REDOX BIOLOGY IN HEALTH AND DISEASE

Monday August 29th to Friday September 20th
Unidad de Posgrado, UNAM
Instituto de Investigaciones Biomedicas, UNAM

INSTRUCTORS

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AUDIENCE

This course is designed for 20-25 graduate students (Ph.D. or masters) to be enrolled. It is expected that students interested will have a research area/project somehow linked to Redox Biology. Students should have a general background on cell/molecular biology, biochemistry, physiology. It is not necessarily to be an expert in all the topics to be discussed. A basic background on oxidative stress and redox biology, or experience in this area is preferable as this course will provide an advanced overview of the subject. This course is registered as part of the **Posgrado en Ciencias Biológicas, Biología Experimental y Biomedicina**, but can be attended by students from other Graduate Programs and Institutions. This course involves some lectures and presentations in English by the students.

COURSE OBJECTIVES

1. Provide a broad and advanced overview of redox-based biochemical processes (including energy generation, metabolism, oxygen transfer, cell signaling, gene regulation, protein modification, and enzyme catalysis) with an emphasis on recent progress.
2. Develop depth of knowledge regarding redox-active species and radicals, and antioxidant molecules and enzymes, and the roles for redox cofactors in structure and function of cellular macromolecules.
3. Overview the biochemical, molecular and genetic basis of redox-related diseases and therapeutics.
4. Introduce commonly utilized methods for redox biology research.
5. Integrate redox-related research topics and questions through the discussion or recent literature.

COURSE MATERIALS

1. Redox Biochemistry (by R Banerjee, Published by Wiley) Free Radical Biology and Medicine (by B Halliwell and JMC Gutteridge, Published by Oxford)
2. Redox Signaling and Regulation in Biology and Medicine (by CS Jacob and PG Winyard, Published by Wiley)
3. Oxidative Stress and Redox Regulation (by U Jacob and D Reichmann, Published by Springer)
4. Molecular Basis of Oxidative Stress (by FA Villamena, Published by Wiley)
5. Reference books: Any medium level biochemistry textbook (e.g., D Voet and JG Voet, 3rd edition; Lehninger, 5th edition)
6. Redox Biology Center educational resource: http://genomics.unl.edu/RBC_EDU/
7. A Dropbox link to articles and course materials will be provided. https://www.dropbox.com/sh/l9l7l79idh0272n/AABV_njCTyeTJrHJQjF8PtPRa?dl=0

COURSE EVALUATION (100 POINTS = 10 GRADE)

(1) One written multiple-choice final exam to be held on September 16th (50 points)

(2) One lead paper/topic discussion (25 points):

- Everyone should read ALL the papers before coming to class including additional commentaries and supplementary information and be ready to actively participate in the discussion.
- Papers will be reviewed in 1 hr, and the discussion will be led by a student (each student leads one paper).
- The student that leads the discussion will present a review on background information and provide an introduction to the area of research (no more than 15 min) prior to starting the discussion of the paper. Paper assignments will be done at the initial meeting on August 8 (see calendar below). The leading student should prepare no more and no less than 9 full Figures (from the main manuscript or Supplementary Data) in a Power Point Presentation so that 9 students present the data individually. (the student is welcomed to select from the supplementary data those figures that he/she considers more important for the discussion).
- Throughout and at the end of the paper discussion, the leading student has to integrate the data published in other relevant papers with the manuscript revised, and this will also include:
  - Criticize data
  - Emphasize significance and impact of presented results.
  - Provide future research directions

(3) Class participation (25 points)

- Attendance of 80% required to pass the course
- Participation in the discussion of papers. Students will individually describe the data presented in the paper figures.

IMPORTANT: You must understand that this course requires a bit of reading and participation. The complete list of papers is given below so plan to read and prepare the papers thoroughly ahead of time for their active discussion or presentation, particularly when you have to lead the paper discussion. It is expected that you will spend August (before the course starts) working on the papers, taking and notes, so that the afternoon before the class you just review your notes.

Discuss this in detail with your advisor. **Two papers will be discussed per day. If your plan to read them the night before, it is very unlikely that you will be ready to discuss them.** Usually, a full afternoon should be dedicated per paper. "I did not read the papers" is not an excuse!!! Attend the initial Meeting (August 8th) to discuss class expectations, grading and paper assignations, or contact the instructors. All papers will be provided in a dropbox link, but you should be able to find them online and if not you should take initiative and contact the authors to provide you with a pdf copy that would include all supplementary data.

Certificates of Attendance will be given at the end of the course for all attendees (auditing or enrolled students) as long as they have attended the course (80%), participated in the class and discussion of manuscripts and obtained a pass grade in the exam (60% or correct answers). Only enrolled students will be required to lead and present a paper. Final grade will be given no later than one week after the final exam.

COURSE CONTENT:

Introduction to the Course *(Dr. Franco)*
Course overview

Redox-based biochemical process *(Dr. Khalimonchuk)*
Evolution and redox-based biochemical reactions, Reduction/Oxidation Reactions, Oxygen metabolism & Mitochondria, Redox enzymes, Protein folding-disulfide bond, Cofactors, Fe-S clusters, Redox-active Inorganic elements

Oxidative Stress and Antioxidant systems *(Dr. Gonsebatt and Franco)*
Free Radicals, Reactive Species of Oxygen and Nitrogen, Glutathione, Ascorbate, Superoxide dismutase, Catalase, Protein Oxidation and Turnover, Lipid oxidation, Oxidative DNA-damage and Repair

Redox Homeostasis and Signaling *(Dr. Franco)*
Signal transduction pathways regulated by Hydrogen Peroxide, Nitric Oxide, Hydrogen Sulfide. Thiol-based oxidoreductases and Oxidative Post-translational Modifications.

Redox-Related Diseases & Therapeutics *(Dr. Franco)*
Host Defense, Cancer, Neurodegeneration, Diabetes, Aging and others. Programmed Cell Death Pathways. Combating disease – Research progress, Success and challenge in the clinics

Methods in Redox Biology *(Dr. Franco)*
Detection of reactive oxygen and nitrogen species. Use and determination of antioxidants. Redox Proteomics, Redox Metabolism and Redox Sensors. Determination of Redox Potential

SCHEDULE AND LOCATION

This course will be held at the Unidad de Posgrado of the Universidad Nacional Autónoma de México. Circuito de Posgrado S/N, Coyoacán, Cd. Universitaria, 04510. Ciudad de México, México. This course is scheduled from **Monday to Friday 8.30-11.00 AM**, a break of 1 h and a second session from **12.00-2.30 PM**, for a 25 h of course in one-week, 65 h total. At the end of the course, a certificate of attendance and/or a grade will be provided according to the guidelines of the institution.

The mini-symposium will be held at the Instituto de Investigaciones Biomédicas Sede del Tercer Circuito Exterior, Coyoacán, Cd. Universitaria, 04510. Ciudad de México.

REDOX BIOLOGY IN HEALTH AND DISEASE COURSE
Unidad de Posgrado, UNAM

Schedule	Description
08/08/16 9.00 AM-11.00 AM	Initial Meeting to discuss class expectations and grading *If you cannot attend this meeting you should contact the instructors for them to inform you about the specifics of the class.*
29/08/16 8.30 AM-11.00 AM	Course Overview *(Dr. Franco)* "***Redox-based biochemical processes***" *(Dr. Khalimonchuk)*
11.00 AM-12.00 PM	Break
12.00-2.30 PM	Papers to be discussed 1. Martinez-Reyes I et al. (2016) TCA Cycle and Mitochondrial Membrane Potential Are Necessary for Diverse Biological Functions. Mol Cell. 61:199 2. Martelli A et al. (2015) Iron regulatory protein 1 sustains mitochondrial iron loading and function in frataxin deficiency. Cell Metab. 21:311
30/08/16 8.30 AM-11.00 AM	"***Redox-based biochemical processes***" *(Dr. Khalimonchuk)*
11.00 AM-12.00 PM	Break
12.00-2.30 PM	Papers to be discussed 3. MacDonald G et al. (2014) Memo is a copper-dependent redox protein with an essential role in migration and metastasis. Sci Signal. 7(329):ra56. doi: 10.1126/scisignal.2004870. 4. Tsunoda S et al. (2014) Intact protein folding in the glutathione-depleted endoplasmic reticulum implicates alternative protein thiol reductants. Elife. 2014 29;3:e03421.
31/08/16 8.30 AM-11.00 AM	***"Oxidative Stress and Antioxidant systems"*** *(Dr. Gonsebatt, Dr. Franco)*
11.00 AM-12.00 PM	Break
12.00-2.30 PM	Papers to be discussed 5. Zucker SN et al. Nrf2 amplifies oxidative stress via induction of Klf9. Mol Cell. 53(6):916-28. 6. Bailey AP et al. Antioxidant Role for Lipid Droplets in a Stem Cell Niche of Drosophila. Cell. 163(2):340-53.
01/09/16 8.30 AM-11.00 AM	***"Oxidative Stress and Antioxidant systems"*** *(Dr. Franco)*
11.00 AM-12.00 PM	Break
12.00-2.30 PM	Papers to be discussed 7. Gad H et al. (2014) MTH1 inhibition eradicates cancer by preventing sanitation of the dNTP pool. Nature. 508(7495):215-21. 8. Wei N et al. (2014) Oxidative stress diverts tRNA synthetase to nucleus for protection against DNA damage. Mol Cell. 56(2):323-32.
02/09/16 8.30 AM-11.00 AM	***"Redox Homeostasis and Signaling"*** *(Dr. Franco)*
11.00 AM-12.00 PM	Break
12.00-2.30 PM	Papers to be discussed 9. Shao D et al. (2014) A redox dependent mechanism for regulation of AMPK activation by Thioredoxin1 during energy starvation. Cell Metab. 19(2):232-45.

	10. Manček-Keber M et al. (2015) Toll-like receptor 4 senses oxidative stress mediated by the oxidation of phospholipids in extracellular vesicles. Sci Signal. 8(381):ra60. doi: 10.1126/scisignal.2005860.
05/09/16 8.30 AM-11.00 AM	"***Redox-Homeostasis and Signaling***" *(Dr. Franco)*
11.00 AM-12.00 AM	Break
12.00-2.30 PM	Papers to be discussed 11. Hisatsune C et al. (2015) ERp44 Exerts Redox-Dependent Control of Blood Pressure at the ER. Mol Cell. 58:1015 12. Gurzov EN et al. (2014) Hepatic oxidative stress promotes insulin-STAT-5 signaling and obesity by inactivating protein tyrosine phosphatase N2. Cell Metab. 20(1):85-102.
06/09/16 8.30 AM-11.00 AM	"***Redox-Related Diseases & Therapeutics***" *(Dr. Franco)*
11.00 AM-12.00 PM	Break
12.00-2.30 PM	Papers to be discussed 13. Yee C et al. (2014) The intrinsic apoptosis pathway mediates the pro-longevity response to mitochondrial ROS in C. elegans. Cell. 2014 157(4):897-909. 14. Piskounova E et al. (2015) Oxidative stress inhibits distant metastasis by human melanoma cells. Nature. 527(7577):186-91.
07/09/16 8.30 AM-11.00 AM	***"Redox-Related Diseases & Therapeutics"*** *(Dr. Franco)*
11.00 AM-12.00 PM	Break
12.00-2.30 PM	Papers to be discussed 15. Schreiner B et al. (2015) Astrocyte Depletion Impairs Redox Homeostasis and Triggers Neuronal Loss in the Adult CNS. Cell Rep. 12(9):1377-84. 16. Belenky P et al. (2015) Bactericidal Antibiotics Induce Toxic Metabolic Perturbations that Lead to Cellular Damage. Cell Rep. 13(5):968-80.
08/09/16 8.30 AM-11.00 AM	***"Methods in Redox Biology"*** *(Dr. Franco)*
11.00 AM-12.00 PM	Break
12.00-2.30 PM	Papers to be discussed 17. Paul BD et al. (2014) Cystathionine γ-lyase deficiency mediates neurodegeneration in Huntington's disease. Nature. 509(7498):96-100. 18. Lewis CA et al. (2014) Tracing compartmentalized NADPH metabolism in the cytosol and mitochondria of mammalian cells. Mol Cell. 55(2):253-63.
09/09/16 8.30 AM-11.00 AM	***"Methods in Redox Biology"*** *(Dr. Franco)*
11.00 AM-12.00 PM	Break
12.00-2.30 PM	Papers to be discussed 19. Kirstein J et al. (2015) Proteotoxic stress and ageing triggers the loss of redox homeostasis across cellular compartments. EMBO J. 34(18):2334-49. 20. Menger KE et al. (2015) Fasting, but Not Aging, Dramatically Alters the Redox Status of Cysteine Residues on Proteins in Drosophila melanogaster. Cell Rep. 2015 11(12):1856-65.

REDOX MINI-SYMPOSIUM
Instituto de Investigaciones Biomedicas

12/09/16 8.45-9.00 AM	Opening
9.00-10.15 AM	**"Effect of antioxidant treatment on mitochondrial alterations in the experimental renal disease"**

	Jose Pedraza-Chaverri, Facultad de Química UNAM
10.15-11.30 AM	**"Reactive oxygen species in fungal cell differentiation"** Jesús Aguirre Linares, Instituto de Fisiología Celular, UNAM
11.30 AM-12.00 PM	Break
12.00-1.15 PM	**"Air pollution particles and oxidative stress: implications in systemic toxicity"** Andrea de Vizcaya Ruiz, Departamento de Toxicología, CINVESTAV
1.15-2.30 PM	**"Biogenesis of oxidative phosphorylation complexes in mitochondria"** Xochitl Pérez Martínez, Instituto de Fisiología Celular, UNAM
13/09/16 9.00-10.15 AM	**"Cellular Redox regulation by HGF/c-Met: implications in liver diseases"** Luis Gomez Quiroz, Div. de Ciencias Biológicas y de la Salud, UAM Iztapalapa
10.15-11.30 AM	**"Physiological and pathological aspects of liver pro-oxidant activity"** Mauricio Díaz Muñoz, Instituto de Neurobiología, UNAM
11.30 AM-12.00 PM	Break
12.00-1.15 PM	**"Oxidative stress and aging: Is the free radical´s theory still valid?"** Mina Konigsberg, Div. de Ciencias Biológicas y de la Salud, UAM Iztapalapa
1.15-2.30 PM	**"Oxidative stress and inflammation in animal models of stress: therapeutic relevance of antioxidants"** Abel Santa Maria del Ángel, Instituto Nacional de Neurología y Neurocirugía
14/09/16 9.00 AM-10.15 AM	**"Neurotoxicity of arsenic exposure"** Ma. Eugenia Gonsebatt, Instituto de Investigaciones Biomédicas, UNAM
10.15-11.30 AM	**"Studying amyloid-β-copper interactions: Insights into redox properties and aggregation pathways"** Liliana Quintanar Vera, Departamento de Química, CINVESTAV
11.30 AM-12.00 PM	Break
12.00-1.15 PM	**"Reactive oxygen species, NADPH-oxidases and neuronal differentiation"** Julio Morán Andrade, Instituto de Fisiología Celular, UNAM
1.15-2.30 PM	**"Energy metabolism and oxidative stress in neurodegeneration"** Rodrigo Franco, Redox Biology Center, UNL
2.30-2.45 PM	Closing Remarks
19/09/16 8.30 AM-10.30 PM	Final Exam
11.30 AM	Delivery of Certificates

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