BIOLOGY OF AGING

Lecture course by Alex Lyakhovich, Office: FENS 1043, Tel. 9506
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Name: **BIOLOGY OF AGING (other name Aging and Gerontology)**

Codes: **BIO446/546**

When/Where: #**Monday 10.40AM-11.30AM/ FASS G018***

#**Tuesday 2.40PM-4.30PM/ FASS 1008-1010***

#Subject to change, please see final schedule

Aim: The course intends to provide an up-to-date overview of the biology of aging, one of the fastest growing scientific disciplines of the 21st century, located at the intersection of biology, mathematics, computer science and medicine.

Course Description: While all of us intuitively know what the aging is, many basic questions about aging are mysterious. Is aging itself a disease, and can we successfully intervene in the aging process? Or is it a program that one can hack? In this course, we will explore the scientific discoveries made from studies of model organisms, which have led to revelations about the molecular biology of aging. We will look at aging at different angles – from population genetics to the "reliability theory" of mechanical engineering. We are going to understand why older people more likely to experience neurodegenerative disorders, stroke, and cancer and what kind of changes happen at the molecular and cellular levels that are associated with these diseases. We will look at the molecular mechanisms of aging, and during the practical exercises we will try to come up with some theories of aging of our own. We will discuss some medical interventions that can extend the lifespan of organisms as diverse as yeast and primates, and the implications for successfully intervening in age-related diseases.

Format: This course consists of approximately 20+ lectures separated by 2 discussion sessions and 2 tests. Students will be required to read and analyze at least one seminal paper for each lecture and come to class prepared to discuss them.

Prerequisites: A basic level understanding of biology, molecular and cell biology, biochemistry and statistics is a highly prerequisite.

Attendance and participation: Required in at least 70% of the lectures (offline preferred)

Evaluation criteria: T1- 15%, T2-15%, Midterm-30%, Final – 40%

! For midterm and final exams, participation in the discussion is just as important as successfully submitting the assignment!

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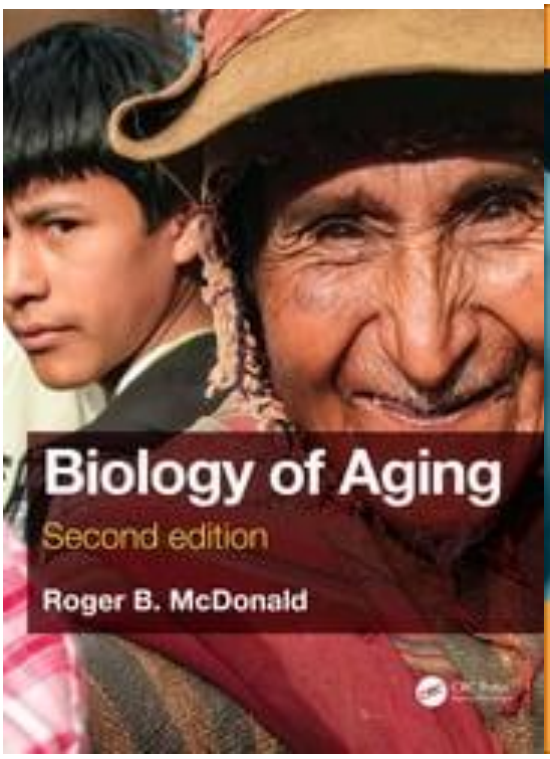
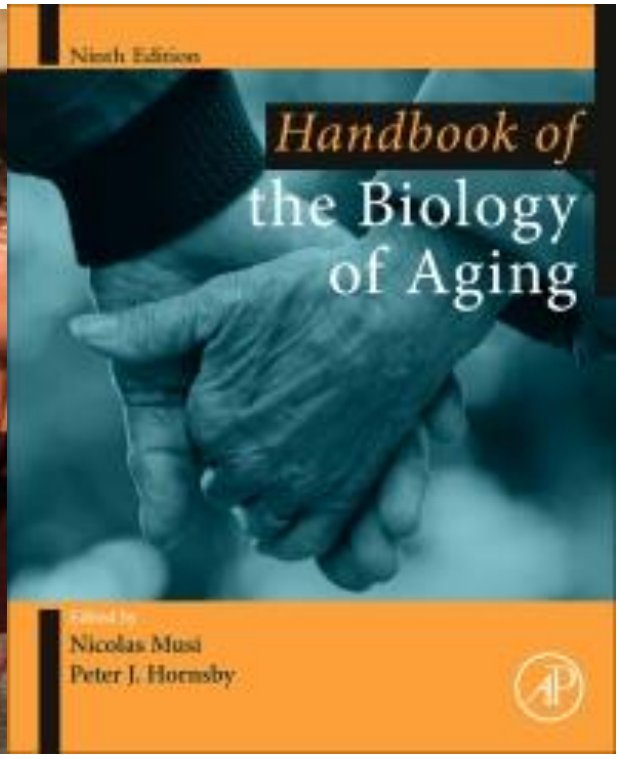
Any of the following books can be used as supportive materials:





Handbook of the Biology of Aging 9th Edition Editors: Nicolas Musi Peter Hornsby eBook ISBN: 9780128162835 (we have 6th Edition in SU information unit, also OK)
Biology of Aging, 2nd Edition, Roger B. McDonald ISBN 9780815345671

Fortunately, or unfortunately, no good textbooks on aging have yet been written. Therefore, **the above handbooks supplement rather than replace the lectures.** In addition, starting with the second lecture, I will offer you to read some original articles and ask questions about them. The idea is for you to develop critical thinking. You should not take every published paper as dogma, but should pick out the important points and pay attention to the weaknesses.

If you want to use other books on aging, show them to me.

Letter Grade Criteria for Earning Grade

A 100 – 90 %

A - 89 – 85 %

B+ 84 – 80 %

B 79 – 75 %

B - 74 – 70 %

C+ 69 – 65 %

C 64 – 60 %

C - 59 – 55 %

D+ 54 – 50 %

F Less than 49 %

Disability Accommodations

If you need disability-related accommodations for this course, please contact Ş. Ceren Başak Araz at the Disable Students Support Unit Center of Individual and Academic Development (CIAD) address: Orhanlı, Tuzla, 34956, Istanbul, Turkey, e-mail: specialneeds@sabanciuniv.edu telephone: + 90 216 483 9448

website: http://ciad.sabanciuniv.edu/en/disabled-students-services

How to communicate with me

Drop by my office, drop me an e-mail, whatsup me (+34 600 79 84 27), or leave a message via SUcourse, where all announcements and amendments will be placed.

Important notes: - Life is full of the unexpected, and sometimes we are faced with unavoidable situations such as illness, urgent household needs, or off-campus events (such as spot competitions or student conferences). All of these issues are handled on a case-by-case basis. For example, illness and inability to attend lectures must be accompanied by an appropriate report from the medical center; off-campus duty usually happens once, and those who are required to participate must provide me with a letter from your supervisor.

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Week 1

Introduction. A small survey about aging. Aging: definition of the term. The phenomenon of aging in wildlife. Human aging. Signs of aging, the problem of determining biological age. Average, maximum and life expectancy. Survival curves. Chronological and biological aging. Demographic parameters reflecting aging. The significance of the phenomenon of aging: social, medical, political, economic aspects. Redundant systems. Reliability theory of aging. Ageless organisms.

Week 2

How to measure aging. Physiological aspects of aging. Age-related changes in the immune, cardiovascular, musculoskeletal, nervous and reproductive systems. Methods for quantifying the rate of aging. Mortality and age-specific mortality rate. Life expectancy. Average and maximum lifespan. Gompertz-Makeham law and mortality rate doubling time.

Week 3

Theories of aging -I. The rate-of-living theory. Aging as a program to make room for the next generations. Accumulation of mutations. Original research papers describing each theory. Discussion.

Theories of aging-II. Aging as a genetically controlled process. Population genetics of aging. Peter Medowar and his test-tubes. Antagonistic pleiotropy. Original research papers describing each theory. Discussion.

Week 4

Modern theories of aging -I. Denham Harman's theory of oxygen poisoning and free radical accumulation. Cellular aging. Hayflick's theory of cellular (replicative) aging. Hayflick limit. Original research papers describing each theory. Discussion.

Modern theories of aging -II. Telomere attrition. A compromise in the distribution of the body's resources between reproduction and self-preservation. The disposable soma theory. Original research papers describing each theory. Discussion.

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Week 5

Biological models to study aging – from unicellular organisms to human being. Advantages and disadvantages. Premature aging caused by genetic diseases. Progeria. Life as a transmission of genetic texts. Basics of modern molecular and cellular biology. Discussion of original papers.

DNA damage and repair. Mutations. Changes in the properties of structural proteins: collagen, crystallines. Discussion of original papers.

Week 6 (Apr 11-12) and midterm exam

We are going to have a small test (**T1**) and discuss home assignment (**HA1**) based on previous lectures. Option 1 -students are required to type a 4-5 pages report on a topic related to the biology of aging and aging theories. A summary of the paper will be presented in class as well. Option 2 - students will choose a paper from either of the lectures, and will write a 2-page-brief analysis. In this assignment, students will be expected to describe the questions that the authors wanted to answer, analyze the experiments that addressed these questions (focusing on the key experiments and controls), and provide a feedback of the authors' interpretations of their results.

Week 7

Molecular mechanisms of aging in prokaryotes and eukaryotes. Difference in accumulation of mutations. Seminal papers to discuss.

Mitochondria. Reactive oxygen species (ROS) – from good to bad. Role of ROS in biomolecule damage. Apoptosis, ferroptosis and lifespan; the relationship between apoptosis and cellular aging.

Week 8

Mutant and transgenic animals -I. Study of the aging mechanisms. Mutations that accelerate aging in mice. The role of DNA repair genes. Transgenic mice with overexpression of the Cu, Zn-superoxide dismutase gene.

Mutational and transgenic models- II. Immune aging and age-related neurodegenerative diseases. Mice with knockout p53 gene. Germ cell deficient mutant mice. Circadian rhythm gene mutations. Genetic modifications slowing aging in mice.

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Week 9

The relationship between cancer and aging- I. Increased incidence of spontaneous tumors and changes in susceptibility to carcinogens with age. The role of telomeres and telomerase in the development of tumors.

The relationship between cancer and aging- II. Possible relationships between oxidative stress, aging and carcinogenesis. Increased risk of cancer with longer lifespan.

Week 10

Reproductive strategy and evolution of life expectancy. The phenomenon of menopause and its significance. The role of sex hormones in aging and carcinogenesis. Hormone replacement therapy and its effect on the aging process.

DNA methylation, protein glycosylation, accumulation of mutations. Age-related changes in gene structure and expression. Longevity inheritance in humans. Any genes for longevity? Programmed aging, "large biological clock" and the hypothesis of phenoptosis.

Week 11

Methods of slowing down aging I. Pharmacological agents that increase life expectancy. Antioxidants. Hormones of the thyroid gland and adrenal cortex. Corticosteroids. Dehydroepiandrosterone. Estrogens and hormonal contraceptives; a growth hormone. Antidiabetic drugs.

Methods to slow down aging -II. Melatonin: Effects on aging in mice, rats, fruit flies, worms. The effect of melatonin on the development of neoplasms. Mechanisms of the geroprotective action of melatonin. Immunomodulators. Enterosorbents. Other drugs and effects. Side effects of geroprotectors: risk of developing tumors.

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Week 12

Methods to slow down aging-III. Calorie restriction of food. The influence of calorie restriction on life expectancy, on the development of age-related pathology, on gene expression, on the level of oxidative stress, on the glucose-insulin-growth hormone-IGF-1 system, on the reproductive system. The evolutionary aspect of calorie restriction.

Methods of slowing down aging -IV. Mitochondrially targeted antioxidants of the. Operating principle. Impact on life expectancy. Influence on selected pathologies associated with aging.

Week 13 and Final exam

Conclusion remarks - the current state of gerontological research in the world. The main directions and prospects for further research in the field of gerontology. Chronological and biological clocks.

First we will have a short test (**T2**) and then we will discuss a homework assignment (**HA2**) based on all previous lectures. HA2 will be considered a final exam. The format depends on the number of students in the class. Students will prepare an oral presentation on a paper of their choice. Students must identify a topic of interest from the course, conduct a literature search to find other works on that topic, and select one (with instructor approval) to present. Each student will have to present his/her chosen work to the class and answer questions from his/her classmates and the instructor.