PATHOGEN CO-INFECTION - THE PROBLEM

Acquired immune deficiency **(AIDS),** tuberculosis **(TB)** and **malaria are the primary infectious diseases causing death worldwide. TB** is responsible for a third to a half of **human immunodeficiency virus type 1 (HIV-1)-associated deaths,** particularly in sub Saharan Africa and South East Asia. **Malaria** is widely spread in tropical Africa and accounts for approximately 800,000 deaths every year. In addition to these pathogens, 170 million people are infected with **hepatitis C virus (HCV),** which leads to chronic liver disease. Because of shared routes of transmission, **HCV co-infection** is recognized as a major cause of **morbidity and mortality among HIV-1 infected persons.**

The epidemiology and clinical features of co-infected subjects is well documented, however, there is a paucity of basic scientific studies addressing the interactions between these pathogens. There is undoubtedly a complex interplay between pathogens and the host immune response.

PATHCO FOCUS AND OUTCOME

PathCo consortium proposes that pathogen evasion and dysregulation of host immune responses play a key role in co-infection associated morbidity. Within this Project will test this hypothesis by developing ***in vitro* and *ex vivo* co-infection model systems** to study co-pathogen interactions. The specific objectives of PathCo are to improve our understanding of pathogen co-infection effect(s) on host innate and adaptive immune responses and to develop new approaches to dissect pathogen interactions: ranging from the genesis of fluorescent labelled viruses to state-of-the-art tissue explant culture systems and novel humanised mouse models. Translational studies of infected subjects will define pathogen-specific effects on host immune responses and consequences for disease progression. It is imperative that such interactions are elucidated before evaluating new prophylactic or therapeutic strategies in co-infected individuals.

PathCo is split into 5 basic research areas encompassing the following objectives

- **To define the genetic and molecular basis underlying TB regulation of HIV-1 replication**
- **To define the role of HIV-1infectionand associated inflammation on HCV replication**
- **To identify common pathways defining Malaria and HCV liver tropism**
- **To generate humanized mouse model systems that support pathogen co-infections**
- **To identify the effect(s) of HIV-1 infection on HCV specific host immune responses**

The PathCo project brings together powerful multidisciplinary technologies that will improve our understanding of **the complex interactions between infectious agents and the host immune response** that will significantly improve the management of co-infection associated disease. Recent developments in each of the disease disciplines enable the design of model systems that support pathogen co-infection, highlighting the timeliness of **PathCo's mission to study the biological and immunological consequences of co-infection(s).**

Ultimately such knowledge will be instrumental in the **rational design of new therapies and vaccines to control HIV-1, TB, malaria and HCV.** In parallel to generating and utilizing new tools to understand the basic biology of pathogen co-interactions the **PathCo consortium members** will develop novel anti-microbials for translational research. **The PathCo project** will identify new targets for therapy and vaccine design, whilst validating known agents for their ability to block pathogen transmission and to target antigen or anti-pathogen components to dendritic cells (DCs).

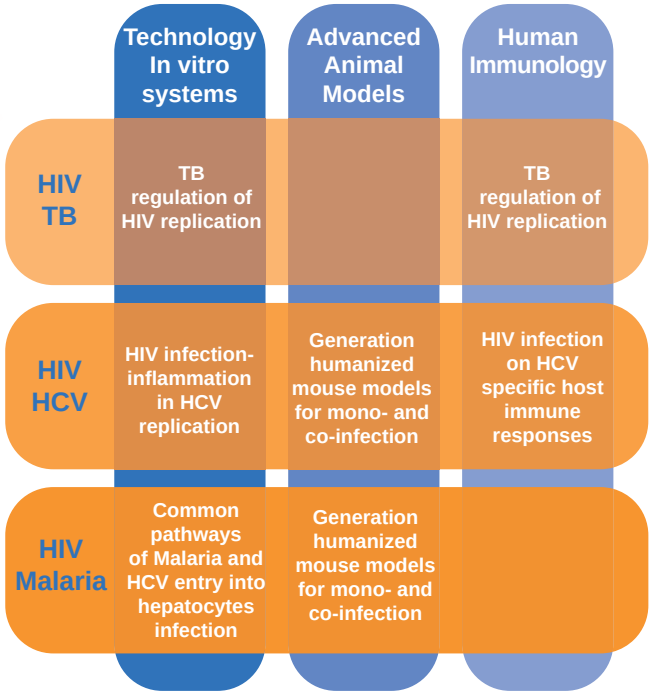
PATHCO ALLIANCE

The PathCo consortium consists of nine beneficiaries from four EU different countries (UK, France, Germany and Italy) and one beneficiary from non-EU countries (South Africa).

PathCo is a well-balanced team of immunologists, virologists, clinicians, statisticians, epidemiologists with expertise in HIV/AIDS, TB, malaria and hepatitis C infection research and has the most appropriate scientific and technical background as well as the animal models and instrumentation required to fulfill the goals of this project and to succeed in its mission.

PathCo beneficiaries will have access to well-characterised established cohorts of co-infected patients from different geographical locations.

PROJECT ORGANIZATION



PathCo

PATHCO PARTNERS

UNIVERSITY OF LIVERPOOL
Bill Paxton - United Kingdom
www.liv.ac.uk

UNIVERSITY OF BIRMINGHAM
Jane McKeating - Gurdyal Besra
United Kingdom
www.birmingham.ac.uk

INSTITUT NATIONAL DE LA SANTÉ ET DE LA RECHERCHE MÉDICALE
Olivier Silvie - France
www.inserm.fr

UNIVERSITAETSKLINIKUM FREIBURG
Robert Thimme - Germany
www.uniklinik-freiburg.de

UNIVERSITY OF OXFORD
Tao Dong - United Kingdom
www.ox.ac.uk

IMPERIAL COLLEGE OF SCIENCE, TECHNOLOGY AND MEDICINE
Carolina Herrera - Xiao-Ning Xu
United Kingdom - www3.imperial.ac.uk

UNIVERSITY OF CAPE TOWN
Robert Wilkinson - South Africa
www.uct.ac.za

INSTITUT PASTEUR
James Di Santo - France
www.pasteur.fr

ALTA RICERCA E SVILUPPO IN BIOTECNOLOGIE S.R.L.U.
Riccardo Bertini - Italy
www.altaweb.eu

PathCo

PATHOGEN CO-INFECTION:
HIV-1, Tuberculosis, Malaria and hepatitis C virus

COORDINATOR:
Prof William A Paxton PhD DIC
Department of Clinical Infection, Microbiology and Immunology
Institute of Infection and Global Health
University of Liverpool
216e, Ronald Ross Building
8 West Derby Street
Liverpool L69 7BE
w.a.paxton@liverpool.ac.uk

www.pathco.org

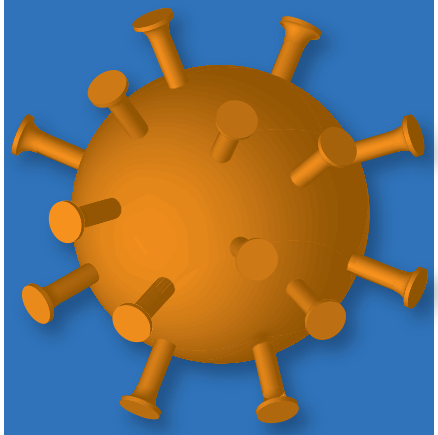
EC Contribution: € 5.909.690
Duration: 60 months
Starting date: 01/11/2012

SEVENTH FRAMEWORK PROGRAMME

PathCo

PATHOGEN CO-INFECTION:

HIV-1, Tuberculosis, Malaria and hepatitis C virus



SEVENTH FRAMEWORK PROGRAMME