Free Radicals and Redox Biomedicine (BIOC 791B)

Spring Semester 2019

Theme	Dates
January 2019	
Introduction/Overview of the course. Free radicals/ROS in disease and normal physiology. Oxygen history. Oxygen paradox: energy benefits vs oxygen toxicity. **Definition /Terminology** of Free Radicals, ROS and redox reactions. Classification of the radicals. **Defining redoxome.** Redox signaling vs. oxidative stress. Quantitative Free Radical and Redox Biology: vocabulary, methods, quantitation.	Jan 8
Thermodynamics of Free radicals and Redox Active compounds. Oxidation state, redox half reactions, redox couples and reduction potentials. Pecking order of free radicals.	Jan 10
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 15
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 17
Reactive Oxygen and major biological sources of free radicals. Dioxygen as widely spread biradical (triplet state). 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. The sources of free radicals in biological systems: an active forms of metabolism of oxygen, specific enzyme systems, free-radical steps in biochemical reactions, radiation damage, ecological factor (contamination of pro-oxidants in atmosphere and in the food).	Jan 22
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 24
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 29 and Jan 31
February 2019	
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 5 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 12
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 19
NOx-species. Physiological functions and toxicity: reactions with biomolecules. NO-donors and NO acceptors as therapeutic agents. Experimental approaches of NOx detection.	Feb 21

Midterm week: Summary of the previous lectures/discussion of the exemplified potential problems for the midterm exam. Midterm exam.	Feb 26 Feb 28
March 2019	
Peroxynitrite. Chemical reactivity, reactions in biological fluids and cells, methods of generation and detection.	March 5
Alkoxyl and alkylperoxyl radicals. Physico-chemical properties and reactivity. The sources. Lipid peroxidation, oxidative damage of proteins and nucleic acids. Reactions of recombination and biochemiluminescence. Inhibitors: ascorbic acid, alpha-tocopherol, ubiquinone, etc. Methods of detection.	March 7
Spring Break	March 9-17
Thiols and thyil radicals. Redox State and thiol redox code. Oxidative stress and oxidative stress markers.	March 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 26
Free Radical Theory of Aging. The basics theories of aging. Nutrition and role for antioxidants. Free radicals and Ionizing Radiation.	March 28
April 2019	
Free radicals, tumor microenvironment (TME) and redox imbalance in disease: roles in tumorigenesis, cancer progression and aggressiveness.	Apr 2
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 9, 11, 16, 18, 23, 25
Final. Paper presentations	Apr 30
May 2019	
Final. Paper presentations	May 2