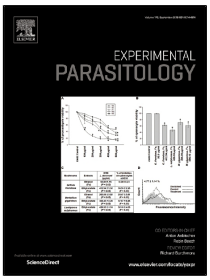
Accepted Manuscript



Prophylactic treatment of L-Arg improves malaria outcomes by regulating host immune responses during *Plasmodium yoelii* 17XL infection

Qiubo Wang, Yonghui Feng, Xiaodan Sun, Wei Pang, Weixin Fu, Yaming Cao

PII:	S0014-4894(17)30256-4
DOI:	10.1016/j.exppara.2018.09.013
Reference:	YEXPR 7611
To appear in:	*Experimental Parasitology*
Received Date:	23 May 2017
Accepted Date:	20 September 2018

Please cite this article as: Qiubo Wang, Yonghui Feng, Xiaodan Sun, Wei Pang, Weixin Fu, Yaming Cao, Prophylactic treatment of L-Arg improves malaria outcomes by regulating host immune responses during *Plasmodium yoelii* 17XL infection, *Experimental Parasitology* (2018), doi: 10.1016/j.exppara.2018.09.013

Prophylactic treatment of L-Arg improves malaria outcomes by regulating host immune responses during *Plasmodium yoelii* 17XL infection

Qiubo Wang[a], Yonghui Feng[b], Xiaodan Sun[a], Wei Pang[a], Weixin Fu[c]*, Yaming Cao[a]*

a. Department of Immunology, College of Basic Medical Sciences, China Medical University, Shenyang, Liaoning Province, P.R. China

b. Department of Laboratory Medicine, The First Hospital of China Medical University, Shenyang, Liaoning, P.R. China

c. Science Experiment Center of China Medical University, Shenyang, Liaoning Province, P.R. China

Abstract

L-arginine (L-Arg), the precursor of nitric oxide (NO), plays multiple, important roles in nutrient metabolism and immune regulation. Hypoargininemia is one of the distinctive features of malaria patients in endemic areas. To understand the immunoregulatory function of L-Arg in malaria, we investigated the effects of L-Arg, pre- or/and post-treatment, on the cellular/humoral immune response during *Plasmodium yoelii* 17XL (*P.y*17XL) infection in DBA/2 mice. Populations of splenic $CD4^+$T-$bet^+IFN\text{-}\gamma^+$ T cells (Th1), $F4/80^+$ macrophages, $CD4^+GATA\text{-}3^+IL\text{-}4^+$ T cells (Th2), $B220^+CD138^+$ plasmacytes and antibody-producing cells ($IgG^+/IgG1^+$-plasma cells) were assessed by flow cytometry. Pro-inflammatory cytokines and antibodies (IgG and IgG1) were quantified by immunoassays. We found that treatment with L-Arg significantly decreased parasitemia and shortened disease duration. Prophylactic treatment with L-Arg promotes an enhanced Th1 cell response during the early stages of *P.y*17XL infection, and treatment with L-Arg in the course of infection facilitates the later humoral immune response. Our findings suggest that treatment with L-Arg may decrease parasite burden and control the host's susceptibility to parasite synchronously by regulating host immune responses against *P.y*17XL, producing better outcomes for malaria infection. This implies that the supplementation of L-Arg may be a promising adjunctive therapy to reduce malaria-associated mortality in endemic areas.

Key words malaria; L-Arginine; *P.y*17XL; Th1/Th2 responses; antibody