BUILDING CROSS-DISCIPLINARY COLLABORATIONS IN AGING RESEARCH WEBINAR MONDAY 09.24
Multidisciplinary Collaborations

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Outline

• Examples of interdisciplinary collaborations
  • The Longevity Consortium
  • The Study of Muscle Mobility and Aging (SOMMA)
  • The Parkinson’s Fracture Prevention Trial

• Review the questions

• If time, Pharmaceutical & Silicon Valley collaborations
My approach to basic science collaboration

• Immersed myself in the literature
• Found a mentor in that discipline
• Attended basic science meetings and lectures
• To develop a translational proposal, organized meetings with scientists from other disciplines.
Examples
Read the world’s literature on the biology of longevity

• Mostly from model species.
• Understanding basic research is essential
Attended basic science conferences

• Local lectures on longevity
• Gordon Conferences
• Basic Science sections of our national meetings
• Learned about the terminology and methods
• Met mentors / collaborators
The Longevity Consortium

• Proposed and funded by NIA over 20 years ago
• Understanding the biological basis of human longevity would require combined efforts of
  • Basic scientists
  • Clinical scientists
  • Genetic epidemiologists
Longevity Consortium

• Retreats every 6 to 12 months
• Goal: learn each other’s language
• Immersion in each other’s science
• Presented their work to each other
• Everyone was encouraged to ask dumb questions
Longevity Consortium

• Retreats every 6 to 12 months
• Goal: learn each others language & methods
  • 1st meeting / retreat in Iceland
  • Immersion in each others work
  • Start friendships
• Presentations; ok to ask dumb questions
Example: Dramatic research in worms

Mutations that reduce the activity of a gene called daf-2 double the worm’s lifespan.

Daf-16 mediates the effect. Its homologue is FOXO3A, a transcription factor.
Example: Dramatic research in worms

Daf-16 mediates the effect
It’s homologue is FOXO3A a transcription factor

I had to learn new concepts: c.elegans, knock-out, wild-type, dafs, lifespan...
Translation from worms to humans

• Cynthia: Mutations in IgF/insulin signaling pathway. extended life-span of worms

• *LC renewal grant funded to test 291 common variants in 30 genes encoding proteins in that pathway in humans*

• Using cohort studies we identified and replicated associations between variants in FOXO3A and in AKT1 and survival

Pawlikowska...Ziv. Aging Cell 2009;8:460
SOMMA  
(Study of Muscle Mobility and Aging)  
• Started about a decade ago  
• Test the role of muscle in loss of mobility disability
Learning about muscle

Went back to school about the basics

• Read textbooks about muscle by physical therapists and biologists
• Review articles about muscle cell biology
• A retreat in an isolated location
• It became clear that there was a need to assay human muscle cells in a large cohort to predict change in mobility
Mentors

• Brett Goodpaster, part of the Health ABC Study
  • Called people he recommended

• Found an expert, Karyn Esser (University of Kentucky)
  • Liked the idea of a basic-clinical translational study
  • Connected me with others

• Luigi Ferrucci, NIA, was also excited and made other connections and contributed experience
Invited workshops

• Workshops in S.F.
  • Co-led by Karyn Esser
  • ~12-20 experts invited for 1-2 days (identified by
    • Basic scientists, scientists from pharmaceutical companies

• Goal: new ideas, measurements, & potential collaborators
Face to face meetings about a proposal

• Drafted a research plan
• Assembled a team – clinical and basic scientists
• A series of meetings about the proposal with the team
• Presentations and intense discussion about Energy and Muscle
• Meetings at NIA, hosted by Luigi Ferrucci
• Resulted in a proposal for a Study of Energy and Aging (SEA)
SOMMA and predecessor proposals

Simply

• Muscle biopsies in ~900 older adults to assay pathways in muscle cells that predict mobility disability

• Top clinical geriatric scientists (especially Steve K, Anne Newman)
  • Expert in the design and conduct of clinical and translational research

• Top basic scientists and labs in each key area biology of muscle
  • Energetics/mitochondria, denervation, autophagy, oxidative damage
Reactions from basic science reviewers

• Reviewed by special panels that included clinical and basic scientists
• The 1st 5 proposals got good, not fundable, scores
• A few negative reviews from the basic scientists
  • The study is “only correlational”
  • Not novel: “the ideas have already been proven in mice”
• It was important to have pre-reviews, especially from other critical basic scientists.
Similar issues with medical specialists
A trial in Parkinson’s disease

• A trial of zoledronate to prevent fractures in older patients with Parkinson’s disease
  • Did a meta-analysis of all studies of fracture risk in Parkinson’s
  • Teamed up with a leading neurologist (Caroline Tanner) who recruited others and the Parkinson’s Foundation
  • 2 day F2F start-up meeting in S.F.

• Incorporated aspects important to neurologists (e.g. teleneurology exams; recruitment by neurologists)
Reviews by a Special Emphasis Panel, mostly Parkinson’s disease specialists

• Why so many internists? The trial needs more neurologists.’
• Modest significance. This is not to improve Parkinson’s. Will it worsen the disease? Increase falls?
• Won’t be used in practice: neurologists aren’t trained or interested
The questions
How should you prepare for talking with someone from another field?

• Don’t let lack of preparation be a barrier to starting a conversation.
  • A friend / mentor can help you learn

• Eventually, you must read, attend lectures and/or meetings
  • It is important to know, in general, latest developments
  • See who is doing the best work to talk with, perhaps include

• Stay focused
What aspects of the other disciplinary culture should you understand?

• Whatever you need for your collaboration
  • At a minimum, key words, methods, and measurements
  • E.g. “conditional knock-out,” ”lifespan,” ”State 3 and 4 respiration.”

• The landscape of competition and relationships
  • Currently, trying to manage uncomfortable competition between two pairs of labs.
  • Must listen to all sides and be fair.
What aspects of your disciplinary culture should you take care to communicate?

• You don’t know what your collaborators don’t know
• Encourage even ’stupid’ questions. Don’t dominate conversations.
• A few key concepts that influence their work
  • E.g. misunderstanding a “case-cohort design” led to insufficient budget for assays.
What does a good multidisciplinary collaboration look like?

• A funded proposal. Impactful papers.
• Fun. People enjoy the conversations and calls.
What are signs that a potential collaboration will end poorly? What conflicts can be anticipated?

• Tension

• Slow or no response to emails or meeting requests.
How to judge? Will interdisciplinary research be beneficial or harmful my career?

Beneficial

• The expertise and/or measurements will enable you to answer more interesting and important questions.

• You can expect an enjoyable long-term relationship. Mutual respect.
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**Beneficial**
- The expertise and/or measurements will enable you to answer more interesting and important questions.
- You can expect an enjoyable long-term relationship. Mutual respect.

**Potentially harmful**
- A distraction? How will the interdisciplinary methods improve the design or conduct of your studies.
- Dysfunctional relationships. Tension. Lack of timely responses
Summary

• Extend your research outside your area of expertise
• What do you need to answer the question in the best way?
• If your research would benefit from biology
  • Learn: read, attend conferences
  • Find a partner/mentor to help you learn & introduce you to other experts
  • Have meetings of potential translational partners
    • Share presentations
    • Learn each others languages
    • Develop aims and plans together
• Avoid or get out of ones that are unclear, tense, or nonresponsive.
How does collaboration work at the academic-industry interface?

• I’ve had collaborations with > 10 pharmaceutical and 4 silicon valley companies
• Excellent experiences; learned a lot.
• Best ones have been based on friendships and mutual benefit.
• Worst: industry wants you to do something (recruit patients, provide data) with little or no input about the design or participation in analysis and writing.
  • Being a clinical site in a many multi-site trial; paid per patient
• Best: true collaboration about the design of a project or funding your ideas
  • Investigator-initiated studies (IIS)
Thank you!

We are recruiting post-docs and faculty for translational research on aging

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