

Genetic markers for SSG-resistance in *Leishmania donovani* and SSG-treatment failure in visceral leishmaniasis patients of the Indian subcontinent

Manu Vanaerschot¹, Saskia Decuypere¹, Suman Rijal², Shyam Sundar³, Jean-Claude Dujardin¹

¹ Institute of Tropical Medicine Antwerp, Antwerpen, Belgium; ² B.P. Koirala Institute of Health Sciences, Dharan, Nepal; ³ Banaras Hindu University, Varanasi, India

Antimony-resistant (SSG-R) *L. donovani* is widespread in the visceral leishmaniasis endemic regions in India and Nepal. The current standard to identify SSG-R *Leishmania* is a laborious *in vitro* assay of which the result has little clinical value since SSG-R parasites are also found in SSG-cured patients. In this study, candidate genetic markers for clinically relevant SSG-resistant parasites identified by full genome sequencing were validated on a large set of clinical strains. This showed that 3 genomic locations suffice to specifically detect the SSG-resistant parasites found only in patients experiencing SSG-treatment failure (sensitivity: 77.8%, specificity: 100.0%, positive predictive value: 100.0%, negative predictive value 92.0%). These parasite genetic markers show not only a better performance to detect and predict SSG-treatment failure of the patient, they are also much easier to apply compared to the current laborious *in vitro* SSG-susceptibility test. These findings allow the development of rapid assays to monitor the emergence and spread of clinically relevant SSG-resistant *Leishmania* parasites.