Announcements

• http://www.pitt.edu/

• http://www.pharmacy.pitt.edu/
Strategic Review and Planning Sessions

- PharmD Admissions
- International Programs
- Advising
- Electives, ARCOS, Special Topics
- Getting to Expert Faster
- Graduate Program Self Study
- Promotion and Tenure
- Big Data

Altered Conditional Acceptance Criteria
Strategic Review and Planning Sessions

- PharmD Admissions
- **International Programs**
- Advising
- Electives, ARCOS, Special Topics
- Getting to Expert Faster
- Graduate Program Self Study
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- Big Data

Shannon Young: International Partnerships Coordinator
Strategic Review and Planning Sessions

- PharmD Admissions
- International Programs
- Advising
- Electives, ARCOS, Special Topics
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- Graduate Program Self Study
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FYII on September 26!
Strategic Review and Planning Sessions

- PharmD Admissions
- International Programs
- Advising
- Electives, ARCOS, Special Topics
- Getting to Expert Faster
- **Promotion and Tenure**
- Graduate Program Self Study
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FYII on October 17
Strategic Review and Planning Sessions

- PharmD Admissions
- International Programs
- Advising
- Electives, ARCOS, Special Topics
- Getting to Expert Faster
- Promotion and Tenure
- Graduate Program Self Study
- Big Data

FYII on November 21!
Putting the “Clinical” in Pharmacy

Patricia D. Kroboth, PhD
Dean
School of Pharmacy
Three Categories of Learning

Basic Science:

Therapeutic Modules
- Cardiovascular Disease, Endocrinology, Pulmonology, Oncology, and others

Professional and Clinical Development
- The Emerging Professional, Profession of Pharmacy, Experiential Learning
Putting the Clinical in Pharmacy

“. . . prepares student pharmacists to be health care practitioners who optimize the health of patients . . . through the effective use of medicines and other interventions. . .”
Putting the “Clinical” in Pharmacy
Required Experiences
Simulations and Real Patient Experiences

Required Clinical Experiences
During PharmD Program
= 370

Year of PharmD Program

Experiences per Student (#)

P1  P2  P3  P4

51  92  71  156

- Std Patient
- SimMan
- Silver Scripts
- VirPt Cases
- Real Pts
Putting the “Clinical” in Pharmacy

1. **Classroom:** lecture, discussions, group work

2. **Controlled clinical environments:** *Simulated* clinical situations
   a) Standardized Patients (Trained Actors)
   b) Computer Cases with Branched Questions
   c) Human patient simulator

3. **Experiential Learning—Real Patients**

4. **Student Organized Health Fairs, Outreach**
Group Work in Large Classroom Setting

Students learn:
- Critical thinking
- Communication skills
- Team work and collaboration
Seven Drug Therapy Problems

1. Unnecessary drug?
2. Need additional drug?
3. Need a different drug product?
4. Dosage too low?
5. Dosage too high?
6. Adverse drug reaction?
7. Non-compliant with therapy?

For All Patients: Hospital and Ambulatory
Second Category
Controlled Situations for Clinical Skills Development

a) Standardized Patients (Trained Actors)

b) Computer Cases with Branched Questions

c) Human patient simulator

All three:

• Have known answers.

• Provide a safe environment for learning.

• Protect patients from medication errors.

• Provide immediate feedback to students on their performance.
Standardized patients are trained about details:
- disease and symptoms
- their “family history”
- medications and side effects

Advantages
1. Every student has same experience
2. Patients can be questioned by the student.
3. SPs (and faculty) give feedback to the student
4. Interviews can be filmed
Human Patient Simulators: Life-like mannequins to teach clinical therapeutics

The mannequin:
- Breathes and can change sounds
- Sweats
- Responds to drugs--bar code reader for drug and dose
- Pupils dilate
- Seizes
- Coughs
- Eyes produce tears
- Bleeds
- Can check vital signs—blood pressure, respiratory rate, pulse
- Can have arrhythmia
- Dies from inappropriate drug dose
- AND more!
Computerized Patient Cases with Branched Questions

Students:
• See patient data.
• Decide which data is important
• Make decisions about drug therapy and monitoring
• Receive immediate feedback through the computer program.
Third Category: Student Pharmacists Working with Real Patients

- Faculty have less control over the patients and situations students experience.
- The “real” solutions to patient problems are unknown.
Silver Scripts

On visit #1, student:
1. Meets patient
2. Reviews medications
   *Goes home. . .*

Visit #2
3. Develops a plan
4. Finalizes plan with faculty member
5. Meets with patient and acts on plan on visit #2

Student pharmacists:
- Learn patient interaction skills
- Self direct learning for specific patient
- Become highly motivated to learn more pharmacology and therapeutics—BEFORE it is offered in the curriculum.
## ONE Silver Scripts Session
### Summary of 108 Student Experiences

<table>
<thead>
<tr>
<th>Type of Problems &amp; Interventions</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication Education</td>
<td>56</td>
</tr>
<tr>
<td>1. Unnecessary Drug</td>
<td>21</td>
</tr>
<tr>
<td>2. Needs additional drug</td>
<td>107</td>
</tr>
<tr>
<td>3. Needs different drug</td>
<td>20</td>
</tr>
<tr>
<td>4. Dosage too low</td>
<td>16</td>
</tr>
<tr>
<td>5. Adverse drug reaction</td>
<td>26</td>
</tr>
<tr>
<td>6. Dosage too high</td>
<td>15</td>
</tr>
<tr>
<td>7. Non-compliance</td>
<td>62</td>
</tr>
<tr>
<td>Referral to other health care provider</td>
<td>43</td>
</tr>
</tbody>
</table>

**Total Drug Therapy Problems Identified and Addressed** 267
Silver Scripts

Top “Diseases and Risk Factors of Patients

2014

• Hypertension
• Pain
• Cough/ cold
• Diabetes
• GI disorders
• Depression
• Hyperlipidemia
P2: Experiential Learning in Community Pharmacies

Students:
- Teach patients to use inhalers correctly
- Educate Patients about medicines
- And more.
### P2: Experiential Learning in Community Pharmacies

<table>
<thead>
<tr>
<th>Year</th>
<th># Students</th>
<th># Patient Encounters</th>
<th># Drug Therapy Problems Identified</th>
<th># Interventions Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>109</td>
<td>3,542</td>
<td>1,400</td>
<td>883</td>
</tr>
</tbody>
</table>
Experiential Learning: P2 Year Students Provide Patient Education in Community Pharmacies
Experiential Learning: P2 Year
Students Do Interventions in Community Pharmacies

Students learn to contact physicians to make changes in prescription medications.
P3 and P4: Interactions with Real Patients In Hospitals, Clinics, Community- With Other Health Professionals
P3 and P4 Years: Working in Hospitals

Patients are sicker and more acutely ill.

Students learn:

• How to work as a member of a health care team
• Their boundaries.
• Trust in other health professionals

Students develop confidence.
Fourth Category: Student Organized Health Screening
White Coat Ceremony: P1 Students

Professionalism

Oath of a Pharmacist:
Ethics
Responsibility
Summary: Putting the “Clinical” in Pharmacy

1. **Classroom**: lecture, discussions, group work

2. **Controlled clinical skills development**: *Simulated* clinical situations—provide immediate feedback
   a) Standardized Patients (Trained Actors)
   b) Computer Cases with Branched Questions
   c) Human patient simulator

3. **Experiential Learning**—Real Patients

4. **Student Organized Health Fairs, Outreach**
Excellence, Innovation, Leadership

Required Clinical Experiences During PharmD Program

- Std Patient
- SimMan
- Silver Scripts
- VirPt Cases
- Real Pts

Year of PharmD Program

Experiences per Student (#)

- P1: 51
- P2: 92
- P3: 71
- P4: 156

Total: 370
For faculty to consider: How can we do better?

1. Do we need more cases in P3 year?
2. Do students need to have a required number of patients to graduate?
3. How do we decrease the variability in experiences and assure the best possible training for our students?
Professionalism

- Are we as a faculty continuing to hold high expectations of professional behavior—throughout the entire time students are in class and in our program?
- Do we need to be more demanding of classroom behavior?
Research Data Management

School of Pharmacy Faculty Meeting

August 19, 2014
Melissa Ratajeski
HSLS Data Management Committee Chair

Michele Klein-Fedyshin
Liaison Librarian to the School of Pharmacy

http://hsls.libguides.com/school-of-pharmacy
Data Management

- Development and execution of policies and procedures in order to manage data throughout its lifecycle

- **Before** the cycle begins is the time to make decisions
Research Data Lifecycle

- Creating Data
- Processing Data
- Analysing Data
- Preserving Data
- Giving Access to Data
- Re-using Data
Data Management and YOU

University of Pittsburgh
School of Pharmacy
The Art and Science of Excellence
Does your lab/research group currently use a naming convention to save your data files?

- Yes
- No

What is a naming convention?

n = 9
Retraction: Spontaneous pre-stimulus fluctuations in the activity of right fronto-parietal areas influence inhibitory control performance

A retraction of the Original Research Article:
Spontaneous pre-stimulus fluctuations in the activity of right fronto-parietal areas influence inhibitory control performance


The authors and the journal wish to retract the 12 March 2013 article cited above.

While applying the same analyses to another dataset, the authors discovered that a systematic human error in coding the name of the files had been made during the extraction of the EEG template topographic maps best differentiating the two experimental conditions at the single subject level. Because the subsequent processing steps were based on these EEG maps, this error has ultimately modified the final result of the paper, which is therefore not correct. For this reason, the authors request to withdraw the article.

All the authors concur with this retraction and sincerely regret any inconvenience this may have caused to the reviewers, editors, and readers of Frontiers in Human Neuroscience.
How do you make your data accessible to those outside of your lab/research group?

- Publish in peer reviewed journals
- Present at conference
- Provide raw data on request
- Provided analyzed data on request
- Deposit raw data into repository
- Deposit analyzed data into repository
- I typically do not share my raw data
- I typically do not share my analyzed data

n = 8
“Publications are arguments and data is the evidence”

What might prevent you from sharing your raw data?

- Concern that proper credit will not be given
- Patient privacy issues
- Fear of competition
- Fear of wrongful use
- Restricted due to commercial/patent
- My raw data would not be useful to others
- N/A: I am willing to share
- Other

n = 8
In the past 2 years, have you written a DMP as part of a grant proposal?
Federal Guidelines
NIH Data Sharing Policy

- $\geq 500,000$ in direct costs in any single year are expected to include a plan for data sharing or state why data sharing is not possible

- Data sharing should occur in a timely fashion
NSF DMP Requirements

- Proposals must include a supplementary document labeled Data Management Plan (DMP)
- Describe how the proposal will conform to NSF policy on the dissemination and sharing
Office of Science and Technology Policy (OSTP)

- Federal agencies with > $100M in research and development expenditures
- develop a plan to support increased public access to the results of federally funded research
Journal Requirements
The Joint Data Archiving Policy (JDAP) describes a requirement that supporting data be publicly available.

JDAP has been adopted by journals across various disciplines.

Journals that adopt JDAP often recommend Dryad as an appropriate data repository.

http://datadryad.org/pages/jdap
Some JDAP Journals

- BMJ
- Ecology
- Genetics
- Heredity
- Nucleic Acids Research
- PLoS
- Systematic Biology
Clonal relationships in breast cancer in situ and invasive

outside the reference distribution of independent pairs, and is considered suggestive for clonality (equivocal) if the \( P \) value is within the range of the reference distribution but more extreme than the 5th percentile (that is, \( P < 0.05 \)). Further details of the method are described in Ostrovnaya and colleagues [21], and software is available in the Bioconductor package [23].

The source data used in this study are available in Dryad Repository [doi:10.5061/dryad.6354b].

Results

LCIS was identified in 44/65 (68%) patients subject to the array; among these, 21 patients had a paired DCIS and/or a paired invasive lesion for comparison. Seven patients were excluded due to poor-quality DNA/array data, leaving 14 patients with 17 paired samples for analysis (three patients each had three samples for comparison). The characteristics of each of the LCIS and paired samples are described in Table 1.
Questions??

mar@pitt.edu
Pursuing Chemical Biology in the School of Pharmacy

Paul A. Johnston
Drug Development Pipeline

Pre-clinical drug development

- SAR
- Analytical method
- PK
- Formulation
- MOA pharmacology
- ADME
- Acute Toxicity
- In vivo disease models
- Tox-safety pharmacology

PD biomarker bioimaging

Efficacy
Lead Generation & Optimization

Genomics, Proteomics & Molecular Biology

Screen Throughput
- UHTS > 100K/day
- HTS 10K to 100K/day
- MTS 100 to 10K/day
- LTS < 100/day

Targets

Assay Development

Compounds → Actives → Hits → Leads

Screen → Follow up → Validation

Automation

Chemistry

Combinatorial synthesis

Structural Verification

SAR

Natural Products

ADME-Tox

Robotic Liquid Handling Platforms
Detection Instruments

Janus 96-well & 384-liquid transfer platform

ImageXpress Micro
High Content Imaging Platform

M5e Microtiter HTRF Plate Reader
Multi-mode Detection: Abs, FI, FP, FRET, TR-FRET, & Luminescence
School of Pharmacy Compound Libraries

• **50,000 Compound Pharmacy School Diversity Library (PSDVL)**
  – Diversity subset of 410K ChemBridge 410K core library
  – Widest coverage of pharmacophore space but maintaining structural diversity
  – Filtered for physiochemical properties while exploring chemical space
    • MW ≤ 500, clogP ≤ 5, tPSA ≤ 100, rotatable bonds ≤ 8, H-bond acceptors ≤ 10, & H-bond donors ≤ 5
  – Non-drug like compounds, undesirable chemical groups removed
    • Michael acceptors, crown-ethers & analogs, disulfides, epoxides, etc.
  – Full 3D conformational analysis used to select all 3-point pharmacophores

• **Smithgall 10,000 Compound Mon-peptide Peptido-mimetic Protein-protein Interaction (PPI) focused library**
  – Subset of ChemDiv 142K PPI library
  – Includes mimetics of α-helices and β/γ-turns
  – Di- & tri-peptide mimetics & RGD, AVPI, PDZ, & VIP domain-binding motifs
  – Combinatorial templates modified with both flexible and rigid substituents
  – Geometry related to dihedral angles reported for ‘natural’ β- and γ-turn motifs
Dotmatics Laboratory Information Management System (LIMS) & Database Server

- 4TB Data Storage
- HCS Image & HTS Databases
- Data Security - Tape Backup

**REGISTER**
Chemical registration

**BROWSER**
Querying and reporting

**BIOREGISTER**
Biological registration & sequence management

**STUDIES**
Data screening and workflows

**STUDIES NOTEBOOK**
Electronic Laboratory notebook

**PINPOINT**
Chemical cartridge

**GATEWAY**
Document management and collaboration

**VOXEL**
Advanced analytics and visualisation

**ELEMENTAL**
Chemical sketching

**D2O**
Microsoft Office™ add-in

**NUCLEUS**
Database upload
Castration Resistant Prostate Cancer

Ligand dependent & independent mechanisms of castration resistance in prostate cancer

Harris et al, 2009, Nature Clinical Practice 6: 76-85

Agoulnik et al, Cancer Res 2006, 66: 10594-10602

Prostate cancer with intermediate TIF2 staining index 4

Prostate cancer with strong TIF2 staining index 9
Androgen Receptor::Transcription Intermediary Factor 2
Protein-Protein Interaction Biosensor Assay

TIF2-GFP Biosensor Adenovirus
TIF2 LXXLL 725-840 NLS/NaLS GFP

AR-RFP Biosensor Adenovirus
AR-LBD-AF2 662-919 NLS/NES RFP

1. DHT/AR-Agonist
2. Inhibitor then DHT
3. DHT then Inhibitor

AR-TIF2 PPI Phenotype
PPI Inhibitor Phenotype
AR Binding ↓ HSP70/90 ↓ Translocation ↓ Phenotype
Translocation Enhanced Image Analysis Module Segmentation: TIF2-GFP Derived Masks in FITC and Texas Red Channels

DMSO

TIF2-GFP
AR-RFP

20 nM DHT

TIF2-GFP
AR-RFP

Image

Mask
AR-TIF2 Protein-Protein Interaction Biosensor Validation:
A) AR-TIF2 PPI Formation & B) Inhibition Curves
3 x 3 Drug Combination Matrix
20 Compounds and 10 Cell Lines

Trellis Scatter Plot by Cell Line - NSC # Vs % Growth

NCI 60
Project Team:
David Close
Seia Comsa
Richard DeBiasio
Tong Ying
Shun

School of Pharmacy
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Flagged Synergy

SK-MEL-5 Cells, Drug A AJAY-4 - Drug B Vemurafenib

- Positive % cell growth indicates proliferation
- Negative % cell growth indicates cell death
- 0% Cell Growth indicates cytostasis

Drug combinations:
- Matrix controls
- Replicate controls

Treatment Group:
- A1
- A2
- A3
- B1
- B2
- B3
- Average A1
- Average A2
- Average A3
- Average B1
- Average B2
- Average B3

Synergy
Additive

Negative % cell growth indicates cell death
Positive % cell growth indicates proliferation
0% Cell Growth indicates cytostasis

Barry Gold

NSC332395 AJAY-4
AJAY-4 & Vemurafenib Drug Combination
SK-Mel-5 (BRaf-V600E) Vs SK-Mel-2 (WT-BRaf)

A. Growth Inhibition of Melanoma Cell Lines by APE-1 (AJAY-4) & BRAF Inhibitors (Vemurafenib)
   SK-MEL-5 (BRAF-V600E) & SK-MEL-2 (WT BRAF)

B. AJAY-4: Vemurafenib Drug Combination Ratio
   SK-MEL-5 Cells 3:2 Constant Ratio
   SK-MEL-2 Cells 3:8 Constant Ratio

Drug Combination Index (CI)

CI > 1.0
Drug Combination Effect < Additive

CI = 1.0
Drug Combination Effect is Additive

CI < 1.0
Drug Combination Effect is Synergistic

Stanton Kochanek
APEX1 in HNSCC

Analysis performed by Dr. Da Yang

TCGA Head and Neck Cancer (279 Cases)

Gene Amplification: APEX1 (Base excision repair)

Cal33

Cal 27

David Close & Danying Qin
HNSCC 3D Spheroid Assay Development

Shilpa Sant
Shilpaa Mukundan
Fnu
David Close

24hr
48hr
72hr
96hr

Unstimulated
EGF
EGF + Cetuximab

Total ERK1/2 Antibody

pERK1/2 Antibody

Cal33 300 µM Spheroids 384-well Seeding
Cell Titer Glo

Image Analysis

Visual Scoring

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Acknowledgements

Johnston Lab
- Yun Hua
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- Thomas Smithgall
- Barry Gold
- Donna Huryn
- Shilpa Sant
- Da Yang
- Nathalie Wong
- Harold Smith
- Nancy C. Reich

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The Society of Biomolecular Imaging and Informatics
FIRST ANNUAL CONFERENCE
SEPTEMBER 10–12, 2014
JOSEPH B. MARTIN CONFERENCE CENTER at HARVARD MEDICAL SCHOOL, BOSTON

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http://www.sbi2.org/2014-registration/

HCS/HCA SHORT COURSES
- Introduction to Fluorescence Image Acquisition & Analysis
- Assay Development/Optimization
- Data Analysis: feature selection, normalization/transformation, & statistics
- Pharmacodynamics & Tissue-based HCS
- Systems Approaches & Analytics
- And more...

PREMIER SCIENTIFIC PROGRAM
- Assay development & HCS Case Histories
- Image Analysis & Informatics
- Physiologically Relevant Models
- Emerging Frontiers

SPECIAL PUBLICATION
- Open Access for 6 months

NETWORKING OPPORTUNITIES
- Meet Leaders in the field & build collaborations with colleagues
- Exhibits, lunchtime seminars, & meet-and-greet sessions with vendors

EXHIBITORS

KEYNOTE SPEAKER
Dr. Stuart L. Schreiber
Harvard University & The Broad Institute
Partnership in Graduate Program with Sun Yat-Sen University (SYU) School of Pharmaceutical Sciences (July 1 - July 31, 2014)
Goals:

The goal is to develop a partnership with Sun Yat Sen University (SYU) that will help our graduate program to attract academically qualified and scientifically prepared students from a top tier School of Pharmacy in China. The process would be sustainable, and will represent a great pipeline for highly qualified candidates for our graduate program.
Laboratory Safety Training

- Pre-arrival: Small Animal, Bloodborn pathogens, Chemical Hygiene (Completed on-line)
- Post-arrival: Isotope Safety (classroom)
Welcome Session
Weekly faculty presentations

Xiaochao Ma, Tom Nolin, Sam Poloyac, Haitao Yang
Weekly meetings with graduate student interest group

Led by Ziv Kirshner
Department of Pharmaceutical Sciences Seminar

Huichang Bi, PhD
Associate Professor
School of Pharmaceutical Sciences
Sun Yat-sen University

Metabolomic analysis of pancreatic cancer cells

Tuesday, July 29, 2014
12:00  1:00 PM
456 Salk Hall
Graduate Program Information Session

Led by Maggie Folan
NCI visit

Led by Xiaochao Ma
Picnic
Washington DC visit
What’s next?

• Intern experience sharing (at SYU, September 2014)

• Graduate application for the 2015 class

• Summer intern program for 2015?