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Human and Mosquito Lysozymes in Malaria: Old Molecules for New Approaches towards Diagnosis, Therapy and Vector Control

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As a consequence of the global eradication program recently launched by charity foundations [1], World Health Organization (WHO) officially registered in 2010 a decline in estimated malaria cases and deaths, with 655.000 deaths counted among more than 200 million clinical cases worldwide, of which 91% due to Plasmodium *falciparum* [2]. Nevertheless, malaria remains so far an alarming emergency in developing countries, as the vast majority of cases occur in Africa (81%) and South-East Asia (13%) [2]. Thus, it appears still urgent to identify any parasite or host molecules which might serve as new affordable markers for early diagnosis of malaria complications [3], or as new targets for primary and adjuvant therapy [4] along with vector control [5].

In this context, lysozymes could be good candidate molecules. These enzymes are antibacterial proteins defined by their ability to hydrolyze β-1,4-glycosidic linkage between N-acetylmuramic acid and N-acetylglucosamine of peptidoglycan in the cell wall of bacteria (muramidase activity) [6]. Three major distinct lysozyme types showing high level of homology have been identified in the animal kingdom: c-type (chicken-type), present in several members of the Chordata, including humans, and different classes of the Arthropoda, including mosquitoes; g-type (goose-type), in few members of the Chordata and in some bivalve mollusks; and i-type (invertebrate-type), in the invertebrates [6]. Human lysozyme was the first mammalian lysozyme to be sequenced and served as a model protein for a wide variety of studies [7]. Interestingly, in the recent years the involvement of both human and mosquito lysozymes in malaria has been observed independently by several research groups.

Natural haemozoin (nHZ, malarial pigment), a lipid-bound ferriprotoporphyrin IX crystal produced by *Plasmodium* parasites after haemoglobin catabolism, was shown to promote *in vitro* the early release of human lysozyme from adherent monocytes [8]. Such an effect was mediated by the increased production of three pro-inflammatory molecules (TNFα, IL-1β and MIP-1α/CCL3), and was dependent on activation of p38 mitogen-associated protein kinase (MAPK) and NF-κB pathways [9]. Moreover, 15-hydroxyeicosatetraenoic acid (15-HETE), a major component of the lipid moiety of nHZ, was identified very recently as the molecule responsible for the most part of these effects [10].

Consistently, the plasma levels of lysozyme [11] and the number of nHZ-containing leukocytes in the peripheral blood of *P. falciparum*-infected patients [12-14] correlated well with parasitaemia degree or disease severity. On the other hand, the mosquito homologue of human lysozyme was shown to bind to oocysts of *Plasmodium berghei* and *falciparum* in *Anopheles gambiae*, *stephensi*, and *dirus*, and therefore facilitate their development within the vector [15,16].

These findings suggest that human lysozyme may represent a likely marker for early diagnosis of complicated malaria as well as a putative target for adjuvant therapy, whereas mosquito lysozyme could be addressed as a new target for insecticides to be used in vector control. Although further investigation is certainly required, it is intriguingly to speculate that old well-known enzymes such as lysozymes might reveal themselves as very relevant molecules to be targeted by innovative and cost-effective tools to fight malaria.

References

1. Khadjavi A, Giribaldi G, Prato M (2010) From control to eradication of malaria: the end of being stuck in second gear? Asian Pac J Trop Med 3: 412-420.
2. WHO (2011) World Malaria Report 2011.
3. Lucchi NW, Jain V, Wilson NO, Singh N, Udhayakumar V, et al. (2011) Potential serological biomarkers of cerebral malaria. Dis Markers 31: 327-335.
4. Prato M, Giribaldi G (2012) New Perspectives for Adjuvant Therapy in Severe Malaria. J Bacteriol Parasitol 3: 1-2.
5. Prato M, Khadjavi A, Mandili G, Minero VG, Giribaldi G (2012) Insecticides as Strategic Weapons for Malaria Vector Control. In: Perveen F, editor. Insecticides - Advances in Integrated Pest Management: InTech, 91-114.
6. Callewaert L, Michiels CW (2010) Lysozymes in the animal kingdom. J Biosci 35: 127-160.
7. Peters CW, Kruse U, Pollwein R, Grzeschik KH, Sippel AE (1989) The human lysozyme gene. Sequence organization and chromosomal localization. Eur J Biochem 182: 507-516.
8. Prato M, Giribaldi G, Arese P (2009) Hemozoin triggers tumor necrosis factor alpha-mediated release of lysozyme by human adherent monocytes: new evidences on leukocyte degranulation in *P. falciparum malaria*. Asian Pac J Trop Med 2: 35-40.
9. Polimeni M, Valente E, Aldieri E, Khadjavi A, Giribaldi G, et al. (2012) Haemozoin induces early cytokine-mediated lysozyme release from human monocytes through p38 MAPK- and NF-kappaB-dependent mechanisms. PLoS One 7: e39497.
10. Polimeni M, Valente E, Aldieri E, Khadjavi A, Giribaldi G, et al. (2012) Role of 15-HETE in haemozoin-induced lysozyme release from human adherent monocytes. Biofactors, in press.
11. Mohamed AO, Elbashir MI, Ibrahim G, Ismail M, Venge P (1996) Neutrophil leucocyte activation in severe malaria. Trans R Soc Trop Med Hyg 90: 277.
12. Amodu OK, Adeyemo AA, Olumese PE, Gbadegesin RA (1998) Intraleucocytic malaria pigment and clinical severity of malaria in children. Trans R Soc Trop Med Hyg 92: 54-56.
13. Nguyen PH, Day N, Pram TD, Ferguson DJ, White NJ (1995) Intraleucocytic malaria pigment and prognosis in severe malaria. Trans R Soc Trop Med Hyg 89: 200-204.

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14. Were T, Davenport GC, Yamo EO, Hittner JB, Awandare GA, et al. (2009) Naturally acquired hemozoin by monocytes promotes suppression of RANTES in children with malarial anemia through an IL-10-dependent mechanism. Microbes Infect 11: 811-819.

15. Kajla MK, Shi L, Li B, Luckhart S, Li J, Paskewitz SM (2011) A new role for an old antimicrobial: lysozyme c-1 can function to protect malaria parasites in Anopheles mosquitoes. PLoS One 6: e19649.

16. Lapcharoen P, Komalamisra N, Rongsriyam Y, Wangsuphachart V, Dekumyoy P, et al. (2012) Investigations on the role of a lysozyme from the malaria vector Anopheles dirus during malaria parasite development. Dev Comp Immunol 36: 104-111.