Research Teams of the Future: Interdisciplinary and Translational

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Questions/Goals

- What is interdisciplinary research?
- What is translational research?
- What sort of institutional structures facilitate this research?
- What is the role of mentoring and collaboration in preparation for interdisciplinary and translational research?
Introduction to the NIH Roadmap

“Health research traditionally has been organized much like ... cottage industries, ...grouping them into distinct, departmentally based specialties. But, as ... the molecular secrets of life have become more accessible, two fundamental themes are apparent: the study of human biology and behavior is a wonderfully dynamic process, **and the traditional divisions within health research may in some instances impede the pace of scientific discovery.**”

NIH Roadmap
Multi- vs Interdisciplinary Research

“Over the years, the Institutes and Centers of the NIH have developed many initiatives, mechanisms and programs to support either disciplinary or multidisciplinary research (where multidisciplinary research is defined as bringing together different disciplines to focus on a circumscribed problem, but keeping the disciplines distinct).”

NIH Roadmap
Interdisciplinary Research

“Interdisciplinary research integrates the analytical strengths of two or more often disparate scientific disciplines to create a new hybrid discipline. By engaging seemingly unrelated disciplines, traditional gaps in terminology, approach, and methodology might be gradually eliminated.”

NIH Roadmap
Examples?

“Historical examples include the development of **genomics**, which was formed from genetics, molecular biology, analytical chemistry, and informatics. Another example in which multiple disciplines have, …blended and evolved into a new discipline is **neuroscience**. Thirty years ago, students of the brain might have identified themselves as anatomists, physiologists, or psychologists, but today most would consider themselves neuroscientists.”

NIH Roadmap
Modifying the Infrastructure

- **Clinical Research Networks.** …focused on improving and expanding existing clinical research data networks and standardizing data reporting to improve networking (assessment instruments).
- **Clinical Outcomes Assessment.** …to develop new technologies to improve the assessment of patient-reported clinical outcomes, such as fatigue, pain, and mood changes (craving, alcohol use, relapse).
- **Clinical Research Training.** … increasing the number of clinical researchers, diversifying the settings in which clinical research is conducted, and providing clinical research training for medical and dental students.
- **Clinical Research Policy Analysis and Coordination.** …to address the difficulties clinical researchers confront in satisfying the multiple requirements of diverse regulatory and policy agencies.
- **Translational Research.** … see next slides

NIH Roadmap
Indiana CTSI Structure

1. Overview
   1.1. Indiana University
   1.2. Purdue University
   1.3. Indiana CTSI

1.1. Create Translational Research Acceleration Programs
   1.1.1. Novel Clinical & Translational Studies
   1.1.2. Pilot Collaborative & Translational Studies

1.2. Milestones & Implementation

1.3. Tracking & Evaluation

2. Governance

II. Train a New Cadre of Translational Researchers

II.1. Education, Training & Career Development
   II.1.1. CITE - K30, K12, T32

III. Foster Robust Community Engagement

III.1. Informatics Program
III.2. Community Health Enhancement Program (CHEP)

IV. Build Facile and Comprehensive Research Resources and Technologies

IV.1. Study Design & Biostatistics
IV.2. Regulatory Knowledge Support
IV.3. PCIR
IV.4. TTR Cores
IV.5. Disease Modeling
IV.6. Biomaterials & Nanotechnology

V. Leverage Resources of the Greater Indiana Community

V.1. Future Directions
   V.1.1. Global Health
   V.1.2. WellPoint

Improved Health of Indiana & Beyond

Trainee

Researcher

Community
How do we define translational research?

Translational Circle

Bench

Basic Research
Preclinical studies
Animal studies

T4
Translation into Practice - TRIP
Disease Modeling
-Omic studies
Pharmacogenetics

Healthcare

Translation into Practice - TRIP
Care Acceptance
Health economics

T3
Dissemination & Implementation research

Clinical Research
Phase III studies
Efficacy studies

T1
Case series
Phase I & II studies

Practice Based Research
Phase IV studies
Best Practice studies

T2
Meta-analyses
Systematic Reviews

Bedside

Product Development
Licensing
IP management
Industry Partnership

Commercialization

Community
To increase translational biomedical research and improve the health of the people of Indiana and beyond.
Streamlining Translational Research

CTSI HUB

Open Access

Researcher/Trainee/ Community

CTSI Access Officer

New Project Ideas

Resource Allocation & Funding Team

RFAs

Specific Resource Requests

Project Development Team

Funded Projects

MOP Team

Release Funds

Provide Resources

Study Design and Biostatistics

Regulatory Knowledge & Support

Bioethics & Subject Advocacy

Translational Technology Cores

Participant & Clinical Interaction Resources

Medical and Bio-Informatics
Expanding the pool of investigators

**Curriculum**
- MS in Clinical Research
- MS in Translational Research
- PhD in Translational Research

**Scholars**
- K-12 postdoctoral
- T-32 predoctoral
- Others (K-23, other T-32)

**Purdue University**

**Indiana University**

**CITE Core Program**

**Translational Scholars**

**Informed Consumers**

**PhDs**
- Minor in Clinical or Translational Research

**Residents**
- Research Electives

**Medical Students**
- Pilot Program

**College Students**
- Summer Internships
Preparation for interdisciplinary and translational research

• Mentoring, and your responsibilities as the protégé
• Understanding how collaboration works
• Understanding “cultural differences” you will encounter in moving between disciplines.
• Understanding how translation occurs
The voyagers brought their ship to the shore and Telemachus sprang from it. But before him went the goddess, grey-eyed Athene, in the likeness of the old man, Mentor. And the goddess...bade him now go forward...and ask [King] Nestor for tidings of his father Odysseus.

But Telemachus said to her, “Mentor, how.. Should I greet him? And how can I, a young man, question such a one as Nestor, the old King? “

The goddess, grey-eyed Athene, encouraged him: the right words, she said, would come.

Homer. Iliad, Chapter VII
Another Mentor

“The appearance of his *Handbuch der Physiologie des Menschen* between 1833 and 1840 (translated into English by Dr William Baly, and published in London in 1842) marked the beginning of a new period in the study of physiology. In it, for the first time, the results of human and comparative anatomy, as well as of chemistry and other departments of physical science, were brought to bear on the investigation of physiological problems.” Wikipedia

Adapted from Andrew Schaefer, APM winter meeting 2009
Many successes

Adapted from Andrew Schaefer, APM winter meeting 2009
Many successes (and new disciplines)
Roles of the Mentor

Provide a positive role model and guide in ethical practices
Be available and responsive
Evaluate protégé progress and performance
Help protégé develop writing and communication skills, including grantsmanship
Encourage and foster collegiality
Help transform a student into a colleague
Encourage life balance outside the research

From Justin McArthur, APM Winter meeting 2009
Responsibilities of the Mentor

Mentoring requires commitment of time, energy and goodwill (and in many/most institutions this is not explicitly paid for)

Each trainee must be allocated a significant portion of time, and the trainee needs to understand the commitment that is being made

The mentor uses his or her experience and contacts to help the trainee establish a professional network

From Justin McArthur, APM Winter meeting 2009
Characteristics of a Good Mentor

Sets high standards for research: rigor and logic

Encourages efficient use of time

States expectations and lets others know when they are not meeting them

Offers criticism in a way that doesn’t discourage people

Reviews laboratory records to guard against sloppiness; monitors for plagiarism.
Responsibilities of the Protégé

Establish a relationship with a set of mentors; some may be informal.

Add new mentors as you need help, but don’t let go of the old ones.

Seek advice from others, openly and diplomatically. If a mentor isn’t working out, change mentors.

From Justin McArthur, APM Winter meeting
Characteristics of a good Protégé

Brings a set skills to the laboratory/mentor: specific experience (statistics, software expertise), techniques from other laboratories.

Knows the mentors’ work (and provides them papers or references that they might be interested in).

Comes to meetings with an agenda, prepared to discuss progress, problems, and solutions.

Remembers that the mentor is a peer who provides support; mentors are not supervisors, monitors, or managers.

From Justin McArthur, APM Winter meeting 2009
In the long run...

“Technology will make hard-earned human skills worthless at an ever faster pace (who does Northerns, Southerns, manual DNA sequencing or PCR...anymore?)

Security is found in constant retooling to bring new value to one’s division/department/institution (not in a credential like tenure)

Cultivate a career “Lattice” rather than career “Ladder”.

This means you must learn to collaborate.

From Barry Coller, Vice President for Medical Affairs and Physician-in-Chief, The Rockefeller University, APM Winter meeting 2009; used with permission
Insights into collaboration
Three Simple Rules

1. Researchers collaborate, not research programs
2. The coin of the realm at academic medical centers is extramural funding
3. Success requires that all collaborators benefit as measured by the coin of their realm

Adapted from Christopher Callahan, Regenstrief Institute, Indianapolis, IN; used with permission
Three Simple Realities

1. Silence is not golden. Tension, debate, and conflicts are expected.
2. Some collaborations fail. If some don’t, you are not taking enough risks.
3. Collaborations are not forever. They end when a simple rule is violated.
Why Collaborate?

• Each of the partners will be more competitive for extramural funding
• The partnership will lead to synergy in discovery
• Stakeholders will benefit
• Society will benefit
• It’s fun
National Conference of Disease X

IU researcher A presenting study of disease X

IU researcher B presenting study of disease X

NIH program officer funding both researcher A and B. Inquiring whether B has ever met A?
Potential Partners- Good Qualities

- Shared vision for a specific research project
- Complementary (synergistic) resources
  - Scientific expertise, leadership, or maven
  - Research infrastructure including professional staff
  - Research population, samples, database, or toys
  - Extramural funding
  - Intermediary to research resources
- Enjoyable personality is a plus
- Mutual respect is a requirement
Potential Partners - Poor Qualities

- Non-overlapping research focus
- Good will but no specific research project
- Incompatible or conflicting style
  - Ineffective finisher
  - Low emotional intelligence
  - Questionable integrity
  - Functions at a different speed
  - Working with an incompatible coin of the realm
Ten Steps to Successful Collaborations

1. Define the goals of the project and expected outcomes
2. Communicate face-to-face at the outset
3. Communicate often and regularly
4. Choose a leader or leadership structure
5. Define roles and responsibilities of each participant
Ten Steps to Successful Collaborations

6. Discuss administration of the budget
7. Discuss administration of data
8. Identify intellectual property issues
9. Discuss publication and authorship plans
10. Identify when the project is expected to end
Reasons for Getting a Rejection

- Bad timing
- Lack of appreciation of potential partner’s focus, priorities, expertise, or strategic direction
- Maturation, culture, or style differences
  - Early - promiscuous with high risk taking
  - Middle - more discerning and targeted
  - Late - full roster of ongoing and planned projects
- Every “yea” equals a thousand “nays”
Collaboration and Junior Faculty

- Keep both eyes open—must be very clear about level of risk and the timeline
- Identify how your participation leads to specific first-authored publications and the timeline for submitting a specific grant as PI
- A high risk project must be balanced with a low risk project (or two)
- High risk, long-term yield collaborations are for senior researchers
Broadening Concept of Collaboration

- Industry
- State or Federal Government
- Community Agencies
- Advocacy Groups
- Community Organizations
- Different Fields: Agriculture, Engineering, etc.
The Story of Penicillin

- Fleming (1928), but also Florey and Chain (1938)
- Florey and Chain did not set out to make an antibiotic for human application
- WWII set in motion the idea for human use but no practical way to make penicillin in quantity
- Through philanthropy, met AJ Moyer, an expert in deep tank fermentation in Iowa with access to culture medium
- US Office of Scientific Research and Development formed largely to facilitate mass production of penicillin
- Government incentives facilitated collaboration among multiple pharmaceutical companies for production
Translational Research

Adapted from Barry Coller, Vice President for Medical Affairs and Physician-in-Chief, The Rockefeller University; APM Winter Meeting 2009; used with permission.
The paradox (and life) of the clinical translational researcher

“[We] are considered to be clinicians by physiologists, biochemists, and immunologists; and considered to be physiologists, biochemists, or immunologists by most clinicians.“

Dr. Isaac Starr, President, American Society for Clinical Investigation, 1940
Comparison of scientific discovery with translational research

<table>
<thead>
<tr>
<th>Scientific Discovery</th>
<th>Translational research</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Based on scientific opportunities</td>
<td>• Based on a health need</td>
</tr>
<tr>
<td>• Progress by taking the next logical step</td>
<td>• Progress measured by a final goal: a vaccine, drug, device, public health measure</td>
</tr>
<tr>
<td>• Any valid outcome of an experiment generates KNOWLEDGE</td>
<td>• Negative outcome generate relatively little useful knowledge</td>
</tr>
</tbody>
</table>

Adapted from Barry Coller, Vice President for Medical Affairs and Physician-in-Chief The Rockefeller University, APM Winter meeting 2009
Inverse approaches of Scientific Discovery and Translational Research

Scientific Discovery
- Background and Significance
- Preliminary data
- Specific aims
- Experiments
- A paper

Translational Research
- Health need
- Devise assays, formulate study, assemble collaborators
- Perform large scale trial
- Move results to medical practice
Spanning two cultures

Medicine

- Timely action required despite uncertainty
- Focus on that which is unique
- Many uncontrolled variables
- Follow practice guidelines
- Error to be avoided at all costs

Basic Science

- Reserve judgment until evidence is compelling
- Focus on the reproducible and generalizable
- Identify and control all variables
- Be bold and take risks
- Error is valuable and can lead to new ideas

Adapted from Barry Coller, Vice President for Medical Affairs and Physician-in-Chief, The Rockefeller University, APM winter meeting 2009
Spanning two cultures

**Medicine**
- Physicians apply new knowledge
- Expert opinion valued in absence of firm evidence
- Read NEJM, Annals Internal Medicine, specialty journals
- Wears coat and tie, work hours dictated by other responsibilities

**Basic Science**
- Scientists discover new knowledge
- Expert opinion is suspect (favorite tribal story is the great discovery first rejected by study section or editor)
- Read Cell, Science, Nature
- Wears jeans and teeshirt, flexible work hours

There are yet more cultural issues in working with other partners: industry, government, foundations

Adapted from Barry Coller, Vice President for Medical Affairs and Physician-in-Chief, The Rockefeller University
Essential skills of the translational research investigator or team

“1. The ability to articulate a health need with the precision of a basic science hypothesis
2. The ability to create a robust and practical assay (molecular, cellular, organismal, behavioral) to begin to address that health need
3. The ability to conceptually design a phase 3 trial to assess safety and efficacy before embarking on the project.”

Adapted from Barry Coller, Vice President for Medical Affairs and Physician-in-Chief, The Rockefeller University  APM Winter meeting 2009
Practical approaches for trainees wishing to prepare for translational research careers

1. Create, with your mentor’s assistance, a multi-disciplinary thesis, post-doc, or junior faculty committee
2. Cross the disciplines yourself: at meetings, in conferences, in your reading
3. Consider a minor in translational research (in other words, this is becoming more systematic)
Practical approaches for trainees wishing to prepare for translational research careers

4. If a basic scientist, get the advice of clinical specialists to help you understand the opportunities for translation of your work to a health problem

5. If a clinician, get the advice of basic and social scientists to understand the discoveries that may be translated to the health problem you wish to solve
Summary

1. There is much emphasis on development of interdisciplinary research with a translational focus (and therefore funding)

2. Success will depend on your training and your ability to collaborate

3. Understand the cultures of the disciplines you are trying to span
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