Free Radicals and Redox Biomedicine (BIOC 793B)

Spring Semester 2022

Theme	Dates
January 2022	
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 11
Thermodynamics of Free radicals and Redox Active compounds. Oxidation state, redox half reactions, redox couples and reduction potentials. Pecking order of free radicals.	Jan 13
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 18
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 20
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 25 and Jan 27
February 2022	
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.	Feb 1
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 3 and Feb 8
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 10
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 15 and Feb 17
Peroxynitrite. Chemical reactivity, reactions in biological fluids and cells, methods of generation and detection.	Feb 22
NOx-species. Physiological functions and toxicity: reactions with biomolecules. NO-donors and NO acceptors as therapeutic agents. Experimental approaches of NOx detection.	Feb 24

March 2022	
Thiols and thyil radicals. Redox State and thiol redox code. Oxidative stress and oxidative stress markers.	March 1, 3
Midterm week: Summary of the previous lectures/discussion of the exemplified potential problems for the midterm exam. Midterm exam.	March 8, 10
Spring Break	March 12-20
Antioxidant enzymes. SOD, catalase, glutathione-dependent antioxidant enzymes, reparation systems of proteins, lipids and nucleic acids.	March 22
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 24
Free Radical Theory of Aging. The basics theories of aging. Nutrition and role for antioxidants. Free radicals and Ionizing Radiation.	March 29
Free radicals, tumor microenvironment (TME) and redox imbalance in disease: roles in tumorigenesis, cancer progression and aggressiveness.	March 31
April 2022	
Free Radicals, TME and Redox in Cancer: Imaging of TME in vivo.	Apr 5
Free radicals and redox imbalance in disease: roles in ischemic heart disease, organ transplantation, neurodegenerative diseases, inflammatory bowel disease, diabetes, obesity, etc.	Apr 7, 12, 14, 19, 21, 26
Final. Paper presentations	Apr 28
May 2022	
Finals week.	May 2-6