

This is the author's manuscript



## AperTO - Archivio Istituzionale Open Access dell'Università di Torino

## The function of P450 enzymes in malaria and other vector-borne infectious diseases

Original Citation:	
Availability:	
This version is available http://hdl.handle.net/2318/2040430	since 2024-12-20T12:22:07Z
Terms of use:	
Open Access	
Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.	

(Article begins on next page)

## The function of P450 enzymes in malaria and other vector-borne infectious diseases

## Oleksii Skorokhod, Ekaterina Vostokova, Gianfranco Gilardi

Department of Life Sciences and Systems Biology, University of Torino, via Accademia Albertina, 13, Torino, Italy. <u>olexii.skorokhod@unito.it</u>

Vector-borne infectious diseases such as malaria, Zika virus disease, dengue fever, yellow fever disease, West Nile virus disease, Japanese encephalitis, leishmaniasis, and others continue to pose a significant global health concern. Malaria is standing out as the foremost threat, particularly affecting pediatric populations and posing life-threatening risks. Parasites, bacteria, and viruses transmitted by vectors contribute to a substantial burden on public health and incur significant economic costs. The vector control, with consideration for ecological and biodiversity conservation, has the potential to prevent most vector-borne diseases. While chemical control using pesticides and insecticides is commonly utilized as a prevention measure, the escalating resistance to insecticides poses a significant challenge in vector control efforts. Metabolic resistance, primarily through insect enzyme systems such as CYP P450 enzymes (e.g. Anopheles gambiae CYP4, 6, 9, 12, 314 and 325 families)<sup>1</sup>, presents a major obstacle. These enzymes are crucial for metabolizing insecticides, leading to resistance. The identification and utilization of natural inhibitors or blockers specific to vector P450 enzymes, alongside conventional pesticides, offer a promising avenue for environmentally friendly insecticide practices. The exploitation of host CYP enzymes, which possess detoxification properties and are involved in immune responses and other biological processes (e.g. CYP1, 2, 3 and 4 families)<sup>2,3</sup>, offers an additional strategy for combating vector-borne diseases.

Here, we summarize the known data on P450 enzymes from all contributors to vector-borne infections, including pathogens, vectors, and hosts, exploring the potential involvement of CYPs in disease progression<sup>4</sup>.

- 1. Nauen R, Bass C, Feyereisen R, Vontas J. The Role of Cytochrome P450s in Insect Toxicology and Resistance. Annu Rev Entomol. 2022;67:105-124. doi: 10.1146/annurev-ento-070621-061328
- 2. Skorokhod O, Triglione V, Barrera V, Di Nardo G, Valente E, Ulliers D, Schwarzer E, Gilardi G. Posttranslational Modification of Human Cytochrome CYP4F11 by 4-Hydroxynonenal Impairs ω-Hydroxylation in Malaria Pigment Hemozoin-Fed Monocytes: The Role in Malaria Immunosuppression. Int J Mol Sci. 2023;24(12):10232. doi: 10.3390/ijms241210232
- 3. Carvalho RS, Friedrich K, De-Oliveira AC, Suarez-Kurtz G, Paumgartten FJ. Malaria downmodulates mRNA expression and catalytic activities of CYP1A2, 2E1 and 3A11 in mouse liver. Eur J Pharmacol. 2009;616(1-3):265-269. https://doi.org/10.1016/j.ejphar.2009.05.030
- 4. Skorokhod O, Vostokova E, Gilardi G. The role of P450 enzymes in malaria and other vector-borne infectious diseases. Biofactors. 2024;50(1):16-32. doi: 10.1002/biof.1996