BIOL 575:
BENCH TO BEDSIDE TRANSLATIONAL RESEARCH

SUMMER PROGRAMME 2013

George Mason University VA

The National Institute for Cellular Biotechnology (NICB)

Dublin City University

Beaumont Hospital/RCSI

In collaboration with:

3U Partnership Research Programmes in Tissue Engineering, Proteomics, Cancer & Diabetes

Molecular Therapeutics for Cancer Ireland (MTCI)

22 July – 26 July 2013

BIOL 575: Bench to Bedside Translational Research

Summer Programme July 2013

George Mason University and Dublin City University

Lecture MTWTh: 9:15am-12:30pm and 1:35pm-2:15pm (Dublin City University, NICB, Main Seminar Room 1st Floor)

Lab MTWTh: 2:45pm-6:00pm (Dublin City University & Beaumont Hospital/Royal College of Surgeons Ireland)

Lab Friday: 9:15am-12:30 (Dublin City University, NICB)

Course Directors: Lance A. Liotta (GMU) and Martin Clynes (DCU)
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Course Description

The new era of personalized therapy and molecular medicine is a perfect example where the functional aspects of genomics, proteomics and bioinformatics can come together at the patient's bedside. This course will focus on the practical use of these three areas for the diagnosis, prevention and treatment of disease. Hands-on technical workshops will be used to illustrate and educate students, as well as touch on issues related to implementation of new platforms and assays.

Faculty teaching this course invented Reverse Phase Protein Microarray, Laser Capture Microdissection, and harvesting Nanoparticles, which you will learn to use, to address molecular questions arising from scientific insights and inquiry. The laboratory workshops will encourage scientific inquiry through the analysis of "unknown" specimens. On the last day of the course, students will present the results of their analysis and propose a brief experimental plan with which they can apply genomic/proteomic technology to a research question.

Course Philosophy

In the sciences, theories are tested and modified continually as emerging technology allows us to delve into the molecular underpinnings of disease. The nature of scientific inquiry often means you end up with new questions instead of a nice, simple conclusion. We will be examining the cutting edges of scientific knowledge in proteomcis and genomics, and some of the technologies used in translational research laboratories. A continual quest for knowledge is what we consider to be the beauty of science: experimental observations are paramount for creative insights and problem solving; nothing is held sacred (even if it is considered dogma); everything is tested and re-examined; and debate fuels the formulation of new ideas and hypotheses to be tested.

Creative ideas often arise from connecting disparate observations, ideas or facts. Collaborations and exposure to multiple "ways of doing things" provides fundamental knowledge for generating these creative insights. Our collaborative course is fast paced, but low-key, with an emphasis on interactive discussions and hands-on training.

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Course Goals

1. Exposure to recent concepts in translational research. Understand the role of translational research in clinical medicine.
2. Exposure to proteomic and genomic technologies used in translational research via small group training/analysis workshops. Application of technologies to solve research questions.
3. Ability to synthesize hypotheses and experimental plans for research projects.

Course materials

Lectures will be based upon information from review articles, primary literature, and *Molecular Profiling* (Methods in Molecular Biology series) edited by Virginia Espina/Lance Liotta. You do not need to purchase the book. USB drives containing the course materials will be provided. Students are encouraged to bring a laptop computer for viewing the course material and preparing their final project.

Laboratory materials

Lab notebooks are required. The notebooks can be any style and are intended to be resources for the students for note taking, data recording, and data analysis.

Attendance

We will not actively monitor attendance in lecture during the course, but consistent lecture attendance is necessary to do well in this course. Missing laboratory workshops may negatively impact your grade, and due to the nature of the laboratory workshops, it is impossible to make up the work.

Evaluation

The grading scale will be: A+ (97-100), A (93-96), A- (90-92), B+ (87-89) B (83-86), B- (80-82), C+ (77-79), C (73-76), C- (70-72), D+ (67-69) D (60-66), F (59 and below).

Rubric

Summary of laboratory assays (how and why assay is used) (25 points), Data Analysis (10 points), Discussion of potential errors and types of specimens (15 points).

Laboratory report (Due by Friday, 26 July 2013 at 17:00 (Irish local time) 50 points (2 page maximum, single spaced, Arial font, 11 point, 1" margins on all sides)
USB drives: Course materials will be provided on Lexar 4GB USB drives, which will be provided to each student for use during the course. • **The laboratory report and data should be stored on the USB drive, which will be collected Friday, 26 July 2013 at 17:00 (Irish local time)** • **Laboratory reports must include your name and student number (#1-#29) to receive a grade. The USB drives will not be returned to the students.** • **Please keep copies of any course information that you may need in the future.**

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Course Timetable

Location: Dublin City University
National Institute for Cellular Biotechnology (NICB)
Main Seminar Room, 1st floor

Monday Morning Lectures 09.15 - 12.30

Day One
Monday 22 July: Introduction to proteomic and genomic techniques

09.15 The upcoming revolution in individualized therapy.
Lance Liotta (GMU)
Review of cancer medicine and the basics of cancer molecular biology and cancer metastasis
Discussion of basic principles of molecular medicine, including the definition and the need for individualized diagnostics and therapeutics.

09.50 New technology for biospecimen analysis.
Ginny Espina (GMU)
Introduction to laser capture microdissection and reverse phase protein microarrays for personalized medicine and clinical trials. Overview of the technology, troubleshooting, and applications.

Coffee break 10.30-10.55

11.00 Next generation genome sequencing: implications of the low cost personal genome
Bryan Hennessy (Beaumont Hospital/RCSI)

11.45 Nanoparticles that harvest biomarkers: improving analytical sensitivity and preserving analytes in one step
Alessandra Luchini (GMU)

Introduction to the use of novel hydrogel nanoparticle-based technology traps, to concentrate and protect potential low abundance disease biomarkers directly from blood, urine and saliva samples, in one step.

Lunch (not included) 12:30-1:30 (cafés and shops on campus)

Monday Afternoon Lecture 13.35 - 14.15

13.35 Current applications of biomarker detection in routine pathology practice.
Tony O'Grady and Robert Cummins (RCSI)

Tuesday Morning Lectures 09.15 - 12.30

Day Two
Tuesday 23 July: Translational Research

09.15 Pre-analytical variability: the tissue is alive
Ginny Espina (GMU)
Preservation of samples (tissue, blood) is critical to maintain cell morphology and stabilize tissue biomolecules for accurate downstream proteomic and genomic analysis. Various tissue fixation strategies will be compared and contrasted in relation to a unique phosphoprotein tissue preservative.

10.00 Ethical issues in biotechnology research
Martin Clynes (Dublin City University)

Coffee break 10:30-10:55

11.00 Diabetes and kidney disease in the era of systems medicine
Susan Mulroney (Georgetown University)

11.45 Cardiovascular disease in the era of systems medicine
Adam Meyers (Georgetown University)

Lunch (not included) 12:30-1:30 (cafés and shops on campus)

Tuesday Afternoon Lecture 13.35 - 14.15

13.35 Quality of Life and Cancer Therapy
Michael Moriarty (St. Luke's Hospital)

Wednesday Morning Lectures 09.15 - 12.30

Day Three
Wednesday 24 July: Genomics, Biobanking, Pharmacokinetics

09.15 Genomic sequencing of cancer: How do we distinguish driver from bystander mutations?

David Hughes (RCSI, Dublin)

Large-scale sequencing analyses have revealed hundreds of mutations in human tumors. However, not all mutations are created equal. Cancer cells acquire mutations in genes critical for controlling cell proliferation, survival and differentiation. Often, tumors continue to depend on these so-called driver mutations, providing the rationale for targeted anticancer therapies. However, without their functional validation it remains unclear which mutations correspond to driver, or rather bystander, mutations and, therefore, whether the mutated gene represents a target for therapeutic intervention.

10:00 microRNAs in health and disease
Niall Barron (NICB, Dublin City University)

Coffee break 10:30-10:55AM

11:00 Biobanking is critical for the future of medicine: Cutting through ethical, social and economic barriers
Eoin Gaffney (St. James's Hospital & Biobank Ireland Trust)

11:45 Targeted treatment of breast cancer
John Crown (SVH & MTCI)

Lunch (not included) 12:30-1:30 (cafés and shops on campus)

Wednesday Afternoon Lecture 13.35 - 14.15

13.35 Cancer drug pharmacokinetics
Robert O'Connor (School of Nursing, Dublin City University)

Thursday Morning Lectures 09.15 - 12.30

Day Four

Thursday 25 July: Stem Cells: Current state of the art, and Industry involvement in translational research

09.15 Stem cell therapy: promises and challenges
Lance Liotta (GMU)

09.50 Targeting premalignant cancer stem-like cells: killing pre invasive lesions for cancer prevention
Ginny Espina & Lance Liotta (GMU)

Breast DCIS cells survive in the hypoxic, nutrient deprived intraductal niche by upregulating autophagy. Autophagy, "self eating", is a normal, cyclic cellular process designed for producing energy during cellular stress. Autophagy represents a therapeutic target for chemoprevention of breast cancer.

Coffee break 10:30-10:55

11.00 Stem Cell transplantation in human eye disease
Finbarr O'Sullivan (NICB, Dublin)

11.45 New clinical trial design and pharma-biotech cooperation
Sinead Toomey (Beaumont Hospital/Royal College of Surgeons Ireland)

Lunch (not included) 12:30-1:30 (cafés and shops on campus)

Thursday Afternoon Lecture 13.35 - 14.15

13.35 Commercialization of biomedical research discoveries and inventions
Naoise Gaffney

19.30 Student/Faculty Dinner: Le Bon Crubeen, Dublin City Centre

Friday Morning Mini-Workshops 09.15 - 12.30

Day Five

Friday 26 July: Mini Workshops

- **Affymetrix Microarrays**
  (Sinead Aherne, Helena Joyce)

- **Quantitative PCR**
  (Niall Barron)

- **Software packages for expression microarray and pathway analysis**
  (Colin Clarke, Stephan Madden)

Lunch (not included) 12:30-1:30 (cafés and shops on campus)

Friday Afternoon - Student Papers due at 17.00 local Irish time

Daily Workshops

Monday-Thursday: AFTERNOONS 14.45 - 18.00

Students will participate in one workshop each afternoon based on the group assignments.

Workshop: **Laser capture microdissection**
(Ginny Espina, Kathy Sheehan, Seán Fitzgerald, Alan Carpino [Life Technologies])

and Sequenom
(Robert Cummins, Tony O'Grady, Kathy Sheehan)
Location: Beaumont Hospital/RCSI
Depart by bus from DCU to Beaumont Hospital: 14.45
Return by bus to DCU: 18.15

Workshop: **Immunohistochemical (IHC) Techniques and Reverse Phase Protein Arrays (RPPA)**
(Annemarie Larkin, Deirdre O'Flynn, Ginny Espina, Mattia Cremona)
Location: Dublin City University, NICB

Workshop: **Nanoparticle Protein Fractionation and Proteomics/Mass Spectrometry Protein Fractionation, Protein I.D. by MALDI.**
(Alessandra Luchini, Lance Liotta, Paul Dowling, Michael Henry, Paula Meleady)
Location: Dublin City University, NICB

Workshop: **Introduction to Basic Cell Culture Techniques**
(Finbarr O'Sullivan, Clair Gallagher)
Location: Dublin City University, NICB

Workshop Groups Monday-Thursday Afternoon

	Group 1	Group 2	Group 3	Group 4
Monday 22 July	LCM/Sequenom	Cell Culture	Nanoparticle/MS	IHC & RPPA
Tuesday 23 July	IHC & RPPA	LCM/Sequenom	Cell Culture	Nanoparticle/MS
Wednesday 24 July	Nanoparticle/MS	IHC & RPPA	LCM/Sequenom	Cell Culture
Thursday 25 July	Cell Culture	Nanoparticle/MS	IHC & RPPA	LCM/Sequenom