Healthy Lives for All

Worm infections are widespread in low to middle income countries. Prof. Clarissa Prazeres da Costa conducts research into how these neglected tropical diseases affect the immune system. As Co-Director of the Center for Global Health at the TUM School of Medicine, she furthermore promotes interdisciplinary and international research collaborations.
Approximately 1.5 billion people around the world are infected with parasitic worms. These trematodes, cestodes and nematodes are known in technical language as helminths. They can enter the human body in food or drinking water contaminated with urine and feces, through mosquito bites or by burrowing directly through the skin. They have complex life cycles and circulate between the environment and their hosts – humans. Until about a 100 years ago, these worms were as widespread in Germany and other economically developed countries as is now only the case in countries without adequate public sewage systems and sanitation facilities. Today, however, such infections are almost unheard of in Germany. Consequently, they are now classified as a group of so-called neglected tropical diseases (NTDs) strongly associated with poverty and are the subject of comparatively little research.

These parasitic worms have developed or co-evolved with the human immune system for a long time. They occupy almost every organ in the human body, with each parasite gradually carving out its own niche, from the skin and the liver to the brain. Symptoms of infection can range from mild digestive problems or anemia to severe growth and development disorders in children. Nevertheless, as Clarissa Prazeres da Costa explains, “it is relatively rare for people to die from these infections, though they often unknowingly carry the infection their entire lives.” Prof. da Costa is Head of the “Infection and Immunity in Global Health” Working Group at the Institute for Medical Microbiology, Immunology and Hygiene (MIH) at TUM. In order to survive in their host for as long as possible, worms need to outsmart the human immune system – and precisely how they achieve this is a fascinating process that da Costa wants to understand better.
She and her team have discovered, for instance, that helminths release molecules that actively inhibit the body’s immune response. In addition, the worms induce increased release of suppressor cells, which further suppresses active responses from the immune system. This “immunomodulation” also influences how people infected with helminths react to other conditions such as allergies, other infections like hepatitis B and C, and even vaccinations, namely by weakening the body’s response in many cases. “As immunologists, we can learn a lot from our ‘old friends’ by better understanding how they manage to trick our immune system,” says da Costa.

Interestingly, experiments in animals have shown that parasitic infections during pregnancy can have an impact on the development of the immune system even in the next generation. Studies are currently underway in the sub-Saharan country of Gabon to examine whether this also occurs in humans and the extent to which parasitic infections affect women’s health in general. In fact, Prof. da Costa is driving this research forward at the TUM Center for Global Health (CGH), which she co-founded and leads with her fellow Co-Director, Andrea Winkler (Department of Neurology). “We feel obligated to pursue the UN Sustainable Development Goals, particularly the third goal of ‘ensuring healthy lives for all’.” Achieving this will require – among other measures – the elimination of neglected tropical diseases. This calls for multidisciplinary research approaches to facilitate sustainable innovation, something the CGH at TUM is seeking to promote. “We want to use the CGH to promote an exchange that spans disciplinary boundaries, especially during the COVID-19 crisis, that is impacting scientific research and scientists alike,” says da Costa.

Pandemics like the novel coronavirus present particular challenges for countries in the Global South. In total, there are only around 2,000 ventilators across 42 African countries. By way of comparison, Germany alone has a regular working stock of 23,000 and is capable of ramping this up to 30,000. African countries also lack sufficient personal protective equipment for medical staff. Da Costa hopes to counter this lack of resources with innovation. Together with Fabian Jodeit and Petra Mela from the Chair of Medical Materials and Implants and Andreas Pichlmair from the Institute of Virology, as well as a
Infection of water snails
Cercariae are set free
Skin penetration
Schistosomes develop
Pairing
Adult schistosoma
Egg production
Eggs pass through bowels and bladder

Collaboration with a firm called Plasmatreat, da Costa is seeking to explore potential methods of sterilizing disposable items with plasma-activated water vapor to thereby inactivate the SARS-CoV-2. This would enable the reuse of ventilators, protective masks and protective suits. “This method is cost-effective and mobile, providing the ideal preconditions for deployment in regions where infrastructure is lacking,” says da Costa, outlining the benefits.

In collaboration with Eugénia da Conceição-Heldt and Janina Steinert from the TUM School of Governance and Martin Schlegel from the Clinic for Anesthesiology, she is also working on a project to investigate the role of the WHO as a crisis manager during the COVID-19 pandemic. An example of this is the WHO’s international SOLIDARITY Trial, a drug trial in which the Klinikum rechts der Isar is also registered.

In her work, da Costa feels bound by the motto of “ensuring healthy lives for all” – both in her basic research into helminths and her commitment to promoting interdisciplinary research at the CGH.

Claudia Doyle

Prof. Clarissa Prazeres da Costa
Physician and infectious disease consultant Clarissa Prazeres da Costa specializes in tropical medicine, parasitology and immunology. She is the Head of the Department of Diagnostic Parasitology and lecturer at the Institute for Medical Microbiology, Immunology and Hygiene. Da Costa heads the “Infection and Immunity in Global Health” research group since 2005 and is Co-Director of the Center for Global Health (CGH), which she co-founded at the TUM School of Medicine in 2016.

A complex life cycle: Parasitic worms like schistosomes enter the human body as larvae called cercariae, which are released by the intermediate host, the fresh water snails. They penetrate the intact skin and undergo several development stages in the body. Eventually, the female worms release eggs, which enter the bowel or bladder. This inflammatory process can cause typical disease symptoms. Miracidia larvae hatch from the excreted eggs. They infect the intermediate host and multiply again. The cycle is thus complete.
Global Health Needs a Multidisciplinary Approach

Since the onset of the COVID-19 pandemic, the topic of global health has once again come into sharp focus. “Ensuring healthy lives for all”, one of the United Nations’ Sustainable Development Goals, is also a key focus for Prof. Clarissa Prazeres da Costa, a specialist in the fields of medical microbiology and infectious disease epidemiology. Together with Prof. Andrea Winkler she founded the Center for Global Health at the TUM School of Medicine.

**Prof. da Costa, what exactly is “Global Health”?**
It is both a concept and a global commitment on the part of UN Member States to ensure healthy lives and promote wellbeing for all. However, the topic of global health is not limited to the field of conventional biomedicine. Instead, the focus is on the prospects for healthcare systems. It is therefore vital that we adopt a multidisciplinary approach to the issue.

**As someone who conducts basic research, how did you become involved in the topic?**
My father is of Indian descent; he worked for an American company and we traveled a lot. I have worked as a doctor in Nepal and the Philippines, where I saw the extent to which people suffer from avoidable acute and chronic infectious diseases. After completing my medical training, I immersed myself in the field of infectious diseases. Since then, I have expanded my focus, which now ranges from the lab to hospital beds. I just want to provide tangible benefits through my research and raise students’ awareness of global health through my teaching.

**What diseases do poorer countries typically face?**
Unlike in high-income countries, infectious diseases are among the most common causes of death in low-income countries. Even putting their generally weak healthcare systems to one side, these countries also lag behind in the development of new medications. To give you an example, 230 million people currently suffer from schistosomiasis, a worm infection that can result in chronic inflammation of the bladder and liver if left untreated. For context, the same number of people have malaria. Only one medication is currently capable of fighting the infection – but it is often not affordable and unavailable. This is why it is donated by pharma companies and administered in mass-medication
programs supported by the World Health Organization, primarily to school children. This approach, however, raises the risk that the parasites will develop resistance to the medication. Although drug development is urgently needed, this work is rarely supported because the enormous costs involved make it less lucrative for pharma companies. At the same time, however, we also urgently need innovative diagnostic techniques that are robust and inexpensive in order to measure the success of such large therapy programs.

How can research become established in countries where there is little structure?
By initiating research networks. We are part of specific programs set up by the German Research Foundation and the Federal Ministry of Education and Research (BMBF) aiming to do exactly that. Another example would be the German Center for Infection Research (DZIF) – a research association bringing together more than 500 doctors and scientists working on new methods to prevent, diagnose and treat infectious diseases. It also has partnerships with four institutions in sub-Saharan Africa.

Could you briefly explain the objectives of the projects you are involved in?
In Cystinet Africa, a sub-Saharan research network supported by the BMBF, my colleague Andrea Winkler and I are working on an interdisciplinary approach to containing a parasitic pork tapeworm infection. This involves taking a “one health” approach to humans, animals and the environment. In another DFG-supported project in the Central African nation of Gabon, our working group is researching the immunological effects of worm infections, more specifically schistosomiasis, during pregnancy. In previous investigations, we have been able to show that an infection during pregnancy can protect the progeny against allergies. It is important to understand the mechanisms involved in order to understand their effects; initial indications are that maternal infection could even have an impact on the efficacy of vaccinations in children. German and African doctoral students are working hand in hand on this project. At present, we are establishing a network on the topic of global women’s health together with academics at TUM and internationally at the Center for Global Health. The research field of immunity and pregnancy will become embedded in this network.

Interview by Eve Tsakiridou