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# Malaria and matrix metalloproteinases: New perspectives for adjuvant therapy

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Besides primary therapy including quinine and artesunate, effective against Plasmodium parasite, several new adjunctive therapies to reduce clinical symptoms and mortality of severe malaria have undergone recent trials. However, results have been disappointing, with albumin being so far the only promising adjuvant therapy. Thus, research for new targets aimed at defining new affordable treatment appears urgent. Recently, convincing evidence on the involvement of human Matrix Metalloproteinases (MMP) in malaria pathogenesis emerged. In vivo, enhanced mRNA/protein levels of a large kaleidoscope of MMP, including MMP-1, -2, -7, and -9, were described in human or murine models of cerebral malaria (CM). In vitro, a tight relationship between human MMP-9 and haemozoin (HZ, malarial pigment), a Plasmodium parasite product resulting from haemoglobin digestion, was demonstrated by my group. In human monocytes and endothelium, HZ enhanced expression, release and activity of MMP-9 and several MMP-9-related molecules, including cytokines (TNFalpha, IL-1beta), chemokines (MIP-1alpha, IL-8), and enzymes/inhibitors from gelatinase granules (lysozyme, tissue inhibitors of metalloproteinases/TIMP). Enhancement of MMP-9 and related molecules appeared dependent on HZ lipid moiety, and a major role for 15-hydroxyeicosatetraenoic acid (15-HETE), a HZ lipoperoxidation derivative, was suggested. Additionally, p38MAPK and NF-kappaB signalling activation was required. Since MMP play a major role disrupting endothelial tight junctions and sub-endothelial basement membrane, along with modulating pro-inflammatory activity, they could be crucial for eliciting blood-brain barrier permeability and inflammation during CM. Therefore, further studies on MMP involvement in malaria will help to clarify mechanisms underlying severe malaria etiopathogenesis, in order to design new targeted adjuvant therapies.

## Biography

Mauro Prato graduated in Medical Biotechnology in 2001 and completed his PhD in Biochemistry and Cellular Biotechnology in 2005 at the University of Torino, Italy, where he has been working as an Adjunct Professor of Biochemistry since 2008. His main research interests cover the investigation of the involvement of human matrix metalloproteinases in malaria, a new research field that he successfully pioneered. He has published 19 papers in peer-reviewed journals, 3 chapters in international books and more than 40 communications in well-established conferences. He is serving as an editorial board member of the Journal of Bacteriology and Parasitology (OMICS Group).

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