirome - MSc		Public Health		Completed
Sikateyo - PhD	HIV	Informed consent process in HIV trials in Zambia	Participants in an HIV vaccine trial in Lusaka	Completed
Yindom - PhD	HIV	Immunogenetics for HIV vaccine design	600 unrelated adults in Gambia	Completed
Yimer - PhD	TB	TB drug and ART interaction and metabolism	758 ART naïve TB, TB-HIV and HIV infected individuals	Completed
Mthiyane - PhD	TB	Interferon gamma responses in TB-HIV coinfected individuals	TB-HIV infected patients	Completed
Mwai - PhD	Malaria	Lumefantrine resistance	250 in vitro culture isolates	Completed
Ramatoulie - PhD	Malaria	Pharmcogenetics of chlorproguanil in adults and children	Malaria patients in The Gambia	Completed
Arama - PhD	Malaria	Immungenetic factors in malaria prevention	77 patients in Mali	Completed

2.1 Alasan Jobe

EDCTP Project Coordinator:	Alasan Jobe (National Malaria Control Program, Department of State for Health and Social Welfare, The Gambia)
EDCTP Call Title:	MSc Studentship
EDCTP Project Title:	Masters in Reproductive and Sexual Health Research
EDCTP Project Code:	TA.2005.40205.001
EDCTP Project Start Date:	10 August 2006
EDCTP Project End Date:	30 October 2007
Supervisor(s):	
Goal:	
Objective(s):	
Status:	Completed
Results and Outcomes:	
Site Principal Investigator(s):	Malang Fofana (The Gambia)
Collaborators:	Joanne Cooper (UK)

2.2 Sunny Oyakhirome

EDCTP Project Coordinator:	Sunny Oyakhirome (Medical Research Unit, Albert Schweitzer Hospital, Gabon)
EDCTP Call Title:	MSc Studentship
EDCTP Project Title:	MSc in Public Health
EDCTP Project Code:	TA.2005.40205.002
EDCTP Project Start Date:	27 June 2006
EDCTP Project End Date:	27 June 2007
Institution:	London School of Hygiene and Tropical Medicine (LSHTM, UK), Distance learning in MSc in public health
Supervisor(s):	• Saadou Issifou (Medical Research Unit, Albert Schweitzer Hospital, Gabon) • Peter Kremsner (University of Tübingen, Germany) • Bertrand Lell (Medical Research Unit, Albert Schweitzer Hospital, Gabon)
Goal:	Candidate aim: Improvement in the health of populations, communities and particular groups within them (e.g. children), through the evaluation of practical, effective interventions against major public health diseases: Malaria, Tuberculosis; AIDS. With emphasis on evidence based methods of analysis of treatment and care; investigation, development and critical evaluation of conceptual models.
Objectives:	To provide a sound ability to apply knowledge of the core disciplines; statistics, epidemiology, health economics, and social research, to real health problems. In addition, graduates should be able to: 1. Demonstrate knowledge and understanding of the principle theories, methods and interventions used in health promotion 2. Demonstrate knowledge and understanding of the development of health promotion internationally and its evolution as a multidisciplinary field 3. Assess the appropriate use of population-wide versus targeted health promotion interventions 4. Consider how to develop health promotion policy and practice that is relevant to varying public health issues in diverse contexts 5. Show competence in critically evaluating and communicating research evidence 6. Apply the knowledge and analytical skills they have gained to inform health promotion policy-making, programme planning, implementation and evaluation, and research design.
Status:	Completed
Results and Outcomes:	The MSc training from the London School of Hygiene & Tropical Medicine on Public Health was completed in June 2007.

2.3 Bornwell Sikateyo

EDCTP Project Coordinator:	Bornwell Sikateyo (Central Board of Health, Zambia)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Understanding participants' consent undertaken by in an Entero-Toxigenic vaccines trial in Misisi Township in Lusaka, Zambia
EDCTP Project Code:	TA.2005.40204.026
EDCTP Project Start Date:	1 November 2006
EDCTP Project End Date:	30 March 2011
Supervisor(s):	• Roger Beech (University of Keele, UK) • Nancy E. Kass (Johns Hopkins Bloomberg School of Public Health, USA) • Douglas Wassenaar (University of KwaZulu-Natal, South Africa)
Objectives:	The specific objectives of this PhD project were: • To describe the interactions between research staff and participants in which "consent" is negotiated and maintained • To explore participants' social and economic characteristics, everyday life and situations as these impact the "consent process" • To assess how negotiations of participant consent evolve and change over the course of the trial in view of the complex procedures.
Status:	Completed
Results and Outcomes:	This study found that study participants in a vaccine trial in Missi in Zambia enrolled to gain access to resources, such as improved health care and cash incentives.

2.4 Louis Marie Yindom

EDCTP Project Coordinator:	Louis Marie Yindom (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	The role of Human leukocyte antigen (HLA) and killer immunoglobulin-like receptor (KIR) in HIV-2 infection: a key component to HIV vaccine design and its evaluation in Africa
EDCTP Project Code:	TA.2005.40204.013
EDCTP Project Start Date:	1 August 2006
EDCTP Project End Date:	31 August 2009
Supervisor(s):	• Assan Jaye (MRC Laboratories, The Gambia) • Sarah Rowland-Jones (MRC Laboratories, The Gambia) • Giorgio Sirugo (MRC Laboratories, The Gambia)
Goal:	To comprehensively characterise the distribution of HLA class I molecules in populations in the Gambia and Guinea-Bissau and to look at immunogenetic associations, focusing on HLA and KIR genotypes, with clinical outcome in HIV-2 infection which is largely confined to West Africa and provides a valuable model of attenuated HIV disease
Objectives:	The major objectives of this project are to: 1. Determine the distribution of HLA class I and KIR genes among HIV-2 cases and healthy individuals in Caio (Guinea-Bissau) and Fajara (Gambia) 2. Study the association of individual HLA-A, HLA-B, HLA-C, and KIR genes with susceptibility or resistance to HIV-2 infection The secondary objectives are to: 1. Determine the epistatic effect between HLA and KIR gene variants in HIV-2 disease outcome using indicators of disease 2. Progression such as CD4+ T cell count and plasma viral load (PVL) 3. Develop sequence specific techniques for subsequent detection of KIR and HLA alleles from genomic DNA
Status:	Completed
Results and outcomes:	The study showed that HLA-KIR compound genotypes did not affect risk of HIV-2 acquisition in Gambia.
Publications:	J.Virology 2010 Aug;84(16):8202-8. doi: 10.1128/JVI.00116-10. Epub 2010 Jun 2. Influence of HLA class I and HLA-KIR compound genotypes on HIV-2 infection and markers of disease progression in a Manjako community in West Africa. Yindom LM1, Leligdowicz A, Martin MP, Gao X, Qi Y, Zaman SM, van der Loeff MS, van Tienen C, Jaye A, Aveika A, Worwui A, Diatta M, Vincent T, Whittle HC, Rowland-Jones SL, Walton R, Carrington M.

2.5 Getnet Yimer

EDCTP Project Coordinator:	Getnet Yimer (Department of Pharmacology, Medical Faculty, Addis Ababa University, Ethiopia)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Anti tuberculosis-anti retroviral drugs induced Hepatotoxicity and interaction of these drugs at the level of CYP 450 metabolism
EDCTP Project Code:	TA.2005.40204.005
EDCTP Project Start Date:	2 August 2006
EDCTP Project End Date:	2 December 2010
Goal:	To evaluate the prevalence, severity, and outcome of hepatotoxicity associated with intake of anti TB and/or ARV drugs when taken concomitantly and when taken alone; and to determine the pharmacokinetic drug-drug interaction between anti TB and ARV at the level of drug metabolism and thereby assess the distribution of CYP 3A4, 3A5, 2C9/19, 2B6, and NAT2.
Objectives:	To assess and compare the prevalence, severity and prognosis of anti-TB and ARV drugs induced hepatotoxicity and evaluate the drug-drug interaction at the level of CYP 450 among Ethiopian patients. Specific objectives 1. To determine the prevalence of DIH in HIV positive TB patients taking anti-TB alone 2. To determine the prevalence of DIH in HIV positive TB patients taking anti-TB and ART 3. To see the distribution of CYP 3A4, 3A5, 2C9/19, 2B6 polymorphism in our study participants 4. To see the effect of CYP 3A4, 3A5, 2C9/19, 2B6 polymorphism on the development of DIH 5. To assess the drugdrug interaction between the anti-TB and ARV drugs 6. To assess the severity as well as outcome of DIH in our study participants.
Status:	Completed
Results and outcomes:	The study is reported to have shown that drug induced liver injury (DILI) is common among Ethiopian TB-HIV patients who have a slow acetylation status related to CYP2B6 516TT genotype. This is particularly relevant to patients on efavirenz based regimen. Through these findings close follow up and regular monitoring of plasma efavirenz concentration and liver enzymes during early therapy particularly in patients with, and those with elevated serum amino-transferases, lower haemoglobin, platelet count and albumin at baseline is recommended for early management of efavirenz-based HAART induced liver injury.
Publications:	1. Yimer,G; Gry, M; Amogne, W; Makonnen, E; Habtewold, A; Petros, Z; Aderaye, G; Schuppe-Koistinen, I; Lindquist, L; Aklillu, E. Evaluation of Patterns of Liver Toxicity in Patients on Antiretroviral and Anti-Tuberculosis Drugs: A Prospective Four Arm Observational Study in Ethiopian Patients. *PLoS One*. 2014; 9(4): e94271.

2.6 Thuli Mthiyane

EDCTP Project Coordinator:	Thuli Mthiyane (Medical Research Council, South Africa)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Safety tolerability and monitoring of combined anti-tuberculosis and antiretroviral therapy (Reconstitution of TB antigen specific IFN-γ responses in TB-HIV co-infected participants)
EDCTP Project Code:	TA.2005.40204.025
EDCTP Project Start Date:	10 November 2006
EDCTP Project End Date:	31 October 2011
Supervisor(s)	• Graham Rook (University College London, UK) • A. W. Sturm (Nelson R Mandela School of Medicine University of KwaZulu Natal, South Africa) • Alimuddin Zumla (University College London, UK)
Goal:	To evaluate contribution of anti-TB and ART to hepatotoxicity through tests for NAT2 and Cytochrome P450 and to assess quality of life of patients on these drugs
Objectives:	1. To determine if there is a difference in the experience of 2. adverse events (AEs) and serious adverse events (SAEs) 3. hepatotoxicity grade 1-4 4. immune Reconstitution Syndrome in TB/HIV co-infected patients receiving TB treatment and HAART concomitantly and TB/HIV co-infected patients receiving TB treatment then commencing HAART 5. To determine if patients starting ARVs early during TB treatment have a better HRQOL than patients starting ARVs after completion of TB treatment in TB/HIV co-infected patients 6. To determine polymorphisms in cytochrome P450 and N-acetyltransferase and their relationship to hepatotoxicity 7. and efavirenz bioavailability in participants receiving anti-TB treatment and HAART 8. To determine the kinetics of mycobacterial cellular immune responses in patients treated with HAART and tuberculosis drugs using an INF-γ release assay.
Status:	Completed
Results and outcomes:	The first PhD project was entitled “Reconstitution of TB antigen specific IFN-γ responses in TB-HIV co-infected participants”. The hypothesis was that IRIS may be facilitated by the absence of regulatory T-cell (Treg) activity preventing the development of pathogen specific memory T cells. The plan was to measure T-cell responses to immunological profile change during treatment and assess adverse events associated with levels of CD4, IFN-γ and viral load. This was changed mid-way to study “Safety tolerability and monitoring of combined anti-tuberculosis and antiretroviral therapy”. The justification for the change has been given. The second study aimed to assess treatment responses to combined TB and HIV therapy in co-infected patients recruited in a WHO funded study called “Bioavialability of fixed dose formulation Rifafour coantaining isoniazid, rifampicin, pyrazinamide and ethambutol”. The data to be assessed was in terms of adverse events, interferon gamma release assays in respsonse to treatment, quality of life and genetic polymorphisms affecting drug pharmacokinetics. The achievements in the projects are: Registration of PhD moved from University of Kwa Zulu Natal to University of Cape Town under Professor Keertan Dheda; recruitment of 89 study participants and completed 24 months follow up

2.7 Leah Mwai

EDCTP Project Coordinator:	Leah Mwai (Kenya Medical Research Institute (KEMRI)/Wellcome Trust Research Program, Kenya)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Understanding the mechanism of resistance to lumefantrine by *Plasmodium falciparum*
EDCTP Project Code:	TA.2005.40204.011
EDCTP Project Start Date:	18 July 2006
EDCTP Project End Date:	1 October 2010
Supervisor(s):	• Alexis Nzila (KEMRI)/Wellcome Trust Research Program, Kenya) • Steve Ward (Liverpool School of Tropical Medicine and Hygiene (LSHTM), UK)
Objectives:	To clarify the mechanisms of LM/PQ/DEAQ resistance, and to identify molecular markers that could be used to predict LM-ATM, DHA-PQ and AQ efficacy
Status:	Completed
Results and outcomes:	This study, which was studentship under Dr Alexis Nzila's supervision, showed mechanisms of emerging resistance to three artemesinin combination therapies against malaria and the molecular markers linked to the resistance patterns.
Publications:	1. Mwai L, Kiara SM, Abdirahman A, Pole L, Rippert A, Diriye A, Bull P, Marsh K, Borrmann S, Nzila A. *In vitro* activities of piperaquine, lumefantrine and dihydroartemisisn in Kenyan *Plasmodium falciparum* isolates and polymorphisms in Pfcrt and pfmdr1, *Antimicrob Agents Chemother*. 2009 Dec;53(12):5069-73. Epub 2009 Sep 21 2. Mwai L, Ochong E, Abdirahman A, Kiara SM, Ward S, Kokwaro G, Sasi P, Marsh K, Borrmann S, Mackinnon M, Nzila A. Chloroquine resistance before and after its withdrawal in Kenya, Malar J. 2009 May 18;8:106 3. Nzila A, Mwai L. *In vitro* selection *Plasmodium falciparum* drug-resistant parasite lines. *J Antimicrob Chemother*. 2009 Dec 18; 65(3):390-8 4. Sasi P, Abdulrahaman A, Mwai L, Muriithi S, Straimer J, Schieck E, Rippert A, Bashraheil M, Salim A, Peshu J, Awuondo K, Lowe B, Pirmohamed M, Winstanley P, Ward S, Nzila A, Borrmann S. In vivo and in vitro efficacy of amodiaquine against *Plasmodium falciparum* in an area of contimued use of 4- aminoquinolines in Africa. *J Infect Dis*. 2009 Jun 1;199(11):1575-82 5. Kokwaro G, Mwai L, Nzila A. Artemether-lumefantrine in the treatment of uncomplicated *falciparum* malaria. *Expert Opin Pharmacother*. 2007 Jan;8(1):75-94 6. Mwai L, Diriye A, Masseno V, Muriithi S, Feltwell T, et al. Genome Wide Adaptations of *Plasmodium falciparum* in Response to Lumefantrine Selective Drug Pressure. *PLoS ONE.* 2012;7(2): e31623. doi:10.1371/journal.pone.0031623

2.8 Janha Ramatouli

EDCTP Project Coordinator:	Janha Ramatouli (Medical Research Council (MRC) Laboratories, The Gambia)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Investigating the effects of inactive CYP2C19 alleles on chlorproguanil pharmacokinetics in adults and in children with mild malaria following Lapdap® treatment
EDCTP Project Code:	TA.2005.40204.018
EDCTP Project Start Date:	23 August 2006
EDCTP Project End Date:	1 March 2010
Supervisor(s):	• Munir Pirrmohamed (University of Liverpool, UK) • Robert Walton (MRC Laboratories, The Gambia) • Fatoumatta Sisay-Joof (MRC Laboratories, The Gambia)
Goal:	To investigate whether CYP2C9 and its genetic polymorphs participate in the biotransformation of the antimalarial biguanides
Objectives:	This project aims to: 1. Survey the range of genetic variation present in CYP2C19, an enzyme important in activating antimalarial drugs 2. Identify and biochemically characterise new genetic variants of this enzyme 3. Determine whether existing and newly defined variants affect response to therapy in large randomised controlled clinical trial.
Status:	Completed
Results and outcomes:	This project has described the frequency of the gain-of-function polymorphism and the loss-of-function polymorphism that influence variable pharmacokinetics of chlorcycloguanil in Gambian adults. The conclusion is that genetic variations in CYP2C9 and CYP2C19 influence chlorcycloguanil pharmacokinetics and may lead to the accumulation of toxic dapsone. These factors need to be taken into consideration in future clinical trials involving antimalarial biguanides/dapsone to avoid the adverse events of haemolytic anaemia that could be severe and therefore improve on the success of the trials.

2.9 Charles Arama

EDCTP Project Coordinator:	Charles Arama (Malaria Research & Training Center, Mali)
EDCTP Call Title:	PhD Studentship
EDCTP Project Title:	Host immunogenetic factors involved in the susceptibility to malaria in sympatric ethnic groups (Dogon and Fulani) in Mali
EDCTP Project Code:	TA.2005.40204.003
EDCTP Project Start Date:	10 August 2006
EDCTP Project End Date:	10 December 2010
Supervisor(s):	• Amagana DOLO (Malaria Research & Training Center, Mali) • Ogobara K. Doumbo (Malaria Research & Training Center, Mali) • Troye-Blomberg, Marita (Stockholm University, Sweden)
Objectives:	To investigate whether antigen presenting cells (APCs) obtained from Fulani and Dogon children exhibited differences in terms of activation status and toll-like receptor (TLR) responses during malaria infection
Status:	Completed
Results and outcomes:	The study results showed that *Plasmodium falciparum* infection impairs the phenotype of blood dendritic cells and alters toll-like receptor responses (TLR) of peripheral blood mononuclear cells (PBMC) from Dogon children. On the other hand, specific dendritic cells subsets are activated in the Fulani children and their PBMC respond normally to TLR stimuli. In particular, malaria infection induces differential innate IFN-γ release in the two ethnic groups.

3 Master's Fellowship in Epidemiology and Medical Statistics

Project Coordinator	EDCTP Fellow	Disease area	Project title	Status
Jim Todd (Kilimanjaro Christian Medical University College, Tanzania)	Asungushe Bonaventura Kayombo	HIV/AIDS	Access to Pre-ART care and treatment, and Pre-ART mortality and loss to follow up among HIV-infected in Kagera	Ongoing
Helen Anne Weiss (London School of Hygiene and Tropical Medicine, United Kingdom)	Sungai Tafadzwa Chabata	HIV/AIDS	Estimating the size of hard to reach populations – comparison of three methods of size estimation of sex worker communities in Zimbabwe	Ongoing
Mala Rakoto Andrianarivelo (University of Antananarivo, Madagascar)	Rivonirina Andry Rakotoarivelo	HIV/AIDS	Study of the prevalence and risk factors associated with Cryptococcus neoformans complex in HIV-infected patients in Antananarivo, Madagascar	Ongoing
Kathy Baisley (London School of Hygiene and Tropical Medicine, United Kingdom)	Patience Nyakato	HIV/AIDS	Sample-based tracing of HIV-positive patients in rural and urban Uganda to estimate linkage to and retention in care before the initiation of antiretroviral therapy	Ongoing
Andrea Mary Rehman (London School of Hygiene and Tropical Medicine, United Kingdom)	Joseph Musaazi	Tuberculosis	Comparison of tuberculosis (TB) treatment completion in HIV and tuberculosis co-infection patients receiving care from rural and urban health service providers in Uganda	Ongoing
Susana Scott (Medical Research Council (UK) Unit, The Gambia)	Ngozi Moneke-Anyanwoke	Malaria	The effects of community-based scheduled screening and treatment (CSST) of malaria in pregnancy on infant mortality, malaria parasitaemia and health seeking behaviour	Ongoing
Lameck Diero (Moi University, Kenya)	Philip O. Owiti	Tuberculosis	Pre-treatment loss to follow-up in the tuberculosis program in western Kenya: The burden and determinants	Ongoing
Eveline Geubbels (Ifakara Health Institute, Tanzania)	Tumaini Nicholas Jackson Kilimba	Cross-cutting	A validation study of a self-triggered health and demographic surveillance data collection system	Ongoing

3.1 Asungushe Bonaventura Kayombo

EDCTP Project Coordinator:	Jim Todd (Kilimanjaro Christian Medical University College, Tanzania)
EDCTP Fellow:	Asungushe Bonaventura Kayombo (International Center for AIDS Care and Treatment Programs (ICAP), Tanzania)
EDCTP Call Title:	Master's Fellowship in Epidemiology and Medical Statistics
EDCTP Project Title:	Access to Pre-ART care and treatment, and Pre-ART mortality and loss to follow up among HIV-infected in Kagera
EDCTP Project Code:	MF.2013.40205.007
EDCTP Project Start Date:	22 July 2014
EDCTP Project End Date:	21 July 2016
Collaborators:	Wambura Mwita (Tanzania)
Type of Project:	Training Award
Goal:	The goal of this study is to examine access to Pre-ART care and treatment, Pre-ART mortality and loss to follow-up by using routine CTC electronic data and structured interviews. CTC electronic data, upon careful framing of research questions and rigorous analysis, can provide information needed by programme managers and policy makers. Structured interviews can provide additional information with regard to Pre-ART retention and engagement in care.
Objectives:	1. Determine the proportion of HIV positive in Kagera region that have enrolled in CTC from 2009 – 2014 2. Describe the baseline characteristics of those that have enrolled in CTC from J2009 – 2014 3. Determine pre-ART mortality rate among ART-naïve adult patients attending the CTC clinics from 2009 – 2014 4. Determine pre-ART lost to follow-up rate due to other causes than death among ART-naive adult patients attending the CTC clinics from 2009 – 2014 5. Determine the predictors of mortality and lost to follow-up among ART-naïve adults patients who attended the CTC clinics from 2009 to 2014 6. Conduct structured interviews to gather relevant baseline information on potential determinants of non-retention and non-engagement in HIV care.
Results and Outcomes:	In progress

3.2 Sungai Tafadzwa

EDCTP Project Coordinator:	Helen Anne Weiss (London School of Hygiene and Tropical Medicine, United Kingdom)
EDCTP Fellow:	Sungai Tafadzwa Chabata (Centre for Sexual Health, HIV and AIDS Research (CeSHHAR Zimbabwe), Zimbabwe)
EDCTP Call Title:	Master's Fellowship in Epidemiology and Medical Statistics
EDCTP Project Title:	Estimating the size of hard to reach populations – comparison of three methods of size estimation of sex worker communities in Zimbabwe
EDCTP Project Code:	MF.2013.40205.014
EDCTP Project Start Date:	13 August 2014
EDCTP Project End Date:	12 August 2016
Collaborators:	Frances Cowan (United Kingdom)
Type of Project:	Training Award
Goal:	The overall goal of the project is to compare how different methods of estimating the size of most-at-risk populations affect i) the estimate of population size and ii) the characteristics of the population recruited.
Objectives:	1. Estimate the size of the sex work population using the multiplier method in four urban centres in Zimbabwe. Programmatic data collected at sex work clinics in the four communities will be combined with data collected during the endline survey for the SAPPHIRE trial 2. Describe the socio-demographic characteristics, health seeking behaviours and HIV prevalence and HIV viral load of women included in the size estimation survey 3. Conduct additional survey work to estimate the size of the sex work population in these four communities using community mapping and capture re-capture 4. Compare size estimates and characteristics of participants identified using the three approaches 5. Compare the cost of each approach.
Results and Outcomes:	In progress

3.3 Rivonirina Andry Rakotoarivelo

EDCTP Project Coordinator:	Mala Rakoto Andrianarivelo (University of Antananarivo, Madagascar)
EDCTP Fellow:	Rivonirina Andry Rakotoarivelo (Ministry of Health, Madagascar)
EDCTP Call Title:	Master's Fellowship in Epidemiology and Medical Statistics
EDCTP Project Title:	Study of the prevalence and risk factors associated with Cryptococcus neoformans complex in HIV-infected patients in Antananarivo, Madagascar
EDCTP Project Code:	MF.2013.40205.018
EDCTP Project Start Date:	14 July 2014
EDCTP Project End Date:	13 July 2016
Collaborators:	• Bénédicte Contamin (Madagascar) • Mamy Jean de Dieu Randria (Madagascar) • Rado Andrianasolo (Madagascar) • Mihaja Raberahona (Madagascar) • Philippe Vanhems (France) • Muriel Cornet (France)
Type of Project:	Training Award
Goal:	To develop a simple and reliable method for diagnosing neuro-cryptococcal meningitis, and to identify circulating serotypes responsible for this life-threatening infection.
Objectives:	1. Assess the prevalence of cryptococcosis in patients infected with HIV 2. Assess risk factors associated with cryptococcosis in patients infected with HIV.
Results and Outcomes:	In progress

3.4 Patience Nyakato

EDCTP Project Coordinator:	Kathy Baisley (London School of Hygiene and Tropical Medicine, United Kingdom)
EDCTP Fellow:	Patience Nyakato (Infectious Disease Institute, Makerere University, College of Health Sciences, Uganda)
EDCTP Call Title:	Master's Fellowship in Epidemiology and Medical Statistics
EDCTP Project Title:	Sample-based tracing of HIV-positive patients in rural and urban Uganda to estimate linkage to and retention in care before the initiation of antiretroviral therapy
EDCTP Project Code:	MF.2013.40205.020
EDCTP Project Start Date:	13 August 2014
EDCTP Project End Date:	12 August 2016
Collaborators:	• Andrew Kambugu (Uganda) • Helen Weiss (United Kingdom) • Agnes Kiragga (Uganda)
Type of Project:	Training Award
Goal:	The overall aim of the project is to obtain accurate estimates of linkage and retention in care among HIV positive patients not yet eligible for antiretroviral therapy (ART), to evaluate programme effectiveness and to guide future strategies for retention in care among patients newly diagnosed with HIV.
Objectives:	1. Estimate the proportion of newly-diagnosed HIV positive patients who get linked to care within three months of testing positive at an HIV care, in rural and urban Uganda 2. Use a sample-based approach to determine time to first linkage to care, outcomes among patients who do not link to care and factors associated with non-linkage to care 3. Use a sample-based approach to estimate the proportion of newly-diagnosed HIV positive patients not yet eligible for ART who are retained in care after linkage, and identify factors associated with non-retention.
Results and Outcomes:	In progress

3.5 Joseph Musaazi

EDCTP Project Coordinator:	Andrea Mary Rehman (London School of Hygiene and Tropical Medicine, United Kingdom)
EDCTP Fellow:	Joseph Musaazi (Infectious Diseases Institute (IDI), Uganda)
EDCTP Call Title:	Master's Fellowship in Epidemiology and Medical Statistics
EDCTP Project Title:	Comparison of tuberculosis (TB) treatment completion in HIV and tuberculosis co-infection patients receiving care from rural and urban health service providers in Uganda
EDCTP Project Code:	MF.2013.40205.025
EDCTP Project Start Date:	13 August 2014
EDCTP Project End Date:	12 August 2016
Collaborators:	• Dr John Bradley (United Kingdom) • Andrew Kambugu (Uganda) • Agnes Kiragga (Uganda)
Type of Project:	Training Award
Goal:	Identifying modifiable factors which lead to better treatment outcomes from the urban care facilities that could potentially be implemented in rural areas so as to lead to a general improvement in TB treatment outcome.
Objectives:	1. Identify and compare TB treatment outcomes in HIV/TB co-infected persons receiving care from rural and urban settings 2. Assess the potential predictors associated with successful TB treatment outcome (the sum of those completing treatment and those cured).
Results and Outcomes:	In progress

3.6 Ngozi Moneke-Anyanwoke

EDCTP Project Coordinator:	Susana Scott (Medical Research Council (UK) Unit, The Gambia)
EDCTP Fellow:	Ngozi Moneke-Anyanwoke (Medical Research Council (UK) Unit, The Gambia)
EDCTP Call Title:	Master's Fellowship in Epidemiology and Medical Statistics
EDCTP Project Title:	The effects of community-based scheduled screening and treatment (CSST) of malaria in pregnancy on infant mortality, malaria parasitaemia and health seeking behaviour
EDCTP Project Code:	MF.2013.40205.036
EDCTP Project Start Date:	28 August 2014
EDCTP Project End Date:	27 August 2016
Type of Project:	Training Award
Goal:	To determine if the use of community health workers for scheduled screening and treatment of malaria in pregnancy will have a positive impact on infant malaria morbidity and mortality.
Objectives:	1. Determine the long term protective efficacy of CSST of malaria in pregnancy against malaria infection in their offspring 2. Determine the effects of CSST on infant mortality 3. Evaluate the impact of CSST on the health seeking behaviour and perception of mothers towards malaria treatment.
Results and Outcomes:	In progress

3.7 Philip O. Owiti

EDCTP Project Coordinator:	Lameck Diero (Moi University, Kenya)
EDCTP Fellow:	Philip O. Owiti (Academic Model Providing Access to Healthcare (AMPATH), Kenya)
EDCTP Call Title:	Master's Fellowship in Epidemiology and Medical Statistics
EDCTP Project Title:	Pre-treatment loss to follow-up in the tuberculosis program in western Kenya: The burden and determinants
EDCTP Project Code:	MF.2013.40205.048
EDCTP Project Start Date:	22 August 2014
EDCTP Project End Date:	21 August 2016
Collaborators:	1) E. Jane Carter (USA, Kenya) 2) Adrian Gardner (Kenya, USA) 3) Judy Gichoya (Kenya)
Type of Project:	Training Award
Goal:	To establish the burden and determinants of pre-treatment loss to follow-up in the tuberculosis programme in western Kenya.
Objectives:	1. Establish the burden of pre-treatment loss to follow-up in western Kenya from January 2011 to June 2014 2. Describe the socio-demographic and geographic factors associated with pre-treatment loss to follow-up in western Kenya 3. Describe the trends in pre-treatment loss to follow-up over the three and a half year period.
Results and Outcomes:	In progress

3.8 Tumaini Nicholas Jackson Kilimba

EDCTP Project Coordinator:	Eveline Geubbels (Ifakara Health Institute, Tanzania)
EDCTP Fellow:	Tumaini Nicholas Jackson Kilimba (Ifakara Health Institute, Tanzania)
EDCTP Call Title:	Master's Fellowship in Epidemiology and Medical Statistics
EDCTP Project Title:	A validation study of a self-triggered health and demographic surveillance data collection system
EDCTP Project Code:	MF.2013.40205.051
EDCTP Project Start Date:	24 September 2014
EDCTP Project End Date:	23 September 2016
Collaborators:	Shamte Amri (Tanzania)
Type of Project:	Training Award
Goal:	To enhance efficiency in Health and Demographic Surveillance (HDSS) while maintaining data quality
Objectives:	To assess yield, timeliness and costs of a new model of acquiring field data in HDSS sites, using participant-triggered data collection visits
Results and Outcomes:	In progress