



MALARIA

CU characterization:

CU name:

Malaria

Scientific area acronym:

BM

Duration:

Semiannual

Working hours:

78

Contact hours:

22

ECTS:

3

Observations:

Mandatory CU

Teacher in charge and respective teaching load in the CU:

Fátima Nogueira - 6 hours

Other teachers and respective teaching load in the CU:

Ana Paula Arez - 3 hours

Carla Sousa - 3 hours

Henrique Silveira - 5 hours

João Pinto - 3 hours

Luís Varandas - 1 hours

Intended learning outcomes (knowledge, skills and competences to be developed by the students):

After this unit, students should be able to:

1. Know and perform some basic techniques for the study of malaria in the laboratory, following the life cycle of the parasite in the vertebrate host and in the vector.
2. To deepen the knowledge on the biology of the parasite's life cycle and parasite's the relationship with the host vertebrate and mosquito vector.



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Intended learning outcomes (knowledge, skills and competences to be developed by the students): (continuation)

3. Recognize the different areas of interest in the study of malaria and its relevance.
4. Understand, analyze and evaluate the applicability of some methodologies for the study and control of malaria, through interaction with IHMT researchers, guests outside the institution and autonomous research.

Syllabus:

- I. Control vs eradication. Control tools: parasite, vector, community education. Obstacles to sustainability.
- II. Systematics of genus *Anopheles*. Life cycle and external morphology. Bio-ecology and behaviour aspects with medical importance
- III. Biodiversity of genus *Anopheles*. Reproductive and digestive physiology. Interaction vector/parasite during esporogony
- IV. Dissection of female anophelines, wet-mount preparations, midguts observation, oocyst count
- V. Resistance to antimalarials: Mechanisms of resistance, molecular markers; Geographic distribution
- VI. Selection and spread of resistant parasites; Concepts of treatment failure and parasite resistance
- VII. Monitoring of resistance to antimalarial drugs (methods in vivo and in vitro)
- VIII. Determination of the dynamics of parasitaemia in two species of murine plasmodia. Determination of parasitemia, spleen and liver index

Teaching methodologies (including assessment):

Direct teaching by the expository method (theoretical classes) and indirect teaching by guided discovery learning and solving problems in a simulation and laboratory environment (theoretical-practical).

The final classification of the course: written test and attendance of at least 2/3 of the practical classes and theoretical-practical.

References for consultation / mandatory existence:

- Das D, Dahal P, Dhorda M, Citarella BW, Kennon K, Stepniwska K, Felger I, Chappuis F, Guerin PJ. A Systematic Literature Review of Microscopy Methods Reported in Malaria Clinical Trials. *Am J Trop Med Hyg.* 2020 Dec 21;104(3):83641. doi: 10.4269/ajtmh.20-1219. Epub ahead of print. PMID: 33350371; PMCID: PMC7941839.
- Dhorda, M., Ba, E., Kevin Baird, J. et al. Towards harmonization of microscopy methods for malaria clinical research studies. *Malar J* 19, 324 (2020). <https://doi.org/10.1186/s12936-020-03352-z>



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References for consultation / mandatory existence: (continuation)

- Global Malaria Programme. <https://www.who.int/teams/global-malaria-programme/case-management/diagnosis/microscopy>
- Machado et al, (2016) Whole-Cell SYBR Green I Assay for Antimalarial Activity Assessment. *Ann Clin Med Microbio* 2(1): 1010.
- Johnson, et al, 2007; DOI: 10.1128/AAC.01607-06.
- Arieu et al, 2014; DOI: 10.1038/nature12876
- Witkowski et al, 2017; DOI: 10.1016/S1473-3099(16)30415-7 Leang et al, 2015; DOI: 10.1128/AAC.00835-15
- WHO Global database on antimalarial drug efficacy and resistance (https://www.who.int/malaria/areas/drug_resistance/drug_efficacy_database/en/ ; Last update: 24 January 2020).
- WHO Drug resistance and response (https://www.who.int/malaria/areas/drug_resistance/en/).
- SOP - Ring-stage Survival Assays (RSA) to evaluate the in-vitro and ex-vivo susceptibility of *Plasmodium falciparum* to artemisinins (<https://www.wwarn.org/sites/default/files/attachments/procedures/INV10-Standard-Operating-Procedure-Ring-Stage-Survival-Assays-v1.2.pdf>).
- SOP - Piperaquine Survival Assays (PSA) to evaluate the in-vitro and ex-vivo susceptibility of *Plasmodium falciparum* to piperaquine (<https://www.wwarn.org/tools-resources/procedures/piperaquine-survival-assays-psa-evaluate-vitro-and-ex-vivo-susceptibility>).
- SOP - Quantitative PCR to assess *P. falciparum* plasmepsin 2 gene copy number v1.0 (http://samara.needsolutions.fr/documents/site/sop_pfplasmepsin_v1_may2016_1_pdf). SOP - PCR-Sequencing for genotyping candidate *P. falciparum* artemisinin resistance SNPs PF3D7_1343700 Kelch protein propeller domain v1.0 (http://samara.needsolutions.fr/documents/site/sop_sequencing_kelch_protein_propeller_v1_2013.pdf).
- Cirimotich CM, Dong Y, Garver LS, Sim S, Dimopoulos G 2010. Mosquito immune defenses against *Plasmodium* infection. *Developmental and comparative immunology*, 34: 387-95.
- Sangare I, Dabire R, Yameogo B, Da DF, Michalakis Y, Cohuet A 2014. Stress dependent infection cost of the human malaria agent *Plasmodium falciparum* on its natural vector *Anopheles coluzzii*. *Infection, genetics and evolution pii: S1567-1348(14)00128-2*.
- Yassine H, Osta MA 2010. *Anopheles gambiae* innate immunity. *Cellular microbiology*, 12: 1-9.
- Lamb TJ, Brown DE, Potocnik AJ, Langhorne J. (2006). Insights into the immunopathogenesis of malaria using mouse models. *Expert Rev Mol Med*. 8:1-22.



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References for consultation / mandatory existence: (continuation)

- Longley R, Smith C, Fortin A, Berghout J, McMorran B, Burgio G, Foote S, Gros P. (2011). Host resistance to malaria: using mouse models to explore the host response. *Mamm Genome*. 22:32-42.
- Ayi K, Min-Oo G, Serghides L, Crockett M, Kirby-Allen M, Quirt I, Gros P, Kain KC 2008. Pyruvate kinase deficiency and malaria. *The New England Journal of Medicine*, 358: 1805-1810
- Duffy PE, Fried M 2006. Red blood cells that do and red blood cells that don't: how to resist a persistent parasite. *Trends in Parasitology*, 22: 99-101
- Lelliott PM, Huang HM, Dixon MW, Namvar A, Blanch AJ, Rajagopal V, Tilley L, Coban C, McMorran BJ, Foote SJ, Burgio G 2017. Erythrocyte β spectrin can be genetically targeted to protect mice from malaria. *Blood Advances*, 1: 2624-2636.
- Luzzatto L, Bienzle U 1979. The malaria/G6PD hypothesis. *The Lancet*, 1: 1183-1184.
- Machado P, Manco L, Gomes C, Mendes C, Fernandes N, Salomé G, Siteo L, Chibute S, Langa J, Ribeiro L, Miranda J, Cano J, Pinto J, Amorim A, do Rosário VE, Arez AP 2012. Pyruvate kinase deficiency in sub-Saharan Africa: identification of a highly frequent missense mutation (G829A;Glu277Lys) and association with malaria. *PLoS ONE*, 7: e47071
- Alonso P. et al. (2011). A Research agenda to underpin malaria eradication. *PLoS Medicine*, 8: e1000406.
- Beales P.F. & Gilles H.M (2002). Rationale and technique of malaria control. In: *Essential Malariology*. Warrel D.A. & Gilles H.M. & (Eds.), 4th Ed. Edward Arnold, Kent: 107-190.
- Mendis K et al. 2009. From malaria control to eradication: The WHO perspective. *Tropical Medicine and International Health*, 14: 802-809.
- Nájera J.A. et al. (2011). Some lessons for the future from the Global Malaria Eradication Programme (1955-1969). *PLoS Medicine* 8: e1000412.
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- WHO (1998). Test procedures for insecticide resistance monitoring in malaria vectors, bio-efficacy and persistence of insecticides on treated surfaces. WHO/CDS/CPC/MAL/98.12. WHO (2015).
- Global technical strategy for malaria 2016-2030. Global Malaria Programme, World Health Organization, Geneva. 29pp
- WHO (2015). World malaria report, 2015. Global Malaria Programme, World Health Organization, Geneva. 243pp.
- WHO (2016). Test procedures for insecticide resistance monitoring in malaria vector mosquitoes (2nd Edition). Global Malaria Programme, World Health Organization, Geneva. 48pp.