PhD Advanced Course

Title: Redox signaling and redox systems in Health and Disease: Implications for drug design and development.

Date: September 13th to 17th 2021

ECTS: 6

Classes: 22.5 hours

Course Coordinator: Vasco Branco

Teaching staff: Vasco Branco (FFUL), Cristina Carvalho (FFUL), Nuno Oliveira (FFUL) Susana Solá (FFUL), Andreia Carvalho (FFUL), Lucia Coppo (Karolinska Institute); Other External (national and international) lecturers to be invited.

Short Introduction

Redox signaling achieved by reactive oxygen species (ROS) is a key aspect of signal transduction in various cellular processes such as cell death, differentiation and inflammation.

However, the line separating redox signaling from oxidative stress is a thin one and redox homeostasis is reliant on the action of redox active systems. These systems are complex arrays of enzymes controlling ROS levels but also the oxidation-reduction cycle of critical protein residues (e.g. cysteines) that enable signal transduction.

Disruption of redox signaling has been implicated in the etiology of several pathologies including cancer and neurodegenerative diseases. Moreover, redox enzymes have very reactive residues (cysteines and selenocysteines) and are, therefore, candidate targets for inhibition by electrophilic compounds, creating opportunities for therapeutic strategies. This Advanced Course will approach these aspects in detail which are of widespread interest for many PhD candidates in Pharmacy.

Goals and Learning Outcomes

The overall Goal of this course is to provide PhD students with the knowledge on oxidative stress and redox signaling to enable the understanding of related health and disease outcomes and to create opportunities for the design and development of novel therapeutic strategies.

Specifically, students are expected to:

- Acknowledge the biological significance of redox reactions;
- Understand the process of oxidative species formation and distinguish between redox signaling and oxidative stress;
- Recognize existing therapeutic opportunities to modulate the activity of redox elements;
- Comprehend the functional redundancy and backups between redox elements and the implications for disease progression and treatment;
- Conceive a research plan using acquired knowledge to address a relevant issue in their PhD work;

Assessment

Students will be required to conceive a mini project showing how they could integrate ROS and redox signaling related topics in their PhD work.

Prior to submission students will present and discuss their projects with their peers and teaching staff to receive feedback on their proposal. The idea is to foster student learning.

Following project submission, these will be randomly distributed by other students for anonymous peer-review. The reviewer should identify the strong points of the proposal and highlight parts where there is room for improvement. The review will be sent back to the author which may or may not include the suggestions of the reviewer. In either case a response to reviewer comments has to be submitted with the final version of the proposal.

The final evaluation will encompass assessment of the written proposal including response to reviewers (70%) and the pertinence of the written feedback given to colleagues during the peer review stage (30%).

Programme

TOPIC A – Reactive oxygen species and oxidative stress

Lecture A1 – Oxidative stress and oxidative species;

Lecture A2 – ROS as signaling molecules in physiology;

Flipped classroom A: methods to evaluate ROS and oxidative stress

TOPIC B – Antioxidant molecules, Redox enzymes and Redox systems

Lecture B1 – Redox active systems: thioredoxin and glutathione

Lecture B2 – Selenoproteins, important targets in drug design

Flipped Classroom B – Natural and custom-design inhibitors, emulators and modulators of redox elements.

TOPIC C – Redox signaling and cancer

Lecture C1 – Redox regulation in cancer cells

Lecture C2 – Redox systems and therapy resistance – case study (glioblastoma)

Flipped classroom C: MAPK cascades: major pathways of redox signal transduction.

TOPIC D – Oxidative stress and neurodegenerative diseases

Lecture D1 – Redox regulation in the CNS and neurodevelopment

Lecture D2 – Oxidative modifications in neurodegenerative diseases

Flipped classroom D: Redox signaling in glia cells

Preliminary timetable

	Monday (13/09/21)	Tuesday (14/09/21)	Wednesday (15/09/21)	Thursday (16/09/21)	Friday (17/09/21)
09:00 -10:30	LA1 – Oxidative stress and oxidative species: major concepts	LB1 – Redox active systems: thioredoxin and glutathione	LC1 – Redox regulation in cancer cells	LD1 – Redox regulation in the CNS: implications for neurodevelopment	Student's Project Presentation and Discussion
10:30-11:00	Coffee Break	Coffee Break	Coffee Break	Coffee Break	
11:00-12:30	LA2 - ROS as signaling molecules in physiology	LB2 – Selenoproteins, important targets in drug design	LC2 – Redox systems as a factor in therapy resistance	LD2 – Oxidative modifications in neurodegenerative diseases	
12:30-11:00	Lunch	Lunch	Lunch	Lunch	
14:00-16:00	FC - Methods to Evaluate ROS and Oxidative Stress	FC - inhibitors, emulators and modulators of redox elements	FC - MAPK Cascades: Major Pathways of Redox Signal Transduction	FC - Redox Signaling in Glia Cells	

L – Lecture; FC- Flipped Classroom; TOPIC A; TOPIC B; TOPIC C; TOPIC D