

MCB/PMB C134 Chromosome Biology / Cytogenetics Spring 2014

Time and Room

Lecture MW 9-10 125 Li Ka Shing

First discussion section: Fridays 9 AM, 103 GPB

Second discussion section: Fridays 10 PM, 107 GPB

Instructors:

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Grading: (point totals)

Discussion presentation	75 pts	
Discussion questions	25 pts	
Midterm	100 pts	(Cande lectures)
Final	100 pts	(Karpen lectures)
Total	300 pts	

Readings:

To gain a general overview, you will want to look at the texts used for MCB 104, or any other Genetics or Cell Biology course. These include Molecular Biology of the Cell, Alberts et al, 5th edition, Chapters 4, 5 or Genetics: From Genes to Genomes, Hartwell et al, 3rd edition, Chapters 4, 13, 14, 18, 20. The 4th edition of Alberts is also available on line at pub med. You can search the text using terms such as chromosomes, mitosis, meiosis. For each lecture one or more review articles will be posted on line at bspace. You will be given guidance as to what to emphasize in your readings.

Discussion:

We will read and discuss original papers for each discussion section. Several members of the class will be selected ahead of time to present the paper and lead the discussion (value=75pts). You will be expected to have read the papers ahead of time even if you are not discussion leaders. Each student will hand in a half page essay at the discussion section answering a question about the paper to be discussed (2pts/essay). The students presenting the paper will consult at least one week ahead of time with the instructors, and help write the questions, and they will look over the answers. The questions will be provided at Wednesday's lecture.

Advice:

A Genetics or Cell Biology course the equivalent of MCB 104 and a biochemistry course such as MCB 102 or MCB 100 is recommended. The single most important element in doing well is keeping up to date. Reviewing your notes before the next lecture and looking at the assigned reading ahead of time will make an enormous difference in the final result. You will be given guidelines about what to emphasize in your readings. Do not hesitate to ask the instructors questions. Reviewing the material only before exams is a very poor strategy, since each lecture in turn uses the material in previous lectures and you could get left behind.

Crossword puzzle web site on cytogenetics: <http://www.proprofs.com/games/crossword/31-cytogenetics/>

Topics and Readings

Pdfs of all readings will be on bspace. All reading assignments are tentative and will be modified during the semester.

Week 1

January 22 Wednesday: (ZC)

Introduction and overview

class mechanics, How discussions sections will work

Define cytogenetics, a little history,

Chromosome Structure 1

packaging problem- histones, nucleosomes 30 nm fiber, higher orders of folding

READINGS:

Olins chr history 03 nature rev mol bio

Gall JCB 81 packing problem

Khorasanizadeh, 04 nucleosome str

Henikoff, histones Annu Rev.

Movie histone structure

January 24 Friday (ZC) joint discussion section: meet in 103 GPB at 9 (Paper presented by ZC) Discussion section: Does a chromosome consist of just one piece of DNA? **We will sign up for paper presentations at this meeting.**

1. Gall, J.G. 1963. Kinetics of deoxyribonuclease action on chromosomes. *Nature* **198:36-38.**

2. Gall, J.G. 1981 JCB chr structure review (look at background on unineme)

Week 2

January 27 Monday: (ZC)

Chromosome structure 2: Heterochromatin vs. euchromatin, condensins and cohesins

READINGS:

Gall JCB 81

Henikoff, var histones Annu Rev.

Hirano, SMCs, 06 Nature Reviews Mol Cell Biology

Sedlow, mitotic chr 04 Mol cell.

Nasmyth and Olivera cohesion 2011

January 29 Wednesday: (ZC)

Chromosome structure 3: Metaphase chromosomes, Centromeres and telomeres,

READINGS:

Sedlow mit chr 2011

Czech, telomeres Cell 04

Eckwall, centromeres Ann Rev Gen 07

Telomeres Nobel prize Press release

January 31 Friday (ZC)

Discussion section: sister chromatid cohesion during mitosis

Ivanov, D., K. Nasmyth (2007). A physical assay for sister chromatid cohesin in vitro. *Mol. Cell* **27: 300-310.**

Week 3

February 3 Monday (ZC)

Kinetochores: generating forces to move chromosomes on the spindle

READINGS:

Glover kinetochores
Sharp anaphase 2011
Tooley ndc80, 2011
Movies

February 5 Wednesday: (ZC)

Error correction during chromosome segregation

READINGS:

Tanaka kinetochore orientation 05 Nature
Musacchio sp chpt
Lampson and Cheeseman sp chpt (backgrd for dis sec)

February 7 Friday : (ZC)

Discussion section: checkpoints

Liu et al (2009). Sensing Chromosome Bi-Orientation by Spatial Separation of Aurora B Kinase from Kinetochore Substrates. Science 323: 1350-1353 and supplemental materials (SOM)

week 4

February 10 Monday: (ZC)

Meiosis I: overview:

Leptotene chromosomes and the synaptonemal complex

READINGS:

Hawley meiosis review 03
Nasymth mei 03

February 12 Wednesday: (ZC)

Meiosis II: Pairing and Meiotic recombination

READINGS:

Keeney mei recombination 06
movies
Cande maize handbook 09

February 14 Friday: (ZC)

Discussion section: C. elegans: the relationship between synapsis and recombination

Dernburg AF, McDonald K, Moulder G, Barstead R, Dresser M, Villeneuve AM. 1998. Meiotic recombination in C. elegans initiates by a conserved mechanism and is dispensable for homologous chromosome synapsis. Cell 94(3):387-98

week 5

February 17 Monday: Holiday

February 19 Wednesday: (ZC)

Meiosis III: Chromosome segregation at MI vs MII.

READINGS:

Allshire, sgo1 centromeres
Javerzat sgo1 phosphorylation
Gregan sgo 1 function

February 21 Friday

Discussion Section: Sister chromatid cohesion during meiosis (ZC)

Kitajima, T. S., SA Kawashima, Y. Watanabe (2004). The conserved kinetochore protein shugoshin protects centromeric cohesion during meiosis. Nature 427:510-517.

week 6

February 24 Monday: (ZC)

Meiotic drive

READINGS:

Pardo-Manuel de Villena

Mcdermott Noor meiotic drive male sterility

February 26 Wednesday: (ZC)

The Karyotype and unusual chromosomes:

Metacentric vs. telocentric chromosomes, polytene chromosomes, lampbrush chromosomes, sex chromosomes

READINGS:

Bachtrog sex chr

Lahn human y chr review (backgrd dis sec)

Graves sex chr evolution

Gall germinal vesicle lampbrush chr

Lis polytene chr nature

February 28 Friday (ZC)

Discussion Section: sex chromosomes

Kauppi et al (2011) Distinct Properties of the XY Pseudoautosomal Region Crucial for Male Meiosis Science331:916-920.

week 7

March 3 Monday: (ZC)

Aneuploidy: causes and Human Genetic Diseases

READINGS:

Hassold Hunt human aneuploidy

Torres and Amon aneuploidy

Sheltzer and Amon aneuploidy

March 5 Wednesday: (ZC)

Polyploidy: causes and evolutionary consequences

READINGS:

Pellman aneuploidy polyploidy cancer 04 (backgrd dis sec)

Wolfe polyploidy

Yeast spindle pictures

March 7 Friday (ZC): Discussion section: Aneuploidy and aging

Lister...Herbert 2010. Age related meiotic segregation errors in mammalian oocytes are preceded by depletion of Cohesin and Sgo2. Current Biology 20:1511-1521.

WEEK 8

March 11 Monday: catch up and review (ZC)

March 13, exam. in class

March 15
No DISCUSSION

WEEK 9 (GK)

March 17, Monday “Introduction to Epigenetics”

Genome organization and sequence composition

Plasticity in genome function-Position Effect Variegation

READINGS:

March 19, Wednesday "Histone Modifications and Epigenomic Landscapes "

Histone modifications-types, establishment and propagation

Genome-wide landscapes of epigenomic factors and histone modifications

Chromosome-specific patterns

READINGS:

March 21, No discussion section

WEEK 10

March 24-28 Spring Recess

WEEK 11 (GK)

March 31 Monday “Epigenetic Regulation of Gene Activation and Silencing-Part 1”

Chromatin and gene activation

RNA interference-post-transcriptional silencing by miRNAs and siRNAs

READINGS:

April 2 Wednesday “Epigenetic Regulation of Gene Activation and Silencing-Part 2”

Constitutive heterochromatin and siRNA recruitment of silencing factors

Polycomb silencing-facultative heterochromatin and developmental regulation

READINGS:

April 4, Friday Discussion: Propagation of Histone Modifications

Hathaway, N.A., Bell, O., Hodges, C., Miller, E.L., Neel, D.S., and Crabtree, G.R. (2012).

Dynamics and memory of heterochromatin in living cells. *Cell* 149, 1447–1460.

(for minireview see Carone, B.R., and Rando, O.J. (2012). Rewriting the epigenome. *Cell* 149, 1422–1423)

WEEK 12 (GK)

April 7, Monday “Epigenetic Regulation of Chromosome Functions”

Epigenetic regulation of DNA replication
Centromere plasticity and epigenetic regulation
Assembly of centromeric chromatin in the cell cycle

READINGS:

April 9, Wednesday “Genome Stability: DNA repair”

DNA damage, repair, and consequences of defective repair
Homologous Recombination and Non-Homologous End Joining
DNA damage checkpoints
Impact of chromatin on DNA repair (and vice versa)

READINGS:

April 11, Friday Discussion: Centromere plasticity

Mendiburo MJ, Padeken J, Fülöp S, Schepers A, Heun P (2011) Drosophila CENH3 Is Sufficient for Centromere Formation. *Science* 334: 686-690.
(for minireview see Jansen, L.E.T. (2012). *Genetics*. Sowing the seeds of centromeres. *Science* 335, 299–300)

WEEK 13 (GK)

April 14, Monday "Nuclear Architecture and Genome Dynamics: Part 1"

Chromosome domains
Nuclear ‘factories’ for replication, RNA processing, DNA repair, gene expression/silencing
Associations with the nuclear periphery

READINGS:

April 16, Wednesday "Nuclear Architecture and Genome Dynamics: Part 2"

Homolog pairing
3D ‘touching, kissing and looping’

READINGS:

April 18, Friday DISCUSSION: Nuclear organization

Solovei, I., Kreysing, M., LanctOt, C., KOsem, S., Peichl, L., Cremer, T., Guck, J., and Joffe, B. (2009). Nuclear Architecture of Rod Photoreceptor Cells Adapts to Vision in Mammalian Evolution. *Cell* 137, 356–368.
(for minireview see: Eskiw, C., and Fraser, P. (2009). Inverted rod nuclei see the light. *Nat Cell Biol* 11, 680–681)

WEEK 14 (GK)

April 21, Monday "Nuclear Architecture and Genome Dynamics: Part 3"

Nuclear dynamics in interphase- how do chromosome regions move?
Passive or active mechanisms? -- DNA repair in heterochromatin

READINGS:

April 23, Wednesday “Cancer and Chromosomes”

Models for cancer initiation and progression: Genome instability vs. oncogenes
Chromosomal functions that go awry in cancer
‘Chromothripsis’
Epigenetic regulation of cancer progression

READINGS:

April 25, Friday DISCUSSION: Nuclear architecture and gene regulation

Noordermeer, D., de Wit, E., Klous, P., van de Werken, H., Simonis, M., Lopez-Jones, M., Eussen, B., de Klein, A., Singer, R.H., and de Laat, W. (2011). Variegated gene expression caused by cell-specific long-range DNA interactions. *Nat Cell Biol* 13, 944–951.

WEEK 15 (GK)

April 28, Monday “Environmental Challenges and the Epigenome”

Impact of environmental factors on epigenetic marks and genome functions
Transgenerational inheritance of environment-induced changes

READINGS:

April 30, Wednesday “Catch up and review”

May 2, Friday DISCUSSION: Environmental reprogramming of genome function

Kucharski R, Maleszka J, Foret S, Maleszka R. (2008). Nutritional control of reproductive status in honeybees via DNA methylation. *Science* 319: 1827–30.

WEEK 16 May 5-9 deadweek

May 13-17 (Final Examinations)

Tentative date: Monday May 12: 7-10 PM