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## Characterization of phosphate transporter(s) and understanding their role in *Leishmania donovani* parasite

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**Statement of the Problem:** Inorganic phosphate (Pi) is shown to be involved in excretion of methylglyoxal (MG) in the promastigote form of *Leishmania donovani* parasite. Absence of Pi leads to its accumulation inside the parasite. Accumulation of MG is toxic to the parasite and utilizes glyoxalase as well as excretory pathways for its detoxification. In addition, Pi is also reported to regulate activities of ectoenzymes and energy metabolism (glucose to pyruvate) etc. Thus, it cumulatively affects growth of the parasite. Therefore, the transporters which allow the movement of Pi across the membrane can prove to be a crucial drug target.

**Methodology & Theoretical Orientation:** Bioinformatics analysis approach was applied to identify the phosphate transporters in *L. donovani*. Phylogenetic analysis as well as secondary structure prediction was performed for its characterization. We tried to understand the secondary structure of these two proteins and confirm modulation in their expression with the change in Pi concentration outside. We also tried to detect the expression quantitatively in a log phase culture of promastigote and under various physiological conditions. Moreover, their modes of action were also measured in presence of different inhibitors (LiF, CCCP).

**Findings:** We first characterized two phosphate transporters in *Leishmania*: H<sup>+</sup> dependent myo-inositol transporter PHO84 and; Na<sup>+</sup> dependent transporter PHO89 based on similar studies done previously on other lower organisms and trypanosomatids. We found significantly higher expression of H<sup>+</sup> dependent transporter (LdPHO84) as compared to Na<sup>+</sup> dependent transporter (LdPHO89). We also inhibited the Na<sup>+</sup> as well as H<sup>+</sup> gradient and then confirmed their involvement in the Pi transport across the membrane.

**Conclusion & Significance:** We thus functionally characterized two phosphate transporters of *L. donovani* and its regulation by extracellular Pi for the first time. These computational results offer the possibility of identifying novel compounds which inhibit the transport of Pi across the membrane.

### Biography

Ambak Kumar Rai is an Assistant Professor in Department of Biotechnology at Motilal Nehru National Institute of Technology (MNNIT) Allahabad, India. He has his expertise in "Understanding the molecular and biochemical aspects of drug resistance in *Leishmania donovani*". A detailed approach to understand the drug unresponsiveness offers new possibilities for therapeutic advancement. He is also inclined to understand the immuno-regulatory aspects of *Leishmania* pathogenesis.

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