Free Radicals and Redox Biomedicine (BIOC 793B)

Spring Semester 2023

Credits

2.0 Credits

Levels

Graduate, Professional

Registration Dates:

Oct 01, 2022 to Jan 13 (last day to register), 2023

Class Location/Times:

In person/Online synchronous, 11:00 am - 11:50 am, Jan 10, 2023 - Apr 27, 2023 (Tuesday and Thursday)

Course Information:

An introductory course in Free Radicals and Redox Biomedicine focused on: 1) biologically-relevant free radicals and allied reactive species, 2) physicochemical properties and methods of detection, 3) redox signaling, 4) free radicals in health an disease: physiological and pathophysiological roles.

Prerequisites: Graduate level biochemistry, physical chemistry and/or biophysics. Undergraduates only by permission of instructor.

Instructor:

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Co-Instructors:

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Textbook: (highly recommended): highly recommended: B.Halliwell and J.Gutteridge 2015 "Free Radicals in Biology and Medicine", Oxford University Press; 5 edition.

Homework: Homework will be given after each main theme and is due the next meeting after the theme is finished. Besides, students are expected to reed as much as they can from recommended references/textbooks.

Exams: Midterm tests and comprehensive open book final or alternative paper presentation will be given. There will be no make-up exams.

Term Paper and Presentation. You will have to prepare a review of the paper(s) and give a 15 minute presentation on a course topic. You can pick up your own topic (with lecturer's approval) or ask for one.

Grading: Grade will be based on the results of first (15%) and final exam/presentation (30%), homework (15%) and attendance (40%).

Attendance: Attendance is mandatory at all class meetings. Failure to attend >= 20% of class meeting will result in your grade dropping by one letter (e.g., from A to B or from B to C).

Brief content/schedule of the course

Theme	Dates
January 2023	
Introduction/Overview of the course. Free radicals/ROS in disease and normal physiology. Oxygen history. Dioxygen as widely spread biradical (triplet state). Oxygen paradox: energy benefits vs oxygen toxicity. **Definition /Terminology** of Free Radicals, ROS and redox reactions. Classification of the radicals. Active forms of oxygen: singlet oxygen and superoxide anion. Active oxygen metabolites: hydroxyl ($^{\bullet}$OH), alkoxyl (RO$^{\bullet}$), alkylperoxyl (ROO$^{\bullet}$) and nitroxyl (NO$^{\bullet}$) radicals. **Defining redoxome.** Redox signaling vs. oxidative stress. Quantitative Free Radical and Redox Biology: vocabulary, methods, quantitation.	Jan 10
Thermodynamics of Free radicals and Redox Active compounds. Oxidation state, redox half reactions, redox couples and reduction potentials. Pecking order of free radicals.	Jan 12
Redox State and Redox Environment in Biologicals Systems. "Redox state": an introduction and biological importance. Examples of biologically important redox couples. Redox state of thiols (GSH) and its biological significance. Redox signaling.	Jan 17
Kinetics of free radical reactions. Types of free radical reactions. Kinetic parameters: rate constants, characteristic lifetimes, steady-state concentrations, and diffusion distances. The exemplified chemistry of physiologically relevant free radicals. Methods of generation. Direct and indirect methods of the measurements of the kinetics.	Jan 19
Electron Paramagnetic Resonance (EPR), EPR spin trapping and alternative methods of free radical detection. Introduction in the EPR spectroscopy as direct method of free radical detection. Spectra parameters. EPR spin trapping as a gold standard of free radical identification. Nitrones and nitroso derivatives as main types of spin traps. EPR spectroscopy of nitric oxide in both free and trapped forms, iron-dithiocarbamate traps of NO$^{\bullet}$. Some examples of EPR spin trapping applications in biological systems.	Jan 24 and Jan 26
Singlet oxygen. Delta- and sigma- states. Physico-chemical properties. Methods of generation and detection. Singlet oxygen in living organisms. Sonochemical activation of heamatoproteins and sonodynamic therapy.	Jan 31
February 2023	
Superoxide radical. Physico-chemical properties. Hydroperoxyl radical. Chemical and biological sources of superoxide. Enzymes related to superoxide production: NADPH-oxidase of phagocytes, xanthine oxidase, oxidases of amino acids, etc. Reactivity of superoxide and the main types of its chemical reactions. Biological actions of superoxide, cytotoxicity. Inhibitors/Traps: Superoxide Dismutase (SOD), ascorbic acid, ubiquinone, etc. Methods of detection of superoxide.	Feb 2 and Feb 7
Hydroxyl radical. Reactions of Haber-Weiss and Fenton, and other sources. Reactivity of $^{\bullet}$OH-radical and lifetime in biological systems. Oxidative damage of proteins and nucleic acids. Cytotoxic, mutagenic and carcinogenic action. Methods of detection.	Feb 9
Nitric oxide. Physico-chemical properties and reactivity. Synthesis of NO in living organisms. NO-synthase (NOS), substrates and products. Classification of NOS, structure, cofactors, prosthetic groups, factors of regulation, subcellular localization. Physiological functions of nitric oxide. Endothelium derived relaxing factor (EDRF).	Feb 14 and Feb 16
Peroxynitrite. Chemical reactivity, reactions in biological fluids and cells, methods of generation and detection.	Feb 21
NOx-species. Physiological functions and toxicity: reactions with biomolecules. NO-donors and NO acceptors as therapeutic agents. Experimental approaches of NOx detection.	Feb 23

Thiols and thyil radicals. Redox State and thiol redox code. Oxidative stress and oxidative stress markers.	Feb 28 March 2
March 2023	
Midterm week: Summary of the previous lectures/discussion of the exemplified potential problems for the midterm exam. Midterm exam.	March 7, 9
Spring Break	March 11-19
Antioxidant enzymes. SOD, catalase, glutathione-dependent antioxidant enzymes, reparation systems of proteins, lipids and nucleic acids.	March 21
Low-molecular antioxidants. Preventing and chain-terminating antioxidants (vitamins C and E; superoxide dismutase, $NO^{\bullet}$!). Balance between oxidant and prooxidant properties. Free radicals and disease.	March 23
Free Radical Theory of Aging. The basics theories of aging. Nutrition and role for antioxidants. Free radicals and Ionizing Radiation.	March 28
Free radicals, tumor microenvironment (TME) and redox imbalance in disease: roles in tumorigenesis, cancer progression and aggressiveness.	March 30
April 2023	
Free Radicals, TME and Redox in Cancer: Imaging of TME in vivo.	Apr 4
Free radicals and redox imbalance in disease: roles in ischemic heart disease, organ transplantation, neurodegenerative diseases, inflammatory bowel disease, diabetes, obesity, etc.	Apr 6, 11, 13, 18, 20, 25
Final. Paper presentations	Apr 27
May 2023	
Finals week.	May 1-5