# Dissecting the Immunological Interplay between Poverty Related Diseases and Helminth infections

## An African-European Research Initiative

# PROJECT FINAL REPORT

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## 1.1 Executive Summary

Worm infections are receiving increased attention due to a) the wide geographic overlap in occurrence between worms and poverty related diseases (HIV, TB and malaria, PRD), b) the large proportion of individuals (minimal estimates around 25%) co-infected with worms and HIV/TB/malaria, c) the potential risk of increasing disease burden, d) the very limited understanding of the impact of worm infections on HIV-, TB- and malaria-specific immune responses and on their clinical outcome, e) the lack of established intervention guidelines for treatment of worm infections, and f) the scarce information on the impact of worm infections on vaccination and vaccine-induced immune responses. In order to address these complex and challenging scientific issues, **IDEA** is the first large EC funded program aiming at tackling these very complex scientific challenges. Specifically IDEA focuses on understanding: a) the worm-induced modulation of the functional and molecular profile of HIV-, TB- and malaria-specific immune responses, b) the impact of worm co-infections on measures of disease activity of PRDs, c) the immunologic markers of worm-, HIV-, TB- and malaria-specific immune responses associated with better control of pathogen replication and disease, and d) the modulation by worm co-infections of vaccine-induced immune responses.

To achieve these objectives, **IDEA** project has developed a global and innovative strategy which includes**:** a) the alliance between African and European leading scientists in the field of worms, HIV, TB and malaria, b) the multidisciplinary expertise involving immunologists, parasitologists, epidemiologists, clinicians, and experts in vaccines, c) cutting edge immunology and the most innovative technologies to profile immune response, d) the access to large cohort studies bringing a number of centres working on worms and PRDs in Africa together, and e) the access to experimental HIV, TB and malaria vaccine candidates under clinical development in Africa.

**IDEA** project has contributed to the deciphering the immunological interplay between PRDs and worm infections. Specifically IDEA has delivered the following key scientific outputs:

- Advancing the understanding of worm-induced modulation of the functional (innate and adaptive immunity) and molecular profile of HIV-, TB- and malaria-specific immune responses.
- Advancing the understanding of the impact of worm co-infections on measures of disease activity for HIV, TB and malaria.
- Identification of new potential bio markers associated with helminth co-infection with HIV, TB and malaria.

Alongside the science, another important output of IDEA is integrating capacity building activities in its research projects, entailing North-South but more importantly South-South exchanges. In addition to supporting multiple master and PhD student projects, significant efforts have been made in harmonization and implementation of novel immunological and diagnostic assays, data management, trial conduct in African settings led by African PIs, building African skills. Leveraging with other parallel research programs funded by the EC and international initiatives for sustained development is also a key feature of IDEA.

## 1.2 Project Context and Objectives

HIV, tuberculosis (TB) and malaria, i.e. the three major poverty related diseases (PRDs) represent the greatest causes of death among infectious diseases world-wide. The recent WHO estimates (http://www.who.int/en/) indicate that about 33,000,000 people are infected with HIV and Sub-Saharan Africa remains the region with the highest number of people living with HIV (67% of cases world-wide) and of HIV-related deaths (75% of total deaths world-wide).

TB is a major cause of illness and death world-wide and particularly in Asia and Africa. There were an estimated 9.2 million new cases of TB in 2006. About 0.7 million new TB cases occurred in HIV infected subjects. Among the 1.5 million estimated deaths, 0.2 occurred in HIV infected subjects. Sub-Saharan Africa had the highest incidence of new TB cases in 2006 with particularly large disease burden in South-Africa, Tanzania, Uganda and Nigeria.

Malaria accounts for about 1 million deaths every year and 90% of deaths occur in tropical Africa. Malaria in tropical Africa is also the leading cause of death among children below five years.

Only recently has it become widely appreciated that other infectious diseases, the so called Neglected Infectious Diseases (NIDs), represent a major public health burden with a particularly great impact related to their widespread distribution across most developing countries. NIDs are caused by a large variety of infectious agents and predominantly by different types of worms. Worms are highly prevalent in tropical regions. Although most infections are asymptomatic, heavy infections result in significant morbidity. Despite limited evidence for the intervention, recently significant scale-up of population-based national programmes for integrated control of worms have taken place following concerted advocacy and major philanthropic donations. These programmes raise important research questions about the public health implications of co-infection and treatment for other diseases such as malaria, HIV and TB. Indeed there is growing epidemiological evidence for interactions between worms and these diseases. The most recent estimates indicate that about two billion people are infected with worms corresponding to a large proportion of the world's population. Three hundred million are severely affected and about 50% of cases are children. The worm infections include schistosomiasis and several species of intestinal worms also known as soil-transmitted helminths. WHO estimates that about 200,000 deaths every year are caused by schistosomiasis alone (http://www.who.int/en/).

The soil-transmitted helminths are present in all the developing countries. Schistosomiasis requires an intermediate snail host and is therefore particularly found in lake regions and along major rivers; it affects children and also adults with particular occupations such as fishermen and irrigation workers. The distribution of the various filariases is determined by the habitat of their insect vectors: for example, oncocherciasis (river blindness) is found in areas of fast-flowing streams where the transmitted black flies breed.

Given the wide geographic overlap in occurrence, co-infections between worms and HIV, TB and malaria occur in tens of millions of people and in both children and adults. In this regard, preliminary epidemiological data generated from a small number of studies indicated that globally about 25% of individuals affected by HIV, malaria or worm infections were co-infected. Although worm infections and HIV, TB and malaria have been extensively investigated, only recently there has been increased attention to the potential impact of co-infections between worms and HIV, TB and malaria. It has been suggested that the interaction between these pathogens may be associated with increased susceptibility to infection and disease: this could have major public health implications by increasing the diseases burden, particularly since effective vaccines are not yet available for these infections. Indeed, although the worm-, HIV-, TB- and malaria-specific immune responses have been the target of extensive investigation, the precise immune correlates of protection remain unknown for all these diseases. Further, although there is considerable evidence that worms-induced effects on the immune system can modulate responses to unrelated

antigens, there is little information on the effects by worm infections on the HIV-, TB- and malaria-specific immune responses in humans, and little evidence as to whether such effects are detrimental, neutral or even beneficial: there is limited knowledge of the influence by underlying worm infections on the clinical course of HIV, TB and malaria. Finally, the impact by worm infections on vaccination requires further investigation as the very limited data available suggests reduced effectiveness of vaccines in subjects with worm infections.

**IDEA** was designed to investigate the issues through a multidisciplinary approach by bringing together experts in the fields of immunology, epidemiology, parasitology and vaccines. The four major objectives of **IDEA** are to determine:

- the worm-induced modulation of the functional and molecular profile of HIV-, TB- and malaria-specific immune responses. In particular, it will be determined how worm innate and adaptive immune responses instruct the subsequent development of HIV-, TB-, and malaria-specific immune responses,
- the impact by worm co-infections on measures of disease activity for HIV, TB and malaria. This investigation will allow us to understand better the interactions between different pathogens and their influence on disease activity,
- the immunologic markers of worm-, HIV-, TB- and malaria-specific immune responses associated with better control of pathogen replication and associated disease,
- the modulation by worm co-infections of vaccine-induced immune responses.

On the basis of the objectives outlined above, IDEA aims to test the following hypotheses:

a) modulation of immune responses by worm infections cause quantitative and qualitative changes in the profile of malaria-, TB- and HIV-specific innate and adaptive immune responses,
b) modulation of immune responses by worm infections results in impaired HIV-, TB- and malaria-specific immune responses and higher pathogens load and
c) modulation of immune responses by worm infections affects vaccination and the development of vaccine-induced immune responses.

## 1.3 Main Scientific & Technical Results/Foregrounds

### 1.3.1 Overview

IDEA is composed of 5 Workpackages (WP), with 1 WP on consortium management (WP1), one on capacity building (WP5) and three WPs (WP2-4) on research and development. The inter-relationship of the WPs and their key outputs are shown in Figure 1 below.

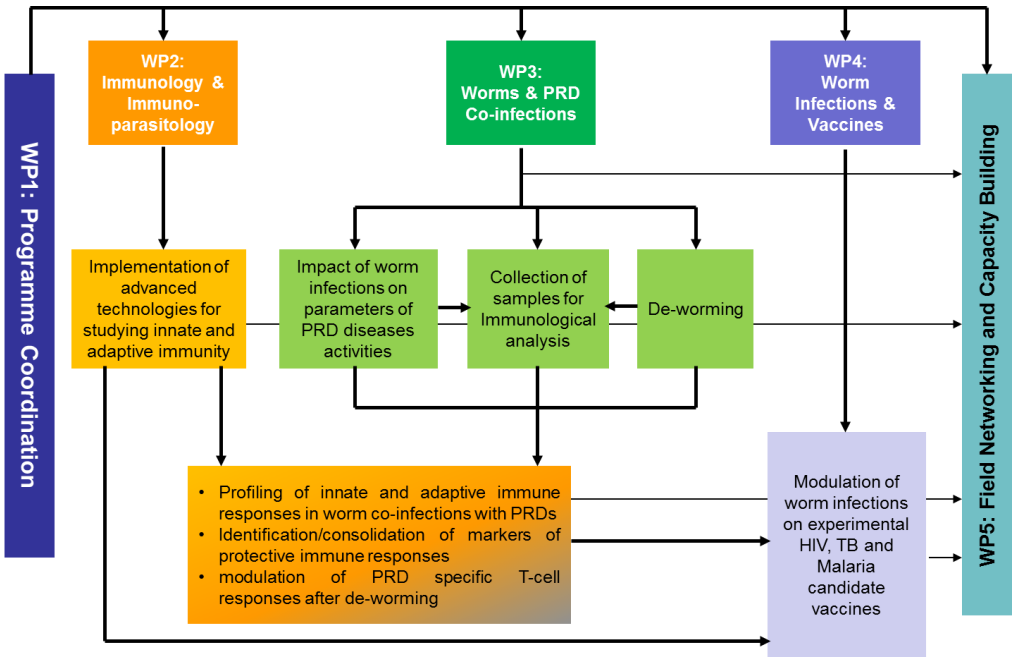
The key strength of **IDEA** is of two folds: 1) State-of-the-Art immunological platform (WP2) and 2) powerful clinical program linking with existing cohorts and studies funded by various international initiatives for access to larger patients dataset (WP3). To ensure data comparability and integration across the different studies, significant harmonization efforts have been made within IDEA on protocol and study design, diagnostic methods and immunological assays and SOPs. These harmonization activities have been performed not just between the different laboratories and clinical sites in the North but also with those in the South. WP2 focuses on profiling the worm-induced immune modulation of the functional and molecular profile of HIV-, TB- and malaria-specific immune responses, while WP3 focuses on understanding the impact of worm infection on the PRD disease activities, including but not limited to acquisition, disease progression and response to treatment. These analyses have led to the identification of new potential biomarkers associated with helminth co-infection with HIV, TB and malaria. In particular these new biomarkers define differences in immune responses against HIV, TB and malaria caused by the underlying helminth infections.

WP4 focuses specifically on understanding the modulation of worm co-infection on PRD vaccination and vaccine-induced immune responses. For the malaria vaccine, the study was linked with the efficacy trial of malaria vaccine of GMZ2. For TB and HIV vaccines, two trials have been conducted using one of the lead vaccine candidates/regimens in the field.

WP5 focuses on field networking and capacity building. The unique feature of **IDEA**'s capacity building activities is the integration with **IDEA** research programme, in addition to master and PhD programs, workshops, courses and short-term exchanges. Many of IDEA studies are led by the African scientists, from clinical trials, to immunological monitoring, to data management and analysis. The major output of this WP is the career development of a new generation of young African scientists, who are playing a leading role in science in SSA.

All the management/coordination/communication activities have been carried out under WP1. All program management tasks in a timely fashion, including timely submission of project scientific and financial report, ensure effective communications between the consortium members through regular tele conferences and face-to-face meetings, as well as maintaining an up-to-date project website. In addition, a central database has also been established that have QCed and imported demographic and clinical data from all key IDEA studies. This central database will also be instrumental for future cross-study analysis beyond the current IDEA lifespan.

**Figure 1 Components of IDEA**




### 1.3.2 WP2 Immunology and Immunoparasitology

The primary objective of workpackage 2 is to determine the worm-induced modulations of the functional and molecular profile of HIV-, TB- and malaria-specific immune responses.

#### *1.3.2.1 Main Activities of WP2*

The main activities include:

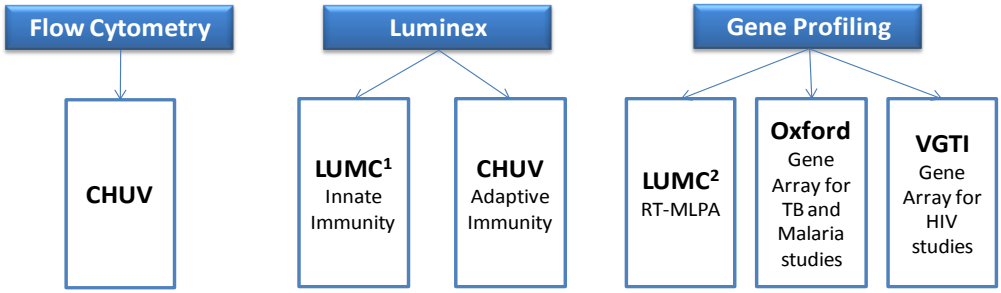
- Harmonization of SOPs for functional polychromatic flow cytometry, luminex and gene profiling
- Profiling the innate immune responses elicited by worm infections, and determine whether the worm-induced innate immune response modulates the innate immune response to HIV, TB and malaria Ags
- Profiling the adaptive immune responses elicited by worm infections, and determine whether the worm-induced adaptive immune response modulates the adaptive immune response to HIV, TB and malaria antigens
- Molecular profiling of innate and adaptive immunity

**Harmonization of Laboratory SOPs**

A key challenge for any large consortium is the harmonization of assays and procedures to ensure comparability and integration of data generated from different laboratories. Significant efforts have been made within IDEA right from the onset of the project in the harmonization of the lab SOPs, primary immunological assays as well as key reagents.

**IDEA** has prioritized three primary immunological assays: 1) functional polychromatic flow cytometry; 2) Luminex, 3) gene profiling. The following laboratories were identified as the core lab for each of these assays based on their track records and expertise (see figure 2 below). The core labs have played a leading role in the harmonization process.

**Figure 2: IDEA Primary Immunological Assays**




LUMC[1]: this is the laboratory led by Dr. Maria Yazdanbakhsh
LUMC[2]: this is the laboratory led by Dr. Tom Ottenhoff

Relevant SOPs have been harmonized across the different laboratories, that include 1) isolation and stimulation of DCs, monocytes & B cells, 2) isolation and stimulation of CD4 and CD8 T cells, 3) PBMC isolation and cryopreservation, 4) ELISpot, 5) functional polychromatic flow cytometry, and 6) Luminex technology.

- ***Harmonization and qualification of Functional Polychromatic Flow Cytometry***

CHUV took the lead in the harmonization of the flow cytometry assay. A vigorous three-step harmonization procedure was defined upfront: Step 1: configuration and setting of flow cytometers; Step 2: Assessment of overall ability of each laboratory to run a standard intra-cellular cytokine staining (ICS); Step 3: Inter-site performance QC to ultimately demonstrate the level of harmonization obtained between all IDEA laboratories. The harmonization process took several reiterative steps, and a number of issues have been identified along the way, such as the instrument configuration and QC, the sample processing SOP, the gating strategy and the analysis workflow. Eight IDEA laboratories (CHUV, MMRP, LUMC, Oxford, Swiss TPH/IHI, INMI, LHSTM and UVRI) have participated and successfully completed the harmonization.

- ***Harmonization of Luminex Assay***

The primary goal for luminex assay is the harmonization of the panel of cytokines and chemokines to be used across the labs and sites and the selection of a common provider for these reagents. LUMC and CHUV have spearheaded a number of pilot studies for innate and adaptive immunity respectively. Based on the outcome of the pilot studies, a panel cytokines and chemokines have been selected. For ***Innate immunity***, a minimum and a full panel have been identified, and the final selection will be based on the cost. The minimum panel includes: 1) helminth/malaria: IFNg, IL-10, IL-13, TNFa, IL-6; 2) helminth/HIV: IFNg, IL-10, IL-13, IFNa, MIP1a and 3) helminth/TB: IFNg, IL-10, IL-13, IL-12p70, IL-23. The full panel includes IFNa2, IL1b, IL6, IL10, IL12p70, IL-13, IL-23, IFNg, MCP1, MIP1a, MIP1b, TNFa and IP-10. For ***adaptive immunity***, a panel of 11 plex has been selected: TNF-$\alpha$, IFN-$\gamma$, IL-2, IL-4, IL-5, IL-13, IL-17A, IL-17F, IL-22, IL-10, and IL-21.

- ***Harmonization and Qualification of Gene Profiling Assay***

Qualification of the RT-MLPA: LUMC took the lead in the qualification of the RT-MLPA assay. The following marker genes have been selected to Innate and Adaptive Immunity. The process of combining, testing and validating the designed RT-primers, hybridisation probes, and positive control template oligos into dcRT-MLPA sets has been completed.

| Innate Immunity | Adaptive Immunity |
|---|---|
| • Genes selectively regulated by live Mtb in MF1 and MF2 macrophage subsets *(Microarray analysis Ottenhoff lab; unpublished data).*<br>• Key MF1 and MF2 cytokines (*IL12A, IL12B, IL23A, CCL5, CCL22, IL10, CCL2,* | • T cell subsets (*CD3, CD4, CD8, CCR7, CD45RO, CD45RA*).<br>• Th1 responses (*CXCL10, IFNG, IL12A, IL12B, IL15, IL1B, IL2, TBX21, TNF*).<br>• Th2 responses (*GATA3, IL10, IL13, IL4, IL5, IL6, IL9, TGFB1*).<br>• Th17 responses (*IL17, IL22RA1, IL23A, RORC*), Th17-associated genes (*Microarray analysis Ottenhoff lab; unpublished data*). |

| | |
|---|---|
| *CXCL13*).<br>• TLRs (*TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, and TLR10*).<br>• Other relevant genes (*NLRP1-4, 6, 7, 10-13, NOD1-2, MRC1-2, NLRC4, CD209, CLEC7A*). | • Treg markers (*CCL4, CTLA4, FOXP3, IL2RA, IL7R, LAG3, GITR*).<br>• T cell cytotoxicity (*GNLY, GZMA, GZMB, PRF1*).<br>• Biomarkers identified that discriminate between TB infection and disease (*CD19, FCGR1A, BLR1; Ottenhoff lab, Genes and Immunity* doi:10.1038/gene.2011.64 2012). |

Further, a "dry run" transcriptomic analysis was conducted between LUMC and VGTI, in order to test the appropriate selection of whole blood RNA isolation kits. Transcriptomic and bioinformatic analysis at VGTI confirmed high quality input material from both methods and no significant differences in the gene expression data between the two kits.

- ***Standardization of Reagents***. At the onset of the **IDEA** project, the group has recognized the importance of standardized reagents and the following has been implemented through the common effort of the consortium:
    - Common panel of antigens to stimulate innate immunity
    - Common antibody panel for the ICS assay
    - Common batch of foetal bovine serum (FBS) for the preparation of PBMCs. CHUV took the lead in the validation of a specific batch of FBS, and subsequently all laboratories ordered the same batch from the same provider.
    - A panel of helminth antigens (for S*. mansoni, S. heamatobium* and *Ascaris lubricoides*) have been produced and provided by LUMC
    - PTE (potential T-cell epitope) peptides were identified as the common peptides to be used for all HIV studies and have been provided by the Vaccine Immune Monitoring Consortium funded by the Bill & Melinda Gates Foundation.
    - ESAT-6/CFP10 fusion protein was identified as the common TB antigen and was produced and provided by LUMC

**Profiling Innate Immune Responses**

The following studies have contributed to this analysis:

- Gabon Malaria Study, analysis was jointly performed by LUMC, EKUT and CERMEL. The study includes three different age groups (newborn, school children and adults) with assessment of: 1) innate responses in infected and uninfected subjects; 2) dendritic cells in adults and cord blood; 3) regulatory cells (B and T cells).
- Tanzania Bagamoyo Malaria Study, analysis was joint performed by Swiss TPH and IHI. The study was done in school children aged 2-9 years, the ex vivo innate immune responses in peripheral blood at the single cell level were measured.
- Uganda HIV Study performed by UVRI in the Fishing Cohort.
- Italian TB Study performed by INMI

LUMC has also conducted a meta-analysis of all published data so far on the effect of helminths on immune responses to malaria. The analysis showed that helminth infections had no effect on Th1, Th2, Th17 or regulatory responses induced by malaria parasites. However, it is noted that species of helminth examined might be important as studies where filarial infections were involved showed stronger effects on malaria induced immune responses.

Further, an IDEA multicentre analysis led by LUMC of data generated by examining the innate immune responses in subjects infected with helminth only, malaria/HIV or TB only or co-infected with helminths. The centres involved were Gabon, Tanzania, Uganda and Italy. The data analysis is still underway but the preliminary results indicate that there is strong geographic variation in innate immune responsiveness. The effect of helminths on the innate responsiveness to malaria, HIV or TB is yet to be analysed by newly acquired statistical packages.

In addition, in order to delineate the early steps, cells and factors involved in the development of the polarized worm-induced innate immune response, EPFL has identified: 1) the role of IL-1 beta as an early cytokine involved in the development of the polarized worm-induced innate immune response; 2) acetate as a further early product, induced by worm infection, and involved in the development of type 2 immunity.

**Profiling Adaptive Immune Responses**

The following studies have contributed to this analysis:

- ***Tanzania Bagamoyo TB Study***, analysis jointly performed by CHUV, Swiss TPH and IHI. The objective of the study was to evaluate Mtb-specific and BCG-specific T-cell responses, together with the impact of TB and TB/helminth co-infection on the expression of 1) transcription factors, and 2) activation molecules and on the frequencies and phenotype of regulatory T cells, using a series of experiments including flow cytometry and Luminex panels previously established and validated.

- ***Tanzania Bagamoyo HIV Study***, analysis jointly performed by CHUV, Swiss TPH and IHI. Analysis has been performed to evaluate HIV-specific T-cell responses, together with the impact of helminth infection on the expression of transcription factors expression and on the distribution of the HIV infected cells among blood CD4 T-cell subsets using a series of experiments including flow cytometry/luminex panels previously established and validated and the use of most recent molecular technologies.

- ***Tanzania Mbeya HIV Study***, analysis jointly performed by MMRP and LMU. The partners studied systemic immune activation and HIV-1 co-receptor expression in relation to different helminth infections and in response to helminth treatment in HIV-negative adults with or without helminth infections.

- ***Uganda HIV incidence and schisto intervention studies*** by UVRI in collaboration with CHUV. The main objective is to study the impact of helminth infections on the acquired immune response to HIV and the partner investigated the T cell response to HIV in individuals infected with S. mansoni.

- ***Uganda Kampala TB contact study*** by UVRI. The main objective was to determine the effect of helminths and other co-infections on susceptibility to infection with M. tuberculosis. The study also allowed additional investigation of the effect of isoniazid preventive therapy (IPT) on the immune response to mycobacterial antigens among HIV-negative household contacts aged above five years

- ***UK London TB study*** by LSHTM. The following analyses have been performed to assess the modulation of helminth infections on anti-mycobacterial immunity by 1) flow cytometry; 2) luminex analysis; 3) genes expression analysis of ex vivo blood samples using microarray analysis.

- ***French HIV/TB study*** by INSERM. The study is focused on comparing the frequency of Treg/Th17 populations, the frequency and cytokine production of mycobacterial-specific CD4 T-cell responses in different groups of patients: i) Non HIV-infected TB+ patients to healthy donors (HD), ii) TB+/HIV+ co-infected versus TB-/HIV+, iii) TB+/HIV+ co-infected versus TB+, and iv) TB+ patients depending on the presence or not of sputum bacillary load.

- ***Italian HIV/TB study*** by INMI. The partner evaluated whether the antiretroviral therapy and TB therapy modified the cytokine profile and memory status of TB-specific antigen-response in comparison with other recall antigen responses in both CD4+ and CD8+ T-cells.

- ***In vitro study*** on the effects of parasite antigen on stimulating and skewing CD4 T cell responses and the consequences for HIV-1 infectivity by AMC. The results indicate that helminthic parasite antigen can skew and modulate DC stimulated immune responses with consequences for HIV-1 infectivity.

### Molecular Profiling of Innate and Adaptive Immunity

The molecular profiling are primarily performed by three core labs: dcRT-MLPA by LUMC and gene array by VGTI (for HIV studies) and Oxford (for TB and malaria studies). Analysis have been performed with samples from the following studies: 1) Uganda HIV studies; 2) Bagamoyo HIV study; 3) Bagamoyo TB Study; 4) Gabon malaria study; and 5) Bagamoyo malaria study.

### *1.3.2.2 Significant Results of WP2*

The key results from WP2 are summarized as follows:

**HIV and worms**

- The effects of S. mansoni on HIV specific T cell responses might involve subtle changes in cytokine production rather than indiscriminate downregulation. (UVRI HIV Incidence and Schisto Intervention Studies)
- No significant quantitative and qualitative differences were observed with regard to both CD4 and CD8 T-cell responses analyzed in HIV patients from Switzerland versus HIV patients from Tanzania in the pilot study conducted at CHUV on blood samples collected in the Bagamoyo HIV study. The HIV infected subjects from Tanzania had various helminth infections (CHUV/Swiss TPH/IHI, Bagamoyo HIV Study).
- Increased expression of T cell activation markers was associated with Trichuris and Ascaris infections with relatively little effect of helminth treatment (LMU/MMRP, Mbeya HIV study).
- Worm infection down-regulates the anti-viral interferon response observed in HIV subjects (VGTI/Swiss TPH/IHI/UVRI, HIV Studies) (Gene Array).
- Helminthic parasite antigen can skew and modulate DC stimulated immune responses with consequences for HIV-1 infectivity (AMC).
- Different worm infections have different transcriptional profiles (VGTI/Swiss TPH/IHI/UVRI, HIV Studies) (Gene Array).

**TB and worms**

- Mtb-specific CD4 T cells in patients with active TB from helminth endemic area have a skewed functional Th2 cytokine profile associated with increased GATA-3 expression. (CHUV/Swiss TPH/IHI, Bagamoyo TB Study)
- Preliminary analysis of the data show that most DEGs are detected in the TB only group. No DEGs are detected in the helminth only group and in the co-infection group, suggesting that helminth infection reduces the effects of active TB on the immune response. (UOXF/Swiss TPH/IHI, Bagamoyo TB study)
- Significant increase in the frequency of the CD4+FoxP3+GARP+ population in the helminth-infected patients compared to non-infected patients, further suggesting increased Treg activity in helminth infected patients. (LSHTM, London TB Study)
- Observed no evidence that co-infections influence the cytokine response profile among those with LTBI. (UVRI TB Study)
- Increase production of IP-10 following Mtb-specific stimulation of blood mononuclear cells were higher in household contacts with subsequent TST conversion than in those who remained TST negative, suggesting that this parameter may be useful in identifying individuals at most risk of established Mtb infection. (UVRI TB Study)

**HIV and TB**

- TB infection is characterized by an increased frequency of peripheral Treg expressing low CD39, and a recall response to PPD biased towards Th2/Th17/Th22 and a higher production of IL27, a cytokine already shown as elevated in various fluids and serum of patients infected with TB. (INSERM, France HIV Study)
- When co-infected with HIV, TB patients exhibited a distinct profiles from mono-infected TB patients and are characterized by a significant increase of Treg/CD39+ and a profound decrease in the frequency of Th2/Th17 recall responses to PPD and ESAT-6 antigens suggesting a deleterious effect of HIV infection on Mtb-specific responses. (INSERM, France HIV Study)
- Patients without bacilli in the sputum are characterized by a higher production of IL-1β and IL-27 in response to TB antigens, which may represent a signature of mycobacterial clearance in the pulmonary site and IL-27 may increase the ability of Mtb-specific T cells to inhibit mycobacterial growth in macrophages. (INSERM, France HIV Study)
- For HIV-infected subjects undergoing ART and TB-specific therapy, the detection of IFNγ+ TNFα+ CD4+ T-cells can be a promising biomarker of active TB disease whereas the IL2+ TNFα+ CD4+ T-cells associate with TB control, such as that observed in LTBI. Moreover, we proved that the ART and TB therapy induce the decrease of effector-memory cells in both HIV-TB and HIV-LTBI patients. (INMI, Rome TB/HIV Study)
- Development of new flow cytometry markers to distinguish active TB from LTBI through the assessment of the CD27 modulation on CD4+ T-cells. (INMI, Rome TB/HIV Study)

**Malaria and worms**

- Helminth infections as well as malaria infections affect innate immune responses, however taken all helminths together, they do not appear to have a strong influence on innate immune responses of malaria co-infected subjects. There is variation in the ability of different helminth species to modify innate responses of malaria co-infected subjects. The results of the multicentre studies should provide a final answer to this (expected to be ready in March 2016). Regulatory immune responses are up regulated by helminth infections, for the first time regulatory B cells were shown to have a suppressive role in the context of helminth infections in humans. (LUMC/CERMEL/EKUT, Gabon malaria study)
- Unbiased analysis using gene set enrichment methods, shows in malaria infection, genes associated with immune and defense responses are significantly upregulated, however in the presence of schistosomiasis and malaria, the same pathways are then down regulated, suggesting that the helminth infection is dampening the immune response to malaria. (UOXF/CERMEL/LUMC, Gabon malaria study)
- Significantly reduced production of IL-6 and TNF-α was detected in cDC and monocytes after TLR1/2, TLR4 and TLR7/8 stimulation in E. vermicularis positive children suggesting that E. vermicularis infestation might result in reduced pro-inflammatory cytokine production in peripheral blood. This is the first time description of systemic effects of this widely spread helminth infection in children that has also potential implications for children living in non-malarious countries. In addition, the secretion of IL-6 and TNF-α was reduced in malaria asymptomatic single and helminth co-infected infants and children. Both, IL-6 and TNF-a have been implicated in the progression from asymptomatic to clinical and severe malaria. (Swiss TPH/IHI)
- E. vermicularis infection suppressed the expression levels of genes implicated in Th1 and pro-inflammatory responses correlates with the reduced expression of IL-6 and TNFα in antigen presenting cells following TLR stimulation. Taken together, E. vermicularis infection modified Th1, pro-inflammatory and IFN inducible responses, and this reduced expression remained in the presence of asymptomatic malaria co-infection. (LUMC/Swiss TPH/IHI, dcRT-MLPA)

### 1.3.3 WP3 Worms and HIV/TB/Malaria Co-infections

The primary objective of WP3 is to determine the impact by worm co-infections on the parameters of disease activity for HIV, TB and malaria, in order to better understand the interactions between different pathogens and their influence on disease activity.

### *1.3.3.1 Main Activities of WP3*

The main activities include:

- Harmonization of protocols for worms and HIV, TB and malaria between the different study sites
- Obtaining relevant ethics and regulatory approval
- Analysis on the effect of worm infections and/or anti-worm treatment on incidence, clinical presentation and immune responses against worms and/or HIV, TB and malaria
- Identification of biomarkers associated with helminth co-infection with HIV, TB and malaria

**Protocol Harmonization**

**IDEA** includes in total 18 cohort/studies in 8 different countries in Europe and Sub-Saharan Africa.
Recognizing the diversity of the different cohorts involved in the IDEA project, and that, in some cases, IDEA study is sub-study of an ongoing larger cohorts, the group has made significant effort in identifying the commonality and gaps between the different studies on HIV, TB, malaria and worms. Gaps are minimized through amendment of ongoing studies and in development of new protocols whenever feasible.
Further, significant effort has been made in the harmonization of case definitions for all four diseases (helminth infection, malaria, HIV and TB). The consortium has come to a consensus on a minimum set of criteria for diagnostic methods, acquisition of infection, disease progression and response to therapy.

**Ethics and Regulatory Approval**

**IDEA** partners are committed to perform the studies in accordance to the highest ethical standard, in accordance to the relevant national and international regulations. No IDEA studies have started prior to the relevant ethics and regulatory approval. A copy of all approvals have been sent and stored at the consortium management office.

**Analysis on the effect of worm infections and/or anti-worm treatment on incidence, clinical presentation and immune responses against worms and/or HIV, TB and malaria**

The following IDEA studies have contributed to this analysis:

**HIV Cohorts:**

- Uganda HIV Incidence & Schisto Intervention study has assessed: 1) the effect of Schisto infection on HIV acquisition; 2) the effect of schisto treatment on HIV clinical presentation and disease progression
- Tanzania Mbeya HIV study is a study on HIV incidence and disease progression
- Tanzania Bagamoyo HIV study with the focus on interaction between worms and HIV on HIV clinical presentation
- Nigeria HIV study has studied the prevalence and interaction of intestinal worms with HIV infections in children and pregnant women

**TB Cohorts:**

- Uganda Kampala TB household cohort has evaluated the effect of helminths and other co-infections on susceptibility to TB infection
- Uganda BCG short term birth cohort has investigated the effects of maternal co-infection with worms and TB on the infant response to BCG immunization

Malaria Cohorts:

- Uganda Entebbe Mother-Baby Cohort has investigated the effects of maternal worm infection on the development of immunity to malaria in early childhood.
- Kenya malaria study has investigated the effect of anti-helminth treatment on the incidence and clinical presentation of malaria in school-aged children
- Bagamoyo malaria study in children focusing on the impact of helminth infections on the clinical presentation of malaria

- Gabon malaria studies: 1) Birth cohort to enrolled pregnant women with or without helminths infection or malaria infections and the neonates were followed for one year; 2) School children cohort to study the effect of helminth infections on malaria infection.
- Nigeria malaria has studied the prevalence and interaction of intestinal worms with malaria infections in children and pregnant women

**Identification of biomarkers associated with helminth co-infection with HIV, TB and malaria**

This is a joint effort of all IDEA partners, combining the immunological analysis with clinical outcome. These analyses have led to the identification of new potential biomarkers (see section 1.3.3.2) that has defined differences in the immune responses against HIV, TB and malaria caused by the underlying helminth infections.

### *1.3.3.2 Significant Results of WP3*

**Impact of worm co-infections on measures of disease activity for HIV, TB and malaria**

- **HIV and worms**
  - No evidence that the helminth co-infection causes differences in the clinical presentation of HIV. However, we observed a tendency that the success rate of anti-helminthic treatment in HIV infected population seems to be limited, suggesting that helminth infections were either not treated successfully or reinfection occurred faster compared to non-HIV infected population. (Swiss TPH/IHI Bagamoyo)
  - No evidence that any of the studied helminth infections (Ascaris, Trichuris, Hookworm, S. Mansoni, S. Hematobium) were associated with significantly increased or reduced risk of HIV acquisition. (LMU/MMRP (Mbeya) and UVRI (Uganda)
  - Deworming of HIV-helminth co-infected subjects might have a moderate effect on slowing down HIV disease progression, but that the effect of deworming might differ by helminth infection. LMU/MMRP (Mbeya)
- **TB and worms**
  - We found no evidence that co-infections increase the risk of LTBI, or influence the cytokine response profile among those with LTBI. Prior BCG may influence the immune response during LTBI by an unknown mechanism. (UVRI TB study)
  - Additional investigation of the effect of isoniazid preventive therapy (IPT) on the immune response to mycobacterial antigens among HIV-negative household contacts aged above five years. After adjusting for baseline cytokine or antibody responses, and for presence of a BCG scar, IPT resulted in a relative decline in Mtb specific production of IFN-γ. A similar decline was found in anti-CFP-10 antibody levels. We found no effect on Mtb specific Th2 or regulatory or Th17 cytokine responses, or on antibody concentrations to PPD and ESAT-6. Although correlates of protection against tuberculosis remain elusive, IFN-γ is undoubtedly required, so these results raise questions about the impact of IPT on subsequent immunity in high tuberculosis transmission settings. (UVRI TB study)
  - We also assessed the performance of IP-10 in the diagnosis of LTBI: Household contacts with LTBI (QFN+TST+) had the highest Mtb specific IP-10 responses compared to uninfected household contacts (QFN-TST-) and active TB cases. Also, at baseline, concentrations of Mtb specific IP-10 were higher in household contacts with subsequent TST conversion than in those who remained TST negative, suggesting that this parameter may be useful in identifying individuals at most risk of established Mtb infection. (UVRI TB study)
- **Malaria and worms**
  - Repeated deworming does not alter risks of clinical malaria or malaria parasitemia among school children. On the basis of these results, we suggest that school-based deworming in Africa is unlikely to have adverse consequences for malaria among school-aged children. (KEMRI study)

- Quarterly treatment of pre-school age children with albendazole was associated with a reduced risk of malaria in childhood. (UVRI malaria study)
- No evidence was found that treatment of worm infections during pregnancy altered the risk of malaria in childhood, but we found strong observational associations between maternal hookworm and incidence of malaria in childhood (UVRI malaria study).
- A clear protective effect of E. vermicularis on clinical malaria development was observed in the Bagamoyo malaria study with children. This effect was not seen in the hookworm and S. stercoralis co-infected children, confirming previous reports in literature. In our cohort, the number of uncomplicated malaria cases is smaller in the presence of E. vermicularis infection when compared to other helminth co-infections even though the prevalence of malaria infection (symptomatic and asymptomatic) did not differ. (Swiss TPH/IHI, Bagamoyo Malaria study)

**Biomarker associated with helminth co-infection with HIV, TB and malaria**

- **HIV and worms**
  - Helminth/HIV co infection markedly increase T-cell subset markers, Treg associated markers, and all T-cell cytotoxicity markers (LUMC/Swiss TPH/IHI, Bagamoyo HIV Study) (dcRT-MLPA)
  - Worm infection leads to up-regulation of inflammasome pathways (VGTI/Swiss TPH/IHI, Bagamoyo HIV Study) (Gene Array)
- **TB and worms**
  - Mtb-specific CD4 T cells in patients with active TB from helminth endemic area have a skewed functional Th2 cytokine profile associated with increased GATA-3 expression. (CHUV/Swiss TPH/IHI, Bagamoyo TB Study)
  - A number of genes were identified in the TB cohort that are described in the literature in TB patients or animal models including IL-10 mediated inhibition, suppression of cytokine signalling (SOCS-3) and C1q. Pathway analysis using DAVID also revealed downregulation of many genes associated with the T cell-receptor signalling pathway, including PD-1, CTLA4, CD3 and CD28. (UOXF/Swiss TPH/IHI, Bagamoyo TB study)
  - Strong enrichment for erythrocyte related molecular functions, possible reflecting the impact of hookworm infections with chronic low level infection and latent anaemia (UOXF/Swiss TPH/IHI, Bagamoyo TB study)
- **Malaria and worms**
  - In malaria infection, genes associated with immune and defence responses are significantly upregulated, however in the presence of schistosomiasis and malaria, the same pathways are then down regulated, suggesting that the helminth infection is dampening the immune response to malaria. (UOXF/CERMEL/LUMC, Gabon malaria study)
  - E. vermicularis infection suppressed the expression levels of genes implicated in Th1 and pro-inflammatory responses correlates with the reduced expression of IL-6 and TNFα in antigen presenting cells following TLR stimulation

### 1.3.4 WP4 Worm Infections and Vaccines

The primary objective of WP4 is to determine the modulation of vaccine induced immune response by worm co-infections.

- The **malaria vaccine** study is embedded in the phase IIB efficacy trial with GMZ2 candidate malaria vaccine. Given that the main study is still blinded, the final analysis is not completed at the time of this report. However pilot studies performed on samples from phase 1 trials with GMZ2 have indicated that children infected with T. trichiura have a lower antibodies production when compared to none infected children. Basically, intestinal parasites modulate antibody response to mature gametocytes of Plasmodium falciparum.
- **Tuberculosis vaccine trial**: The clinical trial was successfully completed with recruitment without loss to follow up and no serious adverse events. The ELISpot data analysis is completed and showed no

difference in immunogenicity between infected or non-infected with S. mansoni groups. Luminex and antibody assays are ongoing.

- **HIV vaccine trial**: Successful conduct of the trial. Preliminary immunogenicity data have shown that the vaccine regimen induces high frequency of moderately strong neutralizing antibody responses to MN.3 and IgG binding antibody responses to Env gp120 proteins (A244, 96ZM651, and MN). The trial is ongoing at the time of the report and the unblinded data is expected in Q2 2016.

### 1.3.5 WP5 Field Networking and Capacity Building

The primary objective of WP5 is to support human capacity development in immunology for Africa. Building sustained and integrated research in SSA has been a priority throughout the entire IDEA project. Training for young African scientists has been strengthened through their direct participation from protocol development to immunological assays to statistical analysis.

IDEA has contributed to:

- 5 short courses "Immunology in the Tropics" held at UVRI, Entebbe, Uganda
- Organized 4 cutting-edge technology workshops on:
    - Molecular diagnostics for helminth and malaria
    - Flow cytometry
    - R programming for data analysis
    - Functional genomics and systems biology
- 9 master students and 16 PhD students
- Multiple North-South and South-South exchanges with the primary goal to strengthen the capacity in immunology.

In response to the tremendous interest in immunology generated by the short courses in Uganda and by the establishment of a laboratory at Makerere University College of Health Sciences (MU-CHS), the department of microbiology at MU-CHS has established a Masters course in Immunology and Clinical Microbiology.

## 1.4 Potential Impact, Main Dissemination Activities and Exploitation of Results

### 1.4.1 Potential Impact

HIV, tuberculosis (TB) and malaria, the three major poverty related diseases (PRDs), represent the greatest causes of death among infectious diseases world-wide. Neglected Infectious Diseases (NIDs), caused predominantly by different types of worms, represent a major public health burden in particular given their widespread distribution across most developing countries. There is large geographic overlap in disease occurrence between NIDs and PRDs. Co-infections between worms and PRD occur in tens of millions of people and in both children and adults (estimated around 25%). There has been limited understanding on the interaction between these pathogens, which may be associated with increased susceptibility to infection and disease, and subsequently could have major public health implications by increasing the diseases burden, particularly since effective vaccines are not yet available for these infections.

IDEA is the first large EC funded program aiming at tackling these very complex scientific challenges and has made significant advances in understanding the effect worm infections can have on altering the immune responses against the PRDs. The direct outputs may guide future public health policy as well as disease interventions.

The potential impact of **IDEA** includes but not limited to:

- **Advancing of immunological understanding of the effects that worm infections can have on modifying immune responses (innate and adaptive) against HIV, TB and malaria**

**IDEA** studies have demonstrated that the effects of helminth infections on immune responses against HIV, TB and malaria may differ from worm to worm.

With regard to HIV and worms, it is shown that helminth/HIV co infection markedly increase T-cell subset markers, Treg associated markers, and all T-cell cytotoxicity markers. Gene profiling analysis have shown that worm infection down-regulates the anti-viral interferon response observed in HIV subjects, and up-regulates the inflammasome pathways.

With regard to TB and worms, the data generated have shown that: 1) Mtb-specific CD4 T cells in patients with active TB from helminth endemic area have a skewed functional Th2 cytokine profile associated with increased GATA-3 expression; 2) Significant increase in the frequency of the CD4+FoxP3+GARP+ population in the helminth-infected patients compared to non-infected patients, further suggesting increased Treg activity in helminth infected patients. Gene profiling analysis have shown downregulation of many genes associated with the T cell-receptor signalling pathway, including PD-1, CTLA4, CD3 and CD28, and strong enrichment for erythrocyte related molecular functions, possible reflecting the impact of hookworm infections with chronic low level infection and latent anaemia.

With regard to malaria and worms, there is variation in the ability of different helminth species to modify innate responses of malaria co-infected subjects. Regulatory immune responses are up regulated by helminth infections, for the first time regulatory B cells were shown to have a suppressive role in the context of helminth infections in humans. The gene arrays analysis have shown a dampening effect of helminth infection on the immune responses to malaria. More specifically, E. vermicularis infection suppressed the expression levels of genes implicated in Th1 and pro-inflammatory responses correlates with the reduced expression of IL-6 and TNF-$\alpha$ in antigen presenting cells following TLR stimulation. Both IL-6 and TNF-$\alpha$ have been implicated in the progression from asymptomatic to clinical and severe malaria.

- **Advancing of understanding of clinical outcome in worm/HIV, TB & malaria co-infections**.

**IDEA** studies have found:

- No evidence that the helminth co-infections cause differences in HIV acquisition or the clinical presentation of HIV. However, we observed a tendency that the success rate of anti-helminthic treatment in HIV infected population seems to be limited, suggesting that helminth infections were either not treated successfully or reinfection occurred faster compared to non-HIV infected population.
- No evidence that helminth co-infections increase the risk of LTBI, or influence the cytokine response profile among those with LTBI.
- Strong observational associations between maternal hookworm and incidence of malaria in childhood
- Deworming of HIV-helminth co-infected subjects might have a moderate effect on slowing down HIV disease progression, but that the effect of deworming might differ between the different helminth infections.
- No evidence that treatment of worm infections during pregnancy altered the risk of malaria in childhood
- Repeated deworming does not alter risks of clinical malaria or malaria parasitemia among school children.
- A clear protective effect of E. vermicularis on clinical malaria development was observed in the Bagamoyo malaria study with children.

- **Improving of vaccine design**. The **IDEA** malaria vaccine trial is embedded in the efficacy trial of the malaria vaccine candidate GMZ2. The **IDEA** HIV vaccine trial is evaluating a candidate vaccine regimen for the next efficacy trial. Even though at the time of this report, the final data are still pending, once obtained (targeted within 12 months post IDEA project life span), the data will be very informative for the efficacy trials of these experimental vaccines and subsequently contribute to the design of the next generation vaccine candidates.

- **Public health policy on de-worming**. The findings from IDEA provide supportive evidence to whether de-worming programmes are beneficial for the health of communities with high burden of worms and malaria/HIV/TB. The overall findings that 1) no evidence of helminth co-infection on HIV, LTBI acquisition, 2) repeated deworming does not alter risks of clinical malaria or malaria parasitemia among school children, support that the current deworming program in SSA is unlikely to have adverse consequences.

- Alongside the science, **IDEA** has also made major impact on building African skills. The capacity building activities have been well integrated within **IDEA**'s its research projects, entailing North-South but more importantly South-South exchanges. In addition to supporting multiple master and PhD student projects, significant efforts have been made in harmonization and implementation of novel immunological and diagnostic assays, data management, and trial conduct in African settings led by African PIs.

### 1.4.2 Main Dissemination Activities

IDEA has conducted various dissemination activities aimed at promoting its research to the widest and varied audience possible. Key dissemination activities are described below.

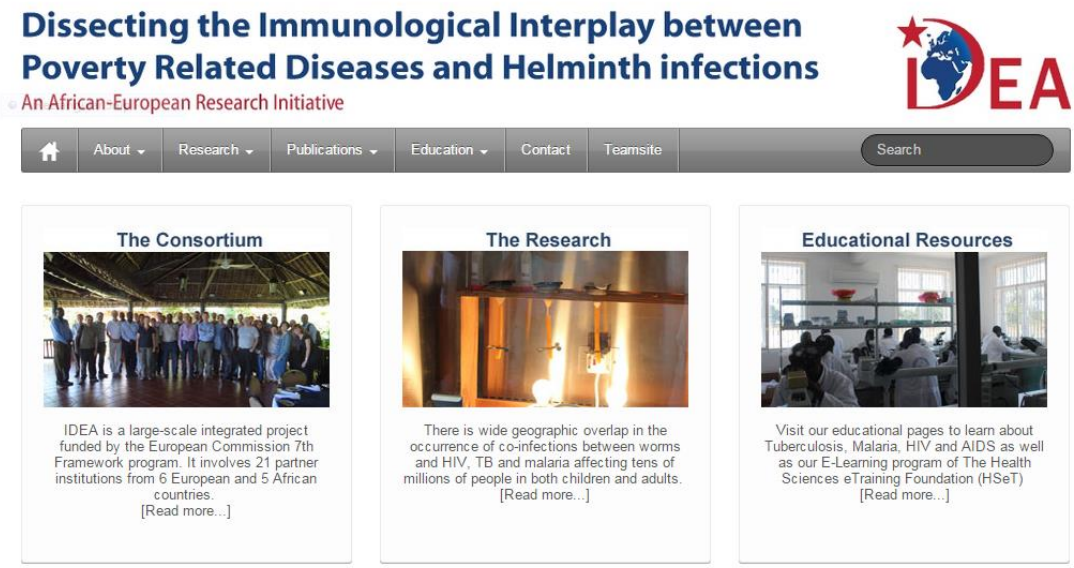
#### *1.4.2.1 Project Website*

The project website www.idearesearch.eu was launched at the start of the project. It has been used as an important tool for both external and internal dissemination and communication. The domain name is renewable on an annual basis and the website will be maintained for at least 3 years after the project ends.

- **Public website**

The public website provides an overview of the **IDEA** project to the general public. It includes an overall summary of **IDEA**, its objectives, update of its research progress and list of publications (both in peer-reviewed journals and posters/presentations at international conferences). Under education, list and links to the most important international conferences in PRDs and NIDs, training courses provided by other relevant organizations are provided. Figure 3 is a screenshot of IDEA home page

**Figure 3 IDEA Home Page Screenshot**




- **Team Site**

The IDEA team site has played an instrumental role for information sharing between the IDEA partners. The team site is secured and access is only possible for IDEA partners with password. The password management is carried out and monitored by the IDEA program management office. Figure 4 is a screenshot of IDEA Team Site.

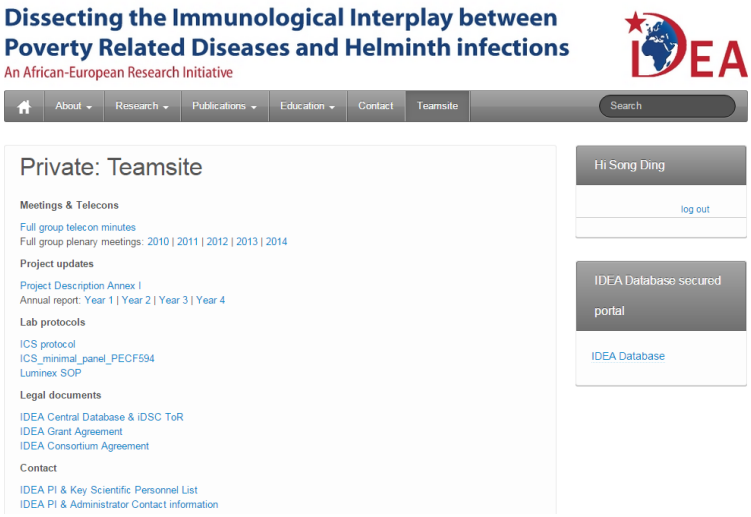
The team site provides the following features to the team members:

- **Meeting minutes/presentations**: minutes of all project meetings, including both teleconferences and face-to-face full group and SAB meetings are posted on the team site. Presentations from the latest full group meeting are also posted on the team site.
- **Project updates**: include annual reports, description of work and its amendments.
- **Laboratory protocols:** Common protocols and SOPs are posted to facilitate the laboratory harmonization process
- **Legal documents**: a repository for official legal documents, such as grant agreement, consortium agreement
- **Contact:** up to date contact information of the key scientific and administrative personnel of each consortium member is provided.

In addition to document repository and sharing, a unique feature IDEA team site is the web-based **IDEA Central Database** portal, providing secured exchange of data between IDEA partners. It allow easy accessibility and increase efficiency in data management and exchange. To ensure the security of the data,

additional log-in is required to access IDEA database. It also has the flexibility to manage different level of access rights depending on the function and input of the consortium partners to the database.

**Figure 4 IDEA Team Site Screenshot**




### *1.4.2.2 Logo and PPT template*

A project logo and template for PowerPoint presentation was created to establish an identity of the project and ensure congruent presentation to external audiences.

### *1.4.2.3 Publications*

IDEA has produced a total of 49 peer reviewed publications and 58 abstracts at various international conferences, from which 24 are oral presentations and 34 are poster presentations. For additional information please see Section 2.1 below.

### *1.4.2.4 Project trainings*

Significant effort has been made within **IDEA** on capacity building activities in SSA.

- **Workshops**: A total of 4 cutting-edge technology workshops have been organized: 1) molecular diagnostic for helminth and malaria (Apr 2011). The workshop was led by Dr. Jaco Verweij from LUMC and attended by partners from both IDEA and SchistoVac (another FP7 project). The helminth PCR technique is now up and running at UVRI in Uganda, NIMR in Tanzania and CERMEL in Gabon; 2) flow cytometry (Feb 2012). This workshop was led by Dr. Alexandre Harari from CHUV and aimed to homogenize the flow cytometry analyses and identify and resolve any discordance between the IDEA laboratories. A consensus SOP was generated at the end of the workshop and distributed to all IDEA laboratories; 3) R programming for data analysis (Dec 2013) and 4) Functional genomics and systems biology (May 2014). Theses workshop was led by Dr. Rafick Sekaly from VGTI and Dr. Marielle Haks from LUMC, with the aim to develop a curriculum in bioinformatics, in particular to a component on the analysis of microarray and multiplex gene array and cytokine data.

- **Immunology Short Courses**: In addition, IDEA as contributed to 6 short courses Immunology in Tropics hosted by Uganda Virus Research Institute between 2010 and 2015. These short courses are co-funded by the Wellcome Trust. The short course have been received very enthusiastically and more than 125

students have attended these courses. The course have greatly motivated the students to continue pursuing a scientific career in Africa.

- **E-Learning**: In collaboration with the Swiss Health Sciences eTraining Foundation, online training program was provided to IDEA partners. Four modules of self-learning programs are made available: Basic Immunology, Tuberculosis, HIV and AIDS, and Basic Concepts in Statistics. More than 70 members of IDEA partners have made use of this E-learning program.

#### *1.4.2.5 Participation in events*

In total, IDEA partners have participated in 45 international events during the project period, presenting and promoting the research results supported through IDEA. 64% of these event are in Europe, 14% in Africa, and 22% in the US/Canada and other parts of the world.

Among these, we would like to highlight two events:

- **European Commission Colloquium: Helminth Infections - Prevention and Treatment of Diseases and Co-infections Involving Helminths:** This event was held on 25 Sep 2012 jointly by four FP7 projects - IDEA, TheSchistoVac, E-PIAF and Settrend. IDEA Project Operation Office provided the management support in the organization of the symposium.

  It has brought together more than hundred scientists in the field of helminth diseases and co-infections with HIV, Malaria and TB, and focused the discussion on helminth drug and vaccine development as well as the immunological interplay between poverty related diseases and helminth infections.

- **European Development Day (3-4 Jun 2015)**: **IDEA** was selected to present a project lab and a stand at the 2015 European Development Day. The central theme for both the project lab and the stand is building sustained research in SSA. Scientists from both Europe and SSA presented their research at this event and concluded that sustained development can only be achieved through integrated approach and international cooperation between policy makers, funding agencies and research communities.

**Figure 4: IDEA Stand at the European Development Day (2015)**


Left: Mr. Wilbert Mbuya, MSc student from NIMR-MMRC. Right: Dr. Annet Nanvubya from UVRI-IAVI, one of the clinical PIs of IDEA HIV vaccine trial.

### 1.4.3 Exploitation of Results

**IDEA** is a unique project in pioneering the global approach of bringing the fields of worms, HIV, TB and malaria together with multidisciplinary expertise in immunology, pathogenesis, clinical epidemiology and vaccinology. The exploitation of IDEA results is multifaceted and can be summarized as:

- **Informative to Public health policy on de-worming**:
    - IDEA findings have shed light on the influence of helminth infections on the clinical course of HIV, TB and malaria. It is important to underscore that the several clinical trials that have investigated this issue have demonstrated lack of any substantial effect, either beneficial or detrimental, of the underlying helmith infection on the clinical course of HIV, TB and malaria, nor on the acquisition of HIV and LTBI.
    - With regard to repeated deworming, it has been demonstrated that it does not alter risks of clinical malaria or malaria parasitemia among school children, and it supports that current deworming programs in SSA are unlikely to have adverse consequences.
    - IDEA has also generated novel information on the geographic distribution and the diversity of helminth infections in different regions in SSA. These new information may be relevant for the implementation of deworming campaigns and of the most appropriate therapeutic interventions in the different areas.

- **Exploitation through IDEA linkage with other international networks**: From the onset of the project, IDEA is linked with various large cohorts/studies funded by various national/international agencies. Such international approach not only enables IDEA to gain access to a larger dataset, but it is also instrumental in the exploitation of the results through the linkage with multiple networks.
    - Worm and malaria vaccine study is embedded in the phase IIB malaria vaccine trial with GMZ2 that involved multiple international stakeholders. The final data on the effect of helminth infection on the vaccine induced immune response will be beneficial for all stakeholders engaged in the development of GMZ2 vaccine.
    - Worm and HIV Vaccine trial is co-funded by International AIDS Vaccine Initiative (IAVI), with additional in-kind contribution from the Collaboration for AIDS Vaccine Discovery of the Bill & Melinda Gates Foundation (for immune monitoring), US Military HIV Research Program (USMHRP) and Global Solutions for Infectious Diseases (GSID) for providing one of the vaccine components. The vaccine regimen under evaluation is also one of the candidate regimens currently planned for the next HIV vaccine efficacy trial. Though the immunological analysis is still ongoing and the final trial results will only be available beyond the IDEA project lifespan, given the trial's engagement of major players in the HIV vaccine field, its outcome will contribute to the design of future vaccine trials in SSA and eventually HIV vaccination campaign when an effective HIV vaccine becomes available.

- IDEA research has also directly contributed to multiple **new research opportunities**:
    - Data from this pilot study on BCG short-term baby cohort supported a successful application to MRC UK for a larger study (involving 300 mother baby pairs) which will commence in 2014. This work was presented at a meeting of the Royal Society in 2014, and published in the Proceedings.
    - The TB study conducted at LSHTM will be continued under the EU funded H2020 TBVAC2020 grant.
    - The IDEA collaboration has led to new collaboration between UVRI and Jenner Institute of Oxford on the genetics of vaccine responses.

In addition, **IDEA** will continue to advertise its outcomes beyond the project duration and promote the visibility of European research on helminth and co-infections. The **IDEA** website remains to be a central tool for future exploitation and dissemination. The website will stay online for at least 5 year beyond the project duration. Regular updates will be made with future publications resulting from the IDEA project or news/discoveries in the field of helminth and co-infections. The web-access IDEA database will be maintained which enables further data mining and meta-analysis beyond IDEA project duration.

## 1.5 Website and Contact:

### 1.5.1 Project Website:

www.idearesearch.eu

### 1.5.2 Coordination:

IDEA is coordinated by Centre Hospitalier Universitaire Vaudois (CHUV)

**Project Coordinator**: Prof. Giuseppe Pantaleo
Centre Hospitalier Universitaire Vaudois (CHUV)
Department of Medicine
Division of Immunology and Allergy (IAL)

### 1.5.3 List of Participants

| Participating Institutions | Acronym | Principal Scientific Contact |
|---|---|---|
| Centre Hospitalier Universitaire Vaudois, Switzerland | CHUV | Giuseppe Pantaleo |
| European Vaccine Initiative – EEIG, Germany | EVI | Odile Leroy |
| Academisch Ziekenhuis Leiden– Leids Universitaire Medisch Centrum, the Netherlands | LUMC | Tom Ottenhoff<br>Maria Yazdanbakhsh |
| London School of Hygiene & Tropical Medicine, UK | LSHTM | Hazel Dockrell |
| University of Oxford, UK | UOXF | Adrian Hill |
| Swiss Tropical and Public Health Institute, Switzerland | Swiss TPH | Marcel Tanner |
| Eberhard Karls Universität Tübingen, Germany | EKUT | Peter Kremsner |
| Kenya Medical Research Institute – Wellcome Trust Collaborative Programme, Kenya | KEMRI | Simon Brooker |
| Medical Research Council on behalf of its MRC/UNRI Uganda Research Unit on AIDS, UK | MRC-UVRI | Pontiano Kaleebu<br>Alison Elliott |
| Istituto Nazionale Malattie Infettive L. Spallanzani – IRCCS, Italy | INMI | Delia Goletti |
| Institut National de la Sante et de la Recherche Medicale, France | INSERM | Yves Levy |
| University of Ibadan , Nigeria | UIMRT | George Ademowo |
| EuroVacc Foundation, Switzerland | EuroVacc | Song Ding |
| Ifakara Health Institute, Tanzania | IHI | Salim Abdulla |
| Academisch Medisch Centrum bij de Universiteit van Amsterdam, the Netherlands | AMC | William Paxton |
| Ludwig-Maximilians-University Munich, Germany | LMU | Michael Hoelscher |
| National Institute for Medical Research - Mbeya Medical Research Program, Tanzania | NIMR | Leonard Maboko |
| Ecole polytechnique fédérale de Lausanne, Switzerland | EPFL | Nicola Harris |
| Vaccine & Gene Therapy Institute Florida, USA | VGTI | Rafick Sekaly |
| Centre de Recherches Medicales de Lambarene, Gabon | CERMEL | Ayola Akim Adegnika |

# 2. Use and dissemination of foreground

## 2.1 Section A - Dissemination Measures

### 2.1.1 Publications

**LIST OF SCIENTIFIC (PEER REVIEWED) PUBLICATIONS, STARTING WITH THE MOST IMPORTANT ONES**

| No. | Title | Authors (Last Name, Initial.) | Title of the periodical or the series | Number, date or frequency | Publisher | Place of publication | Year of publication | Relevant pages | Permanent identifiers (if available) | Is/Will open access provided to this publication? (yes/no) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Effect of repeated anthelminthic treatment on malaria in school children in Kenya: a randomized, open-label, equivalence trial. | Kepha S, Nuwaha F, Nikolay B, Gichuki P, Mwandawiro CS, Mwinzi PN, Odiere MR, Edwards T, Allen E & Brooker S | Journal of Infectious Diseases | pii: jiv382. [Epub ahead of print] | Oxford University Press | - | 2015 | pii: jiv382. [Epub ahead of print] | PMID: 26170395 | Yes |
| 2 | Distribution and risk factors for Plasmodium and helminth co-infections: a cross-sectional survey among children in Bagamoyo district, coastal region of Tanzania. | Salim N, Knopp S, Lweno O, Abdul U, Mohamed A, Schindler T, Rothen J, Masimba J, Kwaba D, Mohammed AS, Althaus F, Abdulla S, Tanner M, Daubenberger C, Genton B. | PLoS Negl Trop Dis | Vol 9 (4) | Public Library of Science | - | 2015 | e0003660 | PMID: 25837022 | Yes |
| 3 | The impact of maternal infection with Mycobacterium tuberculosis on the infant response to BCG immunisation. | Mawa PA, Nkurunungi G, Egesa M, Webb EL, Smith S, Kizindo R, Akello M, Lule SA, Muwanga M, Dockrell HM, Cose SC, Elliott AM. | Philosophical Transactions of the Royal Society B | Vol 370, 2015 | The Royal Society Publishing | - | 2015 | 1671 | PMCID: PMC4527383 | Yes |

| No. | Title | Authors (Last Name, Initial.) | Title of the periodical or the series | Number, date or frequency | Publisher | Place of publication | Year of publication | Relevant pages | Permanent identifiers (if available) | Is/Will open access provided to this publication? (yes/no) |
|---|---|---|---|---|---|---|---|---|---|---|
| 4 | Impact of co-infections and BCG immunization on immune responses among household contacts of tuberculosis patients in a Ugandan cohort. | Biraro IA, Egesa M, ToulzaF, Levin J, Cose S, Joloba M, Smith S, Dockrell HM, Katamba A, Elliott AM. | PLoS One | Vol 9 (11), 2014 | Public Library of Science | - | 2014 | e111517 | PMCID: PMC4221037 | Yes |
| 5 | Interleukin 10 (IL-10)-producing cd1dhi regulatory b cells from schistosoma haematobium-infected individuals induce IL-10-positive t cells and suppress effector t-cell cytokines. | van der Vlugt LE, Zinsou JF, Ozir-Fazalalikhan A, Kremsner PG, Yazdanbakhsh M, Adegnika AA, Smits HH. | Journal of Infectious Diseases | Vol 210, 2014 | Oxford University Press | - | 2014 | 1207-16 | PMID: 24795476 | No |
| 6 | Colorectal Mucus Binds DC-SIGN and Inhibits HIV-1 Trans-Infection of CD4(+) T-Lymphocytes | Stax MJ, Mouser EEIM, van Montfort T, Sanders RW, de Vries HJC, Dekker HL. C Herrera, Speijer D, Pollakis G, Paxton WA | PLoS One | Vol 10, 2015 | Public Library of Science | - | 2015 | e0122020. | PMCID: PMC4368515 | Yes |
| 7 | Cytokine and chemokine profile of the innate and adaptive immune response of schistosoma haematobium and plasmodium falciparum single and co-infected school-aged children from an endemic area of Lambaréné, Gabon. | Ateba-Ngoa U, Adegnika AA, Zinsou JF, Kassa Kassa RF, Smits H, Massinga-Loembe M, Mordmüller B, Kremsner PG, Yazdanbakhsh M. | Malaria Journal | Vol 14, 2015 | BioMed Central | - | 2015 | 94 | PMCID: PMC4365807 | Yes |
| 8 | Schistosoma mansoni and HIV acquisition in fishing | Ssetaala A, Nakiyingi-Miiro J, Asiki G, Kyakuwa N, Mpendo | Tropical Medicine | Vol 20 (9), 2015 | John Wiley & Sons Ltd | - | 2015 | 1190-1195 | PMCID: PMC45 | Yes |

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| 9 | Enterobiasis and strongyloidiasis and associated co-infections and morbidity markers in infants, preschool- and school-aged children from rural coastal Tanzania: a cross-sectional study. | Salim N, Schindler T, Abdul U, Rothen J, Genton B, Lweno O, Mohammed AS, Masimba J, Kwaba D, Abdulla S, Tanner M, Daubenberger C, Knopp S. | BMC Infectious Diseases | Vol 14, 2014 | BioMed Central | - | 2014 | 644 | PMCID: PMC4271451 | Yes |
| 10 | Associations between maternal helminth and malaria infections in pregnancy, and clinical malaria in the offspring: a birth cohort in Entebbe, Uganda | Ndibazza J, Webb EL, Lule S, Mpairwe H, Akello M, Oduru G, Kizza M, Akurut H, Muhangi L, Magnussen P, Vennervald B, Elliott AM. | Journal of Infectious Diseases | Vol 208, 2013 | Oxford University Press | - | 2013 | 2007-16 | PMCID: PMC3836463 | Yes |
| 11 | Helminth-associated systemic immune activation and HIV co-receptor expression: Response to Albendazole /Praziquantel treatment. | Chachage M, Podola L, Clowes P, Nsojo A, Bauer A, Mgaya O, Kowour D, Froeschl G, Maboko L, Hoelscher M, Saathoff E and Geldmacher C. | PLOS Neglected Tropical Diseases | Vol 8 (3), 2014 | Public Library of Science | - | 2014 | e2755. doi:10.1371/ | PMCID: PMC3967945 | Yes |
| 12 | Chronic helminth infection and helminth-derived egg antigens promote adipose tissue M2 macrophages and improve insulin sensitivity in obese mice | Hussaarts L, García-Tardón N, van Beek L, Heemskerk MM, Haeberlein S, van der Zon GC, Ozir-Fazalalikhan A, Berbée JF, Willems van Dijk K, van | FASEB J. | Vol 29, 2015 | Federation of American Societies for Experimental Biology | - | 2015 | 3027-39 | PMID: 25852044 | No |

| No. | Title | Authors (Last Name, Initial.) | Title of the periodical or the series | Number, date or frequency | Publisher | Place of publication | Year of publication | Relevant pages | Permanent identifiers (if available) | Is/Will open access provided to this publication? (yes/no) |
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| | | Harmelen V, Yazdanbakhsh M, Guigas B. | | | | | | | | |
| 13 | CD4+CD25hiFOXP3+ cells in cord blood of neonates born from filaria infected mother are negatively associated with CD4+Tbet+ and CD4+RORγt+ T cells. | Ateba-Ngoa U, Mombo-Ngoma G, Zettlmeissl E, van der Vlugt LE, de Jong S, Matsiegui PB, Ramharter M, Kremsner PG, Yazdanbakhsh M, Adegnika AA. | PLoS One | Vol 9, 2014 | Public Library of Science | - | 2014 | e114630 | PMCID: PMC4273973 | Yes |
| 14 | IL-1β suppresses innate IL-25 and IL-33 production and maintains helminth chronicity. | Zaiss MM, Maslowski K, Mosconi I, Guenat N, Marsland BJ, Harris NL. | Plos Pathogens | Vol 9 (8), 2013 | Public Library of Science | - | 2013 | e1003531 | PMCID: PMC3731249 | Yes |
| 15 | Differences in innate cytokine responses between European and African children. | Labuda LA, de Jong SE, Meurs L, Amoah AS, Mbow M, Ateba-Ngoa U, van der Ham AJ, Knulst AC, Yazdanbakhsh M, Adegnika AA. | PLoS One | Vol 9, 2014 | Public Library of Science | - | 2014 | e95241 | PMCID: PMC3990610 | Yes |
| 16 | Hookworm infection and environmental factors in mbeya region, Tanzania: a cross-sectional, population-based study. | Riess H, Clowes P, Kroidl I, Kowuor DO, Nsojo A, Mangu C, Schüle SA, Mansmann U, Geldmacher C, Mhina S, Maboko L, Hoelscher M, Saathoff E. | PLOS Neglected Tropical Diseases | Vol 5, 2013 | Public Library of Science | - | 2013 | e2408 | PMCID: PMC3764225 | Yes |
| 17 | Ascaris lumbricoides infection and its relation to environmental factors in the Mbeya region of Tanzania, a | Schüle SA, Clowes P, Kroidl I, Kowuor DO, Nsojo A, Mangu C, Riess H, Geldmacher C, Laubender RP, Mhina S, | PLoS One | Vol 18, 2014 | Public Library of Science | - | 2014 | e92032 | PMCID: PMC3958400 | Yes |

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| | cross-sectional, population-based study. | Maboko L, Löscher T, Hoelscher M, Saathoff E. | | | | | | | | |
| 18 | Alterations in Peripheral Blood B Cell Subsets and Dynamics of B Cell Responses during Human Schistosomiasis | Labuda LA, Ateba-Ngoa U, Feugap EN, Heeringa JJ, van der Vlugt LEPM, Pires RBA, Mewono L, Kremsner PG, van Zelm MC, Adegnika AA, Yazdanbakhsh M, Smits HH | PLOS Neglected Tropical Diseases | Vol 7 (3), 2013 | Public Library of Science | - | 2013 | e2094 | PMCID: PMC3591311 | Yes |
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| 20 | Assessment of the effect of Schistosoma haematobium co infection on malaria parasites and immune responses in rural populations in Gabon: study protocol. | Ateba Ngoa U, Zinsou JF, Kassa RF, Ngoune Feugap E, Honkpehedji YJ, Massinga-Loembe M, Kenguele Moundounga H, Nkoma Mouima AM, Mbenkep LH, Wammes LJ, Mbow M, Kruize Y, Mombo-Ngoma G, Bouyoukou Hounkpatin AL, Dejon Agobe JC, Saadou I, Lell B, Smits H, Kremsner PG, Yazdanbakhsh M, Adegnika AA. | Springerplus. | Vol 3, 2014 | Springer | - | 2014 | 388 | PMCID: PMC4128953 | Yes |
| 21 | Priming dendritic cells for th2 polarization: lessons learned | Hussaarts L, Yazdanbakhsh M, Guigas B | Frontiers in Immunology | Vol 5, 2014 | Frontiers Media S.A. | - | 2014 | 499 | PMCID: PMC42 | yes |

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| | from helminths and implications for metabolic disorders | | | | | | | | 02775 | |
| 22 | Randomized, Controlled, Assessor-Blind Clinical Trial To Assess the Efficacy of Single- versus Repeated-Dose Albendazole To Treat Ascaris lumbricoides, Trichuris trichiura, and Hookworm Infection. | Adegnika AA, Zinsou JF, Issifou S, Ateba-Ngoa U, Kassa Kassa FR, Feugap EN, Honkpehedji YJ, Agobe JC, Kenguele HM, Massinga-Loembe M, Agnandji ST, Mordmüller B, Ramharter M, Yazdanbakhsh M, Kremsner PG, Lell B. | Antimicrobial Agents and Chemotherapy | Vol 58 (5), May 2014 | American Society for Microbiology | - | 2014 | 2535-40 | PMCID: PMC3993258 | Yes |
| 23 | Impact of anthelminthic treatment in pregnancy and childhood on immunisations, infections and eczema in childhood: a randomised controlled trial | Ndibazza J, Mpairwe H, Webb EL, Mawa PA, Nampijja M, Muhangi L, Kihembo M, Lule SA, Rutebarika D, Apule B, Akello F, Akurut H, Oduru G, Naniima P, Kizito D, Kizza M, Kizindo R, Tweyongyere R, Alcock K, Muwanga M, Elliott AM. | PLoS One | Vol 7, 2012 | Public Library of Science | - | 2012 | e50325 | PMCID: PMC3517620 | Yes |
| 24 | Epidemiology of coinfection with soil transmitted helminths and *Plasmodium falciparum* among school children in Bumula District in western Kenya | Kepha S, Nuwaha F, Nikolay B, Gichuki P, Edwards T, Allen E, Njenga SM, Mwandawiro CS & Brooker SJ | Parasites and Vectors | Vol 8, 2015 | Biomed Central Ltd | - | 2015 | 314 | PMCID: PMC4486705 | Yes |

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| 25 | Assessment of CD27 expression as a tool for active and latent tuberculosis diagnosis | Petruccioli E, Petrone L, Vanini V, Cuzzi G, Navarra A, Gualano G, Palmieri F, Girardi E, Goletti D | J of Infection | pii: S0163-4453(15)00251-0 | W.B. Saunders Ltd | - | 2015 | doi: 10.1016/j.jinf.2015.07.009. [Epub ahead of print] | PMID: 26253021 | No |
| 26 | IL-4 specific-response in whole blood associates with human Cystic Echinococcosis and cyst activity | Petrone L, Vanini V, Petruccioli E, Ettorre G M, Busi Rizzi E, Schinina V, Girardi E, Ludovisi A, Gomez-Morales M A, Pozio E, Teggi A, Goletti D | J of Infection | Vol 70, 2015 | W.B. Saunders Ltd | - | 2015 | 299-306 | PMID: 25444973 | No |
| 27 | Mycobacterium bovis BCG Vaccination Induces Divergent Proinflammatory or Regulatory T Cell Responses in Adults | Boer MC, Prins C, van Meijgaarden KE, van Dissel JT, Ottenhoff TH, Joosten SA. | Clinical and Vaccine Immunology | Vol 22, 2015 | American Society for Microbiology | - | 2015 | 778-88 | PMCID: PMC4478523 | No |
| 28 | Focused human gene expression profiling using dual-color reverse transcriptase multiplex ligation-dependent probe amplification (dcRT-MLPA) | Haks MC, Goeman JJ, Magis-Escurra C and Ottenhoff THM | Vaccine | Vol 33, 2015 | Elsevier Inc | - | 2015 | 18-6 | PMID: 25917681 | No |
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| 30 | Impact of Short-Time Urine Freezing on the Sensitivity of an Established Schistosoma Real-Time PCR Assay | Kenguele HM, Adegnika AA, Nkoma A, Ateba-Ngoa U, Mbong M, Zinsou J, Lell B, and Verweij JJ. | Am Journal of Tropical Med Hygiene | Vol 90 (6), Jun 2014 | American Society of Tropical Medicine and Hygiene | - | 2014 | 1153-5 | PMCID: PMC4047745 | Yes |
| 31 | Toll-like receptor ligation for the induction of regulatory B cells | van der Vlugt LEPM, Haeberlein S, de Graaf, W, Marthat, TED, Smits HH | Methods in Molecular Biology | 1190 | Springer | - | 2014 | 127-141 | PMID: 25015278 | No |
| 32 | Diagnostic Accuracy of Kato-Katz, FLOTAC, Baermann, and PCR Methods for the Detection of Light-Intensity Hookworm and Strongyloides stercoralis Infections in Tanzania. | Knopp S, Salim N, Schindler T, Karagiannis Voules DA, Rothen J, Lweno O, Mohammed AS, Singo R, Benninghoff M, Nsojo AA, Genton B, Daubenberger C. | Am Journal of Tropical Med Hygiene | Vol 90 (3), Mar 2014 | American Society of Tropical Medicine and Hygiene | - | 2014 | 535-45 | PMCID: PMC3945701 | Yes |
| 33 | Combination of gene expression patterns in whole blood discriminate between tuberculosis infection states | Mihret A, Loxton AG, Bekele Y, Kaufmann SH, Kidd M, Haks MC, Ottenhoff TH, Aseffa A, Howe R, Walzl G. | BMC Infectious Diseases | Vol 13, 2014 | BioMed Central | - | 2014 | 257 | PMCID: PMC4041060 | Yes |
| 34 | Polyfunctional T-cells and effector memory phenotype are associated with active TB in HIV-infected patients | Chiacchio T, Petruccioli E, Vanini V, Cuzzi G, Pinnetti C, Sampaolesi A, Antinori A, Girardi E, Goletti D | J of Infection | Vol 69, 2014 | W.B. Saunders Ltd | - | 2014 | 533-45 | PMID: 24975174 | no |
| 35 | In vitro growth of Plasmodium falciparum in neonatal blood. | Sauerzopf U, Honkpehedji YJ, Adegnika AA, Feugap EN, Mombo Ngoma G, Mackanga JR, Lötsch F, Loembe MM, | Malaria Journal | Vol 13, 2014 | BioMed Central | | 2014 | 436 | PMCID: PMC4242501 | yes |

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| 37 | Rapamycin and omega-1: mTOR-dependent and -independent Th2 skewing by human dendritic cells. | Hussaarts L, Smits HH, Schramm G, van der Ham AJ, van der Zon GC, Haas H, Guigas B, Yazdanbakhsh M. | Immunology and Cell Biology | Vol 91 (7), 2013 | Nature Publishing Group | - | 2013 | 486-9 | PMID: 23835553 | No |
| 38 | Cystic echinococcosis in a single tertiary care center in Rome, Italy. | Petrone L, Cuzzi G, Colace L, Ettorre GM, Busi-Rizzi E, Schininà V, Pucillo L, Angeletti C, Pane S, Di Caro A, Bordi E, Girardi E, Pozio E, Corpolongo A, Teggi A, Brunetti E, Goletti D. | BioMed Research International | doi: 10.1155/2013/978146 | Hindawi Publishing Corporation | - | 2013 | Id: 978146 | doi: 10.1155/2013/978146 | yes |
| 39 | Autophagy in Mycobacterium tuberculosis infection: A passepartout to flush the intruder out? | Goletti D, Petruccioli E, Romagnoli A, Piacentini M, G Fimia M | Cytokine and Growth Factor Reviews | Vol 24, 2013 | Elsevier | - | 2013 | 335-343 | PMID: 23395260 | No |
| 40 | IFNg/TNFa specific-cells and effector memory phenotype associate with active tuberculosis | Petruccioli E, Petrone L, Vanini V, Sampaolesi A, Gualano G, Girardi E, Palmieri F, Goletti D | J of Infection | Vol 66, 2013 | W.B. Saunders Ltd | - | 2013 | 475-96 | PMID: 23462597 | No |
| 41 | Effects of helminths and *Mycobacterium tuberculosis* infection on HIV-1: a cellular | Mouser EEIM, Pollakis G, Paxton WA | Curr Opin HIV AIDS. | Vol 7, 2012 | Wolters Kluwer | - | 2012 | 260-267 | PMID: 22411452 | No |

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| 42 | Vaccines against tuberculosis: where are we and where do we need to go? | Ottenhoff THM and Kaufmann SHE | PLoS Pathogens | Vol 8, 2012 | Public Library of Science | - | 2012 | e1002607 | PMCID: PMC3349743 | Yes |
| 43 | The knowns and unknowns of the immunopathogenesis of tuberculosis | Ottenhoff THM | Int J Tuberc Lung Dis. | Vol 16, 2012 | International Union Against Tuberculosis and Lung Disease | - | 2012 | 1424-32 | doi: 10.5588/ijtld.12.0479 | No |
| 44 | Epidemiology of malaria and helminth interaction: a review from 2001 to 2011. | Adegnika AA, Kremsner PG | Current Opinion in HIV & AIDS. | Vol 7, May 2012 | Wolters Kluwer | - | 2012 | 221-4 | PMID 22418449 | Yes |
| 45 | Troubles never come alone. | Elliott AM, Yazdanbakhsh M | Current Opinion in HIV and AIDS | Vol 7, 2012 | Wolters Kluwer | - | 2012 | 211–213 | PMID: 22418450 | Yes |
| 46 | Specific T Cells Restore the Autophagic Flux Inhibited by Mycobacterium tuberculosis in Human Primary Macrophages | Petruccioli E, Romagnoli A, Corazzari M, Coccia EM, Butera O, Delogu G, Piacentini M, Girardi E, Fimia GM, Goletti D | Journal of Infectious Diseases | Vol 205, 2012 | Oxford University Press | - | 2012 | 1425-35 | PMID: 22457295 | Yes |
| 47 | IP-10 is an additional marker for tuberculosis (TB) detection in HIV-infected persons in a low-TB endemic country | Vanini V, Petruccioli E, Gioia C, Cuzzi G, Orchi N, Rianda A, Alba L, Giancola M L, Conte A, Schinina V, Busi Rizzi E, Girardi E, Goletti D | J of Infection | Vol 65, 2012 | W.B. Saunders Ltd | - | 2012 | 49-59 | PMID: 22465752 | no |
| 48 | Higher Frequency of T-Cell | Chiacchio T, Petruccioli E, | Plos ONE | Vol 6(11), | Public Library | - | 2011 | e27539 | PMCID: | yes |

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| | Response to M. tuberculosis Latency Antigen Rv2628 at the Site of Active Tuberculosis Disease than in Peripheral Blood | Vanini V, Butera O, Cuzzi G, Petrone L, Matteucci G, Lauria F N, Franken KL. M. C., Girardi E, Ottenhoff T.H. M., Goletti D | | 2011 | of Science | | | | PMC3213161 | |
| 49 | Epidemiology and immunology of helminth-HIV interactions | Webb, E. L., A. O. Ekii and Pala, P. | Curr Opin HIV AIDS | Vol 7, 2012 | Wolters Kluwer | - | 2012 | 245-253 | PMID: 22411451 | No |

### 2.1.2 Dissemination Activities

| No. | Type of activities | Main Leader | Title | Date/Period | Place | Type of audience | Size of audience | Countries addressed |
|---|---|---|---|---|---|---|---|---|
| 1 | Website | CHUV | IDEA website: www.idearesearhc.eu | Mar 2010 | International | Scientific Community (higher education, Research), Industry, Civil Society, Policy makers, Medias | - | International |
| 2 | Workshops | UVRI | Immunology in the Tropics | Sep 2010 | Entebbe, Uganda | Scientific Community (higher education, Research) | 25 | International |
| 3 | Oral Presentation at the European Respiratory Society Annual Congress | INMI (Goletti) | Analysis of multifunctional $CD4^+$ T cells responding to RD1 and Rv2628 antigens in whole blood vs bronchoalveolar lavage in active tuberculosis. | 18-22 Sep 2010 | Barcelona, Spain | Scientific Community (higher education, Research) | - | International |
| 4 | Poster at the European Respiratory Society Annual Congress | INMI | Autophagy modulation by Mycobacterium tuberculosis after in vitro infection of human primary macrophages. | 18-22 Sep 2010 | Barcelona, Spain | Scientific Community (higher education, Research) | - | International |
| 5 | Poster at the Italian Society of Infectious and Tropical Diseases, | INMI | Analisi delle cellule T CD4+ multifunzionali che rispondono ad antigeni RD1 e Rv2628 valutate nel sangue periferico vs lavaggio bronco alveolare nei pazienti con tubercolosi. | 24-27 Nov 2010 | Rome, Italy | Scientific Community (higher education, Research) | - | Italy |
| 6 | Poster at the Italian Society of Infectious and Tropical Diseases, | INMI | Modulazione dell'autofagia in macrofagi infettati in vitro con M. tuberculosis. | 24-27 Nov 2010 | Rome, Italy | Scientific Community (higher education, Research) | - | Italy |
| 7 | Oral presentation at the | INMI | IP-10 è un potenziale biomarcatore | 24-27 Nov | Rome, Italy | Scientific | - | Italy |

| No. | Type of activities | Main Leader | Title | Date/Period | Place | Type of audience | Size of audience | Countries addressed |
|---|---|---|---|---|---|---|---|---|
| | Italian Society of Infectious and Tropical Diseases, | (Goletti) | alternativo rispetto all'IFN-γ per la rilevazione di risposte M. tuberculosis-specifiche in soggetti con infezione da HIV. | 2010 | | Community (higher education, Research) | | |
| 8 | Poster at the Keystone Symposium | UVRI | The relationship between maternal and infant immune responses to mycobacteria. | 15 – 20 Jan 2011 | Vancouver, Canada | Scientific Community (higher education, Research) | - | International |
| 9 | Workshops | LUMC/ UVRI | Molecular diagnostic for helminth and malaria | Apr 2011 | Entebbe, Uganda | Scientific Community (higher education, Research) | 25 | International |
| 10 | Oral presentation at the 8th International Conference on the Pathogenesis of Mycobacterial Infections | INMI (Goletti) | Autophagy modulation by Mycobacterium tuberculosis after in vitro infection of human primary macrophages. | 30 Jun – 3 Jul, 2011 | Saltsjobaden, Sweden | Scientific Community (higher education, Research) | - | International |
| 11 | Workshops | UVRI | Immunology in the Tropics - Fundamental Immunology, TB and HIV | Sep 2011 | Entebbe, Uganda | Scientific Community (higher education, Research) | 25 | International |
| 12 | Invited Speaker 3rd International Frontiers of Retrovirology conference | AMC (Paxton) | Variant Cell Types and Host Glycoproteins Influencing HIV-1 Infection | 3rd -6th Oct 2011 | Amsterdam, the Netherlands | Scientific Community (higher education, Research)Scientific | 300 | International |
| 13 | Poster at the European Respiratory Society Annual Congress | INMI | IP-10 is an additional marker to evaluate the RD1-specific responses in HIV-infected subjects. | 24-28 Nov 2011 | Amsterdam, the Netherlands | Scientific Community (higher education, Research) | - | International |
| 14 | Oral presentation at American Society for Tropical Medicine and | UVRI (Ndibazza) | Impact of anthelminthic treatment in pregnancy and early childhood on response to immunisation and on the | 4-8 Dec 2011 | Philadelphia, USA | Scientific Community (higher education, | - | International |

| No. | Type of activities | Main Leader | Title | Date/Period | Place | Type of audience | Size of audience | Countries addressed |
|---|---|---|---|---|---|---|---|---|
| | Hygiene | | incidence of infectious diseases and eczema in childhood: results of a randomised, double-blind, placebo-controlled trial | | | Research) | | |
| 15 | Workshop | CHUV | Flow cytometry | 20-22 Feb 2012 | Lausanne, Switzerland | Scientific Community (higher education, Research) | 20 | International |
| 16 | Workshops | UVRI | Immunology in the Tropics: evolution of the immune system, malaria and helminth immunology | Mar 2012 | Entebbe, Uganda | Scientific Community (higher education, Research) | 25 | International |
| 17 | Workshops | UVRI | Immunology in the Tropics - Fundamental Immunology, TB and HIV | Sep 2012 | Entebbe, Uganda | Scientific Community (higher education, Research) | 25 | International |
| 18 | Oral presentation at the European Respiratory Society Annual Congress | INMI (Goletti) | Response to M.tuberculosis Rv2628 latency antigen associates with bacterial containment | 1-5 Sep 2012 | Wien, Austria | Scientific Community (higher education, Research) | - | International |
| 19 | Oral presentation at the European Respiratory Society Annual Congress | INMI (Goletti) | Different polyfunctional characteristics of RD1-specific CD4+ T-cells in active TB disease and LTBI | 1-5 Sep 2012 | Wien, Austria | Scientific Community (higher education, Research) | - | International |
| 20 | Poster at the Tuberculosis 2012 | INMI | Specific T cells restore the autophagic flux inhibited by Mycobacterium tuberculosis in human primary macrophages. | 11-15 Sep 2012 | Paris, France | Scientific Community (higher education, Research) | - | International |
| 21 | Organization of Conference | CHUV | European Commission Colloquium Helminth Infections | 25 Sep 2012 | Paris, France | Scientific Community (higher education, Research), Policy Maker | 100 | International |

| No. | Type of activities | Main Leader | Title | Date/Period | Place | Type of audience | Size of audience | Countries addressed |
|---|---|---|---|---|---|---|---|---|
| 22 | Poster at Regulatory T cell international meeting | LSHTM | Increased frequencies of CD4+FoxP3+ T cells in helminth-infected patients coincide with an impaired immune response to tuberculosis | 13-16 October 2012 | Shanghai (China) | Scientific Community (higher education, Research) | 200 | International |
| 23 | Oral presentation at the 6th Congress of African Society of Parasitology | CERMEL (AA Adegnika) | Efficacy of three regimen of albendazole 400mg to treat Ascaris, Trichirus trichiura and Hookworm au 6e Congrès de la Société Ouest Africaine de Parasitologie | 18-20 Dec, 2012 | Dakar, Senegal | Scientific Community (higher education, Research) and stakeholders | 300 | European and African |
| 24 | Poster Dutch Society for Immunology (NVVI), Winter Symposium | AMC | Helminth parasite antigens bind DC-SIGN and inhibit HIV-1 capture and transfer to $CD4^+$ T lymphocytes | 19-20th Dec 2012 | Noordwijkerhout, the Netherlands | Scientific Community (higher education, Research) | 200 | Dutch |
| 25 | Workshops | UVRI | Immunology in the Tropics: evolution of the immune system, malaria and helminth immunology | March 2013 | Entebbe, Uganda | Scientific Community (higher education, Research) | 25 | International |
| 26 | Poster 15th International Journal of Immunology (ICI) | AMC | Dendritic cell capture and transfer of HIV-1 to $CD4^+$ T lymphocytes is inhibited by helminth parasite antigens | 22nd-27th Aug 2013 | Milan, Italy | Scientific Community (higher education, Research) | 10,000 | International |
| 27 | Poster at 6th MIM PAN African Malaria Conference | UIMRT | Effect of malaria and helminth coinfections on levels of ascorbic acid and tocopherol and impact on oxidative stress in children. | 6-11 Oct 2013 | Durban, South Africa | Scientific Community (higher education, Research) | - | International |
| 28 | Presentation at 6th MIM PAN African Malaria Conference | UVRI | An investigation of the temporal and spatial patterns of childhood malaria and maternal antibody responses, in Entebbe Uganda, an area of high malaria endemicity. | 6-11 Oct 2013 | Durban, South Africa | Scientific Community (higher education, Research) | - | International |
| 29 | Poster at the XII National Congress SIMIT | INMI | Caratterizzazione funzionale di cellule T specifiche per M. tuberculosis in soggetti con infezione da HIV naive per | 27-30 Oct 2013 | Milan, Italy | Scientific Community (higher education, | - | Italy |

| No. | Type of activities | Main Leader | Title | Date/Period | Place | Type of audience | Size of audience | Countries addressed |
|---|---|---|---|---|---|---|---|---|
| | | | terapia antiretrovirale | | | Research) | | |
| 30 | Poster at the XII National Congress SIMIT | INMI | Echinococcosi Cistica In Un Centro Di Cura Specializzato Per Le Malattie Infettive A Roma, Italia. | 27-30 Oct 2013 | Milan, Italy | Scientific Community (higher education, Research) | - | Italy |
| 31 | Poster at American Society for Tropical Medicine and Hygiene, 62nd Annual meeting | UVRI | An investigation of the temporal and spatial patterns of childhood malaria and maternal antibody responses, in Entebbe Uganda, an area of high malaria endemicity | 13-17 Nov 2013 | Washington DC, USA | Scientific Community (higher education, Research) | >300 | International |
| 32 | Poster at American Society for Tropical Medicine and Hygiene, 62$^{nd}$ Annual meeting | UIMRT | Prevalence and interaction of malaria and helminth coinfections among symptomatic and asymptomatic children in Southwest Nigeria | 13-17 Nov 2013 | Washington DC, USA | Scientific Community (higher education, Research) | >300 | International |
| 33 | Poster at American Society for Tropical Medicine and Hygiene, 62nd Annual meeting | CERMEL | Efficacy of single versus repeated dose albendazole to treat Ascaris lumbricoides, Trichuris trichiura and hookworm infection: A randomized controlled assessor-blinded clinical trial | 13-17 Nov 2013 | Washington DC, USA | Scientific Community (higher education, Research) | >300 | International |
| 34 | Workshop | UVRI | R programming for Data analysis | 17-18 Dec 2013 | Entebbe, Uganda | Scientific Community (higher education, Research) | 10 | Uganda |
| 35 | Poster at Dutch Society for Immunology (NVVI), Winter Symposium | AMC | Colorectal mucus inhibits HIV-1 *trans*-infection of CD4$^{+}$ lymphocytes by binding DC-SIGN | 18$^{th}$-19$^{th}$ Dec 2013 | Noordwijkerhout, the Netherlands | Scientific Community (higher education, Research) | 200 | Dutch |
| 36 | Invited Speaker at the Second Annual Global Health and Infectious Disease Conference | UVRI (A. Elliott) | Immunomodulating effects of helminth infections during pregnancy: The Entebbe Mother & Baby Study | March 2014 | St Louis, USA. | Scientific Community (higher education, Research) | - | International |
| 37 | Poster at Keystone HIV-1 vaccine meeting held in | AMC | The influence of helminth components on HIV-1 susceptibility of memory T | 9 –14 Mar 2014 | Banff, Canada | Scientific Community | 1000 | International |

| No. | Type of activities | Main Leader | Title | Date/Period | Place | Type of audience | Size of audience | Countries addressed |
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| | | | cells | | | (higher education, Research) | | |
| 38 | Poster at Keystone HIV-1 vaccine meeting held in | AMC | A universal DNA/RNA assay as a sensitive tool in detection of variant HIV-1 forms | 9 –14 Mar 2014 | Banff, Canada | Scientific Community (higher education, Research) | 1000 | International |
| 39 | Poster at Keystone HIV-1 Vaccines: Adaptive Immunity and Beyond | AMC | Helminthic Parasite Antigens can Modulate $CD4^+$ T-Cell Responses and HIV-1 Infectivity | $9^{th}$ -$14^{th}$ March 2014 | Banff, Canada | Scientific Community (higher education, Research) | 1,000 | International |
| 40 | Invited Speaker at the 1st European Meeting for Young researchers on soil-transmitted Helminths | EPFL (N. Harris) | Interactions of helminths, intestinal bacteria and their mammalian hosts | 23-26 Mar 2014 | Jongny, Switzerland | Scientific Community (higher education, Research) | - | International |
| 41 | Organization of Conference | EPFL (Harris) | $1^{st}$ European meeting for young researchers on soil-transmitted helminths (EMYH 2014) | 23-24 March, 2014 | Jongny, Switzerland | Scientific Community (higher education, Research) | 50 | European |
| 42 | Poster at the Innovation for the Management of Echinococcosis | INMI | Experimental whole blood test to diagnose and monitor cystic echinococcosis disease | 27-29 Mar 2014 | Besançon, France | Scientific Community (higher education, Research) | - | International |
| 43 | Oral presentation at Conference on host-helminth interactions from a Global Health Perspective | CERMEL & LUMC (Adegnika) | Burden of helminths in Lambaréné Gabon | March 2014 | Lausanne Switzerland | Scientific Community (higher education, Research) | 50 | International |
| 44 | Poster at 24th European Congress of Clinical Microbiology and Infectious Diseases | INMI | Functional and phenotypical characterization of M. tuberculosis specific T-cells in HIV-infected patients with active tuberculosis or latent infection naïve to antiretroviral therapy | 10-13 May 2014 | Barcelona, Spain | Scientific Community (higher education, Research) | - | International |

| No. | Type of activities | Main Leader | Title | Date/Period | Place | Type of audience | Size of audience | Countries addressed |
|---|---|---|---|---|---|---|---|---|
| 45 | Poster at 24th European Congress of Clinical Microbiology and Infectious Diseases | INMI | Detection of IL-4 after specific whole blood stimulation to diagnose and monitor cystic echinococcosis disease | 10-13 May 2014 | Barcelona, Spain | Scientific Community (higher education, Research) | - | International |
| 46 | Workshop | UVRI | Functional genomics and systems biology | 26-28 May 2014 | Entebbe, Uganda | Scientific Community (higher education, Research) | 10 | Uganda |
| 47 | Poster presentation at the Italian Conference on AIDS and Retroviruses | INMI | Functional and phenotypical characterization of M. tuberculosis specific T-cells in HIV patients naive to antiretroviral treatment | 25-27 May 2014 | Rome, Italy | Scientific Community (higher education, Research) | - | Italy |
| 48 | Oral presentation at IX National Congress SIMIT | INMI (Goletti) | Functional and memory status of tuberculosis specific T-cells in HIV-infected patients naive to antiretroviral treatment | 28-31 May 2014 | Florence, Italy | Scientific Community (higher education, Research) | - | Italy |
| 49 | Oral presentation at IX National Congress SIMIT | INMI (Goletti) | Functional characterization of AgB-specific T-cells in cystic echinococcosis patients | 28-31 May 2014 | Florence, Italy | Scientific Community (higher education, Research) | - | Italy |
| 50 | Poster at IX National Congress SIMIT | INMI (Goletti) | Experimental whole blood test to diagnose and monitor cystic echinococcosis disease | 28-31 May 2014 | Florence, Italy | Scientific Community (higher education, Research) | - | Italy |
| 51 | Oral presentation at Symposium Parasite in Preganancy UKZN | CERMEL (AA Adegnika) | Global Burden of parasites in pregnancy West Central and East Africa | May 2014 | South Africa | Scientific Community (higher education, Research) | 50 | African |
| 52 | Oral Presentation at the 9th International Conference on the Pathogenesis of Mycobacterial Infections | INMI (Goletti) | Polyfunctional T-cells and an effector memory phenotype are associated with active TB in HIV-infected patients | 26-29 Jun 2014 | Stockholm, Sweden | Scientific Community (higher education, Research) | - | International |

| No. | Type of activities | Main Leader | Title | Date/Period | Place | Type of audience | Size of audience | Countries addressed |
|---|---|---|---|---|---|---|---|---|
| 53 | Plenary talk at 6th Blizard Institute HIV Symposium | AMC (Paxton) | Factors associated with HIV-1 transmission and disease progression | 17th July 2014 | London, UK | Scientific Community (higher education, Research) | 200 | International |
| 54 | Oral presentation At the EDCTP annual meeting | CERMEL (M. Loembe) | Epidemiology and immunology of malaria and helminths co-infection | July 2014 | Berlin Germany | Scientific Community (higher education, Research), Policy makers, media | 300 | Europeans and Africans |
| 55 | Oral Presentation at the European Respiratory Society Annual Congress | INMI (Goletti) | Functional and memory status of M. tuberculosis specific T-cells in HIV-infected patients naïve to antiretroviral treatment | 6-10 Sep 2014 | Monaco | Scientific Community (higher education, Research) | - | Europe |
| 56 | Presentation at 63rd Annual Meeting of the American Society of Tropical Medicine and Hygiene | UVRI | The association between maternal hookworm infection in pregnancy and antimalarial antibody responses in the offspring. | 2-6 Nov 2014 | New Orleans, USA | Scientific Community (higher education, Research) | - | International |
| 57 | Invited speaker at the Royal Society Discussion Meeting: Biological Challenges to Effective Vaccines in the Developing World | UVRI (A. Elliott) | Maternal exposure to infection and the infant response to BCG and other vaccines. | 10-11 Nov 2014 | London, UK | Scientific Community (higher education, Research) | - | International |
| 58 | Plenary lecture, Infection and Immunity Symposium, University of Utrecht | AMC (Paxton) | HIV-1: the Great Escape | 21st-22nd Nov 2014 | Utrecht, the Netherlands | Scientific Community (higher education, Research) | 200 | Dutch |
| 59 | Poster at Federation of African Immunological Societies | UVRI | The role of internship training in immunology capacity building: a case study from the Uganda Virus Research Institute | December 2014 | Nairobi, Kenya | Scientific Community (higher education, Research) | - | International |
| 60 | Poster at Federation of | UVRI | Active tuberculosis disease is associated | December | Nairobi, Kenya | Scientific | - | International |

| No. | Type of activities | Main Leader | Title | Date/Period | Place | Type of audience | Size of audience | Countries addressed |
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| | African Immunological Societies | | with a boost in humoral immune responses to unrelated antigens. | 2014 | | Community (higher education, Research) | | |
| 61 | Oral presentation at Conference of the British Society for Immun-ology | LUMC | Helminth infections and ineffective Th2 response | Dec, 2014 | Brighton, UK | Scientific Community (higher education, Research) | - | International |
| 62 | Poster at Dutch Society for Immunology (NVVI), A Future Heritage | AMC | *Schistosoma mansoni* soluble egg antigen can interfere with HIV-1 R5 infection | 17th 19th Dec 2014 | Katsheuvel, the Netherlands | Scientific | 200 | Dutch |
| 63 | Oral presentation in Acid Fast Club | LSHTM (F. Toulza) | Helminth-induced CD4+FoxP3+ T cells are associated with an impaired immune response to Mycobacterium tuberculosis | 9 Jan 2015 | London (UK) | Scientific Community (higher education, Research) | 120 | UK |
| 64 | Poster at Keystone Conference | UVRI | Active Tuberculosis Disease is Associated with Increased Humoral Immune Responses to Unrelated Antigens. | 22-27 Jan 2015 | Santa Fe, New Mexico, USA | Scientific Community (higher education, Research) | 350 | International |
| 65 | Poster at Keystone Conference | LSHTM | Helminth-induced CD4+FoxP3+ T cells are associated with an impaired immune response to Mycobacterium tuberculosis | 22-27 Jan 2015 | Santa Fe, New Mexico, USA | Scientific Community (higher education, Research) | 350 | International |
| 66 | Poster at CROI Conference | INSERM | Treg/Th17 and T-cell effector responses in tuberculosis patients coinfected with HIV | 22-27 Feb 2015 | Seattle, USA | Scientific Community (higher education, Research) | - | International |
| 67 | Oral presentation at Keystone Sympotium "a global challenge for disease control" | LUMC | Effect of helminths on the immune system, malaria and allergy | March,2015 | Ouro Preto, Brazil | Scientific Community (higher education, Research) | 200 | International |
| 68 | Presentation during a visit of European | UVRI (Eliott) | IDEA research initiative on Poverty related neglected diseases and | 10 Apr 2015 | Entebbe, Uganda | Policy makers, Scientific | 20 | Uganda, Europe |

| No. | Type of activities | Main Leader | Title | Date/Period | Place | Type of audience | Size of audience | Countries addressed |
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| | members of parliament at UVRI, Uganda, organized by Deutsche Stiftung Weltbevoelkerung (DSW) | | helminth infections | | | Community (higher education, Research) | | |
| 69 | Oral Presentation at the 25th European Congress of Clinical Microbiology and Infectious Diseases | INMI (Goletti) | CD27 expression as a new tool to distinguish active tuberculosis (TB) from latent TB infection | 25-28 Apr 2015 | Copenhagen, Denmark | Scientific Community (higher education, Research) | - | International |
| 70 | Presentation / flyer during a visit of German members of parliament at UVRI, Uganda, orgzniaed by DSW for Product Development Partnerships (PDP) funded by the German government | EVI (Leroy) | Research and Development (R&D) through a Product Development Partnership (PDP) Model;<br>IDEA: Dissecting the Immunological Interplay between Poverty Related Diseases and Helminth Infections: An African-European Research Initiative | 29 May 2015 | Entebbe, Uganda | Policy makers, Scientific Community (higher education, Research) | 20 | Uganda, Germany |
| 71 | Lab session at European Development Day | CHUV | Combating poverty-related and neglected infectious diseases | 3 Jun 2015 | Brussels, Belgium | Scientific Community (higher education, Research), Industry, Civil Society, Policy makers, Medias | - | International |
| 72 | Stand at European Development Day | CHUV | Combating poverty-related and neglected infectious diseases | 3-4 Jun 2015 | Brussels, Belgium | Scientific Community (higher education, Research), Industry, Civil Society, Policy makers, Medias | - | International |

## 2.2 Section B - Exploitable Foreground

### 2.2.1 Part B1 Patents

IDEA has filed no patents, trademarks, registered designs, etc.

### 2.2.2 Part B2 Exploitable Foregrounds

| Type of Exploitable Foreground | Description of exploitable foreground | Explanation | Confidential (Yes/ No) | Foreseen embargo date (dd/mm/yyyy) | Exploitable product(s) or measures | Sector(s) of application | Timetable, commercial or any other use | Patents or other IPR exploitation (licences) | Owner & other beneficiary (s) involved |
|---|---|---|---|---|---|---|---|---|---|
| Exploitation of results through EU policies | Deworming does not alter risks of clinical malaria or malaria parasitemia among school children | Deworming does not alter risks of clinical malaria or malaria parasitemia among school children | No | - | Supports the current de-worming program in SSA | M72 & Q96 | tbd | N/A | KEMRI |
| Exploitation of results through EU policies | Lack of any substantial effect, either beneficial or detrimental, of the underlying helmith infection on the clinical course of HIV, TB and malaria, nor on the acquisition of HIV and LTBI | Lack of effect of helminth infection on PRD clinical course nor acquisition | No | - | Impact on the public policy of de-worming | M72 & Q96 | tbd | N/A | All IDEA Partners |
| Exploitation of results through EU policies | Information on the geographic distribution and the diversity of helminth infections in different regions in SSA | Geographic distribution and the diversity of helminth infections in different regions in SSA | No | - | Impact on the implementation of deworming campaigns and of the most appropriate therapeutic | M72 & Q96 | tbd | N/A | All IDEA Partners |

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|---|---|---|---|---|---|---|---|---|---|
| | | | | | interventions in the different areas | | | | |
| Commercial exploitation of R&D results | Active TB Flow cytometry diagnostic Test | Exploitable as a new assay for active TB diagnosis | No | - | Impact on treatment and prevention of transmission | M72 & Q86 | tbd | PCT/IB2011/003145 | CHUV |
| General Advancement of Knowledge | Development of a Universal assay able to quantitate variant expression levels of HIV-1 transcripts to allow for relative expression comparisons in relation to infection and disease. | Exploitable as a new quantitative assay for HIV infection | Yes | - | Further development of quantifiable assay and potential commercialisation | M72 & Q86 | tbd | N/A | ULIV |
| General advancement of knowledge | PCR based helminth diagnostic test | Exploitable as a molecular diagnostic to complement the current diagnostic tests for helminth infections | Yes | - | Implementation of the test in helminth endemic region | M72 & Q96 | tbd | N/A | LUMC |
| General advancement of knowledge | The whole blood assay based on the evaluation of the "CD27 expression in T cells" by cytometry for the diagnosis of tuberculosis disease and infection | Exploitable for the development of a new whole blood assay for TB infection and disease progression | No | - | Diagnostic test for tuberculosis disease and infection | M72 & Q86 | tbd | N/A | none |
| General advancement of knowledge | The whole blood assay based on an antigen of Echinococcus granulosus for the diagnosis of cystic echinococcosis and status of disease activity | Exploitable for the development of a new whole blood assay for the diagnosis of cystic echinococcosis and status of disease activity | No | - | Multicenter study among INMI, University of Pavia (Prof E. Brunetti) and Kantonsspital St.Gallen (dr W. Albricht) | M72 & Q86 | tbd | N/A | none |