

Title: Safety and Health of Agents used in Malaria Vector Control**Acronym:** SHAMAC**Submitted by:**

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Theme: Health**Focus Area:** Translating research for human health**Type of project:** Thematic network on specific research questions

Summary: The current (and potential future) suite of chemical agents that can successfully be applied for interrupting malaria transmission by mosquitoes are limited mainly to DDT, pyrethroids and some carbamates. In almost all cases these pesticides are applied indoors where they come into contact with the inhabitants including infants, pregnant mothers and the aged. The information about indoor exposure and uptake is insufficient to conduct proper risk assessments under the conditions experienced. The testicular dysgenesis syndrome (TDS) hypothesis suggests that four conditions namely cryptorchidism, hypospadias, impaired spermatogenesis and testis cancer are manifestations of perturbed prenatal testicular development (Skakkebaek et al., 2001). The etiology of TDS is possibly linked to genetic and/or environmental factors, including endocrine disrupters such as DDT and metabolites. For ethical reasons a causal relationship between prenatal exposure and TDS cannot be determined in human studies. However, people living in high risk malaria areas where for example DDT or pyrethroids are being used, are continually being exposed to these endocrine disruptive chemicals. Studies on these exposed human and wildlife populations may provide key answers for the gene-environment interactions of endocrine disrupters. Work in progress by the local consortium found high levels of DDT exposure and the occurrence of TDS indicating a potentially serious endocrine related human wildlife health concern. Urgent work is required to better understand the causes, effects and risks, and thereby hopefully to manage and reduce the stress on millions of people protected by these agents against the most deadly vector transmitted disease in Africa.

Expertise offered: We have established contacts and access to malaria endemic areas and have a well functioning framework supported by local people, different levels of governing bodies, scientists etc. Field and laboratory techniques such as sampling, extraction and analysis have been established for both environmental and human samples. We have access to newborns from both sprayed and non-sprayed villages. Both environmental and clinical investigations have been initiated in one such area.

Previous FP involvement: No

Consortium status: Collaboration exists between a number of SA organizations, including University of Pretoria, University of Johannesburg, North-West University, University of Limpopo, Technical University of Venda, CSIR, and Rhodes University

Expertise sought: We are seeking partners to amplify and strengthen the existing network to assess the health and safety consequences of malaria vector control agents where these come into contact with humans and wildlife

Related projects: South African National R&D programmes

Title: In vitro and in silico instead of in vivo design, evaluation and prediction of safe and efficient new bone pharmaceuticals: a knowledge-based approach

Acronym: BP-model

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project (small scale)

Summary: Like in conventional drug design, extensive animal experiments are performed to evaluate in vivo behaviour of potential bone pharmaceuticals with consequent limited success. To reduce this drastically and to be more efficient in finding new drugs, a novel knowledge-base approach is proposed here. Bisphosphonate-based (radio) pharmaceuticals are emerging as the gold standard for palliative action where bisphosphonates are used as an supplementary approach to radiopharmaceuticals. Both are commercially available to relieve the severe pain that many patients experience. Progress in primary cancer management has caused bone metastasis to become the second highest newly occurring tumours. 870,000 worldwide new cases of bone metastases are recorded yearly. For this area no knowledge base to design new therapies exists implying that the expected increase in research for new therapeutics will be carried out mostly using animals. We propose the establishment of a timely in vitro and in silico model will prevent this. Utilising the experience gained in the field of bone palliation agents, the proposal aims to develop a model integrating blood- and bone modeling, cell targeting and bisphosphonate targeted nanocarrier systems in a multidisciplinary fashion. Appropriate model systems will be constructed with innovative tools arrived at through an integration of existing knowledge and new data from dedicated research experiments. This will provide a holistic picture of their mechanism(s) of action and will show how a proposed bone-seeking pharmaceutical is expected to behave from injection until localizing in the target. The product to be delivered consists of conceptual tools in the form of theoretical, computational and experimental procedures that are capable of predicting the therapeutic success of a proposed (bone-seeking) pharmaceutical. It is not the primary intention to develop the ultimate bone pharmaceutical within the term of this project.

Expertise offered: Blood plasma modeling, animal testing and radiopharmaceutical preparation

Previous FP involvement: Yes

Details of previous FP involvement: Submitted proposal to FP-6

Consortium status: 6 partners, TU Delft, the Netherlands; INETI, Portugal; AZU, the Netherlands; UP Chemistry South Africa; Univ. Aberdeen, UK; Necsa, South Africa; Univ. Silesia, Poland

Expertise sought: SME's that do bone-seeking drug research or bone-seeking radiopharmaceutical research

Related projects: South African National R&D programmes

Title: In vivo biological imaging to investigate research questions relating to TB disease

Acronym: TB-imaging

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Theme: Health

Focus Area: Translating research for human health

Type of project: Thematic network on specific research questions

Summary: PET (Positron emission tomography) is a new diagnostic tool in South Africa. Activities and the current use will be limited in the initial stage to the production and routine use of FDG. However this technology provides opportunities for research projects and we as a research group in collaboration with others are interested in labeling molecules as a tool for in vivo biological imaging. An area of importance in the health of our country (as in many third world countries) is TB and other poverty related diseases (HIV and malaria) that are often occurring together. There is a large focus on TB by many researchers here in South Africa as we have the patients around the corner. It is clear that a PET based diagnostic molecule is not an option to detect these diseases (too expensive) but it may be used to elucidate research questions such as differences in drug performance and drug resistance by providing the biodistribution of compounds in different sets of patients. This information can be gathered over a period of time and one could take a video of what happens to a drug in patients and record accurate data of the amount in certain compartments. The levels of both drug and radiation are orders of magnitude lower than therapeutic doses which make it possible to carry out such studies in healthy human volunteers under protocol.

Expertise offered: TB patients with different disease stages. Radiolabelling expertise. Availability of F-18 and C-11. 6 PET centres, 3 in public health care. At our site a 18MeV cyclotron has been installed last year with a GE set-up for FDG production. Two other centres (one at hospital) have been established this year. All the producers have pledged support for R&D.

Previous FP involvement: No

Consortium status: Necsa, Pelindaba; UP Nucl. Med., Pretoria; Little Company of Mary Hospital, Pretoria; MRC Durban

Expertise sought: Writing and running clinical protocols. TB experts

Related projects: None

Title: Understanding the neuroendocrine gonadal - adrenal dual system in relation to emotional behaviour in humans

Acronym: GADS

Submitted by:

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Theme: Health

Focus Area: Translating research for human health

Type of project: R&D project (small scale)

Summary: This project will investigate the neuroactive effects of gonadal and adrenal steroids in relation to emotion and behaviour in human beings. The major focus will be upon the effects of testosterone and cortisol on the processing of anger and fear. Interactions between the HPG and HPA axes will be investigated and factors relevant to disorders of anxiety and violence will be pursued. Another focus will be on the associated neuropeptide and neuroendocrine systems. Methods will include behavioural and emotional assessment, hormonal assays and neuroimaging.

Expertise offered: Dr van Honk has expertise in acute hormone administration studies in human subjects. Dr Morgan has expertise in neuroimaging.

Previous FP involvement: No

Consortium status: Currently there are two partners: Dr Jack van Honk of Utrecht University, Netherlands and Dr Barak Morgan of UCT plus their associated teams

Expertise sought: Partners with experience in functional neuroimaging of neuropeptide neurobehavioural systems are needed

Related projects: None

Title: Antimalarial drug discovery

Acronym: MalDruDisc

Submitted by:

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SOUTH AFRICA

Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: Networking between organisations in same area

Summary: Using structural models of proven targets derived by homology modeling and X-ray diffraction as basis for (1) the in silico design of flexible pharmacophores, (2) docking of potential inhibitors preselected based on similarity of chemical scaffolds, inhibitors of protein super family or other prior knowledge. Also do In vitro testing of inhibitory capacity and toxicity profiles and global effects on parasite metabolism.

Expertise offered: Bioinformatics, molecular biology, functional genomics, homology modeling enzyme assays, soluble expression of target proteins and biochemical characteristics

Previous FP involvement: No

Consortium status: South African Malaria Initiative

Expertise sought: Medicinal chemists, persons with extensive experience in chemogenomics, functional genomics and chemo informatics

Related projects: International bilateral cooperation South African National R&D programmes

Title: Functional genomics as a tool in drug and target discovery in the malaria parasite

Acronym: FuncGenMalDrug

Submitted by:

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Theme: Health

Focus Area: Translating research for human health

Type of project: Networking between organisations in same area

Summary: Functional genomics approaches have become constitutive elements of molecular biology and an indispensable tool in the drug discovery arena. The application of functional genomics strategies to assign functionality to each gene product of an organism has recently attained increased attention in the field of post-genomics research of Plasmodia. With this genus having the most species sequences of any eukaryotic organism so far, the Plasmodia are providing unique opportunities to the study of intracellular eukaryotic pathogens. However, since a major focus of *P. falciparum* research should be oriented towards the discovery of new drug leads (therapeutics) and novel drug targets, the application of functional genomics and mining thereof remains imperative. This includes the understanding of the transcriptome, proteome and interactome of the parasite to elucidate mode-of-action (MOA) of inhibitory compounds, allow optimization of such inhibitor activities, explain resistance mechanisms to known drugs, chemically validate potential drug targets and ultimately identify and/or functionally describe new drug targets.

Expertise offered: Extensive expertise in the in vitro culturing of malaria parasites with specific focus to drug treatment with both cytostatic and cytotoxic drugs. Molecular biology investigations and structural biochemical analyses of drug targets in the parasite. Gene expression profiling analysis using SSH, DNA microarray and proteomics in a comparative fashion of drug treated vs. untreated parasites. Extensive international collaborative network (USA, UK, Germany, France).

Previous FP involvement: No

Consortium status: Collaboration between AI Louw, F Joubert (University of Pretoria), E Marechal, V Breton (CNRS, France) in SAFeTI programme

Expertise sought: Drug target identification and drug discovery expertise. Proteomics and metabolomics related to malaria parasite. Bioinformatic analysis of gene expression profiles of the malaria parasite

Related projects: International bilateral cooperation

Title: Molecular tools for malaria research

Acronym: MolMal

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: Networking between organisations in same area

Summary: Efforts to combat malaria through novel drug discovery and vaccine development are hampered by (1) the low percentage (34%) of putative genes assigned a function, (2) poor expression of many cloned malaria proteins, (3) very few malaria proteins crystallized and structure determined, (4) techniques for knock-down and knock-out for validation of putative target genes are not well developed, (5) there is a lack of appropriate bioinformatic tools for integrated organization and analysis of the malaria information at the genomic, transcriptomic, proteomic and metabolic pathway levels. The project would focus on development of improved tools and techniques for molecular analysis of Plasmodium.

Expertise offered: The South African Malaria Initiative, coordinated through the University of Pretoria is establishing core expertise groups focusing on addressing many of the identified techniques.

Previous FP involvement: Yes

Details of previous FP involvement: Safe Foods and others

Consortium status: Partnership in place in South Africa. Linkages with French researchers and others established, but so far no lead organization identified

Expertise sought: Expertise in malaria functional genomics and bioinformatics

Related projects: South African National R&D programmes

Title: Cellular and molecular mechanisms of phototherapy

Acronym: CELMOLPT

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools and technologies for human health

Type of project: R&D project including technology demonstration (large scale)

Summary: The Laser Research Group in the Faculty of Health Sciences at the University of Johannesburg focuses on Phototherapy using low powered lasers for the treatment of medical conditions including cancer and wound healing. The biochemical effects of phthalocyanine photosensitizers on cancer cell lines and its ability to induce cell death as used for photodynamic therapy (PDT) is investigated. In addition, morphological, molecular and cellular events involved in the wound healing and cell differentiation processes and the contribution of laser light (LLLT) to activate these responses is studied in human skin and human stem cell lines by following the biochemical cell signaling pathways. Genetic integrity, immunological responses, endocrine activation, cytotoxicity and protein expression is studied to determine the effects of laser light as a function of wound healing and cancer therapy. <http://www.uj.ac.za/laserresearchgroup>

Expertise offered: Cell and tissue culture, biochemistry, wound healing, cancer, stem cell biology, apoptosis, cell signaling, proliferation

Previous FP involvement: No

Consortium status: University of Johannesburg and Rhodes University with the National Laser Centre of South Africa are currently collaborating and working as partners on this project

Expertise sought: Biophysicists, Confocal microscopy, stem cell biologists

Related projects: South African National R&D programmes

Title: A consortium to elucidate the biological mechanisms underlying physical inactivity-induced diabetes.

Acronym: INACTIVITY

Submitted by:

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Theme: Health

Focus Area: Translating research for human health

Type of project: Marie Curie Mobility Instruments

Summary: The project will provide a platform for scientists from Europe to come to South Africa for studies that may lead to a better understanding of the mechanisms responsible inactivity-induced diabetes and allow South African scientists and students to visit research institutions in Europe to enhance their research skills. South Africa offers unique opportunity for these studies because the incidence of type II diabetes is rapidly increasing among people whose lifestyles, especially physical activity have drastically changed since the fall of the apartheid regime. According to the International diabetic association, Type II diabetes will be the most challenging public health problem of the 21st century. It will affect children at a much earlier age thereby drastically reducing their quality of life over a much longer period than previous generations. The increased prevalence is expected to result from lifestyle changes, especially decrease in physical activity resulting from increased mechanization. It is imperative to determine the underlying biological mechanisms by which physical inactivity promotes diabetes. The establishment of molecular links is required to convince pro-profit industries and lawmakers to implement pro physical activity changes and to provide the scientific foundations for appropriate individual prescription of physical activity for health. Understanding the biochemical, molecular and cellular mechanisms of physical inactivity will also lay the foundation for drug development to help individuals who are physically inactive due to disability resulting from paralysis or other prohibitive conditions and those who are not responsive to exercise.

Expertise offered: The research unit for exercise science and sports medicine has an active group of scientists who are working towards elucidating the mechanisms by which exercise promotes health and protects against diseases including type II diabetes. The Unit is well equipped and carries out state-of-the art scientific research and hosts international conferences on a regular basis. It collaborates with scientists from the major Universities of South Africa including the University of Stellenbosch and Wits University. The South African group has the expertise to carry out all aspects of the research and to provide help if needed for the European counterparts.

Previous FP involvement: No

Consortium status: None

Expertise sought: scientists with expertise in exercise physiology, molecular biology and / or epidemiology

Related projects: None

Title: Traceable diagnostics for patients

Acronym: Metrology Medical

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Theme: Health

Focus Area: Optimising the delivery of health care to European citizens

Type of project: Thematic network on specific research questions

Summary: There is concern about the integrity of certain medical measurements where traceability to recognized measurement standards is vital for the safety of a patient. The project focuses on the amount of dose patients are exposed to when undergoing a medical X-ray. The NML in South Africa is a regional training centre for the IAEA (International Atomic Energy Agency). The proposed project aims to set up diagnostic reference levels that enable measurements that are traceable to the SI units ensuring appropriate levels of accuracy and long-term reproducibility of dose measurements.

Expertise offered: Staff has been trained at PTB in Germany, and we can assist the EU with providing traceability for the safe measurement of instruments used in brachytherapy and medical X Rays. In addition, we have expertise (to IEC specification) in the calibration of kV meters in terms of a practical peak voltage, calibration of diagnostic dosimeters and implementation of an ISO 17025 laboratory quality system.

Previous FP involvement: No

Consortium status: Project in progress with the IAEA for African region. Can be extended to the EU

Expertise sought: Manufacturers and suppliers of medical instruments, Calibration facilities in the medical industry and hospitals in the EU

Related projects: None

Title: Disease biomarkers for diagnosis, prognosis and therapy

Acronym: DBDPT

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project including technology demonstration (large scale)

Summary: South African National Bioinformatics Institute possesses a wide range of expertise in large-scale, whole genome and multiple genome analyses on relationship of transcription regulation and transcript expression states. Our interest is in finding highly likely targets for biomarkers for diagnosis, prognosis and therapy for a range of diseases including cancers, HIV, TB, malaria, myasthenia gravis, diabetes, allergy and asthma. We have possibility for efficient linking differentially expressed transcripts with hormonal and non-hormonal transcription regulation, as well as for determining dominant transcription regulators responsible for differential gene expression between affected and non-affected individuals. Deregulated transcription behaviour frequently enables identification of key controllers of such deregulation. These, in turn help in reconstruction of the main parts of regulatory networks affected in disease and in determination of associated pathways. This information helps in prioritizing a smaller group of the most promising molecular biomarkers that can be used in diagnosis, prognosis of therapeutic outcomes and sometimes even as drug targets. We look for partners who need this type of support. Keywords: disease, biomarkers, cancer, HIV, TB, malaria, myasthenia gravis, diabetes, allergy, asthma, hormones, transcription, expression.

Expertise offered: Transcription regulation, regulatory networks and links to expression states. Prioritizing disease associated genes. Computational identification of genes affected by several hormone receptors, such as estrogen receptor, androgen receptor, progesterone receptor, glucocorticoid receptor, VDR, PPAR, and some others affected in different diseases. Integration of biological and medical information from various resources for enhanced insights into molecular basis of disease. Biomedical data-mining and text-mining. Large-scale analyses of genomic data and excellent data modeling ability.

Previous FP involvement: No

Consortium status: None

Expertise sought: Looking for partners that can provide experimental support and have access to medical data and samples

Related projects: None

Title: Design and Development of Thin Polymeric Membranes for Modulated Release of Chemotherapeutic Agents

Acronym: DTPMCA

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project (small scale)

Summary: Background: Systemic chemotherapy for brain tumors has shown low efficacy due to the presence of the blood-brain-barrier (BBB) which limits the efficiency of old and new drugs. Research efforts are now focused on the development of new strategies that can circumvent this problem. One of the promising approaches has been the development of implantable drug-polymer systems for local drug delivery at the target site. Gliadel® represents the first product of this type available on the market for the treatment of high-grade malignant glioma patients. The drug-polymer systems are based on biocompatible and biodegradable polymers capable of releasing the drug in a modulated manner by matrix erosion for a prolonged period. HIV infection has contributed to an increased incidence of brain tumors particularly Primary Central Nervous System Lymphoma (PCNSL). This group of patients can benefit from this treatment approach because it reduces systemic toxicities of chemotherapeutic agents especially immunosuppression and has the potential to curb the problem of drug-drug interactions in these patients. Aim and objectives: The aim of this study is to design, develop and characterize different types of drug-loaded polymeric based membranes which can release the drug in a modulated manner over a prolonged period (e.g. several months). The systems are intended to optimize the treatment of brain tumors.

Expertise offered: The following: I. Preparation of drug-free and drug-loaded membranes II. Preparation of drug entrapped nanoparticles III. Fixation of nanoparticles within membranes IV. Morphology characterization of membranes V. Characterization of the physicochemical and physicomachanical properties of membranes and nanoparticles VI. In-vitro matrix erosion and drug release studies VII. In-vivo animal biodistribution studies.

Previous FP involvement: No

Consortium status: None

Expertise sought: European drug delivery scientists as well as clinicians involved in cancer therapy

Related projects: None

Title: Evaluation of Geriatric Health Systems (Public and Private): Implications for Health Policy and Resource Development

Acronym: AAHS

Submitted by:

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Theme: Health

Focus Area: Translating research for human health

Type of project: R&D project (small scale)

Summary: Our aim is to (1) assess the accessibility, quality, equity and governance of health care for the elderly in our province (2) Identify areas of strength and weaknesses relevant to the needs of the elderly (3) Obtain epidemiological data on health resource utilization by the elderly in KZN with respect to burden of diseases and functional disability (4) Evaluate the contribution of the municipal and provincial health departments and the non-governmental organizations (5) Determine the level of expertise available and the human resource needs required in the future (6) Assist in formulating comprehensive and cost effective policy on health care for the elderly including preventative strategies which are relevant to KZN and South Africa.

Expertise offered: Senior Associate Professor of Geriatrics, Nelson Mandela School of Medicine UKZN with extensive experience in Geriatric Care and Rheumatology. Senior health system researcher Ms Jennifer Chipps with extensive experience in health systems evaluation in Australia and New Zealand

Previous FP involvement: No

Consortium status: None

Expertise sought: European partners with experience in development and evaluation of comprehensive active ageing health systems

Related projects: None

Title: AIDS Restriction Genes in South Africa**Acronym:** ARGs**Submitted by:**

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Theme: Health**Focus Area:** Translating research for human health**Type of project:** R&D project (small scale)

Summary: A hallmark of human immunodeficiency virus type 1 (HIV-1) is the heterogeneity seen subsequent to exposure or infection. Numerous studies have identified individuals who remain uninfected despite repeated exposure to HIV-1. Once infected with HIV-1, some individuals show rapid disease progression to full-blown AIDS within 1-5 years while others termed long-term non-progressors are able to control viremia for prolonged periods of time. The mechanisms by which certain alleles influence susceptibility to HIV infection, the rate of disease progression, development of opportunistic infections and response to antiretroviral therapy are only incompletely understood. Furthermore, most of the studies on the contribution of host molecules to HIV pathogenesis have been done in developed country populations where HIV prevalence is low and where prevalent HIV-1 strains differ from those responsible for the severe epidemic in developing countries. There is an urgent need to extend studies of mechanisms involved in differential pathogenesis of HIV-1 to countries most affected by the HIV epidemic because intervention strategies, both prophylactic and therapeutic must be designed for and tested in these populations. Accumulation of data from these populations may also help resolve mechanisms that remain incompletely understood. Human genes with polymorphic variants that influence the outcome of HIV exposure or infection are known as AIDS restriction genes (ARGs). Among such host factors is chemokine receptor polymorphisms, polymorphisms in molecules that play a key role in antiviral immune responses and human molecules involved in HIV replication. The frequencies of some of these host factors differ among populations according to ethnic or racial background and alleles associated with susceptibility or resistance to HIV-1 may differ among racially distinct groups. We will utilize "high value cohorts" to understand the role of AIDS restriction genes in South Africa. Such cohorts include acute and early HIV infection, long term non-progressors (LTNPs) and highly exposed persistently seronegatives (HEPS). Differential expression patterns and/or genetic variants of candidate genes will be analyzed in respect to HIV exposure or infection outcome. Identified genes will be screened in vitro in order to gain a better understanding of their therapeutic or prophylactic potential. This theme will be followed with multiple candidate AIDS restricting genetic factors such as HLA class II genes, killer immunoglobulin receptor genes (KIRs), programmed death 1 (PD-1), etc).

Expertise offered: The staff has expertise in molecular virology techniques such as PCR, real-time PCR, serological techniques, western blotting, automated HIV sequencing, flow cytometry, viral load monitoring using the automated COBAS Amplicor/Ampli Prep HIV-1 Monitor Test V1.5. Currently, the laboratory is using these techniques to study the contribution of various host molecules to HIV resistance and pathogenesis. Cohorts on study are acute and early HIV-1 subtype C infection, and highly exposed seronegatives (HEPS). A long-term non-progressor (LTNP) cohort is planned.

Previous FP involvement: No**Consortium status:** None

Expertise sought: Seeking experts in genetic epidemiology of HIV/AIDS, virologists with expertise in functional analysis of genes, in vitro assays of effects of host gene variants on HIV replication, drug and vaccine design

Related projects: None

Title: Mycolic acids in tuberculosis and other diseases

Acronym: MAinTB

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project (small scale)

Summary: The mycolic acids (MA) that make up the wax coat of mycobacterium are unique in structure and play an important role in the mechanism of entry into and survival of the mycobacterium in the host macrophage. We collaborate with Prof Mark Baird at University of Wales, Bangor, UK, who has achieved the stereo controlled synthesis of the MA waxes and Prof Johan Grooten at Universities of Gent and Brussels in Belgium who has demonstrated that MA constitutes a pattern of recognition to the innate immune system to either accommodate infection or induce an inflammatory state that activates the immune system in a non-standard way. We are investigating the mycolic acids and their antibodies as biomarkers for active tuberculosis. Together we explore whether the understanding of the structure-function relationship of MAs may provide solutions to control tuberculosis, asthma and immune disorders.

Expertise offered: Biomolecular interaction between lipid molecules and lipid antigens and antibodies quantified by laser induced evanescent field biosensor, Chemical synthesis of mycolic acids and Cell biology of the immune response to mycolic acids.

Previous FP involvement: Yes

Details of Previous FP involvement: Flemish bilateral agreement 1997-2003: Immunoregulatory properties of biolipids in TB

Consortium status: University of Pretoria (SA), University of Gent (Belgium), University of Wales (UK) and University of Dusseldorf (Germany) in collaboration and applying for funding

Expertise sought: Partners and their unique expertise are already identified, but the project requires lobby for recognition of research potential

Related projects: International bilateral cooperation EDCTP South African National R&D programmes

Title: The Cape Town HIV Associated TB Project**Acronym:** CHART**Submitted by:**

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Theme: Health**Focus Area:** Translating research for human health**Type of project:** R&D project (small scale)

Summary: The Desmond Tutu HIV Foundation (DTHF), a registered non-profit organization, was established in January 2004. Based in Cape Town with community sites in Nyanga and Masiphumelele, it brings together a unique combination of academic expertise and social activism. The DTHF is involved in a number of initiatives some of which include the prevention, provision of antiretroviral therapy, studies into adherence strategies and research, training of health care professionals and preparing communities for HIV vaccine clinical trials. Currently the HIV epidemic is progressing most rapidly amongst young women as such the DTHF is particularly interested in developing strategies around prevention of HIV among young people. The DTHF is strongly committed to service delivery and community development but works to underscore this with evaluation and relevant research with an aim to impact policy. The DTHF advises for medical practitioners and supports patients with its experienced and dedicated team of over 100 doctors, nurses, researchers and community trained field workers all working together to provide a holistic approach to the HIV epidemic. Our Mission statement is the pursuit of excellence in research, treatment, training and prevention of HIV and related infections in Southern Africa. Currently tuberculosis control strategies are failing to contain the disease in sub-Saharan Africa, largely because of the parallel epidemic of HIV in the region. An estimated 2.4 million new tuberculosis cases and 540,000 tuberculosis -related deaths now occur in sub-Saharan Africa annually. Consequently in August 2005 the World Health Organization declared the epidemic in Africa to be a regional emergency. The Directly Observed Therapy strategy has been shown to be effective in many settings particularly where levels of HIV are relatively low. However, the reasons for failure of this strategy where HIV is prevalent have not been clearly defined. By examining where Directly Observed Therapy strategy has been less successful we may understand the reasons for the breakdown in tuberculosis control efforts and suggest modifications and improvement in current approaches and design new control strategies.

Expertise offered: Highly experienced at running clinical trials, highly experienced HIV clinicians, a number of well established and maintained international cohorts, experienced in protocol and paper writing, biostatistical expertise backup, experienced in health system modeling.

Previous FP involvement: No**Consortium status:** None

Expertise sought: Products in development that need to be tested in an HIV/TB environment, partners who need testing in diagnostics, strategies and methodologies, data partnerships with people doing similar work

Related projects: EDCTP South African national R&D programmes

Title: Treatment adherence to antiretroviral therapy

Acronym: Adherence

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Theme: Health

Focus Area: Translating research for human health

Type of project: Thematic network on specific research questions

Summary: Non-adherence to antiretroviral therapy invariably has a negative effect on AIDS patients' health and quality of life. Yet, the barriers to adherence are poorly understood and interventions designed to enhance adherence have not been systematically tested. This research project examines the problem of patient non-adherence to ARV's in a historically disadvantaged community in the Western Cape. The first specific aim is to qualitatively examine the perceptions of medical professionals and AIDS patients in primary care clinics in terms of barriers and facilitators to treatment adherence. The second specific aim is to develop a psychometric instrument based on the themes identified in the first specific aim to measure culturally and contextually defined barriers to adherence in a larger sample of AIDS patients. The third specific aim is to determine the relationship between patient social support, perceptions of physician-patient relationships, psychological distress, attitudes towards treatment adherence and quality of life. The fourth specific aim is to develop and test a psychosocial intervention programme aimed at enhancing adherence to behavioural and medication interventions with primary care patients with AIDS.

Expertise offered: Qualitative and quantitative research methods, knowledge of theories in health psychology and access to public health clinics for data collection from research subjects.

Previous FP involvement: No

Consortium status: None

Expertise sought: Would like partners interested in adherence issue in the context of developing countries

Related projects: None

Title: Brain monitoring in children with head injury**Acronym:** BMCHI**Submitted by:**

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Postal Address: Room 314 Institute for Child Health Red Cross Children's Hospital Rondebosch Cape Town

Theme: Health**Focus Area:** Translating research for human health**Type of project:** Networking between organisations in same area

Summary: Injury accounts for the majority of deaths in young people worldwide including children aged 5-15 and injury-related death and severe disability are most frequently determined by the severity of the injury to the head. Survivors are often left with neurological disability creating a burden not only to the child and immediate family but also to society with the need for disability grants, special schooling, various therapies, etc. Unfortunately, preventative strategies have had little impact on the incidence of head injuries in children in South Africa. After sustaining the primary injury, the brain remains vulnerable to secondary insults, the occurrence of which are often occult often the effects are registered only after the event has occurred. Key interventional strategies focusing on identification and avoidance of these insults or at least prompt treatment may lead to significant improvements in outcome. Researchers in Cambridge have developed a ground-breaking software program for monitoring and analysis of multiple variables of brain physiology with potential for improving outcome by continuous identification of potential insults. Basic research has been done in head-injured adults but there is no experience with children - an important fact given that brain physiology in the growing child is significantly different to that of adults. In South Africa, there is an exceptionally high incidence of childhood head injury and a very high mortality after severe head injury has been reported. Collaboration between Cambridge University and paediatric neurosurgeons at the University of Cape Town will enable the application of cutting-edge brain physiology monitoring to investigate the pathophysiology of childhood brain injury and guide intervention in a situation that has become a dire emergency. The potential also exists given the flexibility of the software for local configurations to be created based on results in children using the expertise of local clinicians and scientists.

Expertise offered: Researchers at Addenbrookes Hospital, Cambridge University have performed extensive basic validation of the use of the software in head-injured adults. Computerised mathematical tools have been developed for online continuous and non-invasive analysis of secondary brain insults in adults. At Red Cross Childrens Hospital physicians have extensive experience with the management of childhood head injury due to the very high volume of trauma, mainly due to road traffic accidents significantly more than seen in more developed world settings where although injury still accounts for the majority of deaths in the older childhood age groups the absolute incidence is much lower than would be the case in Cape Town. The strong infrastructure at this hospital makes the validation of protocols for this type of software most feasible in this setting.

Previous FP involvement: No

Consortium status: Dialogue between researchers at Cambridge and the University of Cape Town has already been established to evaluate feasibility of study with regard to training, basic infrastructure, use of the software by local researchers and networking.

Expertise sought: Local partnership will be sought with researchers in physics, electronics, signal processing and/or physics

Related projects: None

Title: Metabolic consequences of antiretroviral therapy in HIV-infected South African children

Acronym: P-Met-HAART

Submitted by:

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Postal Address:

Theme: Health

Focus Area: Translating research for human health

Type of project: R&D project (small scale)

Summary: South Africa's HIV prevalence was 5.6% in children under 15 years of age in 2003. Consequently a large number of South African children require highly active antiretroviral therapy (HAART). The benefits of HAART are well known but there are several metabolic problems associated with long term use in adults. These include diabetes/glucose intolerance, lactic acidosis, lipodystrophy and dyslipidaemia. These complications have not been well studied in children. This is a cross-sectional study of the prevalence of dysglycaemia, dyslipidaemia, hyperlactataemia and lipodystrophy in HIV-infected children [including HAART-naïve, HAART (without protease inhibitors (PIs)), HAART (PI-based)] in the Western Cape. The Western Cape is well suited to study the prevalence of these metabolic complications in view of the relatively long-standing donor-funded paediatric HAART programmes in the region. The researchers currently care for over 600 at risk patients. Risk factors for metabolic problems will be assessed. Assessment of growth and metabolism will be done via questionnaire, serum lipid profiles, OGTTs with insulin and glucose measurements, serum lactate levels, clinical anthropometry, body composition and fat distribution by CT scan and DEXA (the investigators have access to a research DEXA machine). These will permit the development of a simple tool for the clinical evaluation of metabolic consequences which can be utilized in the primary health care setting. This project aims to first define the scope of the problem of dysglycaemia and other metabolic complications in HIV-infected children receiving HAART, to assist in the implementation of a strategy for the early identification and management of these metabolic complications on HAART with a view to minimising the long-term sequelae and thus improving health care delivery.

Expertise offered: The researchers constitute of HIV clinicians and paediatricians, endocrinologists, lipidologists, and epidemiologists at the University of Cape Town and University of Newcastle. The involved persons are well published with a wide spectrum of basic science, clinical and epidemiological research experience. The HIV clinics treat over 600 children on HAART and new patients enter the clinic weekly. The cohort of children has been described in numerous publications. The researchers have already secured funding from the World Diabetes Foundation to perform a similar study in adults. The consortium has access to both basic science laboratories at the University of Cape Town, and clinical laboratory monitoring which offers specialized testing. Dexa and CT scanning facilities are available for exclusive research use. Support staff is trained in good clinical and laboratory practice and research experienced.

Previous FP involvement: No

Consortium status: None

Expertise sought: Stronger European partnerships may be necessary

Related projects: None

Title: Understanding immunity during experimental tuberculosis meningitis

Acronym: EXP TB MENING

Submitted by:

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Theme: Health

Focus Area: Translating research for human health

Type of project: R&D project (small scale)

Summary: Tuberculosis remains an increasing global burden with >8million new cases reported in 2005 and mortality exceeding 2million. Currently South Africa rates 8th highest based on incidence per capita and together with 9 other sub-Saharan countries form the global epicentre of the disease. Prior to the advent of HIV/AIDS 10-20% of cases involved extra-pulmonary tuberculosis of which tuberculosis meningitis was the predominant type the risk that has since increased significantly. Diagnosis of the disease is difficult and uncertainty permeates the clinical approach to tuberculosis meningitis due to a lack of definitive information as a consequence of limited basic research. A structured coordinated approach for better treatment or prevention of this disease can only be based on information generated by fundamental research. This project is based on the establishment of an experimental murine model for tuberculosis meningitis in which the underlying immunological mechanisms pertaining to this disease can be elucidated. This project incorporates a novel approach to investigating the role that specific cytokines such as Tumour Necrosis Factor, Interferon gamma and Lymphotoxin, and specific lymphocytic subsets have in immunity during tuberculosis meningitis. The development of stereotactic technology now allows the researcher to perform intercranial infection with precision at defined loci making use of small volumes. The model intends to imitate the onset of tuberculosis meningitis during rupture of Rich's foci through deposition of bacilli directly into the subarachnoid spaces or the initiation of tuberculomata in the brain through direct inoculation. By applying this model to mice that have specific gene modifications do we have a powerful model that will be applicable to investigate the role that specific target genes have in host neuro-immunity. The model will allow us to gain insight into both acute and persistent meningeal infection.

Expertise offered: We offer (1) extensive expertise in respiratory tuberculosis murine models in which mice are challenged by aerosol inhalation using Mycobacterium tuberculosis, a capability unique to South Africa and Africa (2) access to >50 different specific gene deleted mice bred at our institution and >100 through establish collaborators. (3) an independent animal unit facility supported by qualified animal technologists and veterinarians for animal welfare. (3) a complete, established research infrastructure which include Biosafety level 1, 2 and 3 facilities, a newly established animal breeding facility, flowcytometry and cell sorting capability, a pathology laboratory service, electron, confocal, fluorescence and light microscopy, (4) established institutional administrative support capable of dealing with intricate legal and financial matters.

Previous FP involvement: No

Consortium status: None

Expertise sought: Meningeal murine infection models, clinical and experimental meningitis

Related projects: None

Title: Development of a novel drug for the treatment of multi-resistant Malaria

Acronym: New Malaria Drug

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools and technologies for human health

Type of project: R&D project (small scale)

Summary: Introduction Globally over 2 billion people in particular children, live in malaria endemic countries. Of these approximately 400 million contract malaria annually, while over 1 million die annually of which 90% in Sub-Saharan Africa. Not only health is affected, it is estimated that economic growth reduction is over 1.3% while malaria free countries have a three times higher GDP when corrected for the standard socio, economic and political variables. While Malaria can be caused by multiple organisms in Sub-Saharan Africa the main cause is Plasmodium Falciparum against multiple drug resistance occurs. We have identified a small molecular compound demonstrating promising results to multiple resistant strains of the parasite Plasmodium Falciparum. There is a proposal to establish a Malaria Research Laboratory in order to demonstrate the in vivo effectivity of the small molecular compound in primates. If this step is successful, the Malaria Research Laboratory will perform further research in-license, develop and subsequently commercialise follow-on drug candidates. Materials and methods in order to test the compound sophisticated primate research is required, presently the most adequate primate Malaria model exists in Aotus Apes. The laboratory will be established in close co-operation with the Medical Research Council and the University of Cape Town at Delft (Western Cape). Collaboration with the University of Cape Town (the eldest and highest-rated research institution in the African Continent) is crucial to this proposal, since it is the ideal location for Primate Research (tradition of over 30 years) while collaboration with the Red Cross Children's Hospital (the only academic children's hospital in Sub-Saharan Africa) will safeguard the close the clinical connection of the Research Laboratory. Rationale Since 90% of Malaria deaths occur in Sub-Saharan Africa, it is a serious scientific omission that a Primate Malaria model has not been developed locally. The availability of our newly developed small molecular compound provides a unique opportunity to address this issue even in case the compound proves ineffective in Primate (this is however extremely unlikely), a fully developed Primate Malaria Model will be a great asset to have in South Africa for further Malaria research. In his speech in October 2005, at the opening of the plenary debate on NEPAD and the Decade to Roll Back Malaria, the President of the United Nations' General Assembly appealed to all who had a role to play to respond positively to the challenge. This plea was reiterated by the United Nations General Assembly in a Resolution of 19 December 2005, which recognised the importance of developing effective vaccines and new medicines to prevent and treat malaria, and the need for further and accelerated research. The South African National Biotechnology Strategy has repeatedly highlighted the important contribution that biotechnology can make in the area of human health, including the treatment of malaria. In Conclusion the start-up funds required for this Laboratory are estimated at approximately ZAR 2.9 million. Once success is demonstrated in the Primate Model an additional ZAR 10 million will be required, but the expectation is this will be easily obtained from either commercial investors or international aid foundations at that stage.

Expertise offered: 1. in silico drug development 2. Medicinal Chemistry at research and development level including models for understanding multi-drug resistance in parasites 3. Large Primate animal research facility and experience 4. Laboratory Scale manufacture sufficient for animal studies 5. Drug Assay and pharmacokinetics in multi-drug resistance of TB and Malaria (one of three WHO accredited drug monitoring laboratories) 6. Clinical trialing and public health expertise in paediatric and adult populations 7. Experienced project management and financial control capabilities

Previous FP involvement: No

Consortium status: Prof P Folb, WHO Advisory Board, Prof P Smith, Prof K Chibale, Dr K Barnes, Pharmacology, UCT; Prof AB van As, Red Cross Children's Hospital, UCT, Dr C Sutton, Pediatrician Limpopo, Prof J Seier, Animal Unit, MRC, Dr U Dauer, CEO, 4SC AG; Dr T Schierenberg

Expertise sought: At this stage, all necessary partners have agreed in principle.

Related projects: None

Title: Porcine BMP - Osteo-Restore, as a treatment for Osteoporosis

Acronym: BMP Osteo

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project, including technology demonstration (large scale)

Summary: Altis BMP is a porcine bone derived Bone Morphogenetic Protein (BMP) treatment for non-healing bone fractures which has been developed in association with the Tshwane University of Technology Centre for Tissue Engineering and a local Company Altis Biologics (Pty) Ltd. This project is well advanced and human clinical trials are imminent. RESEARCH IDEA This porcine derived osteogenic extract comprises naturally derived osteogenic factors in a synergistic combination of multiple growth factors. They are purified according to a patented high yield process and they are not species specific. The capacity to induce new bone formation, complete with marrow and mineralized component has been illustrated in a clinical trial in 36 patients with weight bearing non-healing fractures using the human derived BMP's, with exceptional results. PROJECT OBJECTIVES Repartox SA (Pty) Ltd and Repharto BV (Netherlands) have signed an agreement with Altis Biologics (Pty) Ltd in terms of which Altis has ceded all IP and patenting rights to a NEWCO for the development and registration of BMP as a treatment for osteoporosis, to be known as Osteo-Restore. PROJECT OBJECTIVES: Osteo-Restore is intended as an alternative to the contemporary treatment of osteoporosis. The Osteo-Restore will be obtained from the existing GMP extraction plant at the Pretoria Centre for Tissue Engineering at Tshwane University of Technology and used in middle stage and final stage human clinical trials of the product in osteoporosis treatment. FUNDING Funding is now required to complete the development and human clinical trials, in order to further the project towards registration of the treatment regimen as a medical device.

Expertise offered: Dr Nicolaas Duneas - Director for Centre for Tissue Engineering Tshwane University of Technology, PhD, MBA, an expert in bone BMP and bone induction Will provide specialised technical development expertise for laboratory and manufacture Dr Len Coetzee - Repharto SA (Pty) Ltd - PhD(CNS Growth Factors), PhD (Exp pathology), MSC Med, BA. Dr Ben Rademaker (CEO Repharto BV), PhD (Pharmacology) will provide Project Management, Master Plan, etc Mr Nune Peres, Business Development Specialist Mr Norman Thomas - Sales, Marketing, Communication, Strategy.

Previous FP involvement: Yes

Details of previous FP involvement: Repharto BV

Consortium status: Partners required for funding of the project through clinical trials and partners required for marketing and sales on registration.

Expertise sought: Altis Biologics (Pty) Ltd, Repharto SA (Pty) Ltd and Repharto BV

Related projects: South African National R&D programmes

Title: Microbial Expression System for Peptide Production/Display

Acronym: FEST

Submitted by:

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Postal Address: CSIR Biosciences PO Box 395 Pretoria 0001

Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project, including technology demonstration (large scale)

Summary: This technology relates to the development of an expression system for the surface display and production of peptides. This proprietary Gram-positive strain is able to over produce and display chimeric gene products as heterologous peptide/protein fusions. This bacterium harbours the endogenous genetic background to over produce the anchoring motif or carrier protein constitutively and continuously. In order to harness this ability as a surface display/expression system a number of key genetic tools were developed such as gene targeted inactivation. In these genetic background peptides ranging in size from 5 to 40 amino acids can be inserted as in-frame fusions and expressed on the cell surface of this strain. An example included peptides encoding the HIV-1 clade C gp120 epitope which was incorporated as an in frame fusion and found to be successfully over produced and displayed on the cell surface. The peptide was shown to be functional through immunological studies. An antimicrobial peptide has also been expressed in this system. The expression system is currently being further improved by target inactivation of key proteases. This research has been under-pinned by fermentation optimization studies and defined media formulations based on cell mass production are in place. There are a number of advantages of this system: Gram-positive bacteria are robust and cell growth is not impaired by the production of chimeric gene fusions, chimeric production is continuous and constitutive and an inducible promoter system is not necessarily required for over-expression, small peptides are over-produced on the cell surface which facilitates peptide isolation, integration of the chimeric peptide fusions into the host chromosome thereby ensuring that no heterologous plasmid DNA or antibiotic markers are present in the production strain.

Expertise offered: This technology could be ultimately developed as an innovative approach to the production of therapeutic peptides. It can also play a role as a vaccine delivery system by displaying immunogenic peptides.

Previous FP involvement: No

Consortium status: None

Expertise sought: Expertise in the pharmaceutical area, peptide therapeutics, immunology and vaccine production

Related projects: None

Title: The Application of Systems Biology to Validate Novel Leads for Malaria

Acronym: VaNoLeMa

Submitted by:

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Postal Address: Discovery Biology, Biosciences Division, Building 20, Pretoria 0011

Theme: Health

Focus Area: Translating research for human health

Type of project: R&D project, including technology demonstration (large scale)

Summary: CSIR Biosciences is a research-based biotechnology entity that provides solutions to improve health and fight disease. A key activity is to delineate and validate the mechanism of action of novel high-quality drug leads that have been developed de novo, and from exploiting the extensive biochemical diversity that exists within natural plant products in South Africa. Validation represents a key requirement to obtaining regulatory and marketing approval where solid scientific evidence is required by authorities before a drug is deemed acceptable for clinical use. CSIR Biosciences is developing an innovative high throughput platform to expedite the development and validation of rationally synthesized leads and plant-derived compounds to treat malaria, a disease which remains amongst the deadliest infections worldwide. The present array of drug targets used to treat the disease represents a significantly small proportion of the enzymes and metabolic processes that could be exploited for the development of new therapeutics. At the same time through mechanisms borne out of existing targets the parasite has developed rapidly growing resistance to the current range of available drugs. This coupled with the unlikelihood of attaining a cheap effective vaccine solution in the near future has led to an urgent need to identify leads that elicit their potency through novel targets and mechanisms. The objective of this platform is to expedite the discovery, validation and development of new leads against malaria, whose efficacy is elicited through novel targets by applying an integrated multidisciplinary approach that exploits the capabilities of functional genomics and systems biology. Through the effective integration of contemporary science and technology, traditional knowledge of plant derived compounds and evidence from modern medicine, the platform will provide a holistic approach to validating diverse and synergistic chemical moieties that bear potential to treat malaria.

Expertise offered: Expertise include malaria cell culturing, protein and nucleic acid extraction, 2D gel profiling, 2D gel imaging and data analysis, MALDI-TOF and Nanospray mass spectrometry protein/peptide characterisation, microarray profiling and data analysis and ontology mapping and data interpretation

Previous FP involvement: No

Consortium status: None

Expertise sought: Seeking partners with expertise in malaria drug development with a particular focus on expertise in functional genomics

Related projects: South African National R&D programmes

Title: A Systems Biology Approach to Validating Traditional Medicines for Clinical Application**Acronym:** SysBiTMe**Submitted by:**

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Postal Address: Discovery Biology, Biosciences Division, Building 20, Pretoria 0011

Theme: Health**Focus Area:** Translating research for human health**Type of project:** R&D project, including technology demonstration (large scale)

Summary: CSIR Biosciences is a research-based biotechnology entity that provides solutions to improve health and fight disease. A key activity is to develop novel high quality drug leads for clinical application by exploiting the extensive biochemical diversity that exists within natural plant products in South Africa. Drug process validation represents a key requirement to obtaining regulatory and marketing approval, and for traditionally used medicinal plants solid scientific evidence is required for authorities to deem them acceptable for clinical use. A reductionist approach is often employed to try to prove activity, typically involving the study of a compounds activity on known targets through bioassays. However for plant-derived medicinal products that elicits their potency through multiple targets, this approach is less successful as it fails to take into account the effects of synergistic mechanisms. For the majority of these products it is therefore essential to consider the entire system. We are witnessing a transition from the molecular level to the systems level that promises to revolutionize our understanding of complex biological regulatory systems. The ability to exploit genomes, proteomes and the metabolome combined with the capabilities of bioinformatics now facilitates a systems biology approach to validating traditional medicines by studying their effects in whole biological systems. CSIR Biosciences is developing an innovative high-throughput platform to expedite the development and scientific validation of plant-derived leads. Through the effective integration of traditional wisdom, contemporary science and technology and evidence from modern medicine this platform will provide a holistic approach to bioprospecting diverse and synergistic chemical moieties, which in combination might act on multiple targets and improve the therapeutic spectrum. The primary focus is currently to develop and validate natural leads for infectious diseases in particular malaria. Further areas of interest and activity include developing and validating leads to treat asthma, arthritis and inflammation, cancer and diabetes.

Expertise offered: A comprehensive bioprospecting science and technology value chain to include gathering of indigenous knowledge and biodiversity samples, extraction and biological evaluation of samples, bioassay-guided isolation and characterization of new biologically active molecules, development of herbal remedies as new drug candidates, GMP production of minimally processed herbal remedies in a FDA approvable Clinical and Botanical Supplies Unit, synthetic and medicinal chemistry for lead optimization, a dedicated department for the transfer of technology to communities for the cultivation and processing of medical plants. Functional genomics capabilities include cell culturing, protein and nucleic acid extraction, 2D gel profiling, 2D gel imaging and data analysis, MALDI-TOF and Nanospray mass spectrometry, microarray profiling and data analysis, and ontology mapping and data interpretation.

Previous FP involvement: No**Consortium status:** None**Expertise sought:** Seeking partners with expertise in metabolomics, proteomics and in vitro and in vivo biological assays**Related projects:** None

Title: Development of novel therapeutic and rapid diagnostic approaches effective against HIV/AIDS and TB using the cutting-edge aptamer technology

Acronym: aptamers HIV TB

Submitted by:

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Theme: Health

Focus Area: Translating research for human health

Type of project: Marie Curie Mobility Instruments

Summary: HIV infection and its associated disease AIDS, remain significant health problems globally. Although the development of combination therapy in the last decade was a major advance issue of cost, compliance and the rapid emergence of drug-resistant HIV strains have encouraged continued efforts to find alternative new antiretroviral drugs with modalities different from those currently in use. The HIV/AIDS problem is intrinsically linked to and complicated by TB and poor TB diagnostic tools in general. Diagnosing active TB is a challenge, especially in HIV positive people. Clearly the TB diagnostic especially in the light of the HIV epidemic needs to be improved. Thus there is a need for collaboration and integration of HIV and TB research. Accordingly, we propose to use the novel aptamer technology to provide cutting- edge solutions to these major and pertinent health problems our world faces. We propose two intertwined projects. In the first project we shall exploit the aptamer technology to dissect HIV infectivity and provide leads to novel antiretroviral therapeutics. The seminal works on isolation of aptamers that bind to the viral surface envelope glycoprotein, called the gp120, and potentially inhibit viral entry and hence infectivity of clinical isolates of HIV from diverse subtypes and different geographic locations has been done (Khati et al., 2003). We now propose to extend and consolidate this seminal work (Khati et al., 2003) by using the anti-gp120 aptamers for analysis and neutralization of endemic, South African strains of HIV from adult and paediatric patients at various stages of disease. The proposed research will also provide structural leads for the development of potent and even smaller candidate drug molecules that can mimic their HIV neutralizing properties. The second parallel project will be de novo and shall also exploit this powerful aptamer technology to develop rapid new TB diagnostics with high sensitivity and specificity.

Expertise offered: Aptamer Technology; HTS & drug discovery; BSL-3 and HIV neutralisation assays.

Previous FP involvement: No

Consortium status: None

Expertise sought: HIV and TB specialists, Aptamer Technology Experts; Structural Biologists

Related projects: None

Title: Affordable herbal treatments for HIV and HIV Opportunistic infections

Acronym: AHTHIVOI

Submitted by:

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Theme: Health

Focus Area: Translating research for human health

Type of project: R&D project (small scale)

Summary: CSIR Biosciences is a research-based biotechnology entity that provides solutions to improve health, fight disease and to support private and public sector industry in a manner that is sensitive to economic realities and the natural environment of the societies in which we live. In the past decade, with the rapid increase in HIV infection in the sub-Saharan region and due to the relatively high cost of the synthetically derived anti-retroviral drugs there is a real need to evaluate medicinal plants which might yield high quality, safe, effective and affordable therapeutic agents for HIV and HIV opportunistic infections. While SA has a rich biodiversity and traditional use of medicinal plants for the treatment of HIV and opportunistic infections (OI), a systematic approach to scientifically evaluate these is lacking. Over the last 10 years considerable evidence has been emerging not only from the many reports and publications but also from controlled clinical studies of the potential of plant-derived substances as important leads for the development of anti-retrovirals. In conjunction with this, CSIR Biosciences has noted an influx of information on claims or anecdotes for herbal HIV and OI treatment. The project aims to lay the groundwork in establishing the research infrastructure through collaboration with various institutions that can provide expertise such as establishing biological assays, a scientific understanding of the various infections and the production of finished dosage forms of plant based products for the validation of African traditional plants for the treatment of HIV and OI. Activities will include the screening of traditional plant based remedies for the treatment of HIV and OIs, establishment of the most appropriate screening methodologies, the isolation and characterization of the active ingredients and biological markers from these plant extracts, production of the herbal formulations in compliance with GMP, standardization of the preparations, enzymatic-based assays for the mode-of-action determination, synthetic modification of lead compounds, preclinical development and early clinical studies. The project also aims to establish a greater knowledge base and scientific understanding of the various opportunistic infections associated with HIV/AIDS. The project as a whole not only seeks to develop novel plant-derived anti-HIV medicines but also provides ideal opportunities for Human Capital Development and to build competencies in areas of research related to drug candidate identification and design.

Expertise offered: A comprehensive bioprospecting science and technology value chain to include gathering of indigenous knowledge and biodiversity samples, extraction and biological evaluation of samples, bioassay-guided isolation and characterization of new biologically active molecules using LC MS/MS and NMR, synthetic modification of lead compounds, computer-aided design of synthetic derivatives, the development of herbal remedies as new drug candidates, GMP production of minimally processed herbal remedies in a FDA approvable Clinical and Botanical Supplies Unit located at CSIR and a dedicated department for the transfer of technology to communities for the cultivation and processing of medicinal plants.

Previous FP involvement: No

Consortium status: CSIR collaborates with South African Universities (KwaZulu Natal and Albert Luthuli Hospital), establishing a collaboration with Prof M Witvrouw Laboratory of Molecular Virology and Drug Discovery, Molecular Medicine, Univ of Leuven

Expertise sought: Appropriate HIV and OI related biological assays (in vitro and in vivo) for the validation of traditional medicineso Enzymatic/protein based assays for mode of action studieso Pre-clinical studies Modern standardization technologies for complex botanical extracts

Related projects: South African National R&D programmes

Title: Synthesis and Biological Evaluation of Novel Bifunctional HIV Inhibitors

Acronym: HIV Inhibitors

Submitted by:

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Postal Address: Chemistry Department University of Cape Town Rondebosch, 7701 South Africa

Theme: Health

Focus Area: Translating research for human health

Type of project: R&D project (small scale)

Summary: South Africa currently has about 15% of the world total infections of HIV and is badly in need of establishing new research platforms. This project currently underway at the University of Cape Town is concerned with the synthesis and biological evaluation of new bifunctional HIV inhibitors. Currently we are working on RT inhibitors comprising a combination of a nucleoside inhibitor (NRTI) with a non-nucleoside one (NNRTI). This is based on the fact that the substrate-binding site for NRTIs is close in proximity to the NNRTI pocket (about 10 angstroms), and thus the hope is that inhibitors can be designed and constructed that synergistically interact with both drug-targets. So far, we have had significant success with d4T-spacer-HI-236 systems with EC50 values of around 100-200nM as determined at Yale University, USA. We intend to extend these systems to cover other types including the double-drug variation in which spacer cleavage occurs to liberate each drug. Of particular interest in this regard is the incorporation of a viral-entry inhibitor into the conjugate.

Expertise offered: My group can synthesize a family of targeted organic derivatives for biological studies including mechanistic ones involving biolabels. We hope to develop a better understanding of how these interesting synthetic products work at the cellular level and therefore be able to develop superior chemical agents.

Previous FP involvement: No

Consortium status: Interaction with Professor Erick Pedersen from the University of Southern Denmark

Expertise sought: Molecular Biologists / Virologists with expertise in HIV and HIV-testing. Modeling capabilities would be highly desirable.

Related projects: South African National R&D programmes

Title: Synthesis and biological evaluation of garlic mimics as novel antimicrobial, anti-cancer and antiviral agents

Acronym: Garlic Mimics

Submitted by:

Roger Hunter (roger@science.uct.ac.za)

Tel: 021 650 2544

Postal Address: Chemistry Department University of Cape Town Rondebosch, 7701 South Africa

Theme: Health

Focus Area: Translating research for human health

Type of project: R&D project (small scale)

Summary: The folklore and therapeutic benefits of the natural product garlic are legendary dating back about five thousand years, and in recent times several in vitro studies have demonstrated the primary product of crushing a garlic clove allicin to have potent antibacterial, antifungal and antiparasitic activity against a range of microorganisms including methicillin-resistant *Staphylococcus aureus*. Antiviral activity has also been demonstrated but synthetic allicin obtained either biomimetically or chemically from diallyl disulfide has never been developed for human use in vivo as a result of its instability. We have recently initiated a medicinal chemistry programme aimed at synthesizing and developing stable allicin mimics as potentially new antimicrobial agents as well as ajoene mimics as novel anti-cancer and cell-virus adsorption inhibitors for extracellular antiviral chemotherapy. To date we have developed two new synthetic organic routes to access the targets. For the allicin mimics, we have developed a new unsymmetrical disulfide synthesis which by regioselective oxidation accesses a family of S-aryl alkyl thiosulfates. The latter with electron-withdrawing groups on the aromatic (aryl) ring have proved to be stable derivatives with antimicrobial activity against *Staphylococcus aureus*. We are now in a position to expand on the medicinal aspects of this part of the programme. Similarly, ajoene is a stable allicin transformation product with a diverse range of bioactivity. We have developed a synthesis of the core structure using a radical addition reaction as a key step and can now access derivatives for testing. We are particularly interested in the anti-cancer properties of these compounds, i.e. their ability to promote apoptosis as well as the known ability of ajoene to chemosensitize drugs that tumours have become resistant to. Ajoene's published ability to interfere with integrin-mediated adsorption processes of relevance to cell-virus entry is also a key focus of the intended future research.

Expertise offered: My group can synthesize a family of targeted organic derivatives for biological studies including mechanistic ones involving biolabels. We hope to develop a better understanding of how these interesting natural products work at the cellular level, and therefore be able to develop superior chemical agents.

Previous FP involvement: No

Consortium status: Links with the Lancashire School of Postgraduate Medicine in the UK (Professor Hassan) as well as UCT Medical School (Professor Parker) for the cancer aspects.

Expertise sought: Partners for biological testing in antimicrobial assays as well as anti-cancer studies. Experts at the cell-virus interaction interface

Related projects: South African National R&D programmes

Title: Nutrigenomics platform South Africa

Acronym: SANF

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: Networking between organisations in same area

Summary: We propose to start a nutrigenomics network within South Africa with the following aims: To acquire and develop hands-on expertise in nutrigenomic techniques; To acquire knowledge and skills in nutrigenomic data analysis; To provide a platform for discussion and collaboration. The network will be linked to the European Nutrigenomics Organisation (NUGO)

Expertise offered: Expertise in nutrigenomics with special emphasis on gene-environment interaction in the African black population. Internships and exchange students can be arranged.

Previous FP involvement: No

Consortium status: Starting up phase (September 2006)

Expertise sought: Nutrigenomics laboratories, academic institutions

Related projects: FP6 International bilateral cooperation South African National R&D programmes

Title: Determining the effect of HIV treatment and investigating the genetic predisposition on HPV viral load and risk of developing cervical cancer

Acronym: CACX

Submitted by:

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Postal Address: Prof. Anna-Lise Williamson Medical Virology University Of Cape Town Medical School Institute Of Infectious Disease And Molecular Medicine (Iidmm) Wernher And Beit South Wing Level 3, Room S3.01 Anzio Road Observatory - 7925 Cape Town Republic Of South Africa

Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: Networking between organisations in same area

Summary: Persistent infection with HPV is a strong risk factor for cervical cancer, though many successfully eradicate the virus and do not develop a cancer. The project will investigate the HPV viral load in a cohort of South African patients of African origin and mixed ancestry population that have been followed from infection with HIV to development of AIDS and subsequently treated with antiretroviral therapy. Cervical cancer smears samples from this cohort will be studied for the presence of HPV type and HPV titer. This study would explore the effect of HIV treatment particularly HAART on HPV viral load and risk of developing cervical cancer in women. The titer values will also be compared with the cytology and disease outcome. This part of the study would involve transfer of technology for HPV viral load determination from the European partner to the South African partner. The second part of the study deals with examining the importance of genetic risk factors for the development of cervical cancer and investigating the genes that predispose to HPV infection and subsequently lead to cervical cancer. A number of genetic risk factors have been proposed including HLA class II loci and a few studies conducted till date have shown association/non-association of genetic factors with the development of cervical cancer in African population. South African case-control cohorts will be used for this part. This would involve the transfer of technology for SNP genotyping from the European partner to the South African partner. The Swedish partner is presently conducting a genetic mapping study to identify such risk factors using affected sib-pair methods. A series of these risk factors will be examined in South African cohorts. The genetic risk-factors will also include a panel of immune related genes that may affect the course of the HPV infection.

Expertise offered: The South African partner represents a major research group both in the HIV and HPV fields. This group has over the years conducted community-based studies and samples suitable for the collaborative studies are available. A case-control cohort of cervical cancer patients has been set up with South African population with people of African origin and mixed ancestry. Controls have been matched by age and ethnicity with the cases. The blood samples have already been collected and frozen. We have developed assays for the determination of HPV viral load using real-time technology. The necessary instruments are available to carry out both the part of the project.

Previous FP involvement: No

Consortium status: One collaboration with Sweden

Expertise sought: Expertise on dealing with genetics of infectious diseases

Related projects: None

Title: Cell therapy for diabetes and metabolic liver diseases**Acronym:** Diabetes**Submitted by:**

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Theme: Health**Focus Area:** Translating research for human health**Type of project:** R&D project (small scale)

Summary: Diabetes mellitus (DM) and comprises a metabolic disease with inherent loss of insulin-producing β -cells which affected more than 200 million people in 2003. Epidemiological investigations surmise an increase of 100% within the next ten years. Both type I and type II DM can cause severe co-morbidity affecting various organs of the body such as retinopathy, nephropathy of the kidney, atherosclerosis, myocardial infarction of the heart, polyneuropathy and many more. Causative treatment options rely on stringent normalization of blood glucose levels via intense insulin application, dietary precautions and activity efforts. Nevertheless, DM can be considered a devastating disease in many patients which requires adequate treatment options such as replacement of all endocrine components known to synergize within islets of Langerhans within the pancreas. At current state, numerous academic approaches are investigating the potential use of stem cells of various sources considered for targeted programming into β -islet-like cells with appropriate insulin release. For this purpose, embryonic stem cells and haematopoietic stem cells are tested as possible candidates (1-4). Both types of stem cells share inflicting biological concerns as to their carcinogenic risks, biological features, immunogenicity, lack of stem cell availability and in vivo function. In contrast to these approaches we have developed a technique to dedifferentiate blood-borne monocytes to gain pluripotent properties which allow further transdifferentiation of these programmable cells of monocyte origin (PCMO) into functional "neo-islets" and "neo hepatocytes". Generation of PCMO-derived Neo-Islets yields three-dimensional clusters of endocrine cellular aggregates containing glucagon, insulin, somatostatin and pancreatic-peptide positive cell types. These Endocrine Units can be considered equivalent to pancreas-derived islets as they enfold normal biological behaviour upon injection into diabetic test animals. In addition these cells can be programmed into hepatocyte like cells. In children metabolic liver diseases can at state only be cured by whole organ transplantation. However the metabolic defect could be substituted by a small number of hepatocytes sparing the risk of a liver transplantation. So far there have been successful attempts to cure these diseases with allogeneic hepatocyte transplantation. Our newly generated "neo-hepatocytes" could be generated autologously or allogeneically and cure children from their metabolic disease the need of a major operation.

Expertise offered: Large animal research facility, stem cell research, cell culture, pediatric surgery, general surgery, expertise in transplantation and immunosuppression, biotechnology, experience in non human primate research and microsurgery

Previous FP involvement: No**Consortium status:** University of Kiel, Germany, Fresenius Biotech, Germany,

Expertise sought: University of Wisconsin Dep. of Transplant surgery, Prof. Sollinger, Prof. Zilla Cardiothoracic surgery, Cape Town, University of Stellenbosch dep. of Anatomy

Related projects: International bilateral cooperation

Title: Health Information Systems

Acronym: HIS

Submitted by:

Carina de Villiers (carina.devilliers@up.ac.za)

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project, including technology demonstration (large scale)

Summary: IS theory: Application of social theories to, and the use of innovative tools and techniques in information system design, development and implementation processes. Systems development: Development of a framework for improving the inclusion of stakeholders specifically health workers and clients in of the design development and implementation of Health Information Systems. Socio-economic implications: Application of a socio-technical framework for understanding information system failure in diverse settings such as ERP in Hospital Information Systems. Curriculum and training: Development of curriculum and teaching Health Information Systems from a practitioner's perspective, teaching methodologies as well as designing curriculum for Health Information Systems in a university setting. IS and health organisations: Improvement of sustainability of similar projects by transferring of knowledge regarding the ongoing maintenance and support of the information system. Development of guidelines and sharing of lessons to assist in the implementation and management of information systems.

Expertise offered: Contributors: Dr E Byrne (elaine.byrne@up.ac.za) Prof PM Alexander (patricia.alexander@up.ac.za) Dr HH Lotriet (hugo.lotriet@up.ac.za) Dr M Matthee (machdel.matthee@up.ac.za) Mrs E Venter (elmarie.venter@up.ac.za) Collaborators: International groups (HISP/BEANISH, INDEHELA) CSIR University of Oslo Department of Health Pretoria Academic Hospital

Previous FP involvement: No

Consortium status: International groups (HISP/BEANISH, INDEHELA)

Expertise sought: Partners must be able to contribute to what is stated in the project summary.

Related projects: International bilateral cooperation

Title: Ethnicity and vulnerability to air pollution

Acronym: EVAP

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project (small scale)

Summary: This project aims to establish how different ethnic groups differ genetically and how this affects their susceptibility to air pollution. The project would explore the use of both biological assessment approaches (such as genetic biomonitoring of different ethnic groups) and environmental exposure assessment techniques. A comparison of the accuracy of both approaches could result in the development of an integrated assessment tool for determining ethnic vulnerability to air pollution

Expertise offered: South African expertise exists in vulnerability assessment techniques and environmental exposure and risk assessment

Previous FP involvement: No

Consortium status: A Norwegian partner has expressed interest in collaborating, but looking for European counterpart

Expertise sought: Expertise in external exposure technologies would be beneficial as well as experience in integrating external (environmental) and internal exposure assessments

Related projects: None

Title: New Approaches in Identification and Development of Candidates for Mycobacterial Chemotherapy

Acronym: MycobacChem

Submitted by:

Christopher Parkinson (cparkinson@csir.co.za)

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project, including technology demonstration (large scale)

Summary: There has been a serious paucity of new treatments for Mycobacterial infections for around 40 years. With the rate of emergence of MDR and XDR strains of M. tb it is fast becoming a global imperative that alternative chemotherapies be developed. The current project seeks to address the issue through a combination of the utilisation of South African botanical diversity as a source of new molecular entities paying particular attention to indigenous knowledge regarding traditional treatments and the elaboration of such entities using medicinal chemistry protocols in such a manner as to address both pharmacodynamic and pharmacokinetic limitations of the parent species. The work will be carried out in parallel with a study of the structure and function of structurally discrete Mycobacterial kinases, in particular with regard to ATP competitive inhibition.

Expertise offered: A comprehensive bioprospecting science and technology value chain to include gathering of indigenous knowledge and biodiversity samples, extraction and biological evaluation of samples, bioassay-guided isolation and characterization of new biologically active molecules using LC MS/MS and NMR, synthetic modification of lead compounds including automated parallel synthesis and purification, computer-aided design of synthetic derivatives, compound handling and management, the development of herbal remedies as new drug candidates, GMP production of minimally processed herbal remedies in a FDA approvable Clinical and Botanical Supplies Unit located at CSIR and a dedicated department for the transfer of technology to communities for the cultivation and processing of medicinal plants.

Previous FP involvement: No

Consortium status: No international partners. Discussions with NM4TB (FP6), University of Witwatersrand, University of Stellenbosch, UCT Medical School

Expertise sought:

Related projects: None

Title: New Approaches in Identification and Development of Candidates for Antimalarial Chemotherapy

Acronym: NewMal

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project, including technology demonstration (large scale)

Summary: Aside from the recent introduction of artemisinin combination therapy (ACT) and the key agents artemether and artesunate, the mainstays of antimalarial chemotherapy have been the aminoquinolines and folate pathway antagonists. Today, resistant strains are common restricting the efficacy of treatment by existing drugs in both of these classes. The current project seeks to address the issue through a combination of the utilisation of South African botanical diversity as a source of new molecular entities paying particular attention to indigenous knowledge regarding traditional treatments for fever (the active components for some of which have now been characterised), and the elaboration of such entities using medicinal chemistry protocols in such a manner as to address both pharmacodynamic and pharmacokinetic limitations of the parent species. The incorporation of structural motifs (such as the peroxy group) will be examined where the parent molecular entity contains the functionality appropriate for such transformations. The work will be carried out in parallel with a study of the structure and function of structurally discrete malarial kinases and ATPases, in particular with regard to ATP competitive inhibition and restriction of metal ion transport.

Expertise offered: A comprehensive bioprospecting science and technology value chain to include gathering of indigenous knowledge and biodiversity samples, extraction and biological evaluation of samples, bioassay-guided isolation and characterization of new biologically active molecules using LC MS/MS and NMR, compound management and handling, synthetic modification of lead compounds, computer-aided design of synthetic derivatives, medium to high throughput synthesis and purification (including automated parallel synthesis) the development of herbal remedies as new drug candidates, GMP production of minimally processed herbal remedies in a FDA approvable Clinical and Botanical Supplies Unit located at CSIR and a dedicated department for the transfer of technology to communities for the cultivation and processing of medicinal plants.

Previous FP involvement: Yes

Details of previous FP involvement: Associated with Antimal consortium, FP6 top up call.

Consortium status: Seeking partnerships. Contacting Liverpool school for tropical medicine (S Ward, AntiMal / FP6 lead), R K Haynes of University of Science and Technology, Hong Kong, Discussions with UKZN, UCT medical school and Witwatersrand Pharmacy department ongoing.

Expertise sought: Preclinical and clinical expertise, toxicology, metabolism expertise, specific target models

Related projects: None

Title: Learning and innovation in Brazil, India, and South Africa: Health systems, communicable diseases, and economic development

Acronym: LIBISA

Submitted by: Jo Lorentzen (jlorentzen@hsrc.ac.za) Tel: 021.466-8091 Mobile: 084.428-9779 Postal Address: HSRC-ESSD, Plein Park Bldg 10th Floor, 69-83 Plein Street Cape Town 8000

Theme: Health

Focus Area: Translating research for human health

Type of project: Thematic network on specific research questions

Summary: In an ideal world, advances in science, technological innovations, institutional and organisational strategies, as well as appropriate policies would jointly combat and defeat debilitating or lethal diseases such as malaria, HIV/AIDS or intestinal helminths. In the real world these diseases compromise the wellbeing and cause the deaths of many people especially in developing countries. This research project aims to analyse how health systems in three advanced latecomer countries - Brazil, India, and South Africa - have been responding to three different types of diseases. It employs an innovation systems perspective to understand how knowledge about these diseases is generated or absorbed, how and with what effect the various private and public sector actors involved in disease prevention, control and treatment relate to each other and how and by whom or what these interactions are governed. In a stylised fashion, developing countries face three different types of health problems. Some problems are identical to those encountered in developed countries but others are not. The first type concerns diseases for which there is either no effective prevention or treatment such as malaria. The second concerns diseases which have a solution either in terms of effective prevention or treatment albeit not necessarily in terms of a cure, and whose costs are high such as HIV/AIDS. The third type resembles the second except that its solution is not costly such as intestinal helminths. Hence each problem is associated with a different type of solution ranging from exposure minimization and vaccine development (malaria), to navigating the emerging global IP regime for ARVs to understanding the shortcomings of public health programmes aimed at prevention or treatment (helminths). Each solution in turn raises different issues for developing countries from dedicated R&D investments to address global market failures to intra-governmental coordination around health and education challenges.

Expertise offered: The team consists of epidemiologists, health system experts and economists from the three countries who work at universities, science councils, in government and in the private sector. Their different backgrounds and expertise make for the interdisciplinary competence required to tackle such a complex study. At the same time, the adoption of the innovation systems approach guarantees a common framework that allows testing hypotheses across different disease profiles and national health systems. Each country has followed its own strategies in fashioning responses to the health challenges analysed here. These strategies can be differentiated both in terms of their content and their relative success. The comparison of different strategies with different outcomes makes it possible to establish cause-effect relationships. Insofar as the accumulation of cross country experiences facilitates learning from good practice, it makes it thus possible to draw lessons for innovation systems in the health sector.

Previous FP involvement: No

Consortium status: The three existing partners have met on three occasions and designed a project proposal for which they have received some seed funding. They now pursue international foundations such as the Gates and Rockefeller Foundations and the ESRC-DfID facility.

Expertise sought: We are looking for partners in Europe who are interested in comparing the challenges to public health systems in developing countries outlined in this proposal to those in developed countries. Ideally partners would combine technical expertise in the three identified diseases (or others that are related) with an understanding of health system management and innovation, and economic analysis.

Related projects: None

Title: Structural Biology

Acronym: SB

Submitted by:

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Theme: Health

Focus Area: Translating research for human health

Type of project: R&D project (small scale)

Summary: Computer analysis of cryo-EM data, data from X-ray crystallography as well as homology modeling

Expertise offered: Computer analysis of cryo-EM data, data from X-ray crystallography as well as homology modeling

Previous FP involvement: No

Consortium status: None

Expertise sought: Partners with experimental data

Related projects: None

Title: THz diagnostic systems

Acronym: TerraDiagnost

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: R&D project, including technology demonstration (large scale)

Summary: Terra-Hertz (THz) radiation is in the electromagnetic spectrum between the far-infrared optical region and the RF microwave region. There are numerous potential applications in the medical and biological field, e.g. in medical diagnostics and drug development. However, since THz photonics is still an emerging field, there are probably many more applications not yet explored. One of the main obstacles is that there are still no compact and efficient THz sources available. In addition to the medical and biological field there are potential applications for THz systems in the security industry. The aim of this project would be research in the following areas: - Novel compact and efficient THz sources, THz optics (including delivery, shaping and focusing), THz detection and imaging, THz applications in medical diagnostics, THz applications in drug development and New THz applications in other fields.

Expertise offered: Efficient high-power mid-IR laser sources as pump lasers for THz generation, Short-pulse operation of lasers and Electronic control of lasers

Previous FP involvement: No

Consortium status: We are currently discussing the project with the Nonlinear Optics Group of the Physics department, University of St. Andrews, UK.

Expertise sought: Non-linear materials for THz generation (e.g. GaAs), THz optics, THz detection and imaging, Experts in the medical and biological field who would potentially utilise this technology.

Related projects: None

Title: Porphyria International Collaboration

Acronym: PORPH

Submitted by:

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Theme: Health

Focus Area: Optimising the delivery of health care to European citizens

Type of project: Thematic network on specific research questions

Summary: The current problems in the field of the porphyrias lie firstly in the identification of patients/carriers and secondly in establishing why some individuals manifest acute symptoms of the disease, needing expensive treatment while others do not. That is trying to explain the incomplete penetrance of these disorders. This project is aimed at identifying other susceptibility factors / modifier genes which may impact on the phenotype/genotype relationship in the porphyrias. Considering the relative rarity of the acute porphyrias, answers to the above questions will only come out of serious, methodical pooling of data and cross-border collaboration in order to increase the size of the patient cohort. Hence funding to allow such interaction and interlinking of data and projects between the various European countries and the well characterised South African pool of patients will be paramount in achieving these goals.

Expertise offered: Our Centre is an internationally recognised centre and is one of the very few fully comprehensive Porphyria-dedicated units worldwide. Our work and interest encompasses all diagnostic, clinical and information aspects related to porphyria and research within the field.

Previous FP involvement: No

Consortium status: A consortium is already being considered under principal direction of Prof Jean-Charles Deybach, Centre Français des Porphyries Inserm U409, Hôpital Louis Mourier, Paris. Other workers in European countries will be approached.

Expertise sought:

Related projects: None

Title: A Corporate Health Intervention Programme: Developing, implementing and measuring the effectiveness of a comprehensive workplace-based physical activity and health promotion programme

Acronym: Workplace PA

Submitted by:

Tracy Kolbe-Alexander (tkolbe@sports.uct.ac.za)

Theme: Health

Focus Area: CO2 capture & storage technologies for zero emission power generation

Type of project: R&D project (small scale)

Summary: Evidence linking physical inactivity to increased burden of non-communicable disease and the relatively high prevalence of insufficient levels of health enhancing physical activity globally highlights the need for interventions in a variety of settings. We will conduct formative research in the workplace with a view to characterising environmental, inter- and intra-personal factors which may need to be addressed in developing an intervention. In addition, the corporate intervention will include the development of a corporate physical activity 'environmental audit', in collaboration with colleagues from Loughborough University. Following the initial phase, we will develop multi-faceted theory-based, best-practice interventions and evaluate implementation. The focus of these interventions programmes will be to increase habitual physical activity in the workplace and school settings and subsequently increase participants' health status. Also, educational components will address knowledge attitudes and beliefs related physical activity and health. This is a quasi experimental intervention study using matched control communities with longitudinal follow up. Community and corporate-based leaders will be trained to implement the intervention thereby ensuring its sustainability and also empowering participating communities to take ownership of the programme.

Expertise offered: The pilot investigator, from UCT/MRC Exercise Science and Research Unit, has played an integral role in developing a work place based physical activity intervention programme, but it has not yet been evaluated. In addition, we have a well-established partnership with a large national health insurance company, who has just launched a comprehensive corporate based product, providing us with a large base of potential participants.

Previous FP involvement: No

Consortium status: We have had preliminary discussions with Dr Fiona Bull from Loughborough University

Expertise sought: Dr Fiona Bull from Loughborough University, together with the British Heart Foundation has developed a health and environmental audit for British companies. They are currently evaluating the effectiveness of this instrument and corporate based interventions.

Related projects: None

Title: Nutritional and Oxidative Phenotype: Metabolic Inflexibility**Acronym:** NOP**Submitted by:**

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Postal Address: MRC/UCT Research Unit for Exercise Science and Sports Medicine Department of Human Biology Faculty of Health Sciences
University of Cape Town PO Box 115 Newlands 7725 South Africa**Theme:** Health**Focus Area:** Translating research for human health**Type of project:** R&D project (small scale)

Summary: Although South Africa is a country undergoing epidemiological transition, obesity particularly in black women contributes a major health risk. Published and unpublished research by this unit implicates dysregulation in hormonal axes, systemically and tissue-specific, inflammatory response, energy and nutrient balance, and certain socio-cultural factors for obesity and associated morbidity in these women. Obesity in black South African women constitutes a major public health risk. Preliminary evidence from our unit suggests it may be possible to characterise healthy/unhealthy phenotypes in black lean/obese women, in part on the basis of nutrient partitioning ($P < 0.025$, $N = 134$, irrespective of obesity). In a case-control design, we will select black women, (36-42/group, $\beta = 0.20$) classified as unhealthy (Karelis et al., 2004), measure energy expenditure and substrate oxidation in a whole-room calorimeter and R'-R' variability (SNS activation) in response to habitual and short-term exposure to high fat diet (4 wks). Recruitment/sampling (4-8 mos), baseline/intervention (6-12 mos) overlapping. This programme will provide the first opportunity to fully integrate the various methodological approaches of the nominee and collaborators to characterize "metabolic flexibility" (Storlien et al., 2004) with specific reference to substrate oxidation against the various 'metabolically healthy obese' and 'metabolically-obese normal weight' phenotypes, in this unique population sample. It would provide capacity development by providing a training grant for a PhD candidate as well as a salary for a project manager. All efforts would be made to employ candidates from within the community and with a previously disadvantaged background.

Expertise offered: We are the only research centre in Africa uniquely equipped to study whole body energy and nutrient balance, body composition and these biochemical responses in healthy/unhealthy, lean/obese African women, in response to various dietary regimens. Insights gained add to understanding mechanisms and risks underlying the 'nutrition' transition. Further, we are fortunate to have one of only 18-20 whole-room calorimeter laboratories in the world and the only one in sub-Saharan Africa (one manuscript in review, on energy expenditure in lean/obese, black/white women; one in preparation). Through this programme we can expand our previous work, in which we have investigated determinants of substrate oxidation, and relationships to insulin and sympathetic axes, in the various contexts of exercise training, high fat feeding, and low birth weight.

Previous FP involvement: No

Consortium status: We have held preliminary discussions with Professor John Blundell from the BioPsychology Research Group Institute of Psychological Sciences, University of Leeds, and control of appetite and macronutrient selection.

Expertise sought: The aforementioned collaborator, as well as potential collaborators at the University of Maastricht, Department of Human Biology, for expertise in calorimetry

Related projects: South African National R&D programmes

Title: Molecular mechanism of oesophageal cancer

Acronym: MMOC

Submitted by:

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Theme: Health

Focus Area: Translating research for human health

Type of project: R&D project (small scale)

Summary: Oesophageal squamous cell carcinoma occurs with a high frequency in many parts of the world. In South Africa oesophageal cancer presents a significant health problem where it occurs with a high frequency and is one of the most common causes of cancer-related mortality in Black males. Patients diagnosed with this disease generally have a poor prognosis. There is a need to characterize the molecular events involved in the development of oesophageal cancer, since this information will allow us to diagnose and treat the disease more effectively. We are currently using various approaches to characterise genes that are differentially expressed in oesophageal cancer tissue (compared to normal oesophageal tissue). In the proposed project, we plan to characterise the expression status of selected genes. Suitable candidates will be further explored to determine their suitability as (i) potential drug targets or (ii) diagnostic markers. Assay systems will be developed to screen a library of natural products and synthesised compounds for activity against potential targets. We will also explore approaches that could be used to screen blood for potential diagnostic markers.

Expertise offered: Molecular biology approaches that include transfection of cultured cells, RNAi knockdown in cultured cells, Real time RT-PCT, basic molecular biology (PCR, northern, DNA sequencing). Cell biology that includes fluorescent immunocytochemistry, flow cytometry, apoptosis and ROS quantitation, immunohistochemistry, cell migration and invasion assays.

Previous FP involvement: No

Consortium status: We currently have an active research group at UCT involved in oesophageal cancer research.

Expertise sought: Partners required who have expertise in screening blood samples for cancer markers. Also partners with experience in developing antibodies that target cancer cells with toxic compounds.

Related projects: None

Title: Web-based Drinking Water Quality monitoring and management information system in poor bandwidth environment

Acronym: DWQMONMIS

Submitted by:

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Theme: Health

Focus Area: Biotechnology, generic tools & technologies for human health

Type of project: Thematic network on specific research questions

Summary: An internet accessible database system utilising open source components (MySQL, XML, etc), is being successfully utilised to track, report on and provide management decision support on drinking water quality at local authority (municipal) level throughout South Africa. The system is specifically designed to not only allow for dynamically updated standard reporting against specifications, but also guides the decision maker in understanding the implication of non-compliance and what management interventions are required to resolve the non-compliant aspects. The system is accessible via the internet for full use providing considerable costs and operational efficiency benefits over local application based systems. However the system can also be used as an independent local application if required. Current functionality includes: Management Dashboard [summarised monthly view of legislative compliance & identification of areas requiring urgent attention; easy colour coding to show compliance (green), failure within Class 1 (yellow), and failure within Class 2 (red)], Overview (map-based interface with "period based" summary of key indicators), Quick Analysis (quick links to regularly used operational efficiency and legislative compliance tables/graphs and trend analysis), Detailed Analysis (dynamic Tables and Graphs with full flexibility), Reports (archive of management reports in Adobe Acrobat format), Data Entry - (mostly via internet and/or Excel and can be adapted to link to existing systems for specific clients), Automation (auto-notification by e-mail of failures, generation of auto-reports and summary reports for feedback to the full range of participating parties). The intention is to adapt the system to allow compliance monitoring applications throughout Africa. This system allows research results to be disseminated to the user in a simple, efficient and effective way thereby assisting and guiding managers that are often not technically or scientifically qualified to take important decisions.

Expertise offered: Practical expertise in the development and implementation of compliance monitoring and management systems in developing countries where local management experience is lacking and low bandwidth exists. Specialist applications to Drinking Water Quality Management.

Previous FP involvement: No

Consortium status: None

Expertise sought: Any specialist application where a stand-alone compliance monitoring and management system needs to be developed and/or installed.

Related projects: South African National R&D programmes

Title: Melanocyte progenitor cells and their role in the repigmentation of skin in vitiligo patients and burn victims

Acronym: VITILIGO

Submitted by:

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Theme: Health

Focus Area: Translating research for human health

Type of project: Thematic network on specific research questions

Summary: Both vitiligo and burns result in depigmented areas of the skin. As these areas are often in exposed parts of the body they can lead to severe psychological stress and often result in discrimination, particularly in darker-skinned individuals. This project plans to adopt a holistic approach to this problem. The basic science component involves understanding the molecular and cellular mechanisms underlying the activation, proliferation and migration of melanocytes in the skin. The psychological component will help us to evaluate patients' perceptions of living with patches of depigmented skin. Together these will ultimately lead to better therapeutic modalities.

Expertise offered: The South African researchers will offer dermatological expertise and the ability to obtain biopsies from patients

Previous FP involvement: No

Consortium status: Consortium has been initiated with specific partners

Expertise sought: The collaborators in Europe will offer tissue culture expertise and advice regarding the media of culture and the molecular mechanisms regarding the cell cultures. The European collaborators will also provide advice and the expertise regarding antibodies and immunocytochemistry techniques for the visualisation of cell proteins

Related projects: None