

SGC5: T1 Translational Research

Co-Chairs:

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Eric Topol (Scripps Research Institute)

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Lisa Guay-Woodford (UAB)

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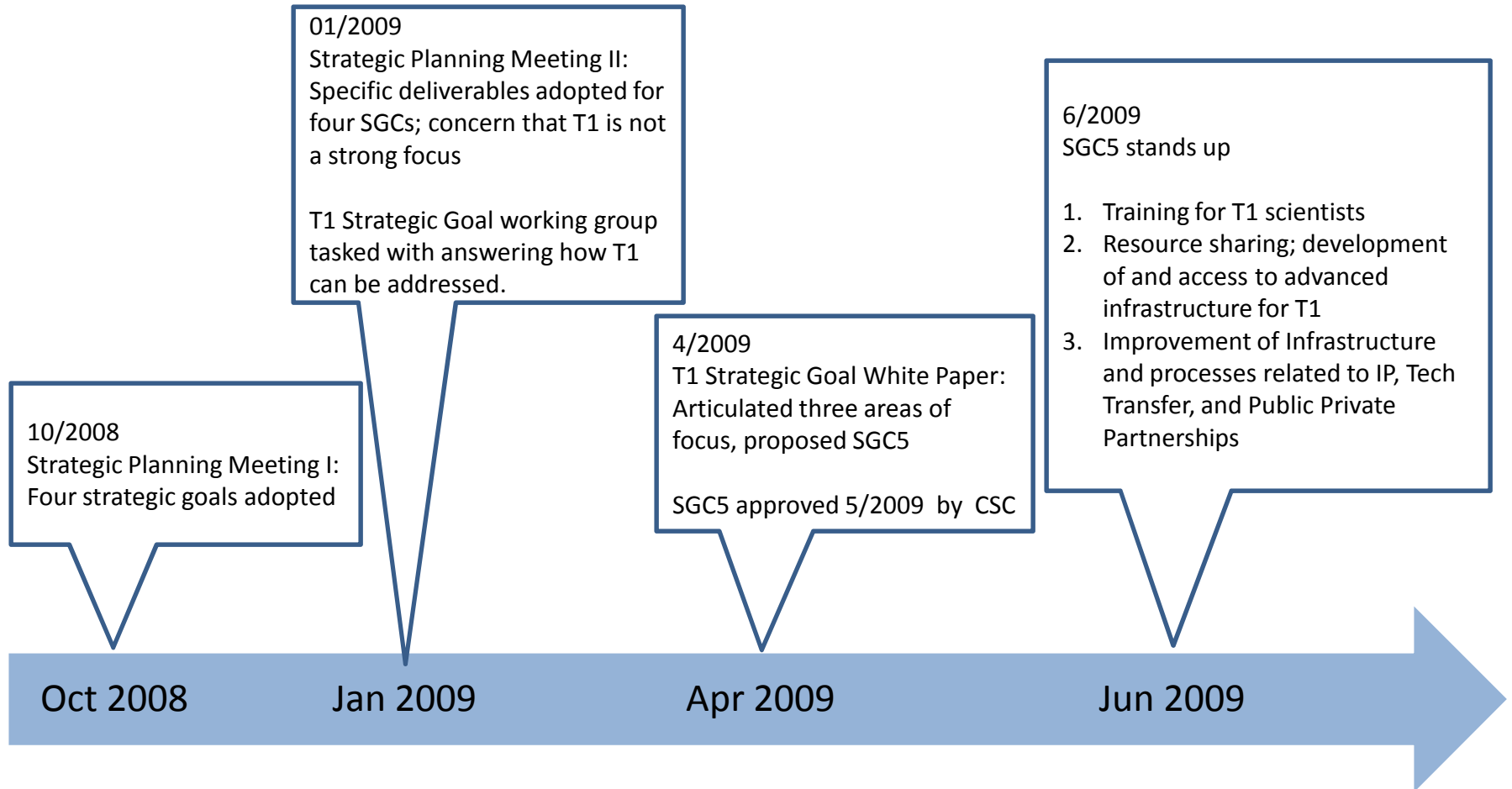
Alice Tarantal (UC Davis)

Geoff Ginsburg (Duke)

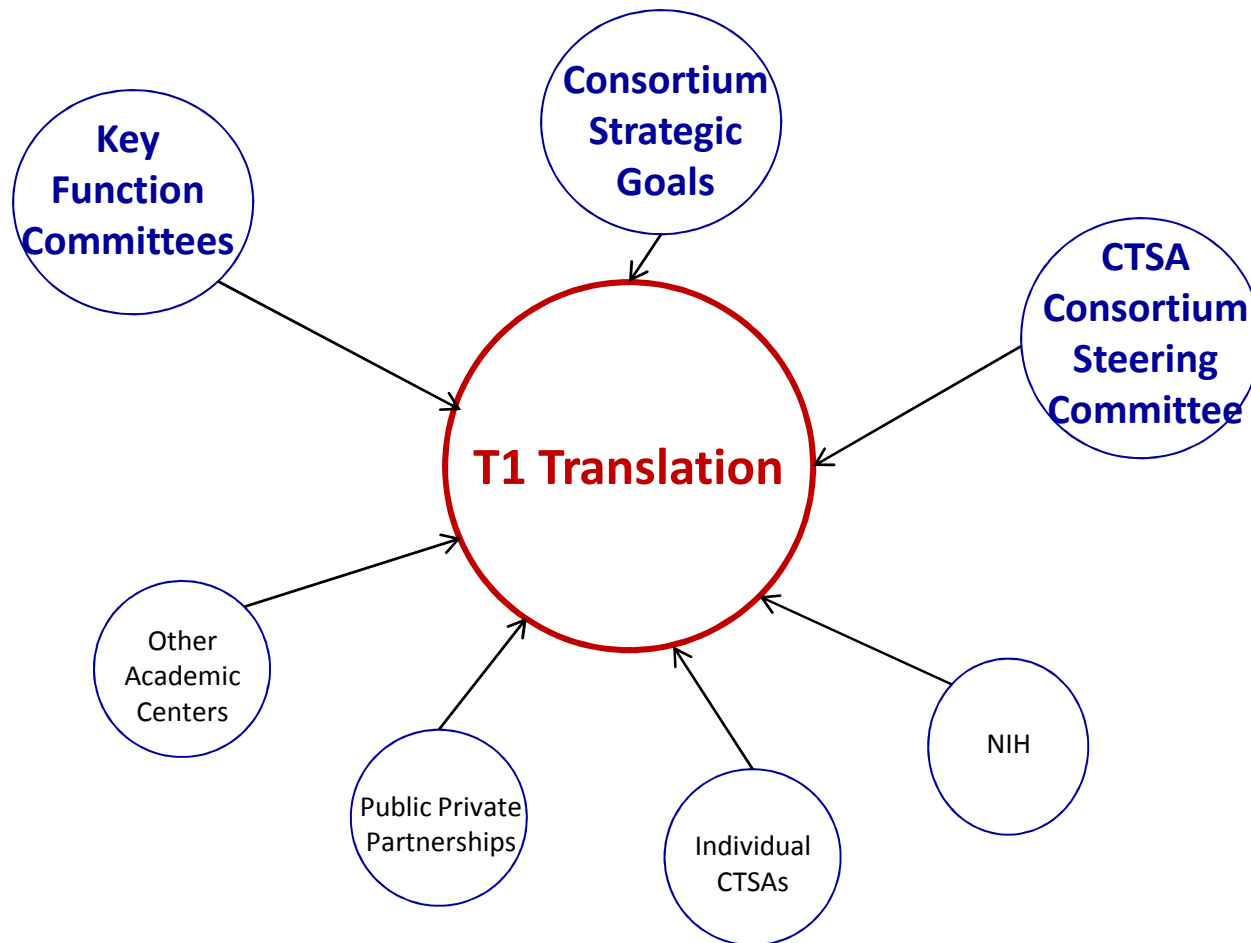
Joseph Kemnitz (Wisconsin)

with Susan Old, Lili Portilla, Jack Harding, Renée Joskow, and Douglas Sheeley (NCRR).

Translational Research Strategic Goal Committee Timeline and Rationale



T1 Translation Moving Forward in the CTSA's



SGC5, Part 1: Rationale, Overview of Goals, and Proposed Scientific Goal

SGC5: T1 Translational Research White Paper, April 2009

I. Definition

T1 research is the component in the continuum of translational research in which scientific advances made in the laboratory are translated into applications relevant for the improvement of human health. This includes developments in diagnosis, therapy, and prevention, through their initial testing in humans, up to the end of phase two in the drug development milieu, incorporating detailed phenotyping in small numbers of patients.

II. Common T1 Research Activities

1. Studies, often mechanistic, in cell-based systems.
2. Studies in animal models of disease.
3. Human studies, often proof of concept studies in small numbers of subjects, well-characterized in terms of phenotype and genotype.

III. Enabling Technologies

1. Genetics and genomics.
2. Proteomics and metabolomics.
3. Pharmacology and medicinal chemistry.
4. Imaging.
5. Bioinformatics and computational biology.
6. Phenotyping.

IV. Training for T1 Investigators: Joint participation by basic and clinical investigators.

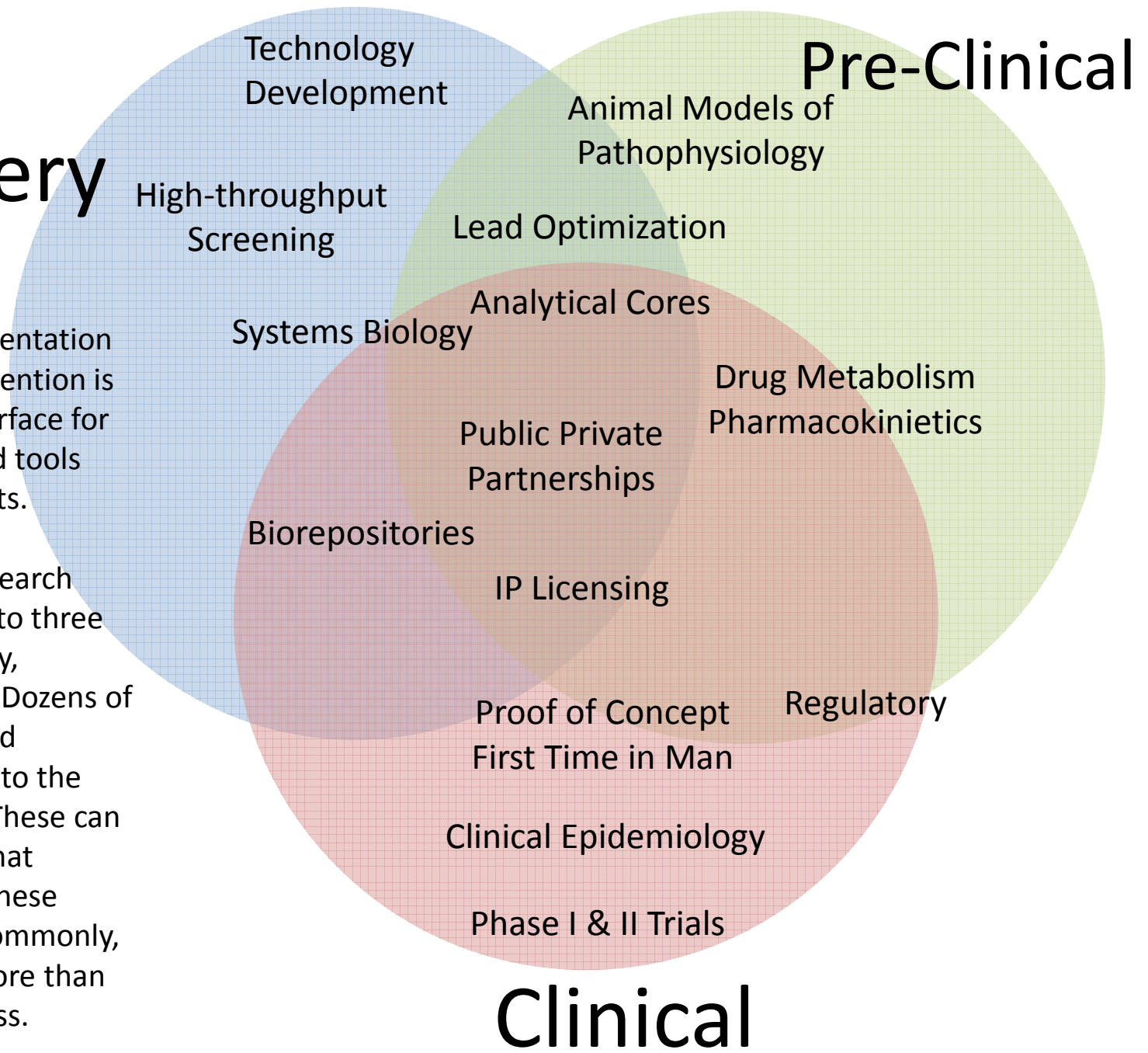
V. Recommendations for a Strategic Goal Committee on T1 Translation.

1. Education and Training Requirements
2. Collaborative Demonstration Projects
3. Support of Technical Resources
4. Technology Transfer and Public/Private Partnerships
5. Disseminate best practices for T1 research across the consortium

Discovery

This diagram is a representation of the T1 space. Our intention is to use it as a visual interface for accessing resources and tools necessary for T1 projects.

The T1 translational research space can be divided into three primary areas: discovery, preclinical, and clinical. Dozens of activities, resources, and processes are essential to the pursuit of T1 projects. These can be roughly and somewhat arbitrarily assigned to these three domains. Most commonly, they are essential to more than one phase of the process.



1. Education and Training Requirements

To be discussed this afternoon is the SGC update session.

2. Collaborative Demonstration Projects

In process of developing a Liaison Work Group with members from SGC1 (clinical research) and SGC5, to keep their respective priorities in equipoise.

Barriers to large, trans-CTSA projects:

- Funding
- What are the advantages over the usual collaborative efforts involving smaller numbers of centers?
- Ownership of results and dilution of credit: Who gets the RO1 or the patent?

2. Collaborative Demonstration Projects (A)

How the CTSA Consortium can bring added value to T1 translational research:

- Organize information on T1 supplements and other T1 ventures in order to identify areas of common interest or areas that might benefit from collaborations (in progress).
- Sharing technologies that are expensive and may not be available at all sites.
- Recruiting subjects with rare diseases.
- Standardizing sophisticated phenotyping protocols across multiple centers.
- Creating large databases of phenotype and genotype data, for example cohorts of healthy controls.

2. Collaborative Demonstration Projects (B)

How the CTSA Consortium can bring added value to T1 translational research:

- Finally, completion of a disease-oriented, practice-changing research project would be an attractive piece to present to the public and Congress to justify continued funding.

2. Collaborative Demonstration Projects (Examples, not necessarily proposals)

Possible examples:

1. Whole genome sequencing and phenotyping of a cohort of healthy elderly to serve as a disease-free control group for many other studies.
 - A resource for the entire CTSA.
 - Study could be funded by NCRN and/or costs could be spread across several Centers

2. Collaborative Demonstration Projects

Possible examples:

2. Adrenal Leukodystrophy: A rare hereditary disorder with highly variable penetrance, from severe childhood neurologic disease to milder adult-onset neuropathy. Disease gene is known, reasons underlying variable penetrance is not.

- Trans-CTSA consortium could accrue enough subjects and pedigrees to do the study.
- Relevant to pediatric and adult medicine.
- Cost sharing or NCRR funding could make possible deep sequencing and proteomic analysis.

3. Support of Technical Resources

- Create and disseminate a catalog of available phenotyping and other research resources (e.g availability of NHANES clinical and DNA sequence data and facilities to aid in drug discovery).
- Sponsor a meeting to give T1 investigators a broad overview of the current capabilities in disease phenotyping: Imaging, proteomics, genomics, metabolic studies, etc.

T1 Translational Research – Integrating with the KFC's and the other SGC's

- How will the KFCs - working with, or independently from, the SGC - support, enhance, facilitate moving the critical needs in T1 Translation forward?
 - Public Private Partnership KFC
 - Engage Industry on collaborating with CTSA Institutions, through Initiatives like the CTSA Industry Forum. Use the forum to develop workgroups between CTSAs, industry, and government to continue to address barriers to collaboration
 - Continued development of the CTSA Pharma Portal to partner investigators with “shelved” compounds and CTSA IP to bundle CTSA technologies
 - Facilitate cross CTSA collaboration opportunities by negotiating agreements efficiently - standardized clauses and templates
 - Compile entrepreneurial educational curriculum for CTSA consortium
 - Continue to participate on national level conference panels (such as BIO) to educate industry on the benefits and how to collaborate with CTSAs
 - Look at leveraging NIH SBIR funding with CTSA PPP goals
 - T1 Translational Research KFC
 - Develop a Federated Information Sharing Architecture (BioBank)
 - Develop a T1 Resource Database across the Consortium
 - Promote Pilot Projects to access and improve the CTSA infrastructure in order to conduct effective and efficient T1 Research Projects
 - Disseminate and promote CTSA facilitated T1 Research success stories

SGC1-SGC5 Liaison Group

- Rationale:
 - The central goal of SGC1 is to transform processes and infrastructure to support more efficient/effective clinical research; whereas the central goal of SGC5 is to make hypothesis-driven T1 translational research happen.
 - Coordination around operational issues, such as best practices, identifying potential partners, and cataloguing available resources is important for both SGCs to achieve their goals.

SGC1-SGC5 Liaison Group

- Members:
 - LM Guay-Woodford (UAB PI); Julie Earnest (OHSU Executive Director); Renée Joskow (NIH/NCRR)
- Charge
 1. Ensure that each SGC is aware of the concerns and operational issues re: clinical research (SGC#1) and T1/translational research (SGC#5).
 2. Liaise with SGCs as well as KFCs (PPP and Translational Research) and CC-CHOC to develop a set of guidelines and a catalogue of public domain resources that could facilitate the design of T1 projects by CTSA Consortium members.

SGC1-SGC5 Liaison Group

- Models for public-private partnerships:

Clinical trials

- Centers for Education & Research on Therapeutics (CERTs)
- UK National Health Service (NHS):
 - Develop the NHS as a world-class environment for collaborative research in the public interest
 - Establish NHS as the preferred host for multi-centre clinical research in partnership with and for industry.

SGC1-SGC5 Liaison Group

- Cataloguing public domain resources:
 - Phenotype data and DNA repositories established by multicenter studies, e.g. NHANES
 - Existing NIH-funded databases, e.g. National Records for Secondary Uses, eMERGE, dbGaP, PheX, caBIG.
- Relevant CTSA Administrative Supplements:
 - T1 KFC: 1) Web-based searchable biobank (CTSA Consortium samples); 2) Database of T1 resources at 7 CTSA Institutions.
 - CC-CHOC: Rare disease biobanking