
Course Number: **CLRES 2710**

Course instructor: **Jennifer Grandis, MD**

Course Title: **Translational Research Tools: How to Navigate Between the Bench and the Beside**

Course Summary: The purpose of this course is to provide an introduction to the general concepts and approaches used in translational research. While each translational research project is necessarily focused on specific hypotheses, diseases and preclinical models, the topics presented in this course represent common themes that are broadly relevant to carrying out translational research. This course will provide an introduction to eight general fields to familiarize students with these areas and how they may be applied to translational research.

Course mechanics: 1 credit (2 hours/session, 1 session/week, for 8 weeks)

Grading: Letter Grade

Location: 305A Parkvale Building

Course requirements: Attendance, Class Participation and Assignments

Required Texts: None

Readings: Readings are placed on reserve at the Institute for Clinical Research Education [Parkvale Building, 3rd floor]).

Topics: There will be a presentation of the issues relevant to the collection of human specimens for research purposes. Areas to be covered include designing protocols and consent, IRB concerns, HIPAA issues and de-identification of specimens, cooperative group and multi-center collections, the role of pathology, “ownership” of specimens, and trouble shooting of potential obstacles.

Learning objectives: This session will provide a broad overview of tissue and biological specimen collection issues. The goal is to provide an introduction to repository design and management, legal, ethical and moral issues and conclude with comments regarding current thinking.

1. Why collect tissues and biological specimens.
2. Brief overview of specimen collection, storage and disbursement: Role of pathology.
3. IRB, HIPAA and consent issues.
4. Honest broker systems, de-identification and multi-institutional collaborations.
5. Ownership issues, prioritization and Tissue Issue committees.
6. Definition of “Human” research and new paradigms.

Readings:

1. Advancing Practice, Instruction and Innovation through Informatics conference (APIII 2005) breakout session D3
HIPAA, Tissue Banking and Data Aggregation: New Tools to Solve Old Problems: Rajiv Dhir, MD and Susan J. Urda, BS, CTR. (view slide presentation – Dhir and view slide presentation – Urda)
2. Grizzle WE, Aamodt R, Clausen K, LiVolsi V, Pretlow TG, Qualman S. Providing human tissues for research : how to estimate a program. *Arch Pathol Lab Med* 122(12):1065-76, Dec. 1998.
3. Qualman SJ, France M, Grizzle WE, LiVolsi VA, Moskaluk CA, Ramirez NC, Washington MK. Estimating a tumor bank: banking, informatics and ethics. *Br J Cancer* 90(6):1115-9, March 2004.
4. The RAND report. Handbook of Human Tissue Sources. A National Resource of Human Tissue Samples. By Elisa Eisemann, Jasen Castillo. http://www.rand.org/pubs/monograph_reports/MR954.

NO LECTURE TODAY

Topics: A discussion of imaging techniques used in translational research will be presented including functional (PET, SPECT, optical, fMRI), as well as anatomic (CT, MRI, ultrasound) imaging strategies. Imaging approaches for preclinical animal models as well as human subject research will be discussed with an emphasis on developing disease-specific strategies.

Learning objection:

1. To understand the rudimentary physics behind image generation using the various available functional (PET, SPECT, optical, fMRI) and anatomic (CT, MRI, ultrasound) imaging techniques.

2. To understand which questions can be best addressed by each imaging technique.
3. To appreciate the approaches to and limitations of response assessment using anatomic and/or functional imaging.
4. To have a clear understanding of the available approaches for labeling/imaging interesting molecules.
5. To appreciate the ways in which imaging can speed new drug development.

Reading:

1. Kelloff GJ, Krohn MA, Larson SM, et al. The process and promise of molecular imaging probes in oncologic drug development. *Clin Cancer Res.* 11(22):7967-7985, Nov. 11, 2005.
2. Ottobriani L, Ciana P, Biserni A, Lucignani G, Maggi A. Molecular imaging: A new way to study molecular processes in vivo. *Mol Cell Endocrinol* Dec. 30, 2005.

Active Learning: Choose a disease that interests you and consider a therapeutic technique or drug which has been recently approved or is still under investigation. Utilizing a MEDLINE search, find examples of how imaging was used in the evaluation of the technique/drug from early preclinical studies in animal models through to late human studies.

Session 4 Processing of Human Tissue Specimens September 27, 2007 Theresa Whiteside, PhD

Topics: There will be a presentation of the issues relevant to the processing of human specimens for research purposes. Areas to be covered include tissue acquisition methods and processing, training in environmental health and safety, sample distribution approaches and storage.

This two-hour class will cover issues relevant to obtaining and processing of human tissue specimens for research purposes. Areas that will be covered include: a process of obtaining IRB approvals, exemptions and types of approvals necessary for research; the organization of a tissue procurement program; procedures for tissue acquisition; triage and sampling of tissues for various purposes (e.g., RNA extraction vs. cryopreservation for sectioning vs. DNA extraction); standard operating procedures for handling and processing of tissues; storage requirements; training necessary for being able to safely process and use human specimens; review of risks associated with handling human tissues; supplies and reagents and record keeping. Current good tissue practice (cGTP) requirements as issued by FDA and compliance with these requirements will be discussed. The students will be provided with the relevant excerpts pertaining to tissue handling from the IRB manual as well as 21 CFR PART 1271 text issues by FDA. The students will also be made aware of depositories of human tissues at the UPMC and at NIH.

Learning objective: to acquire the understanding of rules which are in place for safe handling of human tissues and to learn how to live by the rules without allowing them to interfere with research goals.

Readings: Examples of published papers illustrating how tissue specimens have been successfully used in e.g., tissue microarrays, experimental vaccines, studies of tissue-infiltrating mononuclear cells or genetic analyses will be provided and discussed.

Observation: A 30 minute visit will be arranged at the end of the session to the Tissue Processing Facility at the UPCI to demonstrate the process of tissue procurement and banking as currently practiced in our institution.

Session 5	Stem Cells	October 4, 2007	Kyle Orwig, PhD
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Topics: Stem cells (human embryonic) will be described and discussed. Issues to be covered will include an understanding of how studying normal cell development will allow us to correct the errors that cause a variety of medical conditions. Stem cells as potential medical therapies theoretically offering the possibility of a renewable source of replacement cells and tissues to treat a myriad of diseases, conditions, and disabilities will be presented. Emphasis will be placed on the ethical debate regarding stem cell research.

Learning objectives: Students will understand the definitions, therapeutic potentials and current challenges in the human stem cell field. Through interactive discussion of current research, we anticipate that students will become critical evaluators of new discoveries in this rapidly changing field.

Readings:

1. Thomson, et al. 1998, *Science* 282:1145.

**This is a landmark paper describing the first derivation of human embryonic stem cells. There are alternative methods for deriving pluripotent stems cells, which may appease some opponents of human embryonic stem cell research.

2. Cowan, et al. 2005, *Science* 309:1369.

3. Meissner and Jaenisch. 2005, *Nature* 439:212.

The ethical, political and scientific landscape in the stem cell field is rapidly evolving and we will try to provide the most up to date and relevant materials.

Optional Readings: Optional readings are placed on reserve at the Institute for Clinical Research Education [Parkvale Building, 3rd floor].

Session 6	Genomics	October 11, 2007	Naftali Kaminski, MD
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Topics: The structure and function of the human genome will be discussed with emphasis on applications to translational research. This will include bioinformatics and computational biology approaches to mining the human genome sequence, introduction to high throughput methods to understand genome scale function and regulation, and approaches to identification of genes involved in human diseases.

Learning objectives: The student should be able to:

1. Understand the structure of the human genome.
2. Have a basic knowledge of bioinformatics vocabulary.
3. Use online tools and resources to query genome related databases.
4. Be familiar with high throughput gene expression analysis technologies and their use in clinical/translational research.
5. Appreciate the technical and statistical issues relevant to implementation of high throughput gene expression analysis technologies in clinical and translational research.

6. Use tools for visualization, statistical analysis and mining data generated by high throughput gene expression analysis technologies.

7. Conceptualize data generated by high throughput gene expression analysis technologies in a manuscript or grant proposal.

Session 7

Molecular Diagnostics

October 18, 2007

Alan Wells, MD

Topics: 70% of the information content of the medical record consists of diagnostic testing. More and more of this will come from molecular-based diagnostics. While much of molecular testing is similar to other modes of testing, such as test efficacy parameters, the particulars of molecular testing constitute a new knowledge base that will be required in order to design translational and clinical studies. This 2-hour module will provide basic information as to the various types of testing, an overview of strengths and limitations, and basic aspects of incorporation into such research endeavors.

Learning objectives: The student should be able to:

1. Differentiate between the molecules of target (RNA, DNA).
2. Differentiate between the changes queried (expression level, mutation, polymorphism).
3. Understand the difference between germline and somatic variations.
4. Appreciate the statistical issues inherent in the different assays.
5. Appreciate specimen acquisition issues.

Topics: The use of preclinical animal models in translational research will be discussed. Emphasis will be placed on selection of model(s), knockout and transgenic model development and/or use, animal housing, costs, and ethical concerns.

Learning objectives:

1. To understand the ethical arguments regarding the use of animals in research.
2. To understand the types of animal models that are commonly employed to understand disease processes (diseases are induced genetically or using drugs/chemicals, pathogens, radiation or surgery).
3. To understand the strengths and weaknesses of using different types of animals models.
4. To understand the laws and regulations that governs the use of animals in research.
5. To understand the role of the Institutional Animal Care and Use Committee in providing oversight for research.
6. To understand the expectations of funding agencies regarding the use of animals in research.

Readings:

1. Tolwani RJ, Jakowee MW, Petzinger GM, Green S, Waggle K. Experimental models of Parkinson's disease: insights from many models. *Laboratory Animal Science* 49(4):363-71, 1999.
2. Cryan JF, Holmes A. The ascent of the mouse: advances in modeling human depression and anxiety. *Nature Reviews: Drug Discovery* 4:775-790, 2005.

Active Learning Requirement: Each student should provide a short synopsis of the animal models that are commonly employed to study the disease process of interest.