Could you being by telling us a bit about yourself and how you became interested in studying infectious diseases?

I am currently the Dean of the Faculty of Medicine and Director of University Clinical Research Center of the University of Bamako. Ever since I began my undergraduate degree in medical studies, I have been interested in infectious diseases. I later discovered that they were the primary cause of mortality in Mali. Thus, I decided to do my medical thesis research on schistosomiasis and travelled to several locations across Mali to investigate screening and mass treatment of the disease. I have also been personally disturbed by observing cancers related to this preventable disease.

The need for expertise in epidemiology of malaria and infectious diseases began to come to fruition when our Malaria Research and Training Center was created in 1992; this encouraged me to embark on doctoral studies in infectious diseases (NIAID). The Center was created for building research capacity on the causes, diagnosis, prevention and treatment of neglected tropical diseases in endemic areas. This was facilitated by the existence of research laboratories and local expertise that was built through the long-term collaboration between NIAID and the University of Bamako.

Can you briefly explain what leishmaniasis is and how prevalent the disease is in West Africa?

Leishmaniasis is a neglected disease that is prevalent in more than 90 countries around the world. It affects as many as 12 million people globally, with 1.5 to 2 million new cases every year. Depending on the particular species of leishmaniasis, humans can develop visceral or cutaneous forms of the disease.

It has been documented that cutaneous leishmaniasis (CL) is the most widely reported form of this disease in some West African countries, including Guinea Bissau, Senegal, Niger, Burkina Faso, Mali, Togo and Ghana.

You hypothesise that in an endemic area where sand fly is prevalent, individuals are more likely to be protected against leishmaniasis. How did you come to develop this hypothesis, and how are you testing it?

Our early epidemiological studies of cutaneous leishmaniasis in Mali found high infection rates in the population of some areas associated with no disease. We also uncovered strong in vivo laboratory data that found that repertoires of salivary molecules from Phlebotomus duboscqi may protect mice challenged by leishmanial parasites. These findings have enabled us to formulate more comprehensive questions regarding the development of CL in the field, with the objective of identifying novel ways to prevent and treat this neglected disease.

What role do filarial infections play in an individual’s immune response to sand fly salivary proteins?

We have found that filarial parasites may dampen the response of host antigen-presenting cells to sand fly salivary proteins.

How important is international collaboration in your research project?

International collaboration is crucial for the sustainability of our research project. It empowers local investigators, whilst providing training opportunities in cutting-edge techniques. In addition, it facilitates the transfer of technologies in developing countries like Mali. It also helps develop the careers of young scientists involved in the project.

Finally, to what extent do you hope to further the understanding of leishmaniasis in the next five to 10 years?

We would like to continue investigating the immune response to sand fly salivary gland proteins in populations living in endemic countries, and prepare our research sites for potential vaccine trials.

Dr Seydou Doumbia is Professor of Epidemiology at the Department of Public Health, University of Bamako, Mali. His investigations involve the epidemiology of infectious diseases, including malaria and leishmaniasis. Below, he discusses his background and how he developed his research interests.

In conversation with a tropical diseases expert
Leishmaniasis is a disease caused by a protozoa parasite from more than 20 Leishmania species. The disease is transmitted to humans through the bite of infected female phlebotomine sand flies and affects some of the poorest people on Earth. It is found in both tropical and subtropical countries, such as the rainforests in Central and South America, and the deserts in West Africa and the Middle East. Yet despite the prevalence of leishmaniasis in West Africa, it remains one of the most under-reported and little recognised parasitic infections in the region.

Bites from vector sand flies carrying different species of leishmania dictate what form of leishmaniasis the infected humans develop. There are three main forms of the disease: visceral leishmaniasis (VL), cutaneous leishmaniasis (CL) and mucocutaneous leishmaniasis (ML). Of the three forms, CL is by far the most common and is characterised by skin lesions on exposed parts of the body – lesions that can leave lifelong scars and cause serious disabilities. As many as 12 million people worldwide are affected by the disease, with 1.5 to 2 million new cases reported every year.

Asking the Right Questions

Major risk factors for leishmaniasis include socioeconomic conditions, malnutrition, population mobility and environmental changes. Indeed, the disease is known to be highly climate-sensitive and it is affected by changes in rainfall, temperature and humidity. Despite the severity of the problems associated with leishmaniasis, the treatments for patients with the disease are unreliable. Recommendations for those patients in Africa include a combination of pentavalent antimonials and paromomycin, but these can have significant and severe side effects.

Alarmingly, there is currently no vaccine available to combat leishmaniasis. With that in mind, a team of researchers based at the Tropical Medicine Research Center in Mali are conducting investigations into CL in central and North-West Mali. Led by Dr Seydou Doumbia, the team’s initial epidemiological studies – coupled with their in vivo laboratory data that is now ready for transition to field conditions – has enabled them to begin formulating more comprehensive questions that are helping to widen their understanding of both the transmission and development of CL.

Two Projects to Address Specifics

Doumbia and his team are particularly interested in identifying how the immune responses of individuals living in endemic areas are associated with vector sand fly salivary gland proteins in the development of leishmaniasis. In addition, the team is trying to determine how such immune responses might be modulated by co-infections with filarial worms. To address these questions and achieve their specific aims, the team developed two separate but overlapping projects.

Despite the prevalence of leishmaniasis in West Africa, it remains one of the most under-reported and less recognised parasitic infections in the region.

The first project was centred on epidemiological studies and it set out to investigate whether in vitro T cell responses to vector sand fly salivary proteins correlated with either resistance or susceptibility to CL. Focusing on the Sahelian-Savana areas of Western Mali and Ghana, the team performed baseline studies to identify the prevalence of CL in classical and cryptic foci. Importantly, these studies allowed the researchers to simultaneously study the three most crucial aspects of the disease: the agent that transmits CL to humans and animal
Meanwhile, the second project was centred on immunological studies, it was established to assess the precise ways in which the salivary proteins of a sand fly vector affect human antigen-presenting cells. (Antigen presentation is a process by which the body’s immune system enables immune cells to distinguish between the body’s own cells and infection pathogens). Thus, the team set about examining filarial parasites, concentrating on whether they were able to control the host’s antigen-presenting cells response to sand fly salivary proteins. Ultimately, their aim was to widen understanding of the precise mechanisms involved in the transmission of (or resistance to) CL – findings which would generate potential for the development of a vaccine or improved treatments.

THE NEXT STEP TO COMBATING THE DISEASE

Doumbia and his team’s research has resulted in several key findings that have exciting possibilities for the future of combating CL. By identifying that some of the proteins found in the saliva of sand flies are immunogenic and can produce antibodies for such proteins in both animals and humans, the researchers have uncovered a potential biomarker.

However, perhaps most exciting of all is the group’s work to develop a vaccine for CL. “We have demonstrated that nonhuman primates exposed to uninfected Phlebotomus duboscqi sand fly bites, or immunised with the salivary protein PdSP15, are protected against the form of CL that is initiated by infected bites,” explains Doumbia. Indeed, the vaccine has already been tested on mice and monkeys and will soon be going to clinical trials, providing real hope for millions of people around the world who are at risk of developing CL.

Cutaneous leishmaniasis (ulcerative wet lesion, Keita et al, CNAM).

KEY FINDINGS ABOUT LEISHMANIASIS

Doumbia’s team has made some striking discoveries about leishmaniasis. An improved understanding of this prevalent yet neglected disease is essential to the prevention, treatment and eventual cure of this debilitating and often deadly disease.

Some particularly notable findings made by the researchers include:

- Finding Phlebotomus duboscqi (the common vector of CL in Mali) for the first time in Bamako – mostly within human houses, which confirms the possibility of a local transmission of Leishmania major
- Finding Sergentomyia freetownensis for the first time in Mali, thereby raising the total of sand fly species found in Mali to 15
- Discovering that the parasite Leishmania major is the predominant, possibly exclusive species responsible for CL in Mali
- Identifying Leishmania major as the only species found in sand flies, thereby incriminating Phlebotomus duboscqi as the vector of CL in Mali
- Establishing the ongoing transmission of Leishmania by measuring – for the first time – the incidence of exposure to infected sand flies by a skin test in Central Mali
- Demonstrating a high degree of conservancy among secreted salivary gland proteins from two geographically distant Phlebotomus duboscqi sand fly populations – Mali and Kenya

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FUNDING

NIAID, NIH
Fogarty International Center, NIH

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