Title:

Fighting zoonotic cutaneous leishmaniasis with engineered symbiotic bacteria from vector sand fly

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Abstract

Leishmania development occurs in the lumen of the sand fly midgut, a compartment shared with symbiotic bacteria. Here, we describe a strategy that uses symbiotic bacteria to deliver antileishmania effector molecules to the midgut lumen, thus rendering host sand fly refractory to *Leishmania* infection. *Enterobacter cloacae* a common *Phlebotomus papatasi* symbiotic bacterium was engineered to produce defensin, an anti-*Leishmania* effector protein. Significantly, the proportion of sand flies carrying the parasite (prevalence) decreased by up to 85% for the effector molecule. The mean and median number of *L.major* in the guts were 1,708,090-15.6-1.7 and 78500-0.0-0.0 in the control, wild type, and transgenic groups respectively. We demonstrate the use of an engineered symbiotic bacterium to interfere with the development of *L.major* in the *P.papatasi*. We have produced the first paratransgenic *P.papatasi*. These findings provide the foundation for the use of genetically modified symbiotic bacteria as a powerful tool to combat leishmaniasis.

Key words: *Phlebotomus papatasi,* paratransgenesis, *Enterobacter cloacae, Leishmania major,* defensin