GERONTOLOGY 414 (36250R) NEUROBIOLOGY OF AGING SPRING 2008

Instructors: Caleb Finch cefinch@usc.edu Valter Longo vlongo@usc.edu
Office Hours by appointment

Course location: GERO 230. Course time: Tu,Th 5:00-6:50P

Nature of the course: This course covers a broad spectrum of topics in the neurobiology of normal and pathological aging. It is conceived of as a 'research' course in the challenging mysteries of aging and disease in human brain, most of which remain unexplained. Class discussions are anticipated to advance the thinking of faculty instructors as well as the class. The readings will be posted as Adobe Acrobat pdf files each week. Students who master lecture material and posted pdf file articles will do well n the course. Readings (pdf files) will be posted for each lecture with PowerPoint images on *blackboard*. http://blackboard.usc.edu

Evaluation is based on two midterm essay examinations, a final examination and two oral presentations of assigned papers from the biomedical literature. Exams are not cumulative. Each lecture provides review questions which are the basis for written exams.

Component	Date	Lectures Covered	Percent
Midterm I	Feb 21	Jan15 - Feb 19	20%
WEEK 8 SPRING BREAK MARCH 17 - 22			
Midterm II	April 8	Feb 21-April 3	25%
Final Exam	Wed, May 9 2-4 PM	Apr 3 - Apr 26	25%
Oral presentations (2 per student)			30%
The examinations consist primarily of short answer essay questions.			100%

MAKE-UP EXAMS (with a valid excuse) ONLY SCHEDULED FOR THE FIRST WEEK FOLLOWING THE ORIGINAL EXAM DATE!! If you do not take a make-up exam a score of 0 points will be averaged with the remaining scores. No extra credit is available in this class.

recommended supplemental texts

Alberts B et al. *Molecular Biology of the Cell*, 4th edition, Garland Science, 2002
Arking R. *Biology of Aging*, 3rd edition, Oxford U Press, 2006.
Finch CE. *Longevity, Senescence, and the Genome*, U Chicago Press, 1990
Finch CE, Kirkwood TBL *Chance, Development, and Aging*. Oxford U Press, 2000.
Heimer L. *The Human Brain and Spinal Cord. Functional Neuroanatomy*, 2nd edition, Springer-Verlag, 1995
Kandel ER et al. *Principles of Neuroscience*, 4th edition., McGraw-Hill, 2000
Siegel GR et al., *Basic Neurochemistry,* 7th edition, Elsevier, 2006
Swanson LW *Brain Architecture. Understanding the Basic Plan*. Oxford U Press, 2003
Timiras, P. *Physiological Basis of Aging and Geriatrics*, 4th edition, Informa Healthcare, 2007
Wachter KW, Finch CE. *Between Zeus and the Salmon. The Biodemography of Longevity*. National Academy Press, 1997 http://books.nap.edu/openbook.php?record_id=5740)

Gero 414: Neurobiology of Aging, Spring 2008.
Caleb Finch and Valter Longo

Jan 15: Introduction

Biogerontology and the neurobiology of aging. CF

1. Brain Facts. A Primer on the Brain. http://www.sfn.org/skins/main/pdf/brainfacts/brainfacts.pdf

Theories of aging (cell theories; evolutionary theories). VL

2. Finch CE 2007: *The Biology of Human Longevity*, Chapter 1: pp. 1-49 (PDF).
3. Ricklefs RE and Finch CE1995: *Aging a Natural History*, Chapters 1 and 2 http://docushare.usc.edu/docushare/dsweb/View/Collection-473

4. Kirkwood TB, Austad SN. 2000 Why do we age? Nature. 2000 408:233-8 (PDF).

5. Longo VD et al. 2005 Programmed and altruistic ageing. Nat Rev Genet. 6:866-72. (PFD).

Jan 17:

General Cell Biology and biochemistry VL

1. Alberts B Molecular Biology of the Cell. Chapter 15.
2. Davis E, Ghosh A. 2007 Should I stay or should I go: Wnt signals at the synapse. Cell 130:593-6.

General neuroanatomy. CF

1. Swanson LW 2007 Quest for basic plan of nervous system circuitry. Brain Res Rev 55: 356-72. (PDF)
2. Cotterill RM 2001 Cooperation of the basal ganglia, cerebellum, sensory cerebrum and hippocampus: possible implications for cognition, consciousness, intelligence and creativity. Prog Neurobiol. 64:1-33. (PDF)

Jan 22:

Genetics of longevity:

Model systems of nondividing cells (fly, worm, yeast). VL

1. Longo VD, Finch CE. 2003 Evolutionary medicine: from dwarf model systems to healthy centenarians? Science. 299:1342-6. Review.
2. Longo VD, Kennedy BK. 2006 Sirtuins in aging and age-related disease. Cell. 126:257-68. Review.
3. Kenyon C. 2005 The plasticity of aging: insights from long-lived mutants. Cell.120:449-60. Review.

Environment and human longevity. CF

1. Finch CE, Crimmins EM 2004. Inflammatory exposure and historical changes in human life-spans. Science. 305:1736-9. (PDF) .
2. Finch C 2006. Aging, inflammation, and the body electric. Daedelus March, 68-78. (PDF)
3. Supplemental readings:

*Finch CE. 2000. Chance, Development, and Aging, Chapter 1.
* Crimmins EM, Finch CE. 2006 Infection, inflammation, height, and longevity. Proc Natl Acad Sci U S A. 103:498-503.

Jan 24:

Mechanisms of cell damage and cell death (ischemia, oxidative stress). VL

1, Kermer P et al Neuronal apoptosis in neurodegenerative diseases: from basic research to clinical application. 2007 Trends Neurosci. 30:159-66.

2, Conforti et al 2007 Neuronal death: where does the end begin? Trends NeuroSci 30:159-66.

3. Fabrizio P et al 2001,Regulation of longevity and stress resistance by Sch9 in yeast. Science. 292:288-90.

Neuron migration and death during development. CF

1. Nadarajah B, Parnavelas JG. 2002 Modes of neuronal migration in the developing cerebral cortex. Nat Rev Neurosci. 3:423-32. (PDF)
2. Heck N et al 2007. Activity-Dependent Regulation of Neuronal Apoptosis in Neonatal Mouse Cerebral Cortex. Cereb Cortex, in press. (PDF)
3. Kalb R 2005. The protean actions of neurotrophins and their receptors on the life and death of neurons. Trends Neurosci 28: 5-11. (PDF)

Jan 29:

Synapse loss: neuron death vs atrophy during aging;. CF

1. Finch CE 2007: The Biology of Human Longevity, Chapter 1: pp. 23-27 (PDF).
2. Simić G 1997. Volume and number of neurons of the human hippocampal formation in normal aging and Alzheimer's disease. J Comp Neurol. 379:482-94. (PDF)
3. Finch CE (1993) Neuron atrophy during aging: programmed or sporadic? Trends Neurosci 16:104-10. (PDF)

Neurogenetics of aging: VL

1. Taguchi A et al 2007 Brain IRS2 signaling coordinates life span and nutrient homeostasis. Science. 317:369-72.
2. Libert S et al 2007 ,Regulation of Drosophila life span by olfaction and food-derived odors Science. 315:1133-7.
3. Wolkow CA 2002. Life span: getting the signal from the nervous system. Trends Neurosci. 25:212-6
4. Sievers C 2008 .Insulin-like growth factor-1 in plasma and brain: regulation in health and disease. Front Biosci. 13:85-99.

Jan 31:

Genetics of human brain aging (limits of heritability). CF

1. Finch CE, Tanzi RE 1997 The genetics of aging. Science 278:407-11. (PDF)
2. Finkel D, McGue M.Genetic and environmental influences on intraindividual variability in reaction time. Exp Aging Res.33:13-35. (PDF)

Vascular pathobiology in brain aging. CF

1. Finch CE 2007: The Biology of Human Longevity, Chapter 1: pp. 17; 65-87 (PDF).
2. DeCarli C et al 1999. Impact of apolipoprotein E4 and vascular disease on brain morphology in men from the NHLBI twin study. Stroke. 30:1548-53. (PDF).

Feb 5: Glial cells: white matter, astrocytes, microglia. CF
1. Bartzokis G et al 2001 Age-related changes in frontal and temporal lobe volumes in men: a magnetic resonance imaging study. Arch Gen Psychiatry. 58:461-5.
2. Rozovsky I et al 2005 Reversible age impairments in neurite outgrowth by manipulations of astrocytic GFAP. Neurobiol Aging. 26:705-15.
Student presentations
1. Xie Z et al 2003 Aging and glial responses to lipopolysaccharide in vitro: greater induction of IL-1 and IL-6, but smaller induction of neurotoxicity. Exp Neurol. 182:135-41.
2. Hinks GL, Franklin RJ. 2000. Delayed changes in growth factor gene expression during slow remyelination in the CNS of aged rats. Mol Cell Neurosci. 16:542-56.

Feb 7: Stem cells and regeneration in the CNS. VL
1. Gass P, Riva MA 2007 CREB, neurogenesis and depression. Bioessays. 29:957-61.
2. Morgan D.2007 Amyloid, memory and neurogenesis. Exp Neurol. 205:330-5. Mar 14.
3. Yamasaki TR, et al 2007Neural stem cells improve memory in an inducible mouse model of neuronal loss. J Neurosci. 27:11925-33.
Student presentations
1. Rando TA. 2006 Stem cells, ageing and the quest for immortality. Nature. 441:1080-6.

Yan L et al 2007 Type 5 adenylyl cyclase disruption increases longevity and protects against stress. Cell. 130:247-58.
2. Taguchi A, Wartschow LM, White MF. Brain IRS2 signaling coordinates life span and nutrient homeostasis. Science. 317:369-72.

Feb 12: Biochemistry/molecular biology of memory and aging. Guest lecturer

Student presentations

Feb 14: Cellular mechanisms in memory: LTP and aging. Guest lecturer.

Student presentations

Feb 19: Review and general discussion CF/VL
Feb 21: Midterm exam 1

Feb 28: Memory and aging in humans. Guest lecturer, Mara Mather
1. Hedden, T., & Gabrieli, J. D. E. (2004). Insights into the ageing mind: A view from cognitive neuroscience. *Nature Reviews Neuroscience, 5*, 87-U12.
2. Mather, M., & Carstensen, L. L. (2005). Aging and motivated cognition: The positivity effect in attention and memory. *Trends in Cognitive Sciences, 9*, 496-502.
Student presentations

1. Gazzaley, A., Cooney, J. W., Rissman, J., & D'Esposito, M. (2005). Top-down suppression deficit underlies working memory impairment in normal aging. *Nature Neuroscience, 8*, 1298-1300.
2. Johnson, M. K., Mitchell, K. J., Raye, C. L., & Greene, E. J. (2004). An age-related deficit in prefrontal cortical function associated with refreshing information. *Psychological Science, 15*, 127-132.

Mar 4: Alzheimer disease, the pathobiology. CF
Student presentations

Mar 11: Alzheimer disease: mechanisms and animal models. VL

1. Xie Z et al 2002. Peroxynitrite mediates neurotoxicity of amyloid beta-peptide1-42- an lipopolysaccharide-activated microglia. J Neurosci. 22:3484-92.
2. Ferla FM et al 2007 Intracellular amyloid-beta in Alzheimer's Nat Rev Neurosci. 8:499-509.
3. Goedert M, Spillantini MG2006 A century of Alzheimer's disease. Science 314:777-81.
4. Klein W et al 2001 Targeting small Abeta oligomers: the solution to an Alzheimer's disease conundrum? Trends Neurosci. 24:219-24
Student presentations

Mar 13: Alzheimer disease: drugs in prevention and therapy. CF
Student presentations

Spring break Mar 17-22

Mar 25: Basal ganglia and aging. CF
Student presentations

Mar 27: Parkinsons disease. VL
1. Surmeier DJ 2007 Calcium, ageing, and neuronal vulnerability in Parkinson's disease. Lancet Neurol. 6:933-8. Review.

2. Levy G. 2007 The relationship of Parkinson disease with aging. Arch Neurol. 64:1242-6.

3. Thomas B, Beal MF. 2007 Parkinson's disease. Hum Mol Genet. Spec No. 2:R183-94.
Student presentations

April 1: Huntingtons disease CF
Student presentations

April 3: ALS and peripheral neuropathy. CF
Student presentations

April 8: Midterm exam 2

April 10: Neuroendocrinology of aging: adrenal CF
Student presentations

April 15: Sex steroids in brain aging and Alzheimer disease Todd Morgan
Student presentations

April 17: Diet in brain aging: VL

1. Patel NV et al 2005 Caloric restriction attenuates Abeta-deposition in Alzheimer transgenic models. Neurobiol Aging. 26:995-1000. Epub 2004 Nov 25.
2. Ingram DK 2007 Calorie restriction in nonhuman primates: assessing effects on brain and behavioral aging. Neuroscience.145:1359-64.
3. Mattson MP. 2003 Gene-diet interactions in brain aging and neurodegenerative disorders. Ann Intern Med. 139: 441-4. Review.

Student presentations

April 22: Circadian organization CF
Student presentations

April 24: Exercise in brain aging, Christian Pike
Student presentations

April 29: Brain aging in human evolution: CF
Student presentations

May 1: final review

May 9: Final Exam