

GNET 631 – Fall 2011
Advanced Molecular Biology 1

Section 1 – Taught by Jack Griffith

Aug 24 Wed: Triplet Diseases, genome structure and repeated DNAs
O'Rourke and Swanson, Zu et al

Aug 26 Fri: Repeat diseases continued
Pearson review, Liquori, class notes

Aug 29 Mon: More repeat diseases

Aug 31 Wed: Supercoiling I
Wang 1, 2; C and E news,

Sep 2 Fri: Supercoiling II and unusual DNAs

Sep 5 Mon: No Class – Labor Day

Sep 7 Wed: Telomeres I
Griffith; van Steensel, Zakian review

Sep 9 Fri: Telomeres II
Cesare et al; Wu and de Lange, Mol Cell review, Tomaska

Sep 12 Mon: Chromatin structure
Kornberg, Luger; Griffith; Germon

Sep 13 Tues: Seminar by Tom Kunkel on DNA replication
Biochemistry Dept. 11 AM G202 MBRB

Sep 14 Wed: Chromatin transcription, assembly and phasing
Tyler; Adams

Sep 16 Fri: DNA Replication: general motifs
Dutta and Bell; Benkovic; McHenry

Sep 19 Mon: DNA replication: T7, T4 phage, E. coli
Chastain 2003, Nossal 2007

Sep 21 Wed: DNA replication SV40 and Papilloma viruses

Sep 23 Fri: DNA replication: Herpes viruses (Sezgin Ozgur will speak)

Sep 26 Mon: Wrap up and review (Amanda and Tangi – Teaching Assistants)

Section 2 – Taught by Dale Ramsden

Section 1. Replication control

- 1. Replication origins. Where? (sequence vs. epigenetics)**
- 2. Replications origins. When? (definition of pre-RC, firing of pre-RC)**
- 3. Replications origins. Licensing (not more than once, not less than once either)**
- 4. Fork stability. Translesion synthesis, fork regression**

Section 2. DSB repair

- 5. Double strand break repair1. Chromosome glue.**
- 6. Double strand break repair2; Cell cycle and choice of pathway**
- 7. Homologous recombination 1; Recombinase assembly**
- 8. Homologous recombination 2; Homology search and resolution**
- 9. Nonhomologous end joining**

EXAM 1

Section 3: Genome Editing.

- 10. RNA in DNA**
- 11. Cytidine deamination**
- 12. Active demethylation of 5MeC**
- 13. Mobile elements**
- 14. VDJ recombination**

EXAM 2

Section 3 – Taught by Aziz Sancar

(A) DNA REPAIR

Lecture 1. Wednesday, Nov. 2: Overview of DNA Repair and DNA Damage Checkpoints

- Sancar, A., Lindsey-Boltz, L.A., Ünsal-Kaçmaz, K., and Linn, S. (2004) Molecular Mechanisms of Mammalian DNA Repair and the DNA Damage Checkpoints. *Annu. Rev. Biochem.* **73**, 39-85.
- Heenan, E.J., Sancar, A. (2008) Chemistry of DNA Damage Repair. *Wiley Encyclopedia of Chemical Biology*, DOI: 10.1002/9780470048672.webc131
- Kersge, N., Simoni, R.D., and Hill, R.L. (2009) JBC Classics: 100 years of Biochemistry and Molecular Biology. DNA Repair Mechanisms: the Work of Aziz Sancar. *J. Biol. Chem.* **284**, e19-e20.

Lecture 2. Friday, Nov. 4: Nucleotide Excision Repair

- Sancar A., Lindsey-Boltz L.A., Kang T.H., Reardon J.T., Lee J.H., Ozturk N. (2010) Circadian clock control of the cellular response to DNA damage. *FEBS Lett.* **18**;584(12):2618-25.
- Kang, T.H., Lindsay-Boltz, L.A., Reardon, J.T., and Sancar, A. (2010) Circadian Control of XPA and excision repair of cisplatin-DNA damage by cryptochrome and HERC2 ubiquitin ligase. *Proc. Natl. Acad. Sci. USA* **107**, 4890-4895.

- c) Gaddameedhi, S. Selby, C.P., Kaufmann, W.K., Smart, R.C., Sancar, A. (2011) Control of skin cancer by the circadian rhythm. *Proc. Natl. Acad. Sci. USA*, doi:10.1073/pnas.1115249108

Lecture 3. Monday, Nov. 7: Mismatch Repair

- a) Modrich, P. (2006) Mechanisms in Eukaryotic Mismatch Repair. *J. Biol. Chem.* **281**, 30305-30309.
b) Kadyrov, F.A., Dzantiev, L., Constanin, N., and Modrich, P. (2006) Endonucleolytic Function of MutL α in Human mismatch Repair. *Cell*. **126**, 297-308.

(B) DNA DAMAGE CHECKPOINT RESPONSE

Lecture 4. Wednesday, Nov. 9: Classic Experiments in DNA Damage Checkpoints

- a) Paulovich, A., and Hartwell, H. (1995) A Checkpoint Regulates the Rate of Progression through S Phase in *S. cerevisiae* in Response to DNA Damage. *Cell* **82**, 134-140.
b) Tercero, J.A., and Diffley, J. F. X. (2001) Regulation of DNA Replication Fork Progression Through Damaged DNA by the Mec1/Rad53 Checkpoint. *Nature* **412**, 553-557.

Lecture 5. Friday, Nov. 11: Damage Sensors I: ATM

- a) Bakkenist, C. J., and Kastan, M. B. (2003) DNA Damage Activates ATM Through Autophosphorylation and Dimer Dissociation. *Nature* **421**, 499-506.
b) Lee, J.H., and Paull, T.T. (2005) ATM activation by DNA double-strand breaks through the Mre11-Rad50-Nbs1 complex. *Science* **308**, 551-554.

Lecture 6. Monday, Nov. 14: Damage Sensors II: ATR

- a) Zou, L., and Elledge, S. J. (2003) Sensing DNA Damage Through ATRIP Recognition of RPA-ssDNA Complexes. *Science* **300**, 1542-1548.
b) Choi, J.-H., Lindsey-Boltz, L.A., Kemp, M., Mason, A.C., Wold, M.S., Sancar, A. (2010) From the Cover: Reconstitution of RPA-covered single-stranded DNA-activated ATR-Chk1 signaling. *Proc. Natl. Acad. Sci. USA* **107**, 13660-13665.

Lecture 7. Wednesday, Nov. 16: Damage Sensors III: Rad17-RFC/9-1-1 Complex

- a) Kondo, T., Wakayama, T., Naiki, T., Matsumoto, K., and Sugimoto, K. (2001) Recruitment of Mec1 and Ddc1 Checkpoint Proteins to Double-Strand Breaks Through Distinct Mechanisms. *Science* **294**, 867-870.
b) Majka, J., Niedziela-Majka, A., and Burgers, P.M. (2006) The checkpoint clamp activates Mec1 kinase during initiation of the DNA damage checkpoint. *Mol. Cell* **24**, 891-901.

Lecture 8. Friday, Nov. 18: Mediators

- a) Kumagai, A., Lee, J., Yoo, H.Y., and Dunphy, W.G. (2006) TopBP1 Activates the ATR-ATRIP Complex. *Cell*. **124**, 943-955.
b) Lindsey-Boltz, L.A., Serçin, O., Choi, J.-H., Sancar, A. (2009) Reconstitution of Human Claspin-mediated Phosphorylation of Chk1 by the ATR (Ataxia Telangiectasia-mutated and Rad3-related) Checkpoint Kinase *J. Biol. Chem.* **284**, 33107-33114.

EXAM 1: November 18, Friday (10:00 am) – November 21, Monday (9:00 am)

(C) CELL CYCLE AND CIRCADIAN CYCLE

Lecture 9. Monday, Nov. 21: Overview of Circadian Rhythms

- a) Reppert, S.M., and Weaver, D.R. (2002) Coordination of Circadian Timing in Mammals. *Nature* **418**, 935-941.
b) Hastings, M.H., Reddy, A.B., and Maywood, E.S. (2003) A Clockwork Web: Circadian Timing in Brain and Periphery in Health and Disease. *Nature Rev. Neurosci.* **4**, 649-661.
c) Sancar, A. (2004) Regulation of the mammalian circadian clock by cryptochrome. *J. Biol. Chem.* **279**, 34079-34082.

Lecture 10. Monday, Nov. 28: Connection of the Cell and Circadian Cycles

- a) Matsuo, T., Yamaguchi, S., Mitsui, S., Emi, A., Shimod, F., and Okamura, H. (2003) Control Mechanism of the Circadian Clock for Timing of Cell Division in vivo. *Science* **302**, 255-259.
- b) Nagoshi, E., Saini, C., Bauer, C., Laroche, T., Naef, F., and Schibler, U. (2004) Circadian Gene Expression in Individual Fibroblasts: Cell-autonomous and Self-sustained Oscillators Pass Time to Daughter Cells. *Cell* **119**, 693-705.
- c) Yeom, M., Pendergast, J.S., Ohmiya, Y. Yamazaki, S. (2010) Circadian-independent cell mitosis in immortalized fibroblasts. *Proc. Natl, Acad. Sci. USA* **107**, 9665-9670.

Lecture 11. Wednesday, Nov. 30: Circadian Cycle and Cell Cycle Checkpoints

- a) Ünsal-Kaçmaz, K., Mullen, T.E., Kaufmann, W.K., and Sancar, A. (2005) Coupling of Human Circadian and Cell Cycles by the Timeless Protein. *Mol. Cell Biol.* **25**, 3109-3116.
- b) Gery, S., Komatsu, N., Baldjyan, L., Yu, A., Koo, D., Koeffler, H.P. (2006) The Circadian Gene Per1 Plays an Important Role in Cell Growth and DNA Damage Control in Human Cancer Cells. *Mole. Cell.* **22**, 375-382.

Lecture 12. Friday, Dec. 2: Circadian Cycle and Cancer

- a) Fu, L., Pelicano, H., Liu, J., Huang, P., and Lee, C.C. (2002) Circadian gene *Period 2* Plays an Important Role in Tumor Suppression and DNA Damage Response in vivo. *Cell* **111**, 41-50.
- b) Lee, J.H., Sancar, A. (2011) From the Cover: Circadian clock disruption improves the efficacy of chemotherapy through p73-mediated apoptosis. *Proc. Natl, Acad. Sci. USA* **108**, 10668-10672.

(D) APOPTOSIS

Lecture 13. Monday, Dec. 5: Overview of Apoptosis

- a) Evan, G., and Littlewood, T. (1998) A Matter of Life and Cell Death. *Science* **281**, 1317- 1322.
- b) Hengartner, M. O. (2000) the Biochemistry of Apoptosis. *Nature* **407**, 770-776.

Lecture 14. Wednesday, Dec. 7: Apoptosis Nucleases

- a) Enari, M., Sakahira, H., Yokoyama, H., Okawa, K., Iwamatsu, A., and Nagata, S. (1998) A Caspase-activated DNase that Degrades DNA during Apoptosis, and its Inhibitor ICAD. *Nature* **391**, 43-50.

EXAM 2: December 7, Wednesday (10:00 am) – December 9, Friday (4:00 pm)