Large-Scale Team Science: The EPGP and Epi4K Experience

Dan Lowenstein, M.D.

for

The EPGP and Epi4K Investigators
Disclosure

NeuroVista, Inc.  Scientific Advisory Board
Neurologix, Inc.  Scientific Advisory Board
Learning Objectives

- Appreciate the growth of team science in the current era, and some measures of its impact
- Consider the main challenges in forming and maintaining a team: recognition of contributions, authorship, job security/promotions
- A review of the EPGP and Epi4K experience as it relates to team science
Most of the work still to be done in science and the useful arts is precisely that which needs knowledge and cooperation of many scientists and disciplines.

That is why it is necessary for scientists and technologists in different disciplines to meet and work together, even those in branches of knowledge which seem to have least relation and connection with one another.

Lavoisier, 1793
Figure 3. Number of Authors per Paper in the Boston Medical and Surgical Journal and New England Journal of Medicine for Selected Years from 1886 to 1977.
The Increasing Dominance of Teams in Production of Knowledge

Stefan Wuchty,1* Benjamin F. Jones,2* Brian Uzzi1,2*†

Science 316:1036, 2007
...increasing multi-institutional teams...

Multi-University Research Teams: Shifting Impact, Geography, and Stratification in Science

Benjamin F. Jones,1,2* Stefan Wuchty,3*† Brian Uzzi1,3,4*†

Science 322:1259, 2008
Charters & MOUs

- Guiding principles/Mission statement
  - acceleration of science
  - benefits of collaboration
  - “no surprises”

- Structure and rules
  - Committees
    - Governance group
    - Strategy group
    - Working group
    - Regular members
  - Phenotype repositories
  - DNA repositories
  - Project decisions
  - Publishing/Authorship
The multi-PI option presents an important opportunity for investigators seeking support for projects or activities that require a team science approach. This option is targeted specifically to those projects that do not fit the single-PI model, and therefore is intended to supplement and not replace the traditional single PI model. The overarching goal is to maximize the potential of team science efforts in order to be responsive to the challenges and opportunities of the 21st century.
The Authorship Lottery: An Impediment to Research Collaboration?

Petra Kaufmann, Christine Annis, Robert C. Griggs, and the Muscle Study Group Executive Committee
Authorship Conventions (widely known but unwritten “rules”)

- **“First” authorship**
  - Did the most work
  - Wrote first draft
- **“Final” authorship**
  - PI of grant
  - Head of research team
  - Principal mentor
- **The footnote and asterisk**
  - Equal contributors
  - Corresponding author
When first and final authorship are highly prized, there is an inevitable pressure to subdivide multidisciplinary projects so that each part of the work can have a separate publication. This pressure is particularly great if two or more trainees are each working with a different senior collaborator. Having counseled one’s trainee to strive for first authorship, one is compelled to argue for one’s trainee’s primacy on a multi-authored, multidisciplinary paper. If one fails to hold sway, it then becomes imperative to subdivide the work into more than one first/final authored component, the “least publishable unit.” This usually guarantees that the content and importance of the multiple publications will be “less than the sum of their parts.”

Ann Neurol 2010;68:782-786
Proposed solution

• Adoption of group authorship, accompanied by a detailed table or footnote in the paper that indicates the responsibilities and contributions of all participants, is the most equitable and honest way to report science that represents a team effort.

• Authorship of papers should be defined by a publication policy that is accepted by the research team in advance of the research project.

• The importance of having first authored papers for trainees and named authorship for other investigators should be considered but with efforts to focus trainees and other investigators on publishing secondary or ancillary findings from the original study and thus separate papers.

Ann Neurol 2010;68:782-786
UCSF Committee on Academic Personnel

“A Faculty Handbook For Success
Advancement and Promotion at UCSF

“EVALUATION OF RESEARCH”
...Department chairs, directors of large laboratories who oversee other faculty, and faculty candidates should include a description and evaluation of the faculty candidate’s unique, essential and creative contributions to collaborative research.... To assist in this evaluation, faculty candidates should recommend, and the Chair select, both internal and external references who are familiar with the candidate’s essential and creative contributions to collaborative research, such that the unique contributions of the candidate can be assessed.
A international, multi-center, collaborative research effort funded by the National Institute of Neurological Disorders and Stroke designed to advance our understanding of the genetic basis of epilepsy.
The genesis of the project:

- First-hand awareness of the tremendous impact that epilepsy has on individuals and society, and the current limitations of what we offer our patients
- Recognition of accelerating advances in molecular analyses, and the pivotal role of phenomics
- Indisputable need for a national/international effort to achieve success
- Long-term impact of creating an international resource
- Enthusiasm for working with extremely motivated, experienced, and willing collaborators
Goals:

- Recruit 5250 individuals and parental controls (1500 IGE/LRE pairs, 250 each of IS, LGS, and MCD trios)
- Collect detailed phenotype information, including data on seizure semiology, EEG, MRI, treatment response
- Validate phenotype data using a structured data review process
- Bank DNA/cell lines at Coriell repository
- Work with colleagues to devise an approach for study of genetic data
**Progress (as of 12/5/11):**

<table>
<thead>
<tr>
<th>Activity</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled Participants</td>
<td>3,676</td>
</tr>
<tr>
<td>Completed Units</td>
<td>1,160</td>
</tr>
<tr>
<td>Blood Specimen</td>
<td>3,418</td>
</tr>
<tr>
<td>Subject Demographics</td>
<td>3,496</td>
</tr>
<tr>
<td>Eligibility Screen</td>
<td>3,490</td>
</tr>
<tr>
<td>Dx Interview</td>
<td>1,983</td>
</tr>
<tr>
<td>Med Rec Source Docs</td>
<td>741</td>
</tr>
<tr>
<td>Med Rec Abstraction</td>
<td>2,117</td>
</tr>
<tr>
<td>EEG Upload (total)</td>
<td>1,739</td>
</tr>
<tr>
<td>EEG Site Review (&lt;= 5/1/11)</td>
<td>1,235</td>
</tr>
<tr>
<td>EEG Site Review (&gt;5/1/11)</td>
<td>574</td>
</tr>
<tr>
<td>MRI Upload</td>
<td>1,405</td>
</tr>
<tr>
<td>MRI Site Review</td>
<td>931</td>
</tr>
<tr>
<td>AED</td>
<td>1,164</td>
</tr>
<tr>
<td>Final Dx</td>
<td>2,064</td>
</tr>
<tr>
<td><strong>Total Activities</strong></td>
<td>24,357</td>
</tr>
</tbody>
</table>
Accomplishments to date:

• Collaborative network in which PIs and coordinators feel they have “ownership” of the project
• Group that is entirely committed to sharing credit for successes
• Totally web-based data capturing system
• Unique data monitoring system to allow centralized review of de-identified medical records and phenotypic data, querying of clinical centers, resolution and documentation of data errors
• Centralized data reviews by scientific cores comprised of EEG, MRI, AED, Genome, Phenome, and Data Review and Analysis experts
Accomplishments to date:

• Opportunities for junior investigators and study coordinators to take leadership roles on publications, in collaboration with senior investigators
• Successful, cost-effective national recruitment campaign
• Collaboration with professional and patient epilepsy community and their interest in success of project
Lessons learned:

- Agree on ground rules regarding roles and credit right from the beginning
- Retrospective phenotyping of large epilepsy cohorts is difficult and requires an enormous effort if the goal is reliability and validity
- Incentives must be based on a “per activity” model rather than “% effort” model (but be careful about meeting inclusion criteria).
- A highly functional yet nimble informatics platform is essential for efficient workflow, rapid communications, training, high-throughput data review, etc.
Lessons learned (con’t):

• Start out enrollment and data collection at several pilot centers while system is fine-tuned
• Digitize and store source documentation from the start
• Think long-term regarding future studies and informed consent
• Create a national/international recruitment campaign – create a cost-effective program tailored to specific study needs
• Have a plan in place for handling low performance (volume/quality) sites - and stick closely to it and be prepared to substitute other sites
The primary goal of the Epi4K Center Without Walls is to increase understanding of the genetic basis of human epilepsy in order to improve the well-being of patients and family members living with these disorders. This improvement will come in the form of better diagnostics, treatments and cures. To accomplish this goal, Epi4K aims to analyze the genomes of a large number of well-phenotyped epilepsy patients and families collected by investigators from several major research groups.
Key upfront decisions:

- Epi4K Charter:
  
  A. Guiding Principles

  The driving principle behind Epi4K is that through collaboration and synergy, collectively we will make more rapid progress towards fully understanding the inherited components of epilepsy than can be achieved individually. The Center without Walls provides an unparalleled opportunity for this.

  It follows that membership of Epi4K carries advantages for which some sacrifices of autonomy are considered to be a reasonable price – the corporate benefits considerably outweigh the individual restrictions.

  For any research that would rely wholly or in significant part on Epi4K data or resources, Members are required to present and discuss their ideas within the Epi4K Steering Committee. This principle of “no surprises” extends to all new analyses, poster and oral presentations, manuscripts and other tools of the trade.
Key upfront decisions:

- Publication policy:

  Investigator status in Epi4K signifies an explicit agreement by all investigators to: 1) embrace the concept that Epi4K is a collaborative endeavor; 2) contribute directly to the activities of Epi4K; and 3) share in the credit associated with the collaborative work of Epi4K.

  In light of this agreement, investigator status in Epi4K also signifies a clear acceptance of the policy that all main scientific results (defined below as primary papers) arising from the collaborative work of Epi4K will be attributed to the sole author title: “The Epi4K Consortium”, and the specific contributions of individual investigators will be delineated separately. This policy applies to full-length papers, abstracts, oral presentations, news stories, and any other form of correspondence in which the main scientific results of Epi4K are described and attributed to Epi4K investigators.
Publication policy (con’t):

An additional goal of Epi4K is to facilitate the career development of early-stage and mid-stage scientists. To this end, in situations (described below) where the contributions of individual investigators justify being named as authors on publications, priority will be given to junior investigators (defined as individuals who have not yet achieved the rank of full professor or its equivalent, including senior level postdoctoral fellows). Furthermore, senior investigators (those at the rank of full professor or equivalent) will, in general, not be named authors on the primary and secondary papers (defined below) generated by Epi4K unless they have had a substantive role in being individually responsible for the conceptualization or analysis of the work.
Conclusions and Impact on Clinical Care and Practice

- We are living at the dawn of the era of team science! Essentially instantaneous communications and networking allow multidisciplinary research teams to quickly aggregate and disaggregate as needed to tackle large-scale studies.
- New approaches are facilitating the means by which teams can handle issues related to credit, authorship and promotions.
- The EPGP/Epi4K experience has taught us a great deal about the opportunities and challenges of organizing and managing a large research network – feel free to contact us at any time! (epgp.org)
- EPGP/Epi4K have not yet had a direct impact on clinical care and practice, but we expect to have initial sequencing results within the next year.
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE