Syllabus: GENOMICS

Memorial University of Newfoundland Department of Biology Fall Semester, 2011
Genomics, B-4251 (undergraduate), B-7938 (graduate)
Lecture Room SN 4110
Lab Rooms: SN 4110 for computer-based labs and student seminars, and the molecular teaching lab (SN 3001) for wet labs
Lecture: Tuesday and Thursday, 12:00 – 12:50 pm; Friday 1:00 – 1:50 pm
Lab: Friday 2 – 5 pm

Instructor: Matthew Rise, Ph.D., Associate Professor Ocean Sciences Centre (OSC), Cross-appointed to the Department of Biology; Canada Research Chair (Tier 2) Marine Biotechnology
Office hours by appointment, OSC room AX3001 or on campus (location to be announced)
Office phone: 709-864-7478; Email: mrise@mun.ca

TA: Sabrina Inkpen (M.Sc. student, OSC/Biology)

Guest lecturer and assistant in labs: Tiago Hori, M.Sc. (Ph.D. student, OSC/Biology)

Text for Course: Watson JD, Myers RM, Caudy AA, and Witkowski JA. 2007. Recombinant DNA, Genes and Genomes – A Short Course (Third Edition). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY. ISBN 0-7167-2866-4

Course materials will also come from other books and primary literature posted on the Desire 2 Learn (D2L) website. Some handouts will be provided.

Examples of genomics-relevant books in the QEII library:

- Benfey PN and Protopapas AD. 2005. Genomics. Pearson Education, Inc. (Call number **QH 447 B463 2005**)
- Reece RJ. 2004. Analysis of Genes and Genomes. John Wiley & Sons Ltd. (Call number **QH 442 R445 2004**)
- Campbell AM and Heyer LJ. 2007. Discovering Genomics, Proteomics, and Bioinformatics. Second Edition. Pearson Benjamin Cummings. (Call number **QH 447 C35 2007**)
- Watson JD et al. 2007. Recombinant DNA: Genes and Genomes – A Short Course. Cold Spring Harbor Laboratory Press, New York. (Call number **QH 442 R37 2007**)
- Bowtell D and Sambrook J. 2003. DNA Microarrays : A Molecular Cloning Manual. Cold Spring Harbor Laboratory Press. (Call number **QH 442.2 D6295 2003**)
- Zhanjiang (John) Liu (editor). 2007. Aquaculture Genome Technologies. Blackwell. (Call number **QH 447 A657 2007**)
- J. Sambrook and D. Russell. 2001. Molecular Cloning: A laboratory manual (third edition). Cold Spring Harbor Laboratory Press. (Call number **QH 442.2 M36 2001 V.1**, **QH 442.2 M36 2001 V.2**, and **QH 442.2 M36 2001 V.3**)

Course Description

Genome and functional genomic research are having a profound influence on various fields of study including biomedicine, evolution, environmental biology, and agriculture. This course in Genomics will build on the foundation of Biology Courses involving molecular techniques and genetics, and will provide students with theory and laboratory experience on genomic techniques such as DNA microarray experimental design, hybridization, and data analysis. Genomics (B-4251 & B-7938) has lecture, laboratory, and seminar components. Topics covered include: Technical Foundations of Genomics, Global Gene Expression Profiling, Comparative Genomics, Microbial Genomics, Genomics and Medicine, Genomics and Agriculture, Environmental Genomics, and Epigenetic Modifications of Genomes. Each topic will involve a lecture component, in which theory and methods will be taught using textbooks and journal articles. Some lecture and lab times will be devoted to seminars on methods and papers related to lecture or laboratory components of the course. In the lab component, students will have the opportunity to use state-of-the-art genomic techniques to address research questions. This course has 3 hours of lecture and 3 hours of laboratory per week.

Course Schedule

Note: All research articles that are included as assigned reading are Open Access papers.

Week 1 (Sept. 8, 9): Introduction to Genomics; Technical Foundations of Genomics (Recombinant DNA techniques used in genomic research)

Topic	**Reading Assignment (Text or D2L on-line)**
Recombinant DNA techniques - Review	Text Chapter 4 (Basic Tools of Recombinant DNA)
Gene Discovery: Introduction to cDNA Libraries	Text p. 139 (TA cloning) Creator SMART cDNA Library Manual (Clontech) - Web link Rise et al. 2004 (*Genome Research* paper) Bowman et al. 2011 (*Marine Biotechnology* paper)
Suppression subtractive hybridization (Targeted gene discovery)	Diatchenko et al. 1996 (*PNAS* paper) Rise et al. 2010 (*Physiological Genomics* paper) Hori et al. 2010 (*BMC Genomics* paper) PCR Select cDNA Subtraction Kit Manual (Clontech) - Web link

Lab 1 (Sept. 9): Introduction to DNA Microarray-based Experimentation (Reading: Handouts)
Objective: Become familiar with web and other resources needed for the microarray-based labs

Week 2 (Sept. 13, 15, 16): Technical Foundations of Genomics (Recombinant DNA techniques used in genomic research)

Topic	**Reading Assignment (Text or D2L on-line)**
Normalization of cDNA libraries	Soares et al. 1994 (*PNAS* paper) Zulidov et al. 2004 (*Nucleic Acids Research* paper) Vogel et al. 2011 (*BMC Genomics* paper)
Genomic Libraries (e.g. BAC libraries)	Text Chapter 4 (Basic Tools of Recombinant DNA); also pp. 286-289 (large insert cloning systems and BAC fingerprinting) Osoegawa et al. 2004 (*Genome Research* paper)
Physical maps	Wallis et al. 2004 (*Nature* paper) Krzywinski et al. 2004 (*Genome Research* paper) Thorson et al. 2005 (*BMC Genomics* paper)

Lab 2 (Sept. 16): Microarray Experiment part 1 (experimental purpose and design; RNA extractions)
Equipment required: pipettors, filter tips, microcentrifuges, fume hoods, homogenizers
Guest speaker: Tiago Hori, OSC Ph.D. student (co-supervised by Drs. K. Gamperl and M. Rise). Tiago ran the original heat stress experiment that provided samples for the microarray and QPCR experiment that you will be running in Genomics labs.

Week 3 (Sept. 20, 22, 23): Fundamentals of Whole-Genome Sequencing

Topic	Reading Assignment (Text or D2L on-line)
Introduction to genome sequencing	Text Chapter 10 (Fundamentals of Whole-Genome Sequencing); also pp. 92-93 (Sanger sequencing)
New sequencing technologies (e.g. Roche 454, Illumina, Pacific Biosciences)	Primary literature (to be posted on the D2L website)

Lab 3 (Sept. 23): Microarray Experiment part 2 (DNase I treatment, column purification of RNA)
Equipment required: pipettors, filter tips, microcentrifuges, tube racks

Week 4 (Sept. 27, 29, 30): Fundamentals of Mapping and Sequencing – How the Human Genome Was Sequenced (Text Chapter 11 and assigned reading on D2L website)

Lab 4 (Sept. 30): Microarray Experiment part 3 (quantify and quality check DNAse I -treated, column-purified total RNA templates.
Equipment required: NanoDrop spectrophotometer; everything for running horizontal agarose gels including pipettors and filter tips; gel documentation station.

Week 5 (Oct. 4, 6, 7): Exam I (over Text book Chapters 4, 10, 11 & assigned reading)

- New information presented after Exam I: Gene Expression – From Genome Sequence to Gene Function (Text Chapter 13 and assigned reading on D2L website)

Lab 5 (Oct. 7 and 8): Microarray Experiment part 4 (fluorescent target syntheses, microarray hybridizations, washing, and scanning). Note: This lab will run for parts of two days in the molecular biology teaching lab (SN 3001). Students are encouraged to participate in as much of the Friday – Saturday lab as possible. At the end of the Saturday laboratory, microarrays will be dried in the molecular teaching lab and then transported to the Rise lab at the OSC for scanning. Copies of the primary data (TIF images of fluorescence signal data) will be provided to all students on CD or flash drives.

October 11: Fall semester break (no lecture)

Week 6 (Oct.13, 14): From Genome Sequence to Gene Function (Text Chapter 13 and assigned reading on D2L website) – Introduction to microarrays, SAGE, and next-generation sequencing based transcriptomic analyses.

Lab 6 (Oct. 14): Microarray Experiment part 5: Extraction of microarray data using ImaGene (BioDiscovery, Inc), and quality control (e.g. signal thresholding) of microarray data using Excel.

- ImaGene will be available on the computers in room SN 4110. In addition, students may use ImaGene software in the Rise lab (OSC).

Week 7 (Oct. 18, 20, 21): The Computational Foundations of Genomics – Comparing and Analyzing Genomes (Text Chapter 12 and assigned reading on D2L website)

Lab 7 (Oct. 21): Microarray Experiment part 6: Analysis of microarray data using GeneSpring software (Agilent Corp.) and other software; functional annotation of informative genes using sequence databases, bioinformatic tools, and the primary literature; interpretation of results.

- The software required for this data analysis will be available on the computers in room SN 4110. In addition, students may use GeneSpring or Bioconductor in the Rise lab (OSC).

Week 8 (Oct. 25, 27, 28): Microbial Genomics (Assigned reading on D2L website)
Guest lecturer: Dr. Andrew Lang (Department of Biology, Memorial University)

Lab 8 (Oct. 28): QPCR validation of Microarray Experiment part 1 (QPCR primer design and quality testing).

- ***Graduate students*** *are expected to participate in QPCR primer optimization (e.g. setting up standard curves, calculating amplification efficiencies, etc). Results will be communicated to the rest of the class by electronic files posted on the D2L website, and also via an informal PowerPoint presentation to the class.*

Note: Some of the lab period may be used for continuing microarray experiment data analysis and collection of current BLAST information and functional annotation for microarray-identified informative genes.

Week 9 (Nov. 1, 3, 4): Human Genomics – Finding Human Disease Genes (Text Chapter 14 and assigned reading on D2L website)

Lab 9 (Nov. 4): QPCR validation of Microarray Experiment part 2 (plate set-up, run reactions, statistical analysis of results).

- Interpretation of microarray and QPCR results (e.g. functional annotation of informative genes, literature searches, pathway analysis, etc).
- Note: Part of this lab period will be available for utilization of publicly available databases to collect information required for the Lab Report (e.g. current BLASTx statistics for microarray-identified, informative Atlantic cod sequences, collection of gene ontology information on these genes or their putative orthologues in model species, etc).

Week 10 (Nov. 8, 10): Exam II (over Text Chapters 12, 13, 14 & assigned reading)

- New information presented after Exam II: Epigenetic Modifications of Genomes (Text Chapter 8 and assigned reading on D2L website)
  Guest lecturer: Dr. Sherri Christian, Department of Biochemistry, Memorial University

November 11: Remembrance Day holiday (no lecture or lab)

Week 11 (Nov. 15, 17, 18): Mobile DNA Sequences in Genomes (Text Chapter 7 and assigned reading on D2L website)

Lab 11 (Nov. 18): Seminar 1 (students present papers and facilitate discussions (30 min each).

Week 12 (Nov. 22, 24, 25): Understanding the Genetic Basis of Cancer (Text Chapter 15 and assigned reading on D2L website)

Lab 12 (Nov. 25): Seminar 2: students present papers and facilitate discussions (30 min each).

Lab Report Due (~ 20 pages in the style of *Physiological Genomics* or *BMC Genomics*)

Note: Graduate student lab reports will be expected to have more detailed Results and Discussion sections than undergraduate student lab reports. We will discuss the desired formats for graduate and undergraduate student lab reports in class.

Week 13 (Nov. 29; Dec. 1, 2): Topics in Genomics: Agriculture Genomics, Toxicogenomics, Ecological Genomics, Genomics in Medicine (assigned reading on D2L website)

Lab 13 (Dec. 2): Seminar 3: students present papers and facilitate discussions (30 min each).

Labs and seminars will occur during the weekly lab periods. The laboratory component will present the theory and hands-on application of all steps involved in DNA microarray experiments. Lab periods will be devoted to microarray experimental design, RNA isolation and purification, assessment of RNA quality and quantity, target synthesis, microarray hybridization and washing, microarray scanning, data extraction (e.g. gridding, and design and use of a gene identification file), data analysis (e.g. identification of reproducibly informative transcripts), and data verification or validation [e.g. with quantitative reverse transcription – polymerase chain reaction (QPCR)].

Labs will be run on campus (in SN 3001 for wet labs or SN 4110 for computer-based labs and student seminars). However, some steps (e.g. microarray scanning) may require infrastructure (e.g. scanner) available in M.L. Rise's lab at the Ocean Sciences Centre (OSC room AX3001). These steps may be performed by the graduate student members of a research team, or by Sabrina Inkpen (Genomics TA), Tiago Hori, or Dr. Rise if students are unable to arrange for transportation to the OSC.

Seminars, to be held during lab periods, will cover primary literature pertaining to specific topics in genomic research. Each student will have an opportunity to make a presentation (15 minute, PowerPoint Presentation) and lead a discussion (~15 minute) on an assigned, recent open source journal article on genomics research. Students will be expected to keep a ***neat and complete laboratory notebook****, and to write a* ***formal laboratory report*** *on the microarray/QPCR experiments, data analysis, and interpretation of data.* ***Graduate student lab reports will be expected to have more detailed Results and Discussion sections than undergraduate student lab reports. We will discuss the desired formats for graduate and undergraduate student lab reports in class.***

Evaluation	Exam I (in Week 5):	15%
	Exam II (in Week 10):	15%
	Comprehensive Final Exam:	30%
	Laboratory Notebook:	10%
	Laboratory Report:	20%
	Seminar Presentation and Participation in Discussions:	10%
	Total:	**100%**