Docosahexaenoic Acid–Rich Omega 3 Supplementation Partially Preserves Intestinal Integrity but Fails to Improve Pulmonary Outcomes in Experimental Malaria Caused by P*lasmodium berghei* NK65

Letícia Ferreira Machado[1], Ludmila Ponce Monken Custódio Pereira[1], José Henrique Silva Rodrigues[1], Fernanda Martins Pinheiro[1], Ana Carolina Fonseca da Silva[1], Carolina Brandi Marques[1], Milena Gomes Tavares[1], Gabriel Brum de Souza[4], Heloísa D´Ávila da Silva Bizarro[4], Adolfo Firmino Neto[3], Vinicius Novaes Rocha[3], Flávia Lima Ribeiro Gomes[2], Juciane Maria de Andrade Castro[1], Kézia Katiani Gorza Scopel[1]*

[1]Research Centre of Parasitology. Department of Parasitology, Microbiology and Immunology and Post-Graduate Program in Biological Science, Federal University of Juiz de Fora, Juiz de Fora, Brazil.
[2]Laboratory of Malaria Research. Oswaldo Cruz Institute, Fiocruz, Rio de Janeiro, Brazil.
[3]Research Centre of Pathology and Veterinary Histology. Department of Veterinary Medicine, Federal University of Juiz de Fora, Juiz de Fora, Brazil.
[4]Cell Biology Laboratory, Biology Department, Federal University of Juiz de Fora, Brazil.

Malaria is a systemic inflammatory disease that can cause severe organ dysfunction, including acute respiratory distress syndrome (ARDS) and intestinal barrier impairment. Although ARDS has been extensively studied in experimental malaria models, intestinal inflammation and structural alterations are increasingly recognized as contributors to disease severity. Importantly, distinct *Plasmodium* strains display divergent pathogenic profiles, which may influence the efficacy of immunomodulatory interventions. Our group previously demonstrated that DHA-rich fish oil supplementation attenuates lung inflammation and disease severity in mice infected with *Plasmodium berghei* ANKA, a strain associated with intense inflammation and endothelial adhesion. However, whether similar effects occur during infection with *Pb.* NK65, which induces systemic inflammation without prominent endothelial sequestration, remains unclear. Given the lack of specific therapies for malaria-associated inflammatory complications, this study assessed the effects of DHA-rich omega-3 supplementation on pulmonary and intestinal injury during *Pb.* NK65 infection. Female C57BL/6 mice were orally supplemented with 3 g/kg of DHA-rich omega-3 for 15 days before infection and throughout the course of infection. Lung injury and inflammation were assessed by histopathology, lung edema ratio, alveolar–capillary permeability, cytokine profile, bronchoalveolar lavage fluid analysis, and flow cytometry. Intestinal injury was evaluated by measuring intestinal length and permeability. DHA-rich omega-3 supplementation did not significantly alter lung injury or pulmonary inflammation in PbNK65-infected mice. In contrast, it prevented infection-induced intestinal shortening and showed a non-significant trend toward reduced intestinal permeability. These results indicate that the immunomodulatory effects of DHA-rich omega-3 supplementation are organ-specific and dependent on parasite strain–specific pathogenic mechanisms.