

## **BIO 475: THE BIOLOGY OF AGING**

Fall 2005: T at 6:30 PM – 9:30 PM

Room: Albertus Magnus 404

Credit Hours: 3.00



PROVIDENCE  
COLLEGE

### INSTRUCTOR:

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I am generally in my office (Hickey 252) or in my laboratory (Albertus Magnus 212) from 9:00 AM - 5:00 PM daily and am easily available with a prior appointment. To make an appointment, you may call me on my telephone or email me. I'll keep Tuesday afternoons from 2:00 P.M. to 4 P.M. for drop-in appointments. Please feel free to talk to me about any issue relating either to the course or to your life as a student here at Providence College.

### **A PRAYER BEFORE STUDY**

**St. Thomas Aquinas, O.P.**

**O God, Creator of all things, true source of light and wisdom, graciously let a ray of your light penetrate the darkness of my understanding. Give me a keen intellect, a retentive memory, and the ability to grasp things correctly and fundamentally. Give me the talent of being exact in my explanations and the ability to express myself with thoroughness and charm. Point out the beginning, direct the progress, and help in the completion of all my work. We ask this through Christ our Lord. Amen.**

### COURSE DESCRIPTION:

Why do we grow old? Can we ever expect to live for two hundred years? Understanding the aging process and extending the human lifespan are two of the most cutting-edge and fascinating pursuits in contemporary biology. In this upper-level course, which will be conducted as a journal club that will involve extensive student participation, we will read, analyze, and critique recent papers published in the biology of aging. Topics will include the evolution of aging, theories of aging, and the genetics and molecular biology of aging in different model systems including *S. cerevisiae*, *C. elegans*, *D. melanogaster*, *M. musculus*, and *Homo sapiens*.

Biology is both a science and an art requiring critical skills in reading, listening, thinking, speaking, and writing. It also demands people-skills that facilitate membership in a scientific research team. This seminar course has been designed so that students will

acquire and develop these essential practical skills for the vocation of a scientist or a physician-researcher.

REQUIRED TEXTS:

All the scientific papers and essays we will discuss and critique in this course can be downloaded from the course website on ANGEL. Please print out and bring the papers to class for discussion.

RECOMMENDED TEXTS:

- Robert Arking, *Biology of Aging*, 2<sup>nd</sup> ed. (Sunderland, MA: Sinauer, 1998).
- Stephen S. Hall, *Merchants of Immortality: Chasing the Dream of Human Life Extension* (Boston: Houghton Mifflin, 2003).

ACADEMIC EXPECTATIONS:

This is an upper-level seminar course, and I will expect active participation from all students. Thus, every student should come to class prepared to critically engage each scientific paper and each other. This means that you should read, take notes, and think about all the assigned readings before class. Each week, different students will take the lead and present the papers to the class before we discuss them. At the end of the semester, each student will submit a short 5-10 page grant proposal in the biology of aging based on the format of National Institutes of Health Grant, PHS 398. (For details, see the NIH website, <http://grants.nih.gov/grants/funding/phs398/phs398.html>).

Since this is a course that requires active student participation, regular attendance is expected. Please email the instructor in advance if you expect to miss a class. More than two unexcused absences during the semester could lead to a lower final grade.

GRADING POLICY:

Grades will be calculated as follows:

Grant Proposal (5-10 pages)	50%
Oral Presentations	30%
Class Participation	20%

In the world of science, grants have to be submitted to the funding agency by a particular deadline. There are no exceptions to this rule. Thus, in this class, I expect all work to be handed in on time. Late assignments will be penalized 10% of their point value per calendar day late (not per class day).

Academic dishonesty and plagiarism is not tolerated in science and will not be tolerated in this class. I shall follow and enforce strictly PC's policies regarding academic integrity.

## SCHEDULE OF READINGS:

- Introduction

**N. R. Austriaco, Jr. and L. Guarente, “Changes of telomere length cause reciprocal changes in the lifespan of mother cells in *Saccharomyces cerevisiae*,” *PNAS* 94 (1997): 9768-9772.**

*NEWS*: Karen Hopkin, “Making Methuselah,” in *The Science of Staying Young*, *Scientific American* 14 (2004): 12-17.

- Aging in Bacteria and Yeast

**E. J. Stewart et al., “Aging and death in an organism that reproduces by morphologically symmetric division,” *PloS Biol* 3 (2005): e45.**

**M. Kaerberlein et al., “Genes determining yeast replicative life span in a long-lived genetic background,” *Mech Ageing Dev.* 126 (2005): 491-504.**

**D. Sinclair and L. Guarente, “Extrachromosomal rDNA circles – a cause of aging in yeast,” *Cell* 91 (1997): 1033-1042.**

*REVIEW*: D. Sinclair, “Paradigms and pitfalls of yeast longevity research,” *Mech Ageing Dev* 123 (2002): 857-867.

*NEWS*: Dan Ferber, “Immortality Dies as Bacteria Show Their Age,” *Science* 307 (2005): 656.

*NEWS*: J. Couzins, “Scientific community. Aging research's family feud,” *Science* 303 (2004): 1276-1279.

- Aging in Worms

**N. Arantes-Oliveira, J.R. Berman, and C. Kenyon, “Healthy animals with extreme longevity,” *Science* 302 (2003): 611.**

**C.T. Murphy et al., “Genes that act downstream of DAF-16 to influence the lifespan of *Caenorhabditis elegans*,” *Nature* 424 (2003): 277-283.**

**M.P. Gardner et al., “Aging in a very short-lived nematode,” *Exp Gerontol.* 39 (2004): 1267-1276.**

**K.S. Joeng et al., “Long lifespan in worms with long telomeric DNA,” *Nat Genet* 36 (2004): 607-611.**

*REVIEW*: L. Guarente and C. Kenyon, "Genetic pathways that regulate ageing in model organisms," *Nature* 408 (2000): 255-262.

- Aging in Flies

**S.J. Broughton et al., "Longer lifespan, altered metabolism, and stress resistance in *Drosophila* from ablation of cells making insulin-like ligands," *PNAS* 102 (2005): 3105-3110.**

**D.S. Hwangbo et al., "*Drosophila* dFOXO controls lifespan and regulates insulin signaling in brain and fat body," *Nature* 429 (2004): 562-566.**

*REVIEW*: S.L. Helfand and B. Rogina, "Genetics of aging in the fruit fly, *Drosophila melanogaster*," *Annu Rev Genet.* 37 (2003): 329-348.

- Aging in Mice

**B. Maier et al., "Modulation of mammalian life span by the short isoform of p53," *Genes Dev* 18 (2004): 306-319.**

**M. Bluher, B.B. Kahn, and C. Ronald Kahn, "Extended Longevity in Mice Lacking the Insulin Receptor in Adipose Tissue," *Science* 299 (2003): 572-575.**

**K.K. Wong et al., "Telomere dysfunction and Atm deficiency compromises organ homeostasis and accelerates ageing," *Nature* 421 (2003): 643-648.**

**M. Holzenberger et al., "IGF-1 receptor regulates lifespan and resistance to oxidative stress in mice," *Nature* 421 (2003): 182-187.**

*REVIEW*: H. Liang et al., "Genetic mouse models of extended lifespan," *Exp Gerontol* 38 (2003): 1353-1364.

*NEWS*: Gordon J. Lithgow and Matthew S. Gill, "Physiology: Cost-free longevity in mice?" *Nature* 421 (2003): 125-126.

- Cellular Aging – The Molecular Basis of the Hayflick Limit

**M. Braig, "Oncogene-induced senescence as an initial barrier in lymphoma development," *Nature* 436 (2005): 660-666.**

**M. Collado et al., "Senescence in premalignant tumours," *Nature* 436 (2005): 642.**

**C. Michaloglou et al., "BRAF<sup>E600</sup>-associated senescence-like cell cycle arrest of human naevi," *Nature* 436 (2005): 720-725.**

*REVIEW*: Leonard Hayflick, "The Illusion of Cell Immortality," *Br J Cancer* 83 (2000): 841-846.

*NEWS*: Norman E. Sharpless and Ronald A. DePinho, "Crime and punishment," *Nature* 436 (2005): 636-637.

- Calorie Restriction and Aging

**W. Mair, M.D.W. Piper, and L. Partridge, "Calories Do Not Explain Extension of Life Span by Dietary Restriction in *Drosophila*," *PLoS Biology* 3 (2005): e233.**

**M. Kaeberlein et al., "Sir2-Independent Life Span Extension by Calorie Restriction in Yeast," *PLoS Biology* 2 (2004): e296.**

**B. Rogina and S.L. Helfand, "Sir2 mediates longevity in the fly through a pathway related to calorie restriction," *PNAS* 101 (2004): 15998-16003.**

**J.A. Mattison et al., "Calorie restriction in rhesus monkeys," *Exp Gerontol.* 38 (2003): 35-46.**

*REVIEW*: L. Guarente and F. Picard, "Calorie Restriction – the *SIR2* Connection," *Cell* 120 (2005): 473-482.

*NEWS*: J. Couzzins, "Gene Links Calorie Deprivation and Long Life in Rodents," *Science* 304 (2004): 1731.

- Oxidative Stress and Aging

**S.E. Schriener et al., "Extension of Murine Life Span by Overexpression of Catalase Targeted to Mitochondria," *Science*, published May 5, 2005.**

**W.C. Orr et al., "Effects of overexpression of copper-zinc and manganese superoxide dismutases, catalase, and thioredoxin reductase genes on longevity in *Drosophila melanogaster*," *J Biol Chem* 278 (2003): 26418-26422.**

**S. Melov et al., "Extension of life-span with superoxide dismutase/catalase mimetics," *Science* 289 (2000): 1567-1569.**

*REVIEW*: R.S. Sohal, R.J. Mockett, and W.C. Orr, "Mechanisms of aging: an appraisal of the oxidative stress hypothesis," *Free Radical Biol Med* 33 (2002): 575-586.

*NEWS*: Kathryn Brown, "A Radical Proposal," in *The Science of Staying Young*, *Scientific American* 14 (2004): 30-35.

- Werner's Syndrome and the WRN Gene

**L. Crabbe et al., "Defective Telomere Lagging Strand Synthesis in Cells Lacking WRN Helicase Activity," *Science* 306 (2004): 1951-1953.**

**P. M. Watt et al., "SGS1, a Homologue of the Bloom's and Werner's Syndrome Genes, Is Required for Maintenance of Genome Stability in *Saccharomyces cerevisiae*," *Genetics* 144 (1996): 935-945.**

**C. Yu et al., "Positional Cloning of the Werner's Syndrome Gene," *Science* 272 (1996): 258-262.**

*REVIEW*: Ali Ozgenc and Lawrence A. Loeb, "Current advances in unraveling the function of the Werner syndrome protein," *Mutation Research*, in press.

*REVIEW*: J. W. Lee et al., "Pathways and functions of the Werner syndrome protein," *Mech Ageing Dev.* 126 (2005): 79-86.

*REVIEW*: D. Kipling et al., "What can progeroid syndromes tell us about human aging?" *Science* 305 (2004): 1426-1431.

*NEWS*: Elizabeth Pennisi, "Premature Aging Gene Discovered," *Science* 272 (1996): 193-194.

- Human Aging

**S.J. Olshansky et al., "A potential decline in life expectancy in the United States in the 21<sup>st</sup> century," *N Engl J Med* 352 (2005): 1138-1145.**

**T.T. Perls et al., "Life-long sustained mortality advantage of siblings of centenarians," *Proc. Natl Acad Sci* 99 (2002): 8442-8447.**

**R.G.J. Westendorp and Thomas B.L. Kirkwood, "Human longevity at the cost of reproductive success," *Nature* 396 (1998): 743-746.**

*REVIEW*: G.M. Martin, "Genetic modulation of senescent phenotypes in *Homo sapiens*," *Cell* 120 (2005): 523-532.

*NEWS*: Thomas T. Perls, "The Oldest Old," in *The Science of Staying Young*, *Scientific American* 14 (2004): 6-11.

- Evolution of Aging

**G.C. Williams, "Pleiotropy, natural selection and the evolution of senescence," *Evolution* 11 (1957): 398-411.**

**D.N. Reznick et al., “Effect of extrinsic mortality on the evolution of senescence in guppies,” *Nature* 431 (2004): 1095-1099.**

*NEWS*: P.A. Abrams, “Evolutionary Biology: Mortality and Lifespan,” *Nature* 431 (2004): 1048-1049.

- *Should We Delay Human Aging? The Ethics of Longevity Research*

**Pope John Paul II, *Letter to the Elderly*, October 1, 1999.**

**President’s Council on Bioethics, “Ageless Bodies: IV. Ethical Issues,” in *Beyond Therapy: Biotechnology and the Pursuit of Happiness*, October 15, 2003, pp. 181-202.**

**D. Gems, “Is More Life Always Better? The New Biology of Aging and the Meaning of Life,” *Hastings Cent Rep.* 33 (2003): 31-39.**

*REVIEW*: W.S. Browner et al., “The genetics of human longevity,” *Am J Med* 117 (2004): 851-860.

*NEWS*: Michael R. Rose, “Will Human Aging Be Postponed?” in *The Science of Staying Young*, *Scientific American* 14 (2004): 24-29.

*NEWS*: Mark A. Lane, Donald K. Ingram and George S. Roth, “The Serious Search for an Antiaging Pill,” in *The Science of Staying Young*, *Scientific American* 14 (2004): 36-41.

*NEWS*: S. Jay Olshansky, Leonard Hayflick, and Bruce A. Carnes, “No Truth to the Fountain of Youth,” in *The Science of Staying Young*, *Scientific American* 14 (2004): 98-102.