

77:222 FREE RADICALS IN BIOLOGY AND MEDICINE

(4 Semester hours)

Spring 2005 Course Outline

Instructors:	Dr. Garry R. Buettner	68 EMRB	(319) 335-6749
	Dr. Larry W. Oberley	B-180 ML	(319) 335-8015

Lectures are held **M,T,W,TH 9:30-10:20 in B-180A ML**

This course is designed to give participants an understanding of the fundamental aspects of free radical and antioxidant chemistry, biochemistry, and biology. The goal is to provide the fundamental knowledge required by researchers who wish to pursue problems of human health that involve free radicals, related oxidants, antioxidants, and antioxidant enzymes.

The course will have two exams: March 3 and a final exam in May.

Participants will prepare five papers for the course. Papers I-IV are short papers; *i.e.*, no more than 10 pages, including title page and references. They will describe the fundamental free radical-related **chemistry and biochemistry** of the topic. The papers will be prepared on a word processor. They will be submitted in two stages. The preliminary version will be returned with comments and suggestions (no grade will be assigned). The author then can address these comments as appropriate for the final submission, which will be graded.

In papers I-IV the content should focus on the chemistry, biochemistry, spectroscopy, routes of formation, detection, *etc.* In these papers no more than approximately one short paragraph should be devoted to the biology/health aspects of these species.

Paper I – Radicals, RNS and ROS

Preliminary version due 26. January 2005 9:30 sharp.

Final version due 09. February 2005 9:30 sharp.

Possible topics are:

alkoxyl, RO [•]	HOI	O ₂ ^{•-} /HO ₂ [•] in water
Chloramines	HOSCN	O ₂ ^{•-} /HO ₂ [•] , nonprotic solvent
CO ₂ ^{•-}	LO [•] (PUFA)	O ₃
Cumene-OOH	LOOH (lipid)	ONO ₂ CO ₂ ⁻
DNA-OOH	MDA	Pentadienyl radical
e ⁻ _{aq}	Methyl-radicals	Pentyl-radicals
Ethyl-radicals	N ₂ O	Peroxyl, ROO [•]
GS [•] , glutathyl	N ₂ O ₃	peroxynitrite
H [•]	N ₃ [•]	Phenoxyl radical
H ₂ O ₂	NO [•] , NO ⁺ , NO ⁻	POOH (protein)
HNE	NO ₂ ⁻	Sulfenic acids
HO [•]	NO ₂ [•]	<i>tert</i> -Butyl-OOH
HOBr	O ₂	TO [•] (vitamin E)
HOCl	¹ O ₂	β-Carotene [•]

Paper II - Small-Molecule Antioxidants

Preliminary version due 14. February 2005 at 9:30 sharp.

Final version due 24. February 2005 at 9:30 sharp.

Possible topics are:

β -carotene/vitamin A	DETAPAC	Lipoic acid	SOD mimic
BHA/BHT	DTT	Lycopene	Taurine
Bathocuproine	"E"-analogues	NAC	α -Tocopherol
Bilirubin	EDTA	NADPH	γ -Tocopherol
"C"-analogues	Ergothionine	Nitroxides	Trolox
CAT mimics	Flavonoids	NO [•]	Urate
CoQH ₂	GPx mimics	OTC	Vitamin K
Cysteine	GSH	Pyruvate	Zinc
Desferal®	Lactate	Resveratrol	

Paper III – Enzymes, Proteins or redox regulated transcription factors

Preliminary version due 28. Feb 2005 at 9:30 sharp.

Final version due 10. March 2005 at 9:30 sharp.

Possible topics are:

AP-1	HIF	Oxidative DNA repair enzymes
Ascorbate Oxidase	HRP	Oxidative proteases
Catalase	Kinases	OxyR
CuZnSOD	Lactoferrin	P-450's
EcSOD	Lipoxygenase	P53
Ferritin	LPO	Peroxiredoxin (Prx I, II III, IV, V, VI)
FeSOD	Melanin	Phosphatases
Glucose Oxidase	Methionine sulfoxide reductase	Phospholipase A ₂
Glutaredoxin	Microperoxidase	Protein disulfide isomerases
Glutathione disulfide reductase	MnSOD	Ribonucleotide reductase
Glutathione-S-transferase	MPO	SoxR
Glut-transporter	Myoglobin	Thioredoxin
GPx-1	NADPH Oxidase	Thioredoxin reductase
GPx-2	NF- κ B	Transferrin
GPx-3	NOD	Xanthine dehydrogenase
GPx-4 (PhGPx)	NOS-1	Xanthine oxidase
Heat Shock Proteins	NOS-2	
Hemeoxygenase	NOS-3	
Hepatoglobin	NOS-4	

Paper IV - Xenobiotics

Preliminary version due 24. March 2005 at 9:30

Final version due 04. April 2005 at 9:30

Possible topics are:

Acetaminophine	CCl ₄ metabolism	Misonidazole	PCB
Adriamycin	Chlorpromazine	MPTP	Silica
air pollutants	Cigarette smoke	Nipride	SO ₂
Alloxan and diabetes	Dioxin	Nitroglycerin	Streptozotocin
Asbestos	Ether lipids	Paraquat	"UV-light"
Bleomycin	Hydrazines	PBN	a topic of <u>your</u> choice

Paper V - Disease States and Free Radicals

Topic Selection Date: No later than 3. March 2005

Outline Deadline: 14. April 2005 (Two copies of a detailed outline are to be handed in)

Due: 5. May 2005 at 9:30 a.m. sharp

Length: 15-25 pages

Scientists have increasingly claimed that free radicals are the cause of various diseases and pathologies. However, 90% of these claims are still controversial because not enough evidence is available. We would like you to examine the role of active oxygen species or free radicals. Your discussion should consider alternative hypotheses as appropriate. One of the following diseases or pathologies (or any other of your choice) may be chosen upon consent of the instructors:

The final paper should be from 15 to 25 pages in length, including title page and references. Possible topics are:

Aging (e.g disease treatments)	DNA Damage (Mutations, Aberrations, etc.)	Parkinson's Disease
Alcoholism	Down's Syndrome (Trisomy 21) (Why don't they get cancer?)	Porphyria
ALS/Lou Gehrig's Disease	Inflammation	Radiation-Injury
Cancer (Cause, Cell Biology or Treatment)	Ischemia-Reperfusion Injury	Sickle-Cell Anemia
Cataracts	Lipoproteins and Atherosclerosis	Silicosis
Chemical-Injury (Pick A Chemical)	Malaria	Thalassemia
Chronic granulamatous disease	Muscular dystrophy	Any Other Topic Of Your Choice
Diabetes	Oxygen Toxicity	

You should review the literature, suggest new experiments and if possible propose a mechanism of injury. Take a stand on whether free radicals are involved or not involved. Do not hesitate to argue against free radicals as a mechanism of action. If possible, suggest a treatment for this pathology. At least one page should be devoted to a proposal of new experiments to test a basic hypothesis on the understanding of this health problem.

Paper Format:

All papers should be double spaced with 1" (or 2.5 cm) margins. The font size used in all papers should be equal in size to that of 12 pt Times New Roman. They should have a title page, e.g.,

P.T. Mann

Free Radicals

1

Free Radicals are Great

by

PAR T. MANN

101 The Fieldhouse
Department of Free Thinking
The University of Iowa
Iowa City, IA 52242-1234

Tel: 319/335-5555

Fax: 319/335-0000

Email: par-mann@uiowa.edu

For 77:222, Spring 2005

1. April 2005

At the bottom of the title page put an alphabetical list of any abbreviations used. The top of each page should have a header with name, a short title, then page number on the right.

Then, on page 2 an **outline** with page numbers followed on the same page by the:

Abstract: 25-100 words.

Introduction: one or two paragraphs (Start at the top of page 3.)

Main Text

References (Start a new page, usually.)

In your paper all "facts" should be referenced as to source. If figures from publications are copied, the source is to be given. Each paper must have primary sources when appropriate.

The References are to be consecutively numbered in the text and noted as [1] *etc.* Do not use superscript.

The Reference Formats* are:

Journal:

1. Oberley LW, Buettner GR. (1979) Role of superoxide dismutase in cancer: A review. *Cancer Res.* **39**:1141-1149. (Journal names are to be given with standard abbreviations, italic with only a period at the end, e.g. *J Biol Chem.* *Free Radic Biol Med.* *Free Rad Res.*)

Book:

2. Oberley LW, ed. (1982) *Superoxide Dismutase*. Vol. 2 Boca Raton, FL: CRC Press.

Chapter in Edited Book:

3. Buettner GR. (1982) The spin trapping of superoxide and hydroxyl radicals. In: Oberley LW, ed. *Superoxide Dismutase*. Vol. 2. Boca Raton, FL: CRC Press; pp 63-81.

* Note that complete titles are to be given. Single space within a citation, double space between citations. Note also, the "hanging" format.

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Miscellaneous

This course is given by the College of Medicine. This means that class policies on matters such as requirements, grading, and sanctions for academic dishonesty are governed by the College of Medicine. Students wishing to add or drop this course after the official deadline must receive the approval of the Dean of the College of Medicine. Details of the University policy of cross enrollments may be found at: <http://www.uiowa.edu/~provost/deos/crossenroll.pdf> .

"Truth in Lending" -- Students borrowing extra time to complete their papers will be charged interest at the rate of 1% of their grade per hour. Interest free extensions will be given only in cases of documented emergency. This request must be presented in writing and, of course, be well documented.

"Truth in Learning" -- Portions of The University of Iowa Student Handbook dealing with dishonesty in academic work are incorporated by reference into this course description. Violators will suffer. Plagiarism is the biggest temptation. Plagiarism is the practice of copying from a book or other publication and not acknowledging that the words or figures used are someone else's. Possible consequences for plagiarism are: failing grade for paper, expulsion from the course, or expulsion from the University.

"Administrative Procedures Act" -- Portions of The University of Iowa Catalogue dealing with adding and dropping courses are incorporated by reference into this course description.

"Surgeon General's Warning" -- Smoking is hazardous to your health and to the health of those around you. Smoking is prohibited in all university buildings. The use of other forms of tobacco is hazardous to your health as well as aesthetically repugnant. It is prohibited in our classroom and offices.

"Communications Decency Act" -- Out of respect for your colleagues and to the class, please turn off all pagers and mobile phones during class. Emergency personnel and expectant parents are exempt.

This page is adapted from:

<http://cornell-iowa.edu/politics/red-tape.html>

**77:222 Free Radicals in Biology and Medicine
Tentative Outline**

Space provided below need not correlate with time devoted to the discussion of the topic.
Also, the sequence is bound to vary.

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| <p>I. Introduction</p> <p>A. Current Status of Radicals in Health Issues</p> <p>B. What is a radical</p> <p>C. Free Radicals and Your Life</p> <p>II. Historical Aspects</p> <p>III. Electronic Structure and Bonding</p> <p>IV. Active Oxygen</p> <p>A. Species, O_2, $O_2^{\bullet-}$, HO_2^{\bullet}, 1O_2, H_2O_2, HO^{\bullet}</p> <p>B. Chemistry</p> <p>V. Radical Reactions</p> <p>VI. Free Radical Kinetics</p> <p>A. First-order Reaction</p> <p>B. Second-order Reaction</p> <p>C. Steady-State</p> <p>D. Chain-reactions</p> <p>VII. Radiation Chemistry</p> <p>A. Tools</p> <p>B. Species: e^-_{aq}, H^{\bullet}, HO^{\bullet}, H_2O_2, H_2, $O_2^{\bullet-}$</p> <p>C. Tricks: $CO_2^{\bullet-}$, N_2O</p> <p>D. Pulse Radiolysis/Flash Photolysis</p> <p>VIII. Lipid Peroxidation</p> <p>A. Chemistry</p> <p>B. Measurement</p> <p>C. Effects</p> <p>IX. Antioxidants</p> <p>A. Preventative</p> <p>B. Chain-breaking</p> <p>C. Small molecule</p> <p>1. Vit C and E</p> <p>2. CoQ</p> <p>3. Urate</p> <p>4. Other</p> <p>D. Enzymes</p> <p>E. Chelates</p> <p>X. Iron and Free Radical Chemistry</p> <p>A. Reactions</p> <p>B. Chelates</p> <p>C. Protein</p> <p>1. Transferrin</p> <p>2. Ferritin</p> <p>3. Hemes</p> <p>XI. The Pecking Order</p> <p>A. Thermodynamics</p> <p>XII. DNA</p> <p>A. As a target</p> <p>B. Chemistry</p> <p>C. Products</p> <p>XIII. Protein Oxidation</p> <p>XIV. Photo reactions</p> <p>A. Photochemistry</p> <p>B. Photosensitization</p> <p>C. 1O_2</p> <p>XV. Detection of Radicals</p> <p>A. TBARS</p> <p>B. Fluorescence</p> <p>C. Cyt C /NBT</p> | <p>D. DNA Products</p> <p>E. Strategies</p> <p>1. SOD, CAT, chelates</p> <p>XVI. EPR Detection of Radicals</p> <p>A. Instrumentation</p> <p>B. Direct Detection</p> <p>XVII. EPR, Transition Metals</p> <p>A. Fe</p> <p>B. Cu</p> <p>C. Mn</p> <p>XVIII. EPR, Spin Trapping</p> <p>A. Chemistry</p> <p>B. Biology</p> <p>XIX. Xanthine Oxidase</p> <p>A. $O_2^{\bullet-}/H_2O_2$</p> <p>XX. Heme Peroxidases</p> <p>A. HRP</p> <p>B. Others</p> <p>XXI. NADPH Oxidase</p> <p>XXII. Nitric Oxide/NOS</p> <p>A. $^{\bullet}NO$</p> <p>B. $ONOO^-$</p> <p>C. Nitric oxide synthases</p> <p>XXIII. Organelle Production of ROS</p> <p>XXIV. Cellular Production of ROS</p> <p>XXV. Superoxide Dismutase</p> <p>A. Function</p> <p>B. Physical Biochemistry</p> <p>1. CuZn-SOD</p> <p>2. Mn-SOD</p> <p>3. Fe-SOD</p> <p>XXVI. Assay for SOD</p> <p>XXVII. Catalase</p> <p>XXVIII. Glutathione/Glutathione Enzymes</p> <p>A. GSH</p> <p>B. GPx - 4 types</p> <p>C. GST</p> <p>D. GR</p> <p>XXIX. Thioredoxin Systems</p> <p>XXX. Other Antioxidant Enzymes</p> <p>XXXI. Molecular Biology of AEs</p> <p>XXXII. Cytokines</p> <p>XXXIII. Free Radicals and Cellular Differentiation</p> <p>XXXIV. Free Radicals and Cancer</p> <p>XXXV. Free Radicals in Other Diseases, e.g.</p> <p>A. Inflammation</p> <p>B. Trisomy 21</p> <p>C. Aging</p> <p>D. Ischemia/Reperfusion</p> <p>E. Diabetes</p> <p>F. ALS</p> <p>G. Atherosclerosis</p> <p>XXXVI. Redox Environment of the Cell</p> |
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Web Cites of interest:

Virtual Free Radical School: <http://www.medicine.uiowa.edu/frrb/VirtualSchool/Virtual.html>

Sunrise Free Radical School: <http://www.medicine.uiowa.edu/frrb/SRFERS/sfrs.html>

77:222 (2001, 2003): <http://www.medicine.uiowa.edu/esr/education.htm>

Free Radical Journal Club:

<http://www.uihealthcare.com/depts/med/radiationoncology/frrb/seminarsclubs/freeradical/index.html>

Science Daily: www.sciencedaily.com

Free Radical Nomenclature: <http://www.medicine.uiowa.edu/esr/education.htm>

SI Units: <http://www.medicine.uiowa.edu/esr/education.htm>

Google: www.google.com