## How does antimonial resistance affect the survival skills of Leishmania donovani?

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Leishmania donovani is transmitted between mammalian hosts by phlebotomine sandflies and accordingly grows in 2 life-forms (i) extracellular promastigotes which are adapted to the sandfly and (ii) intracellular amastigotes adapted to macrophages of the host. This parasite expertly survives in these 'hostile' environments with a unique redox system protecting against oxidative damage, and host manipulation skills suppressing oxidative outbursts of the mammalian host. Treating patients imposes an additional stress on the parasite and sodium stibogluconate (SSG) was used for over 70 years in the Indian subcontinent. We evaluated whether the survival capacity of clinical L. donovani isolates representative for the parasite population circulating in Nepal, varies significantly at different stages of their life cycle by comparing proliferation, differentiation, oxidative stress tolerance and infection capacity in several in vitro and in vivo models. In general, the strains that were resistant to SSG attained stationary phase at a higher parasite density, contained a higher amount of metacyclic parasites and had a greater capacity to cause in vivo infection in mice compared to strains sensitive to SSG. Since the SSG-resistant strains had superior survival skills as promastigotes and as amastigotes compared to the SSG-sensitive strains, this could indicate that Leishmania parasites adapting successfully to this particular drug pressure acquire an overall increased fitness. This stands in contrast to what is found for other organisms, where drug resistance is usually linked to a fitness cost.