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Tuesday and Thursday, 9:30 - 11:00 am

Grades: 50% class discussion  
25% student presentation  
25% final paper- Due Dec. 9<sup>th</sup>, 2004.

### Discussion

There will generally be one paper discussed each class period, and it is the responsibility of each student to come to class prepared to discuss the papers in detail. Each required paper is available as a PDF on the Bio382 Blackboard site, or will be given out in class one week before discussion. Please keep these points in mind:

- Active participation in discussion is only possible if the papers are carefully read.
- Active participation includes asking questions as well as answering questions.
- Some papers may include techniques or background information that is not entirely explicated within the papers themselves, and additional background reading may be required. A basic genetics textbook or “Human Molecular Genetics” will be useful for background information. Both are available in the library.
- You should feel free to discuss papers with classmates and work together to prepare for class discussion.

As preparation for the discussion please write a short (4 or 5 sentence) summary of each paper. Please hand the summary in at the beginning of class. The summary should include a brief statement of the main question that the authors attempt to address and the experimental approach used. Finally, state the papers conclusions. The summary will be graded as pass/fail and factored into the discussion grade.

### Student presentations

Each student will be assigned two class sessions to present a paper to the class. All students should be prepared to participate in these discussions.

### Paper

A short paper in the form of a research proposal is due Dec. 9<sup>th</sup>. The paper will propose a series of experiments designed to further investigate an aspect of *wnt* signaling. Details regarding the form of the proposal will be provided.

Background Reading and WWW sites that might be useful:

Strachan and Read. 2001. Human Molecular Genetics. Garland Science.

A basic textbook with good descriptions common techniques used in molecular genetics (particularly human genetics). A copy of Volume 2 will be on reserve in the library.

Hartwell et al. 2000. Genetics: from Genes to Genomes. McGraw-Hill.

A basic genetics text on reserve in the library.

Lawrence, P.A. The Making of a Fly. 1992. Blackwell Scientific Publications.

Background fact book for basic *Drosophila* genetics and molecular biology.

Lal and Gallinger. 2000. Familial Adenomatous Polyposis. Seminars in Surgical Oncology. 18: 314-323.

Review focusing on clinical features of FAP/APC.

The *wnt* homepage:

<http://www.stanford.edu/~rnusse/wntwindow.html>

Online guide to mouse genetics.

<http://www.informatics.jax.org/silver/>

Online Medelian Inheritance in Man (OMIM)

<http://www3.ncbi.nlm.nih.gov/Omim>

This site allows detailed information concerning thousands of human genetic disorders including APC.

<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi>

Use this site from the NIH to search biomedical literature databases.

LocusLink

<http://www.ncbi.nlm.nih.gov/LocusLink/index.html>

Online access to information about a gene or protein of interest.

<http://www.genome.gov/glossary.cfm>

a glossary to look up genetic terms-not very technical or in depth

Date	Topic	Paper for Discussion
September 2	Introduction	none
7	Clonal origin of tumors	Fearon, Hamilton, and Vogelstein. 1987. Clonal Analysis of Human Colorectal Tumors. <i>Science</i> 238: 193-197.
9	Mapping the APC gene	Bodmer et al. 1987. Localization of the gene for familial adenomatous polyposis on chromosome 5. <i>Nature</i> 328: 614-616.  Solomon et al. 1987. Chromosome 5 allele loss in human colorectal carcinomas. <i>Nature</i> 328: 616-619.
14	Positional cloning the APC gene	Kinzler, et al. 1991. Identification of FAP Locus Genes from Chromosome 5q21. <i>Science</i> . 253: 661-665.  Nishisho et al. 1991. Mutations of Chromosome 5q21 Genes in FAP and Colorectal Cancer Patients. <i>Science</i> . 253: 665-669.
16	Mouse Models of APC	Su et al. 1992. Multiple Intestinal Neoplasia Caused by a Mutations in the Murine Homolog of the APC Gene. <i>Science</i> . 256: 668-670.  How to make a transgenic mouse
21	Mouse Models of APC	Oshima et al. 1995. Loss of <i>Apc</i> heterozygosity and abnormal tissue building in nascent intestinal polyps in mice carrying a truncated <i>Apc</i> gene. <i>Proc. Natl. Acad. Sci.</i> 92: 4482-4486.  Moser et al. 1993. <i>Apc<sup>min</sup></i> , a mutation in the murine <i>Apc</i> gene, predisposes to mammary carcinomas and focal alveolar hyperplasias. <i>Proc. Natl. Acad. Sci.</i> 90: 8977-8981.
23	<i>int-1</i>	Nusse and Varmus. 1982. Many Tumors Induced by the Mouse Mammary Tumor Virus Contain a Provirus Integrated in the Same Region of the Host Genome. <i>Cell</i> . 31: 99-109.
28	Fly development	Sharma and Chopra. 1976. Effect of the <i>Wingless</i> ( <i>wg<sup>1</sup></i> ) Mutation on Wing and Haltere Development in <i>Drosophila melanogaster</i> . <i>Developmental Biology</i> . 48: 461-465.  Nusslein-Volhard and Wieschaus. 1980. Mutations affecting segment number and polarity in <i>Drosophila</i> . <i>Nature</i> 287: 795-801.
30	Cloning <i>int-1</i>	Baker. 1987. Molecular cloning of sequences from

		<p><i>wingless</i>, a segment polarity gene in <i>Drosophila</i>: the spatial distribution of a transcript in embryos. EMBO Journal. 6: 1765-1773.</p> <p>Rijsewijk et al. 1987. The <i>Drosophila</i> Homolog of the Mouse Mammary Oncogene <i>int-1</i> Is Identical to the Segment Polarity Gene <i>wingless</i>. Cell. 50: 649-657.</p>
October 5	The <i>wnt</i> signaling pathway	Rubinfeld et al. 1993. Association of the <i>APC</i> Gene Product with $\beta$ -Catenin. Science. 262: 1731-1734.
7		Peifer et al. 1994. <i>wingless</i> signal and Zeste-white 3 kinase trigger opposing changes in the intracellular distribution of Armadillo. Development. 120: 369-380.
12		Willert, Shibamoto, and Nusse. 1999. Wnt-induced dephosphorylation of Axin releases $\beta$ -catenin from the Axin complex. Genes and Development. 13: 1768-1773.
14	Modifier genes	Dietrich et al. 1993. Genetic Identification of <i>Mom-1</i> , a Major Modifier Locus Affecting Min-Induced Intestinal Neoplasia in the Mouse. Cell. 75: 631-639.
19		<p>Cormier et al. 1997. Secretory phospholipase Pla2g2a confers resistance to intestinal tumorigenesis. Nature Genetics. 17: 88-91.</p> <p>Takaku et al. 2000. Suppression of Intestinal Polyposis in <i>Apc<sup>d716</sup></i> Knockout Mice by an Additional Mutation in the Cytosolic Phospholipase A2 Gene. J. Biol. Chem. 275: 34013-34016.</p>
21	Genomics of <i>wnt</i>	
26	student	Roose et al. 1999. Synergy Between Tumor Suppressor <i>APC</i> and the $\beta$ -Catenin-Tcf4 Target <i>Tcf1</i> . Science. 285:1923-1926.
28	student	Ahmed et al. 2002. <i>Drosophila</i> Apc1 and Apc2 regulate Wingless transduction throughout development. Development. 129:1751-1762.
November 2	student	Brault et al. 2001. Inactivation of the b-catenin gene by Wnt1-Cre-mediated deletion results in dramatic brain malformation and failure of craniofacial development. Development. 128: 1253-1264.
4	student	Gong et al. 2004. Planar cell polarity signalling controls cell division orientation during zebrafish gastrulation. Nature. 430: 689-693.
9	student	Jiang and Struhl. 1998. Regulation of the Hedgehog and

		Wingless signalling pathways by the F-box/WD40-repeat protein Slimb. Nature 391:493-496.
11	Review and Discuss expectations for Research Proposal. Due Dec. 9 <sup>th</sup> .	Guide to Grant Writing
16	student	Robitaille et al. 2002. Mutant frizzled-4 disrupts retinal angiogenesis in familial exudative vitreoretinopathy. Nature Genetics. 32: 326-330.
18	student	Gong et al. 2001. LDL Receptor-Related Protein 5 (LRP5) Affects Bone Accrual and Eye Development. Cell. 107: 513-523.
23	student	Reya et al. 2003. A role for Wnt signalling in self-renewal of haematopoietic stem cells
30	student	Okubo and Hogan. 2004. Hyperactive Wnt signaling changes the developmental potential of embryonic lung endoderm. J. of Biology. 3:11.
December 2	student	Wang et al. 2004. Vascular development in the retina and inner ear: control by Norrin and Frizzled-4, a high-affinity ligand-receptor pair. Cell 116: 883-895.
7	Future directions in wnt research	No paper
9	Paper Due-class wrap-up	No paper