The Art and Craft of Team Science

Karen McDonald, Professor
Department of Chemical Engineering and Materials Science, UC Davis

Raymond Rodriguez, Professor
Department of Molecular and Cellular Biology, UC Davis
Presentation Overview

- Experience in Team Science (TS)
- What TS is and what it is not?
- What’s driving TS?
- The gentle yet firm touch of nuanced TS leadership — managing, motivating and inspiring individuals toward a common goal.
- Is TS appropriate for graduate students, postdoctoral fellows and assistant professors
- How we identified collaborators and built TS networks
- How we identified and foster effective lines of communication (in the context of different interdisciplinary languages)
Past Team Science Experience

- **R Rodriguez** Team Science Experience
  - DARPA — Human Butyrylcholinesterase in Plants
  - Global HeathShare Initiative
  - Center of Excellence in Nutritional Genomics
  - Ventria Bioscience Inc.
  - International Rice Genome Organization
  - Co-instructor for MCB263, Instructor for Molecular Biology and Biotechnology Design Methodology

- **K McDonald** Team Science Experience
  - DARPA — Human Butyrylcholinesterase in Plants
  - CREATE IGERT Graduate Training Grant in Plant Biotechnology
  - NSF I-Corps Program
  - NSF Large Interdisciplinary Award, Chevron Grant, and NSF with focus on Plant Production of Cellulase Enzymes
  - Co-instructor for MCB263, Instructor for Biochemical Engineering Capstone Design Course
What TS is and what it is not?

- Team Science is not just a multi-investigator agreement to research the same problem or question (i.e., typical collaboration)
- It is not just interdisciplinary research
- It is not distributed effort on different workpackages to solve the same problem (i.e., distributed computing)
- Team Science is a “transdisciplinary” approach to solving complex problems that integrates and aligns expertise and technologies around a shared vision with common expectations.
Factors Driving Team Science

- Complexity (complex, not complicated problems)
- Translational research
- Tenuous funding environment
- Open access to Internet and cloud-based datasets
- Connectedness
- Globalization
- Need for synergistic and highly non-linear results
Expression of Recombinant Human Butyrylcholinesterase in *Nicotiana benthamiana* and its Postproduction *in-vitro* Glycan Redecoration

University of California at Davis Colleges of:

- Biological Sciences
- Engineering
- Letters and Science
- Agriculture and Environmental Sciences
Syria, August 21, 2013
BuChE as Bioscavanger

1. **Acetylcholine (ACh)** is made from choline and acetyl CoA.

2. In the synaptic cleft, ACh is rapidly broken down by the enzyme **acetylcholinesterase**.

3. Choline is transported back into the axon terminal and is used to make more ACh.
DARPA Butyrylcholinesterase Project

- Goal: To make recombinant BuChE in plants, purify it and use *in vitro* enzymatic methods to modify the glycosylation to generate sialylated glycoforms

- Challenges:
  - Time: 12 month project, milestone oriented
  - Reporting: Monthly telecons with sponsor, quarterly reports, final report
  - Resources: budget reduction – cut one team member and reduced budgets of others, logistics for spending funds
  - Project coordination and communication: 7 faculty from 4 colleges, 2 graduate students, 3 postdocs, 3 research staff members, and 1 undergraduate
Investigator Team and Workflow by Task

1. rBuChE gene design and synthesis
   - rBuChE gene constructs
   - rBuChE (KDEL) gene constructs

2. Cloning into agrobacterium expression vectors
   - 2a
   - 2b

3. Transient production of rBuChE in N. benthamiana
   - 3

4. rBuChE purification and characterization
   - 4

5. rBuChE glycoform analysis
   - 5

6. In vitro glycan modification
   - 6

7. Clone/Express glyco-modifying enzymes
   - 7

8. Post-production glycoform and product characterization
   - 8

9. Sialylated rBuChE
   - 9
Three Steps from Multidisciplinary to Transdisciplinary (Team)Science

knowing, planning, sharing
Step 1: Knowing and understanding the problem and opportunities

- Human Health Biotech
- Problem Space
- Analytical Chemistry
- Plant Molecular Biology
Step 2: Planning innovative ways to accomplish the objective
Step 3: Aligning technology and expertise around a shared vision and expectations

- Human Health Biotech
- Analytical Chemistry
- Plant Molecular Biology

Synergy Efficiency Discovery

Problem Space
Figure A. Schematic of Bioscavenger Structure/Function Analysis*

1. Expression of Bioscavengers in Plants (Dandekar, McDonald, Nandi, Rodriguez)
2. Purified Plant-Expressed Bioscavengers (McDonald, Nandi, Rodriguez)
3. Biophysical, Functional, and In Vitro Binding Characterization (BFBC) (McDonald, Nandi)
4. In Vivo Pharmacokinetic/Immunogenicity Studies (Cerasoli)
5. Glycoform Analysis (Lebrilla)
6. Computational Protein Modeling (Faller)
7. In Vitro Glycan Redecoration Strategy (Chen, Faller, McDonald, Nandi)

*An iterative, feedback-dependent system of analysis based on the impact of glycan redecoration on protein structure/function. Reactions 1-4 represent the various enzymes used in glycan redecoration.
Team Science does not happen spontaneously or come easily!
Fact and Fiction of Team Science Leadership

- **Fiction: Collaboration = Consensus**
  - “In order for us to effectively collaborate we must always be in full agreement with each other to take action.”
  - My needs and opinions are equal to everyone else on the team.
  - “When we collaborate with each other, there has to be an abdication of leadership and decision-making authority is handed over to the group.”

- **Fact: Collaboration ≠ Consensus**
  - Effective TS does not require 100% agreement
  - Effective TS does require visionary leadership that is flexible, fair and competent
  - Effective TS has goals that transcend individual needs, ambitions and affiliations
Three Common Styles of Team Leadership

- **Command and Control:**
  - Emphasis on speed and strict adherence to standard operating procedures (SOPs)

- **Consensus:**
  - All members have equal authority. Emphasis is on buy-in (getting members to share relevant knowledge for the greater good) not on speed or quality

- **Collaborative:**
  - Found in dispersed cross-functional networks where designated team or project leaders have decision making authority. Emphasis on information sharing, discovery and quality over speed.
Nuanced TS Leadership is a Mixture of Leadership Styles

- Command and Control:
  - Ability to make difficult resource decision and mid-course adjustments to the project
  - Ability to meet milestones and deadlines

- Consensus Leadership
  - Ability to achieve buy-in from members who already have productive and well-funded research programs
  - Encourages feedback and self-evaluation

- Collaborative Leadership
  - Ability to bring the best minds and highly specialized technologies to bear on difficult, complex problems
## Assigning Responsibilities

<table>
<thead>
<tr>
<th>Subtask #</th>
<th>Task</th>
<th>Team Members</th>
<th>Time line</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Start growing <em>N. benth</em></td>
<td>BF</td>
<td>X</td>
</tr>
<tr>
<td>1</td>
<td>Produce and purify plant-made AAT for practice</td>
<td>KM, SN, SA</td>
<td>X</td>
</tr>
<tr>
<td>2</td>
<td>Gene and vector design</td>
<td>KM, SN, MP, AD, BF, MH</td>
<td>X</td>
</tr>
<tr>
<td>3</td>
<td>Gene and Vector synthesis (outside)</td>
<td>AD</td>
<td>X</td>
</tr>
<tr>
<td>4</td>
<td>Expression vector construction and confirmation</td>
<td>AD, BF, MH, MP</td>
<td>X</td>
</tr>
<tr>
<td>5</td>
<td>Generation of recombinant agrobacteria</td>
<td>AD, BF, MH, MP</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>rBuChE expression and activity verified in crude extracts</td>
<td>KM, SN, SA, MH, AT</td>
<td>X</td>
</tr>
<tr>
<td>7</td>
<td>Production and purification (including purification process development) of functional rBuChE at µg level for initial characterization and <em>in vitro</em> modification, ultimately produce and purify 1 - 2 mg</td>
<td>KM, SN, CL, RLR, AG, SA, AT</td>
<td>X</td>
</tr>
<tr>
<td>8</td>
<td>Basic biochemical analysis (PAGE, Western, MW, amino acid sequencing, CD, MS, HPLC profile) (outside)</td>
<td>CL, SN, AT</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Basic glycan characterizations of rBuChE before in vitro modification and hBuChE for comparison*</td>
<td>CL, AG</td>
<td>X</td>
</tr>
<tr>
<td>10</td>
<td>Synthesize and clone genes for recombinant enzyme</td>
<td>XC, YL</td>
<td>X</td>
</tr>
<tr>
<td>11</td>
<td>Demonstration of ability to replace and add galactose and sialic acid residues to rBuChE glycans at mg scale</td>
<td>XC, YL, CL, AG</td>
<td>X</td>
</tr>
<tr>
<td>12</td>
<td>Demonstration of homogeneous sialylated glycoforms</td>
<td>XC, YL, CL, AG</td>
<td></td>
</tr>
</tbody>
</table>

BF: Bryce Falk; AD: Abhaya Dandekar; CL: Carlito Lebrilla; XC: Xi Chen; RLR: Ray Rodriguez; KM: Karen McDonald; SN: Somen Nandi; SA: Salem Al-Kanaimsh; MY: My Phu; AG: Andres Guerrero; AT: Aye Tu; YL: Yanhong Li; MH: MinSook Hwang
Is TS Appropriate for Graduate Students, Postdoctoral and Junior Faculty?
TS and Career Development

- Independence:
  - TS participation can make it difficult to develop one’s reputation as an independent investigator.
  - Multi-author publications, even in high-impact journals, can obscure one’s contribution to the project.
  - Establishing one’s creativity, originality, and independence is essential for career advancement. This should be a concern for the TS leader.

- Authorship:
  - Assigning authorship can be challenging because the regular criteria for this process is complicated by TS dynamics.

- Benefits of TS:
  - Participation in a TS project can be a rewarding and life-changing experience, if managed properly. Excellent opportunity to network and interact with science leaders on problems of great importance.
Building a Team and Team Communication

Professor Karen McDonald
Identifying Collaborators and Building a Team

TRANSDISCIPLINARY RESEARCH TEAMS

Desirable Attributes

- Essential and complementary expertise
- Passion (and time) for the project
- Good person – someone you want to be around and enjoy bouncing ideas off of
- Good teacher – someone who will spend time explaining things to you
- Good listener - provides constructive criticisms/critiques
- Contributor
- Upbeat/optimistic
- Sense of humor
- Moderate ego – team player

Methods

- Network, network, network
- Sit in on classes outside of your area
- Seminars/seminar visitors
- Funding opportunities – grant proposal writing
Organophosphorus nerve agents (OPs) are considered to be likely weapons for use both in military and terrorist attacks.

OPs are relatively easy to produce in quantity, and can effectively be used to inflict harm.

Human butyrylcholinesterase is an effective prophylactic bioscavenger but:
- Stoichiometric binding 1:1 requires large doses (400mg)
- High cost from donated plasma ($10,000/dose)
- Complex protein – 340kDa tetramer, highly glycosylated
- Recombinant versions to date lack human-like glycosylation and have reduced circulatory half life
DARPA Butyrylcholinesterase Project

Positive outcomes:
- Tremendous learning experience
- Contribution to science and an important problem - demonstrated in vitro enzymatic sialylation of plant made BuChE
- New proposals and follow on projects with other sponsors
- Expansion of team to include computational expertise
- Joint posters and publications
- Incorporation into undergraduate teaching
“The IGERT program has been developed to meet the challenges of educating U.S. Ph.D. scientists and engineers who will pursue careers in research and education, with the interdisciplinary backgrounds, deep knowledge in chosen disciplines, and technical, professional, and personal skills to become, in their own careers, leaders and creative agents for change.

The program is intended to catalyze a cultural change in graduate education, for students, faculty, and institutions, by establishing innovative new models for graduate education and training in a fertile environment for collaborative research that transcends traditional disciplinary boundaries. It is also intended to facilitate diversity in student participation and preparation, and to contribute to a world-class, broadly inclusive, and globally engaged science and engineering workforce.”
Identifying Collaborators and Building a Team

- TRANSDISCIPLINARY GRADUATE TRAINING TEAMS
  - Additional Desirable Attributes
    - Good mentors
    - Good funding record
    - Champion of diversity, inclusiveness
    - Selflessness
    - Responsiveness/persistence
    - Strategic partners off campus
  
- Methods
  - Start with a small group (PI/Co-PIs) to develop vision, define theme and develop ideas for training components
  - Share vision with broader group of faculty to gauge interest, refine ideas, recruit trainers
  - Utilize expertise of Research Development staff!!
  - Talk to graduate students, post-docs and other faculty
  - Identify faculty who give their time to graduate program activities
  - Develop networks off campus with other academics and industry
The importance of persistence!!!!!
A multi-institutional IGERT with an international component:

Tuskegee University

University of California at Davis

National University of Ireland, Maynooth

Teagasc Oak Park Research Center, Carlow

University College Dublin

National University of Ireland, Galway
The CREATE-IGERT graduate training program integrates:

- Plant sciences
- Cellular and molecular biology
- Engineering

Funded 27 students at UCD and TU over the past 6 years!
CREATE-IGERT Faculty Trainers

34 faculty trainers from 7 colleges/schools

Biological and Agricultural Engineering (Engineering)
- Julia Fan
- Tina Jeoh
- Bryan Jenkins
- Jean VanderGheynst

Biomedical Engineering (Engineering)
- Michael Savageau

Chemistry (MPS)
- Carlito Lebrilla

Chemical Engineering and Materials Science (Engineering)
- Karen McDonald

Food Science and Technology (CAES)
- Bruce German
- Nitin Nitin
- Sharon Shoemaker

Integrative Biosciences (TU)
- Clayton Yates
- C. S. Prakash
- Jesse Jaynes
- Marcia Martinez
- Marceline Egnin
- Ramble Ankumah

Medical Microbiology and Immunology (Med)
- Satya Dandekar

Microbiology (CBS)
- Rebecca Parales

Molecular and Cellular Biology (CBS)
- Ray Rodriguez

Pathology, Microbiology and Immunology (Vet Med)
- Tilahun Yilma

Plant Biology (CBS)
- Katie Dehesh
- John Labavitch
- Clark Lagarias
- Bo Liu
- Steve Theg

Plant Pathology (CAES)
- Gitta Coaker
- Bryce Falk
- Martina Newell-McGloughlin
- Pam Ronald

Plant Sciences (CAES)
- Dianne Beckles
- Eduardo Blumwald
- Abhaya Dandekar
- Daniel Kliebenstein
- Richard Michelmore
- David Neale
- John Yoder

7/8/2015
CREATE-IGERT aims to train PhD students in these integrative skill sets:

1) Desire and ability to work in interdisciplinary research teams.
2) Frequent and effective communication between research team members.
3) Establishment of a common ground (a common set of scientific principles and laboratory skills to build upon).
4) Deep knowledge in one's own field coupled with broad exposure in related areas.
5) A commitment to teach others outside one’s field as well as a desire to learn from others outside of their field.
6) Creativity and "out of the box" thinking.
7) Ethical and responsible conduct in research, development and business.
8) An understanding of the global impact, as well as different needs and/or perspectives on the technology in different parts of the world.
Contributors

- Guest Lectures
- Seminars/Workshops
- Equipment Donations
- Plant Tours
- Internships
- Grant Applications
- External Advisory Board
- Research Funding

Logos of contributing organizations are also displayed.
CREATE IGERT Project

**Goals:**

1) Develop a framework for interdisciplinary graduate training at the interface of plant science, biotechnology, and engineering
2) leading to new scientific knowledge to move the fields of biofuels/biorefineries, plant-made products and environmental sustainability,
3) attract, recruit, retain and graduate a diverse cohort of doctoral students,
4) cultivate the integrative skill set in graduate students as well as faculty trainers.

**Challenges:**

- Project coordination particularly with international and university partners
- Unrealistic expectations for international internships
- Varying levels of faculty participation in training activities
CREATE IGERT Project

Highlights:

- New joint research projects among trainers, co-supervised students
- Interdisciplinary training helped students achieve diverse career goals (faculty positions, AAAS fellowship in plant biotechnology regulatory policy, industry positions, entrepreneur)
- Many new extramural projects have been funded (NSF, DARPA, NSF REU, NSF GK-12) and subteams continue to write joint proposals (STC, ERC, PFI, REU, DOE, USDA, NSF)
- Industrial internships continue (required by DEB at UCD and IBS at TU) as well as joint proposals with industry colleagues, TU and international partners
Team Communication: DARPA Project

• TRANSDISCIPLINARY RESEARCH TEAMS

Project management related: within the team
• Smartsite: Web based data repository, documents, mailtool, calendar
• Monthly meetings prior to telecon and then after telecon, weekly subgroup meetings
• Gantt chart updates
• Email

Project management related: outside of the team
• Single point of communication with sponsor
• Group presentations
• Coordinated requests
Team Communication: IGERT

TRANSDISCIPLINARY GRADUATE TRAINING TEAMS

- Project management related: within the team
  - Smartsite: Web based data repository, documents, mailtool, calendar
  - Website
  - Listserves/Email
  - New trainee orientation, meeting prior to annual reporting
  - Annual retreat and Distinguished Lecture
  - Mid-project “Self Study Report”

Major challenge – keeping all participants, stakeholders, international partners up to date
Toolbox Session with IGERT Team

Michigan State University, University of Idaho,
Boise State University,
University of Alaska, Anchorage & the National Science Foundation

http://www.cals.uidaho.edu/toolbox/index.asp

- A workshop and survey tool to help researchers in a team comprised of members from different disciplines to understand differences in the way they approach science, what they value, what they think is important, etc.
Toolbox Experience

- Interdisciplinary team comprised of 2 PhD students (Immunology and Chemical Engineering), Postdoc (Bio and Ag. Engr) and Faculty Member (Engineering)

- Goal: Increase self awareness and mutual understanding about participant’s assumptions, expectations and values related to scientific research

- Methodology: Pre-questionnaire, facilitated discussion of responses, post-questionnaire

- Deliverables: Toolbox Profile, a collection of documents that serves as a record of the workshop experience including pre and post-questionnaire responses, transcript of discussion, facilitator observations and personalized list of references
Toolbox Findings

- Identifying fundamental differences between the way research is conducted in different fields: value and importance of
  - Clearly stated hypotheses
  - Quantitative vs qualitative studies
  - Basic versus fundamental versus applied research
- "We had not really discussed these issues in the past but just forged ahead on our project"
- "For collaboration to work well, everyone must get something out of it and it helps to know what they think is important, worthwhile, and of value to their career."
Summary

- Team science is an emerging trend for solving complex, multivariate problems that require diverse skillsets, broad knowledgebase and multiple technologies.

- Successful TS project are characterized by:
  - Clearly defined objectives, goals and milestones
  - Goals that transcend individual needs, ambitions and affiliation
  - A project manager with broad technical knowledge and managerial skills (a skilled accounts manager is also good).
  - Nuanced leadership that provides vision, promotes buy-in from all stakeholders, encourages feedback and is capable of making hard decisions.
  - Leaders with integrity, communication and motivational skills and the use of consensus leadership to engage all stakeholders