

Proposals for Collaboration
Stem Cell Translation Laboratory (SCTL)
Division of Pre-Clinical Innovation
National Center for Advancing Translational Sciences
National Institutes of Health

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Introduction to SCTL

The NCATS [Stem Cell Translation Laboratory](#) is an NIH Common Fund Program focused on addressing the key biological and technological roadblocks that impede the translation of induced pluripotent stem cells (iPSCs) into clinical and regenerative medicine applications. As a state-of-the-art research facility, SCTL aims to develop new technologies (e.g. reproducible and scalable cell differentiation protocols), quality control standards, and translational paradigms to improve the efficiency of iPSC utilization. SCTL staff members work as a dynamic multidisciplinary team who apply their diverse scientific expertise to iPSC biology. The SCTL features advanced equipment and resources not available to most laboratories, such as large compound libraries (e.g. small molecules, natural products); quantitative high-throughput and high-content screening; robotic automation of cell culture workflows; multiscale assay development; 3-D bioprinting; next-generation sequencing, and integrated platforms to profile gene and protein expression and measure functional endpoints in standard cultures, as well as on the single-cell level.

The operational model of SCTL is collaboration between NIH intramural and external partners from the public and private sectors. SCTL partners bring actionable existing data and knowledge (e.g. cell characterization methods, differentiation protocols, safety assays) to the collaboration, but they either lack the expertise or resources to move these approaches into quality control, standardization, and robustness that are required for clinical-grade translation.

The minimal starting point for entering into collaboration with SCTL is a solid data package with preliminary data, description of the important problem(s) to be addressed, and outlining the anticipated timeline. SCTL uses a milestone-driven, multi-stakeholder project team approach to drive project execution. Assuming all milestones are met, SCTL commits significant resources to enable completion of a project. In all cases, measurable parameters (deliverables, timelines) will be agreed upon and implemented as a metric for informed decision making. A project will be deemed successful when the corresponding protocol improved by the SCTL team achieves the agreed-upon common goal(s). Upon completion, SCTL will disseminate all relevant data, protocol steps and newly discovered reagents. The joint team will make an effort to publish results in scientific journals.

Proposal Instructions

Overview

This is not a grant application, and no external funding is available. Rather, it is a proposal to collaborate with SCTL scientists, with the goal of moving promising protocols, assays, and iPSC-based technologies into future clinical testing. If accepted into the SCTL program, NIH intramural and extramural investigators will partner with SCTL scientists to develop and execute a milestone-driven iPSC development program. SCTL scientists will provide pluripotent stem cell expertise and operations will use SCTL funds to complete tasks required to meet program milestones. The external collaborator(s) will provide starting points for the project, ongoing expertise (e.g. developmental pathways, disease-area), and, when appropriate, efficacy or other testing of protocols, cells, and small molecules.

The primary focus of SCTL is to optimize and standardize promising technologies so that they can be progressed toward clinical iPSC applications. It is expected that projects will enter SCTL at a stage where a protocol or procedure has already been tested using biological and technical replicates.

Proposals are meant to identify candidate projects for collaborative development. Proposal submissions to collaborate with SCTL will be accepted on a rolling basis and reviewed three times per year.

General Instructions

At this time, SCTL is considering projects on iPSC characterization (e.g. strategies to distinguish normal and abnormal cell lines), directed cell differentiation and maturation under defined conditions, particularly into the neural (neuronal, glial, oligodendroglial) and endodermal lineages (hepatocytes, insulin-producing pancreatic beta cells) but mesodermal lineages will be considered as well.

Proposed projects must target a key roadblock in the currently-used methods. These could be underdeveloped cell differentiation protocols that have significant potential for improvement.

Data from the most relevant protocols and human iPSC models available should be obtained before proposing to collaborate. Projects must be at least at the stage of a validated protocol with a specific outcome.

Interested investigators must register with the online [proposalCENTRAL](#) system and provide a project abstract. The abstract must summarize the proposed collaboration in a way suitable for public dissemination. Describe the goal, the proposed approach, the current state of the project, the resources required to advance development, the public health impact and why SCTL is the desired partner for collaboration. The abstract should be informative to other scientists working in the same or related fields and understandable to a scientifically or technically literate lay reader. Do not include proprietary, confidential information or trade secrets. Following registration, a mandatory pre-proposal call is required with the SCTL program staff to assess project eligibility and orient investigators to the proposal and collaboration processes. Eligible investigators then will be invited to submit a full electronic proposal via [proposalCENTRAL](#).

Required Documents for SCTL Program Proposals

NCATS will assess submitted research proposals for scientific merit, technical feasibility, fit with available resources and alignment with SCTL programmatic goals. Steps include:

1. **Pre-proposal screening** with SCTL staff to confirm eligibility as a collaborating entity and adequacy of the current data package. This process consists of submission of an abstract (no more than one page in 12-point Times New Roman) for the proposed project and a telephone discussion with SCTL staff. Send proposed project abstracts via email to [Ilyas Singec](#)([link sends e-mail](#)).
2. **An actionable existing data package.** This means the applicant must:
 - a. Prove that a protocol has already been tested using biological and technical replicates.
 - b. Provide a complete list of reagents and other details.
 - c. Submit a summary detailing the outcome of prior solid experimentation (e.g., a description of attempts to reproduce the protocol by different researchers in the same group or collaborators; information on optimization steps and troubleshooting carried out).

- d. Manuscripts and other supporting publications can be uploaded during submission.
3. **Submission of a full proposal package.** This includes a formal request (no more than five pages with data and figures, in 12-point Times New Roman) and specific supporting documents not to exceed two pages (e.g. published or preliminary data presented). Identify the current roadblocks to development and the stage to which the project will need to be taken to attract outside development resources. Identify milestones and describe potential challenges and go/no-go decision points. Include specific details as necessary to demonstrate that the project has been well thought out (e.g., the availability of appropriate reporter cell lines and components of the assays to be developed, etc.). References should NOT be exhaustive. Provide a list of no more than 15 references relating directly to the proposal. Provide PDFs of any key papers to ensure that all readers have access to critical data that may be cited. Compile all reference documents into a single PDF upload, if possible, pending individual file size limits in [proposalCENTRAL](#)
 4. **Peer-reviewed, confidential scientific assessment** of the submitted proposal by SCTL staff and advisory group members (composed of NIH staff with expertise in the proposal area). Decision-making criteria include:
 - a. Strength of the data package
 - b. Feasibility and the deliverables timeline
 - c. Synergy with SCTL goals
 - d. Translational sciences impact
 5. **In-depth face-to-face meetings with potential collaborators** and discussion of raw data under the protection of a confidential disclosure agreement.
 6. **Agreement that all data (positive and negative results) and resources generated under the collaboration will be shared with the public.**
 7. **Intellectual Property (IP) Information:** To ensure sufficient freedom to operate on the proposed project, a clear description of the relevant patent space and status of IP is required. This includes a list of any patents issued or pending with respect to either the agent to be developed or any non-commercially available technology or material required for the development of the proposed project. In the event that a project would require the use of non-commercially available technology or equipment that is patented by a third party, the proposal must include documentation verifying that the patent holder does not object to its use in support of the proposed SCTL project. Each SCTL proposal must include the information described below, signed by an authorized staff member overseeing IP and/or technology transfer at the investigator's institution or company. This verifies that he or she has reviewed the SCTL proposal and that the technology is eligible for consideration by the SCTL program. If the technology is found not to be eligible for use as outlined and it is central to the investigator's proposal, submission to the SCTL program is not encouraged.

The following information is REQUIRED. If any of the following are not applicable to your project, state so explicitly (e.g., "There are no confidentiality agreements in place with a third party."):

- Description of the patent space or freedom to operate around the proposed agent.
- Details of all the following rights that are owned by your institution and that will be used in the project (the "institution's IP"):
 - Patents and patent applications
 - Significant knowhow
 - Registered trademarks, applications for registered trademarks and other marks
 - Registered designs, applications for registered designs and significant other designs
 - Significant copyright works and other IP rights
- Details of all employees, consultants, and other parties involved in the development of the institution's IP related to the SCTL project proposal. If there are contributors from outside the institution, describe their role in development.

- A complete list and brief description of all agreements with third parties related to the SCTL project proposal:
 - Granting rights to those third parties under the institution's IP
 - Granting rights under third-party IP to the institution

- A complete list and brief description of all confidentiality agreements with third parties related to the SCTL project proposal, including details of any:
 - Claims made by third parties against the institution related to the project proposal that the institution has infringed a third party's IP rights
 - Circumstances where a third party has or may have infringed the institution's IP or other IP used in the institutions' business related to the project proposal

NOTE: Any IP generated before initiation of SCTL collaboration are retained by the investigator/institution as background IP. The potential for development of new IP will depend on the stage at which the project enters into collaboration with SCTL. However, all collaborators should anticipate that there will be joint IP development with SCTL employees. Inventorship of any new, multi-party IP created from this collaboration will be determined according to U.S. patent law and governed under the collaborative agreements executed at the outset of the formal research partnership.

8. **Key Investigators Biosketch:** All key investigators (i.e., all investigators intellectually involved in the project) must provide biosketches following the current [NIH General Biographical Sketch](#) format. In the list of publications, please highlight any that are directly related to the proposed project by preceding them with a double asterisk (**). All key investigators should list all current external sources of research funds. The lead principal investigator (point of contact) should provide additional contact information.

NOTE: Prior to submission, all documents must be converted to searchable PDF format, free of any digital protection or passwords, to allow compilation and handling by the proposalCENTRAL system.

Selection Process

NCATS staff initially assess proposals to SCTL for scope and availability of internal resources. SCTL staff then seek feedback on select proposals from the governance members of this program including NIH staff in relevant Institutes and Centers and external stem cell experts to measure enthusiasm for the proposed science, competitiveness within the research area, and feasibility of success.

Feedback will be obtained in the following areas:

- Strength of current data package
- Feasibility to complete goals
- Translational impact relative to current standard
- Likelihood of external adoption and broad impact

Details of the NIH and external expert deliberations are kept confidential by the SCTL program, though investigators will receive written communication regarding the proposal's final outcome. All materials submitted to SCTL via [proposalCENTRAL](#) are considered confidential.

Following the scientific assessment, SCTL staff will evaluate select proposals further through due diligence and face-to-face meetings with potential collaborators, during which SCTL staff may request additional supporting data. Portfolio balance and availability of resources also will impact final decisions.

Post-Submission Communications

NCATS staff will inform investigators of the status of their proposal as soon as is feasible. During the selection process, additional (just-in-time) data may not be submitted. Twelve months after a proposal is deferred or declined, investigators may be given an opportunity to provide new data in support of the proposal. Significant

changes to a proposal's scientific direction or available data may require submission of a fully revised proposal document. (See below "Updates to Prior Proposals")

Collaborative Agreements

Research projects are governed by formal NIH collaborative agreements. When a collaborative agreement is agreed to and signed by all parties, the collaborative project will start. More information about the [available standard model agreements](#) may be found on the NCATS website.

Project Initiation, Planning, Termination

1. **Project Team:** Once a collaborative agreement has been executed, a project team will be formed. In consultation with the collaborating investigator, the project team will develop and define the following elements:
 - Project Plan
 - Timeline
 - Milestones and Deliverables
 - Go/No-Go Decision Points
2. **Project Plan:** The Project Plan will be approved by SCTL leadership. Any changes to the Project Plan will need to be approved by SCTL leadership. Go/no-go decisions will be made by the project team based on the Project Plan. In coordination with governance team members, SCTL leadership makes the final decision regarding changes to project scope or termination.
3. **Project Termination:** Upon failure to meet timelines, milestones, and/or deliverables or with the recommendation of the governance team, SCTL will terminate a project. Whenever possible, collaborating investigators will be provided guidance on how to move the project forward.

Updates to Prior Proposals

SCTL may accept updates 12 months after a proposal is initially deferred or declined.

Updates may require:

- A summary letter, not to exceed 2 pages.
 - Explain how the proposal has been modified and strengthened.
 - If the prior proposal received a detailed evaluation by TRND, respond to any comments and recommendations, and address any disagreements.
- An amended proposal.
 - The amended proposal should follow the current "Proposal Instructions" governing required documents and page limits.