GENETICS OF DRUG RESISTANCE IN PARASITOLOGY

CU characterization:

CU name:
Genetics of drug resistance in parasitology

Scientific area acronym:
PA

Duration:
Semestral

Working hours:
56

Contact hours:
31

ECTS:
3

Observations:
Opcional CU

Teacher in charge and respective teaching load in the CU:
Fátima Nogueira - 9 hours

Other teachers and respective teaching load in the CU:
Sandra Antunes – 5.4 hours
Ana Domingos – 5.4 hours
Carla Sousa – 4.3 hours
João Pinto – 3.2 hours
Sofia Cortes – 3.2 hours
Olga Matos – 4.3 hours
Isabel Maurício – 5.4 hours
Manuela Calado – 5.4 hours
Docentes convidados – 9 hours

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

Through interaction with IHMT researchers, guests from externals to the institution and autonomous research, at the end of the curricular unit of Genetics of Drug Resistance in Parasitology, students should:

1. Know notions of antiparasitic resistance genetics, phenotypic adaptation to the environment and the challenges in defining resistance;
2. Recognize different areas of interest in the study of the genetics of antiparasitic resistance and its relevance;
3. Define the main resistance mechanisms and their molecular basis in the context of medical parasitology;
4. Be aware of notions of pharmacogenetics and drug resistance in parasitology;
5. Understand, analyze and evaluate the applicability of some methodologies and tools for the identification of genetic markers of resistance and their applicability in the monitoring, epidemiology and control of parasites with an impact on human health.

Syllabus:

I. Introduction to the concept of drug resistance and parasitic infection. Notion of resistance genomics. Notion of phenotypic adaptation to the environment, resistance to antiparasitics, transmembrane transport of xenobiotics/drugs in eukaryotes.

II. Enzymes of the oxidative stress response system and efflux pumps in response to drugs, using the malaria parasite *Plasmodium falciparum* as an example.

III. Mechanisms of resistance to insecticides. Define the main resistance mechanisms and their molecular basis. Concept of resistance vs tolerance. Types of resistance (physiological, behavioral).

IV. Monitoring the occurrence of drug resistance: example *Pneumocystis jirovecii*.

V. Epidemiological importance of resistance to drugs currently used in the treatment of leishmaniasis.

VI. Resistance to anthelmintics. Difficulties in defining resistance. Genomics of resistance in nematodes, trematodes and cestodes. Individual and community consequences. *Biomphalaria* spp and *Schistosoma mansoni*: Resistant or susceptible. Host specificity and infection.

VII. Basic concepts of tools - metabolomics, proteomics and transcriptomics.

VIII. Post-genomic tools for studying drug resistance: Experimental Design; Bioinformatics; Examples of applications.

IX. Pharmacogenetics and drug-drug interactions. The notions of pharmacogenetics, pharmacogenomics will be addressed. Drug metabolization phenotypes their causes and impacts on drug resistance selection. Some examples in parasitology.

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Teaching methodologies (including assessment):

Teaching of this CU is based on the lecturing method, translated into theoretical classes; In the demonstrative method, in a practical laboratory class; In the active and interrogative methods applied in theoretical-practical classes and in a seminar class. There will also be tutorial sessions to support the autonomous study and preparation of the seminars.

Student evaluation is based on the students' performance in a written multiple-choice test with 30 questions (0.57 values each) and another three short answer questions (one 0.9 points and the other two 1 value each). The approval in the UC implies: i) the accomplishment of a minimum attendance of 75% of the classes and the achievement of a minimum final classification of 10 values (maximum 20 values) in a written test.

References for consultation / mandatory existence:

- O'Neill PM, Barton VE, Ward SA. The molecular mechanism of action of artemisinin--the debate continues. Molecules. 2010 Mar 12;15(3):1705-21.
- Witkowski B, Berry A, Benoit-Vical F. Resistance to antimalarial compounds: methods and applications. Drug Resist Updat. 2009 Feb-Apr;12(1-2):42-50. doi:
- O'Brien C, Henrich PP, Passi N, Fidock DA. Recent clinical and molecular insights into emerging artemisinin resistance in Plasmodium falciparum. Curr Opin Infect Dis. 2011 Dec;24(6):570-7.
- Sá JM, Chong JL, Wellems TE. Malaria drug resistance: new observations and developments. Essays Biochem. 2011;51:137-60.
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- Hemingway J, Hawkes NJ, McCarroll L, Ranson H. 2004. The molecular basis of insecticide resistance in mosquitoes. *Insect Biochem Mol Biol* 34: 653-665
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- Exploiting Knowledge on *Leishmania* Drug Resistance to Support the Quest for New DrugsAya Hefnawy, Maya Berg, Jean-Claude Dujardin, Géraldine De Muylder. Trends in Parasitology, **2017**. 33: 162-174.
- *Leishmania* antimony resistance: what we know what we can learn from the field. Aït-Oudhia K, Gazanion E, Vergnes B, Oury B, Sereno D. Parasitol Res. **2011**. 109:1225-32

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References for consultation / mandatory existence: (continuation)

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- Lopez-Arias et al. 2014. Reduced Efficacy of Commercial Acaricides Against Populations of Resistant Cattle Tick *Rhipicephalus microplus* from Two Municipalities of Antioquia, Colombia. Environmental Health Insights. 8:71.
- Abdel-Hamid, A.H.Z, Rawi, S.M. & Arafa, A. F, 2006. Identification of genetic marker associated with the resistance to *Schistosoma mansoni* infection using random polymorphic DNA analysis. *Mem. Inst. Oswaldo Cruz*, **101** (8): 863-868.
- Lockyer, A.E, Jones, C.S, Noble, L.R. & Rollinson, D, 2004. Trematodes and snails: an intimate association. *Canadian J. Zool,* **82** (2): 251
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- Madeira de Carvalho, L.M. (2008) Importância da resistência aos anti-helmínticos a propósito da "Roundtable Nematode Resistance, Atenas, 11-13 de Maio de 2007". Acta Parasitológica Portuguesa, 15 (1/2): 79-91.
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