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Recent advances in vaccination for leishmaniasis using genetically altered live attenuated parasite

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Visceral leishmaniasis (VL) caused by Leishmania donovani is a vector-borne anthroponotic disease transmitted by a sand fly bite with no available human vaccines. "Leishmanization", deliberate infection with small inoculums, confers strong and durable protection against cutaneous leishmaniasis (CL) suggesting that a vaccine could be effective against visceral leishmaniasis. In this presentation I will address how genetically altered live attenuated L. donovani parasites as vaccines are both safe and protective against leishmaniasis. Briefly, we have developed two attenuated lines of L. donovani by deleting either the gene responsible for cell division or a gene essential for energy generation. These cell lines survive for a limited time in vivo in animal models (mice and hamsters) and do not survive in immune-suppressed animals. Analysis of immune responses in mice immunized with genetically altered parasites and challenged with virulent parasites showed protective Th1-type immunity. The parasite burden was significantly reduced even when challenged after longer immunization time periods, when the attenuated parasites could not be detected, signifying a sustained immunity. Immunization with L. donovani genetically altered parasites was shown to cross-protect against infection from other species that cause either cutaneous or mucocutaneous leishmaniasis. Finally, I will present evidence of visceralization of L. donovani following bites from infected Lutzomyia longipalpis sand flies to mice and hamsters which has not been previously demonstrated. This new finding has an important implication in demonstrating the efficacy of vaccines under field conditions.

Biography

Upon completion of his doctorate in Microbiology at Bose Institute, India in 2006, he joined the Center for Biologics Evaluation and Research (CBER), USFDA as post-doctoral fellow and was recently promoted to a Visiting Associate. From his doctorate study he developed his expertise in host-parasite interaction and immunology in Leishmaniasis. During his tenure at CBER/FDA, he has focused on the development and characterization of gene deleted cell lines as potential live attenuated vaccine candidates and test such parasite cell lines as protective vaccine against Leishmaniasis.

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