

Parasitic disease of humans and livestock remains a worldwide problem. Leishmaniasis impacts both health and economics and drains resources that could be used to promote development. Improving control of this disease would have profound benefits for human health, aid in wealth creation, and enhance quality of life. With no vaccine currently available for use in humans, chemotherapy remains the primary method of intervention, however current drugs are inadequate. New drugs are needed and whilst several promising candidates are in early phase clinical trials, gaining deeper insights into *Leishmania* biology is crucial for supporting drug discovery efforts. *Leishmania* undergoes a tightly regulated differentiation process, known to be regulated by phosphorylation, transitioning between an extracellular promastigote to an intracellular amastigote. Differentiation requires extensive cellular remodelling to adapt to changing environments and this is enacted by peptidases, including the ubiquitination proteasome system (UPS). In this presentation I will describe how we have used CRISPR-Cas9 genome editing of *Leishmania* genes to investigate their function in life cycle progression and establishment of infection. I will also describe how protein kinases and the UPS system are an important target class for potential new anti-leishmanial drugs.