# ***Nsc 312 – Biological Rhythms***

Fall 2007 T 1-2:50
Instructor: Mary Harrington, Bass 417, x3925, mharring@smith.edu,
Office hours: M9-10, W830-930, or by appointment.

Sep 11 Introduction
Sep 18 Human Circadian Rhythms
Sep 25 Fundamental properties
Oct 1 Comparative studies
Oct 16 Molecular Biology of circadian clocks
Oct 23 The SCN
Oct 30 Photic and non-photic entrainment
Nov 6 Photoperiodism
Nov 13 Circadian rhythms and health
Nov 20 Presentations of student research
Nov 27 Presentations of student research
Dec 4 Presentations of student research
Dec 11 Presentations of student research

## ***Sep 11- Introduction***

Background readings:

- Ouyang Y, Andersson CR, Kondo T, Golden SS, and Johnson CH, 1998. Resonating circadian clocks enhance fitness in cyanobacteria. Proc. Natl. Acad. Sci. 95:8660-8664.
- Chapters 1 and 2 in Chronobiology: Biological Timing
- Johnson CH, Elliott JA, Foster R (2003) Entrainment of circadian programs, Chronobiology International, 20: 741-774

## ***Sep 18 – Human Circadian Rhythms***

Background readings:

- Chapters 9 and 10 in Chronobiology: Biological Timing

*Students present articles in groups of three:*

1. Scheer et al. Plasticity of the intrinsic period of the human circadian timing system. PLoS ONE. 2007 Aug 8;2:e721.
2. Revell et al Advancing human circadian rhythms with afternoon melatonin and morning intermittent bright light, J Clin Endo Metab 91 (2006) 54-60
3. Toh KL, Jones CR, He Y, et al., 2001. An hPer2 phosphorylation site mutation in familial advanced sleep phase syndrome. Science 291:1040-3.
4. Zeitzer et al Temporal dynamics of late-night photic stimulation of the human circadian timing system, Am J Physio, 205 289:R839-44.
5. Crowley SJ et al Estimating dim light melatonin onset (DLMO) phase in adolescents using summer or school-year sleep/wake schedules. Sleep 2006 29:1632-41

## ***Sep 25 Fundamental properties***

Background readings:

- Chapter 3 in Chronobiology: Biological Timing.
- Jud et al (2005) A guideline for analyzing circadian wheel-running behavior in rodents under different lighting conditions, Biol Proced Online 7:101-116.
- Pittendrigh and Daan 1976 (five papers)

*Students take turns presenting the figures:*

Johnson CH, Elliott JA, Foster R (2003) Entrainment of circadian programs, Chronobiology International, 20: 741-774

## ***Oct 1- Comparative studies***

Background readings:

- Chapter 5 in Chronobiology: Biological Timing, to p.168
- Circadian organization in reindeer

*Each student serves as leader on one article and discussant on another article:*

1. Zimmerman N.H., and Menaker M., 1979. The pineal: A pacemaker within the circadian system of the house sparrow. Proc Natl. Acad Sci 76:999-1003.
2. Page, T.L., 1982, Transplantation of the cockroach circadian pacemaker. Science 216:73-5.
3. Roenneberg, T, and Morse, D., 1993. Two circadian oscillators in one cell. Nature 362:362-4.(paper copy)
4. Plautz JD, Kaneko M, Hall JC, and Kay, SA, 1997. Independent photoreceptive circadian clocks throughout Drosophila. Science 278:1632-5.
5. Kaneko et al Diversity of zebrafish peripheral oscillators revealed by luciferase reporting.PNAS 2006 103:14614-9.
6. Steele CT, Zivkovic BD, Siopes T, Underwood H. Ocular clocks are tightly coupled and act as pacemakers in the circadian system of Japanese quail. Am J Physiol Regul Integr Comp Physiol. 2003 Jan;284(1):R208-18.
7. Granados-Fuentes D, Saxena MT, Prolo LM, Aton SJ, Herzog ED. Olfactory bulb neurons express functional, entrainable circadian rhythms. Eur J Neurosci. 2004 Feb;19(4):898-906.

## ***Oct 16 Molecular biology of circadian clocks***

Background readings:

- Chapter 7 in Chronobiology: Biological Timing
- Ko and Takahashi (2006) Molecular components of the mammalian circadian clock, Human Molecular Genetics, 15:R271-277.
- Lakin-Thomas PL (2006) Transcriptional feedback oscillators: Maybe, maybe not…. JBR 21:83-92.

*Students work in pairs to lead discussion of articles*

1. Araki et al., 2006, Identification of genes that express in response to light exposure and express rhythmically in a circadian manner in the mouse suprachiasmatic nucleus. Brain Research.
2. DeBruyne at al., A clock shock: Mouse CLOCK is not required for circadian oscillator function, Neuron (2006) 465-477.
3. Gallego M et al, An opposite role for tau in circadian rhythms revealed by mathematical modeling, PNAS 2006.
4. Roybal et al Mania-like behavior induced by disruption of CLOCK, PNAS 2007 104:6406-11.
5. Hong et al Inducible and reversible Clock gene expression in brain using the tTA system for the study of circadian behavior. PLoS Genetics 3:0324-0338
6. Kornmann et al System-driven and oscillator-dependent circadian transcription in mice with a conditionally active liver clock. PLos Biol 5:0179 – 0189

## ***Oct 23 The SCN***

Background readings:

- Chapter 5 p.168 – 175, and Chapter 6 in Chronobiology: Biological Timing

*Students work in pairs to lead discussion of articles*

1. Stephan FK, Zucker I Circadian rhythms in drinking behavior and locomotor activity of rats are eliminated by hypothalamic lesions. Proc Natl Acad Sci U S A. 1972 Jun;69(6):1583-6.
2. Schwartz, WJ, Gross RA, and Morton, MT, 1987. The suprachiasmatic nuclei contain a tetrodotoxin-resistant circadian pacemaker. Proc Natl. Acad Sci.84:1694-8.
3. Ralph, M.R., Foster, R.G., Davis, F.C., and Menaker, M., 1990. Transplanted suprachiasmatic nucleus determines circadian period. Science 247:975-978.
4. Welsh DK, Logothetis DE, Meister M, Reppert SM. Individual neurons dissociated from rat suprachiasmatic nucleus express independently phased circadian firing rhythms. Neuron. 1995 Apr;14(4):697-706.
5. Silver, R., LeSauter, J., Tresco, P.A., and Lehman, M.N., 1996. A diffusible coupling signal from the transplanted suprachiasmatic nucleu controlling circadian locomotor rhythms. Nature 382:810-813.
6. de la Iglesia HO, Cambras T, Schwartz WJ, Diez-Noguera A.Forced desynchronization of dual circadian oscillators within the rat suprachiasmatic nucleus. Curr Biol. 2004 May 4;14(9):796-800.

## ***Oct 30 - Photic and non-photic interactions***

Background readings:

- Yannielli P and Harrington ME (2004) Let there be "more" light: enhancement of light actions on the circadian system through non-photic pathways. Progress in Neurobiology 74: 59-76.
- Atkinson et al Exercise as a synchronizer of human circadian rhythms: an update and discussion of the methodological problems, Eur J Appl Physiol, 2006

*Students work in pairs to lead discussion of articles*

1. Klerman EB, Rimmer DW, Dijk DJ, Kronauer RE, Rizzo JF 3rd, Czeisler CA. Nonphotic entrainment of the human circadian pacemaker. Am J Physiol. 1998 Apr;274(4 Pt 2):R991-6.
2. Maywood and Mrosovsky (2001) A molecular explanation of interactions between photic and non-photic circadian clock-resetting stimuli. Gene Expression patterns 1: 27-31.
3. Dallman R and Mrosovsky N (2006) Scheduled wheel access during daytime: A method for studying conflicting zeitgebers. Physiol Behav 88: 459-465.
4. Mistlberger and Antle (2006) The enigma of behavioral inputs to the circadian clock: A test of function using restraint. Physiol Behav 87: 948-954.
5. Harrington et al Behavioral and neurochemical sources of variability of circadian period and phase: studies of circadian rhythms of npy-/- mice. Am j Physiol 292 (2007) 1306-1314.
6. PC Yannielli, J. McKinley Brewer and M.E. Harrington, Activation of the NPY Y5 receptor suppresses circadian responses to light while its blockade potentiates them: complementary *in vivo* and *in vitro* studies. European Journal of Neuroscience, 18 (2004) 891-897

## ***Nov 6 – Photoperiodism***

Background readings:

- Chapter 4 in Chronobiology: Biological Timing
- Goldman BD Mammalian photoperiodic system: Formal properties and neuroendocrine mechanisms of photoperiodic time measurement, JBR 16 (2001) 283-301
- Prendergast BJ Internalization of seasonal time, Hormones Behav 48 (2005) 503-511.
- Lincoln GA Decoding the nightly melatonin signal through circadian clockwork Mol Cell Endocrinol 252(2006) 69-73.
- Elliott, J.A., Stetson, M.H., and Menaker, M., 1972. Regulation of testis function in golden hamsters: A circadian clock measures photoperiodic time. Science 178:771-3.
- Elliott JA Circadian rhythms and photoperiodic time measurement in mammals Fed proc 35 1976 2339-2346.

*Students select one task and explain to others:*

1. Describe photoperiodic responses. Clarify photosensitivity, photorefractory. Use appropriate figures from Goldman article, Chronobiology text Ch 4, Prendergast.
2. Describe internal coincidence vs. external coincidence models. Use Goldman paper and Chronobiology text (p. 119-120)
3. Present Elliott 1976 paper (fig 4.15 in Chronobiology text, Fig 2 in Goldman)
4. Discuss mechanisms and sites of action for melatonin to mediate photoperiodic responses. Use Goldman, Prendergast, and Chronobiology text.
5. Present Lincoln paper.

## ***Nov 13– Circadian Rhythms and Health***

Background readings:

- Chen-Goodspeed and Lee, Tumor suppression and circadian function. J Biol Rhythms. 2007 Aug;22(4):291-8.
- Laposky et al Sleep and circadian rhythms: Key components in the regulation of energy metabolism.FEBS Lett. 2007 Aug 14;
- Stevens et al. Meeting report: the role of environmental lighting and circadian disruption in cancer and other diseases.Environ Health Perspect. 2007 Sep;115(9):1357-62.
- Spanagel et al Alcohol consumption and the body's biological clock Alcoholism: Clinical and Experimental Research, 29 (2005).
- Wu and Swaab (2005) The human pineal gland and melatonin in aging and Alzheimer's disease. J Pineal Res 38:145-152.

*Students work in small groups to lead discussion of articles*:

1. Megdal et al Night work and breast cancer risk: A systemic review and meta-analysis. Eup J Cancer 41 (2005) 2023-2032
2. De Leersnyder et al. (2006) Circadian rhythm disorder in a rare disease: Smith-Magenis syndrome. Mol Cell Endocrinology
3. Gery S et al, Epigenetic silencing of the candidate tumor suppressor gene Per1 in non-small cell lung cancer, Clin Cancer Res 2007
4. Lewy et al (2006) The circadian basis of winter depression, PNAS , 103:7414-7419.
5. Pallier et al Pharmacological imposition of sleep slows cognitive decline and reverses dysregulation of circadian gene expression in a transgenic mouse model of Huntington's disease. J Nsci 27 (2007) 7869

## ***Nov 20 – Dec 11 Student Research Presentations***

### ***Evaluation of your efforts:***

- 20% Class participation – attendance, discussion, questions, preparedness, summaries
- 25% Term paper
- 25% Presentation
- 15% Research Article presentations
- 15% Annotated Bibliography – due the day of your presentation

Work handed in late will be marked down 5% for each day it is late.

### ***Summaries and brainstorming***

Prior to class Sep 18, Oct 1, 16, 23, 30, and Nov 13 prepare a summary of your target article. List up to 3 experiments that might be sensible as follow-up experiments. Limited to two pages.

## ***Final Presentation***

This will be at least 30-45 min long, and will include an in depth discussion of at least two primary journal articles, assigned for the entire class to read and posted on Moodle at least one week prior to the presentation.

## ***Term Paper***

Topic chosen: 10/23
Preliminary Outline and preliminary Bibliography due: 11/6
Draft due: 11/20
Completed paper due: 12/21

The paper should be 10-15 pages long. It should include a brief discussion of the historical background to your topic, a clear statement of the research problem, a detailed presentation of current knowledge relating to this problem, and a final section proposing at least 3 experiments that would make the most sense as further work on this topic. For each experiment, describe your hypothesis, your method for testing that hypothesis, and your interpretation of the possible results.

## ***Annotated bibliography***

The articles will be the ones you are using or have considered for your term paper. This is a combination of complete citation of the article, along with several sentences summarizing the article. Indicate the most important results, and how you did or did not find this source useful. You should have 20 references. The finished bibliographies will be shared with the entire class.

## ***Suggestions for term paper topics:***

1. How does the SCN control peripheral oscillators in mammals?
2. How is the circadian clock linked to metabolic disease and obesity?
3. Describe and justify several scientifically based treatments for circadian disorders in humans.
4. Is the molecular basis of the circadian clock explained by transcription-translation feedback loops? Describe evidence for alternative explanations.
5. How is the circadian clock linked to neurodegenerative disorders?
6. What explains the links shown between circadian rhythm disruption and increased cancer risk?
7. What events follow the reception of light to produce resetting of the mammalian circadian clock? What is the process by which the cellular and molecular system is reset?
8. Are circadian rhythms related to longevity?

Other topics are possible, providing the focus is on a topic of current interest in the neuroscience of biological rhythms.