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Development of genetically modified live attenuated parasites as potential vaccines against visceral leishmaniasis

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Visceral Leishmaniasis (VL) is a potentially fatal disease caused by the parasitic protozoa *Leishmania donovani*. The major challenges for control of the disease include toxicity of available drugs, emerging drug resistant strains and non-availability of a vaccine. People who recover from *Leishmania* infection develop lifelong immunity against it, hence live attenuated parasites with known genetic defect have great potential as vaccines as they mimic natural infection without causing the disease. It was aimed to develop several genetically modified live attenuated *Leishmania donovani* parasites as potential vaccines that would persist for a brief duration but get eventually cleared. One such gene knockout parasite, deleted for a growth-regulating gene *centrin1* (Ld Cen1^{-/-}), is specifically attenuated at the amastigote stage. Ld Cen1^{-/-} has been shown to be safe, protective and immunogenic in various animal models, with induction of strong Th1 effector response. Pre-clinical evaluation of Ld Cen1^{-/-} *ex-vivo* in human PBMCs from *Leishmania*-exposed healthy individuals shows induction of a strong recall and protective immune responses similar to that observed with wild type parasite, establishing the potential of Ld Cen1^{-/-} as a vaccine against human VL. Studies are in progress for the clinical trial of Ld Cen1^{-/-}. Further, three new lines of *L. donovani* were developed by deletion of distinct amastigote-specific genes, including genes coding for A1 protein, adenosine kinase-like protein (AKLP), and a hypothetical protein on chromosome 30 (HP30). The double knock-out mutants that are confirmed to be safe and protective in animal models will be pursued as live attenuated human vaccine candidates.

Biography

Poonam Salotra has completed her PhD from Delhi University and Postdoctoral studies from Roche Institute of Molecular Biology, NJ, USA. She is the Deputy Director at National Institute of Pathology, New Delhi, India. She is elected Fellow of Indian National Science Academy and a member of the WHO Advisory Panel on Parasitic Diseases. She has published more than 95 papers in reputed journals and holds 2 US patents

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