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Modulation of the immune response and infection pattern to Leishmania donovani in visceral leishmaniasis due to arsenic exposure: An in vitro study

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Abstract

The arsenic contamination of ground water in visceral leishmaniasis (VL) endemic areas in Bihar, India leads to human exposure through drinking water. Possibly, the consumed arsenic (As) accumulates in the tissues of VL patients, who subsequently internalize intracellular amastigotes to confer resistance against chemotherapy to the parasite, leading to modulation in the host's immune response. This hypothesis appears to be consistent with the *in vitro* findings that in arsenic-exposed parasites, the mitochondrial membrane potential became depolarized, whereas the reduced thiol and lactate production was overexpressed with enhanced glucose consumption; therefore, the reduced thiol possibly supports an immunosuppressive state in the host cells. This observation was well supported by the down-regulated expression of pro-inflammatory cytokines (IL-2, IL-12, IFN-γ, and TNF-α) with a suppressed anti-leishmanial function of macrophage (NO, ROS). In contrast, the pathophysiological mechanism of VL has received ample support by the promotion of Th2 cytokines (IL-4 and IL-10) in the presence of arsenic-exposed *Leishmania* parasites (Ld^{AS}). Dysfunction of mitochondria and the overexpression of lactate production raise the possibility of the Warburg effect being operative through the up-regulation of glucose consumption by parasites to enhance the energy production, possibly augmenting virulence. Therefore, we surmise from our data that arsenic exposure to *Leishmania donovani* modulates the immune response and infection pattern by impairing parasite function, which may affect the anti-leishmanial effect in VL.

Biography:

More than 25years research experience in the field of leishmaniasis to reveal the resistant isolates demography, their role in protective cytokine diversion, control of parasitic anemia in visceral leishmaniasis as well as identification of phytopharmaceutical anti-leishmanial candidate and also to identify the candidate for vector based vaccine development against leishmaniasis.

Speaker Publications:

1. Modulation of the immune response and infection pattern to Leishmania donovani in visceral leishmaniasis due to arsenic exposure: An in vitro study. (2019), Plos One, 14(2), p.e0210737.
2. Exploring new immunological insight on SP15 (~ 14kDa) family protein in saliva of Indian sand-fly (*Phlebotomus argentipes*) in experimental visceral leishmaniasis. (2018), Cellular immunology. 332, pp.51-57.
3. *Cedrus deodara: In vitro* anti-leishmanial efficacy & Immunomodulatory activity. (2017), The Indian journal of medical research, 146(6), p.780.

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