

Ga CTSA TL1 Application Writing Workshop

November 2, 2023

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Objectives

- ▶ Understanding the TL1 proposal process
- ▶ Grant Writing Nuts and Bolts
 - ✓ NIH Fellowship Biosketch (*fellowship version – use FORMS H*)
 - ✓ TL1 Personal Statement
 - applicant's training
 - research background
 - career goals
 - ✓ Research and Training Plan: Clinical / Translational Research Proposal (6 pages total)
 - ✓ Resources

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TL1 Overview

	Predocutorial Track - PhD students - Medical Students	Postdoctoral Track - PhD postdoctoral fellows - MD clinical fellows
US citizen or permanent resident	✓	✓
Enrolled at one of the GA CTSA partner institutions - Emory, Morehouse SOM, Ga Tech, UGA	✓	✓
- Award duration	1-2 years - Typically, 1 year for Medical Students	1-2 years - Typically, 1 year for most residents and MD fellows
Dedicated to a career that encompasses clinical and/or translational research	✓	✓
Application due date	February 15, 2024	March 15, 2024
Required mentor research training	✓	✓
Required didactic training	MD / MSCR or CPTR PhD / MSCR or CPTR	CPTR or MSCR (or equivalent with approval)
Budget	NRSA stipend + \$1,500 for travel + health insurance + child care expenses	NRSA stipend + \$11,800 for research supplies + \$1,500 for travel + child care expenses

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Goal of TL1 training

- ▶ **Research Education** is a critical component of the GA CTSA.
 - ▶ The GA CTSA is dedicated to providing predoctoral and postdoctoral trainees with state-of-the-art scientific knowledge, tools and methods to improve human health through rigorous clinical and translational research training.
- ▶ Through the TL1 Core, the GA CTSA will increase the translational research workforce and enhance career development of future leaders of the biomedical research workforce, a major mission of NIH.



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Getting ready to prepare a TL1 fellowship application



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Create HIGH Overall Impact for your proposal

- ▶ Well written, follows the rules outlined in the Application Instructions
 - ▶ <https://georgiactsa.org/training/tl1.html>
- ▶ Clear and focused objectives
- ▶ Doable and feasible given time and support available from your mentor's research environment
- ▶ Entire narrative is a cohesive whole with a focused theme (i.e., *the story of how you will advance in a career in Clinical and Translational Research*)
- ▶ Mentor section is VERY PERSONAL and VERY DETAILED
- ▶ Research plan and training plan are complementary

All this is integrated with your near and long-term career goals

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Articulate your Immediate and Long-term Career Goals



Reviewers will look for the answers to these questions:

1. What new training will you receive and from who?
2. Are you competitive - biosketch, mentoring team, research plan
3. How will this training you describe in the application advance your career and the science you propose given this new skill set?
4. What will be the next step?

→ Preview a research area that you are interested in pursuing.

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Be very specific: What new research skills will you acquire?

- Name the **NEW** laboratory methods, analytical methods, modeling schemes, comparative systems, new animal models, etc.
- itemize the **New** specialized coursework / workshops / seminars

- Hypothesis-driven work is highly valued
- Human-oriented research is required

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From the Application Guidelines - Support

In addition to didactic training (e.g., MSCR program), all TL1 trainees will have **mentored research training** and carry out a **hypothesis driven research proposal (clinical or translational research)** relevant to human health under the guidance of their lead mentor and mentoring team.

The proposed research project must include a well-articulated **human component** and an explanation of how the research **translates** to improving human health.

For example, studies including humanized animal model systems may be eligible.

However, studies that focus on **basic science** are not eligible for this particular TL1 funding mechanism.

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Do what successful grant writers do: Vet your research idea with LOTS of smart people

- ▶ **Is your Research Plan scientifically sound?**
 - ▶ How do you know this?
 - ▶ Let others see your work – review and feedback from other mentors/advisors and peers (not just your mentor)
 - ▶ Do you have preliminary data?
 - ▶ Show data from your own work or from your lab (attribute appropriately)
- ▶ **How will you write about research in an area where you are not an expert?**
 - ▶ Get advice from your mentors
 - ▶ Especially for explaining new techniques or analyses in your proposed aims




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Drobox Resources

- General Scientific Grant Writing materials
- Human Ss materials from NIH
- Information on the NIH NRSA F grants
- NIH Sites on Rigor and Reproducibility
- FindingFundingforResearch(7.2015).pdf
- JAMA ClinTrials(2016).pdf
- Preliminary Research- Don't Stop 'Til You Get Enough.docx

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TL1 Application Nuts and Bolts



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TL1 Application Required Sections

1. **Cover sheet**
2. **Personal Statement** (*up to 2 pages – see directions*)
 - ▶ applicant's training, research background, and career goals
3. **Your NIH Biosketch** (*fellowship version*)
4. **Your lead mentor's NIH Biosketch** (*standard version*)
5. **Any co-mentors' or collaborators' biosketches** (*standard version*)
6. **Clinical / Translational Research Proposal**
 - a) Title of proposal and list of mentors (its own page)
 - b) Abstract/Summary (500 word maximum; separate page)
 - c) **Specific Aims** (1 page maximum, part of 6 pages)
 - d) **Research Plan and Training Plan** (balance of 6 pages)
 - e) Bibliography
 - f) Protection of Human Subjects (<2 pages)
 - g) Inclusion of women, children and minorities (brief statement)
7. **Letters of support** – submitted directly to the administrator
 - ▶ Letter of commitment/support to serve as Lead Mentor and from any co-mentors and advisors
 - ▶ Letter of recommendation from Division Director or Chair or Dean of Students

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Create PDFs

- ▶ Use online portal to attach files and submit grant
- ▶ **Questions:**
 - ▶ GA CTSA Program Coordinator / administrator:
Cheryl Sroka csroka@emory.edu

At each partner institution:

Emory: Cheryl Sroka – csroka@emory.edu
 MSM: Dr. Gianluca Tosini – gtosini@msm.edu
 Georgia Tech: Dr. J. Brandon Dixon – dixon@gatech.edu
 UGA: Dr. James Lauderdale – jdlauder@uga.edu

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Preparing the NIH Biosketch for a TL1 award

Create your biosketch here!

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Preparing the Biosketch for a TL1 award

New Tools to build and store your biosketch

<http://grants.nih.gov/grants/forms/biosketch.htm>
http://grants.nih.gov/grants/policy/faq_biosketches.htm

Create your biosketch here!

<http://www.sph.emory.edu/research/grand-rounds/index.html>
<http://www.sph.emory.edu/research/documents/NewNIHBiosketch.pdf>

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TL1 Review Criteria

(≈ NIH F31, F32, T31, T32)

F- Fellowship Grants Review Criteria Categories
Fellowship Applicant
Sponsors, Collaborators and Consultants
Research Training Plan
Training Potential
Institutional Environment and Commitment to Training

You are not your research, but you are your biosketch

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Which Biosketch should I use?

- ▶ Predocs and Postdocs use the **Fellowship** version of the NIH Biosketch
- ▶ All Faculty → use **Standard** Biosketch

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<https://grants.nih.gov/grants/forms/biosketch.htm>

Biosketch Format Pages, Instructions and Samples

A biographical sketch (also referred to as biosketch) documents an individual's qualifications and experience for a specific role in a project.

NIH requires submission of a biosketch for each proposed senior/key personnel and other significant contributor on a grant application. Some funding opportunities or programs may also request biosketches for additional personnel (e.g., Participating Faculty Biosketch attachment for institutional training awards).

Applicants and recipients are required to submit biosketches

- in competing applications for all types of grant programs,
- in progress reports when new senior/key personnel or other significant contributors are identified, and
- to support prior approval requests for changes in senior/key personnel status and changes of recipient organization.

Biosketch (Fellowship): Biographical Sketch Format Page - FORMS-H

Description
Prepare biographical sketches for applications and progress reports for fellowship applications and awards.

How to Access

FAQs on Biosketch Format Pages, Instructions and Samples

RELATED RESOURCES

- How to Apply - Application Guide
- Format

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Sections of the NIH Biosketch

Name, eRA commons, Position, Education & Training

- Personal Statement
- Positions and Honors
- Contributions to Science
- Scholastic Performance

Instructions: <https://grants.nih.gov/grants/how-to-apply-application-guide/forms-g/fellowship-forms-g.pdf> (follow the layout of the example)

FAQs - <https://grants.nih.gov/faqs#/biosketches.htm>

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BIOGRAFICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow the format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Robertson-Chang, Lellani

eRA COMMONS USER NAME (credential, e.g., agency login): Robertson

POSITION TITLE: Graduate Student Research Assistant

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing; include postdoctoral training and residency training if applicable)

INSTITUTION AND LOCATION	DEGREE (if applicable)	START DATE	END DATE	FIELD OF STUDY
Swarthmore College	BA	08/2008	05/2012	Biology
UC San Diego	PHD	08/2012	05/2016	Molecular Biology

A. Personal Statement

eRA commons user name – obtain this through your department

Emulate this NIH Biosketch example – predoctoral versus postdoctoral
- Pay attention to tone, layout, style, subheaders

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A. Personal Statement

- ▶ Briefly describe why you are well-suited for your role(s) in this project. Relevant factors may include:
 - ▶ aspects of your training
 - ▶ your previous experimental work on this specific topic or related topics;
 - ▶ your technical expertise
 - ▶ your collaborators or scientific environment; and/or
 - ▶ your past performance in this or related fields.
- ▶ You may cite up to four publications or research products that highlight your experience and qualifications for this project. Research products can include, but are not limited to, audio or video products; conference proceedings such as meeting abstracts, posters, or other presentations; patents; data and research materials; databases; educational aids or curricula; instruments or equipment; models; protocols; and software or netware.

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Research Support follows Personal Statement (updated biosketch instructions)

- If you are currently on ANY kind of grant as a pre- or post-doc, show this support using the standard presentation style used in the Standard Biosketch
 - ▶ Examples might include:
 - ▶ F30, 31, T32 trainee
 - ▶ named fellowship grant
 - ▶ Funding as a pre-doc or Postdoc on a PI's R01 grant

Ongoing and recently completed projects that I would like to highlight include:

R01 DA942367
Hunt (PI); Role: Postdoctoral Fellow
09/01/16-08/31/21
Health trajectories and behavioral interventions among older people with substance use disorders

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Personal Statement section recap:

- Personal Statement paragraph
- Up to 4 highly impressive literature citations (otherwise save your literature citations for the Contributions to Science section)
- Research Support (now and recent)
 - ▶ Most medical students and pre-doctoral fellows will not have much to put after the Personal Statement paragraph. This is not a problem.
 - ▶ If you have forthcoming abstracts or manuscripts, you can include these for the fellowship version of the biosketch.
 - ▶ Preprints are allowed (follow citation instructions)
 - ▶ You can also include papers on which you have received an Acknowledgement

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NOTE:

- ▶ There are 2 items labeled "Personal Statement" in this application
- ▶ **#1:** As part of the main application, there is a 2-page required essay describing your training, research background and career goals called Personal Statement
- ▶ **#2:** The **Personal Statement is an important** section of the NIH Biosketch (here 1 para is sufficient)

These are different but very similar; include both

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Suggestions for Writing the NIH Biosketch Personal Statement

1. **Customize the personal statement for each grant proposal**
2. **Mention the name of the grant proposal (e.g., TL1) and speak directly to the purpose of this funding mechanism**
 - ▶ *I envision using the training, experience and research findings from this TL1 award to launch my career in cardiovascular research focusing on the role of shear stress affecting the interface of endothelial cells and leukocytes in maintaining the balance of immune activation and immune tolerance, on cardiovascular diseases.*

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Writing Suggestions

3. Lots of overlap with the required TL1 Personal Statement about your training and career goals
4. Be succinct, revise this several times after you have developed the other essay sections
5. Convey passion and excitement about your work
6. All these sections need to be great – Reviewers really care about these essays
7. **TIPS**
 - ▶ read essays aloud to yourself
 - ▶ - ask someone else to read over your essays for flow, clarity, grammar

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B. Positions and Honors



Positions and Employment

Other Experiences and Professional Memberships

Honors

- ▶ Clarify what specific awards/honors were for

→ You can load this info into My NCBI

- online tool (via SciENcv) to support building/storing your personal data including linking to all your publications

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Examples of additional creative subheaders

- Patents
- Board Certifications
- Consultant/Reviewer
- Course Instructor/Director
- Program Developer (could be an international program, or software)
- External Advisor

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Section C. Contributions to Science

- ▶ Summarize your research contributions using this organization:
 1. Early Career
 2. Graduate Career
 3. Postdoctoral Career
- List **up to 4** four peer-reviewed publications or other non-publication research products (*this includes abstracts, posters, etc.*)
- "Descriptions of contributions may include a mention of research products under development, such as manuscripts that have not yet been accepted for publication. These contributions do not have to be related to the project proposed in this application."
- ▶ In other words, show us EVERY paper or presentation you are an author for

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At the end of Section C.

- ▶ Provide a URL to a full list of your published work as found in a publicly available digital database such as SciENcv or My Bibliography, which are maintained by the US National Library of Medicine.
- ▶ This link will be part of your 'research identity' going forward. It is worth it to start curating this now.
- ▶ This is not required but highly recommended.
- ▶ If you have no publications, you may omit this.
- ▶ Do not use Google Scholar or any other non-governmental link

Complete List of Published Work in My Bibliography:
[http://www.ncbi.nlm.nih.gov/myncbi/.....](http://www.ncbi.nlm.nih.gov/myncbi/)

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C. Contributions to Science *(see directions and examples)*

1. Early Career
 - ▶ Brief narrative (written in 1st person)
 - ▶ Published manuscripts, abstracts, etc. (underline or bold your name)
2. Graduate Career
3. Postdoctoral Career

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C. Contribution to Science

1. Dietary composition has long been identified as a modifiable risk factor in the development of a variety of health outcomes. My undergraduate research, under the mentorship of Dr. Krzysztof Czaja and supported by the CURO research assistantship at the University of Georgia, was focused on the impact of macronutrient composition on gut-vagal-brain physiology. We found statistically significant differences in vagal and hindbrain composition between rats maintained on diets of varying macronutrient composition, with those fed a high sugar, high fat diet showing the highest level of inflammatory markers in the vagus nerve and most significant neuronal restructuring in cerebral feeding centers. I was **acknowledged** in Czaja, K., et al (2017) for my contribution to body fat composition measurement using MRI, macroscopic and microscopic anatomical dissection, cryosectioning, immunohistochemistry, data organization and management, statistical analysis, and preparing text for publication. The results of this work provided a mechanistic framework for the impact of diet on host physiology. The significance of the results gave me an opportunity to present at a university wide research conference and provided scientific background for my honors thesis exploring the connection between broad spectrum antibiotic use and obesity, which was later published under first authorship.

- a) Gawey, B., Czaja, K. (2017). "Broad-Spectrum Antibiotic Abuse and its Connection to Obesity". *Journal of Nutritional Health & Food Science*. 5, 2-21.
 - b) Acknowledgements, Sen, T., Cawthon, C., Ihde, B., Hajnal, A., DiLorenzo, P., de La Serre, C., and Czaja, K. (2017). Diet-driven microbiota dysbiosis is associated with vagal remodeling and obesity. *Physiology & Behavior*. 173, 305-317.
- Abstract:** Gawey, B. "High Dietary Sugar and Fat Content Leads to a Change in Intestinal Innervation and Gut-Brain Communication". CURO Research Symposium. UGA Honors College. Athens, GA. 8 April. 2016. Poster presentation.
- Honors Thesis:** Gawey, B. Broad-spectrum antibiotic use and the connection to obesity. 2016. University of Georgia

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Contributions to Science

1. Medical School Research Experience:

The microbiome is emerging as an important target for influencing health outcomes. During medical school, I have been involved in research in the Clinical Microbiome Program at Emory Clinic under the mentorship of Dr. Smith. I completed an elective focused on exploration of current models of clinical research focused on the investigation of the microbiome. Forthcoming results of our metabolomic analysis of microbial derived small molecules will have important implications for human health, disease biomarker tracking, and preventative medicine, providing additional insight and therapeutic perspective to microbiome and metabolome-based interventions, such as probiotics and fecal transplants as a means of preventing, controlling, and reversing disease.

(this Contribution to Science had no publications - this is ok)

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Contributions to Science

3. Postdoctoral Career:

I worked with the team that created a novel shared decision aid, called iChoose Kidney, for providers (nurses, social workers, or physicians) to use with ESRD patients to help them make treatment decisions about kidney transplantation vs. dialysis. I worked with the PI to calculate the risk prediction models, and convert these to a widely accessible, free mobile tool (on iTunes and on a website). This tool is currently being used in practice by more than 400 providers across the US, and our preliminary scientific studies suggest the tool improves knowledge and decision-making ability among patients. A multi-center, randomized study at 3 of the largest transplant centers across the nation (Emory, Columbia, and Northwestern) is testing the clinical effectiveness of the tool.

- a. iTunes iPad and iPhone app of iChoose Kidney:
<https://itunes.apple.com/us/app/ichoose-kidney-patient-education/id685381934?mt=8>
- b. Website: www.ichoosekidney.emory.edu

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C. Contribution to Science *(e.g. from Standard Biosketch)*

3. **Early caffeine therapy is associated with a lower risk of bronchopulmonary dysplasia**

Caffeine therapy is widely used to treat apnea related to prematurity. A landmark international, multicenter trial demonstrated that caffeine reduces the risk of bronchopulmonary dysplasia, a serious and chronic respiratory complication of prematurity. **My research has focused** on examining the comparative effectiveness of various approaches to initiation of caffeine therapy. Initial studies **at our center**, which we later validated in a large US cohort of over 60,000 very low birth weight infants, **showed** earlier initiation of caffeine therapy, compared to later initiation, was associated with a lower risk of bronchopulmonary dysplasia. **Our initial novel findings** have recently been replicated by several other research groups in the US and internationally.

- ▶ **Patel RM**, Leong T, Carlton DP, Vyas-Read S. Early caffeine therapy and clinical outcomes in extremely preterm infants. *J Perinatol*. 2013;33(2):134-40. PMID: 22538326
- ▶ Dobson N*, **Patel RM***, Smith PB, Kuehn DR, Clark J, Vyas-Read S, Herring A, Laughon MM, Carlton DP, Hunt CE. Trends in caffeine use and association between clinical outcomes and timing of therapy in very low birth weight infants. *J Pediatr*. 2014 May;164(5):992-998.e3 PMID: 3992195 *Contributed equally

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D. Scholastic Performance

- ▶ Scholastic Performance
 - ▶ Follow directions, use grid

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Recommendations

- ▶ Follow the directions – look at the NIH sample and compare your biosketch to it (layout, etc.)
- ▶ Reviewers are looking for specific information in particular places – make it easy for the reviewer by following the rules and the formatting
- ▶ Do not misrepresent any facts
 - ▶ List all publications as they would appear in PubMed or in any other searchable database
- ▶ Advice from reviewers:
 - ▶ “Self-aggrandizing will certainly backfire. Probably better to lean towards humility to increase likability factor.”

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Personal Statement for the TL1 Application



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TL1 Personal Statement (2 pages max.)

- formatting: use Arial 11 font and .5-inch margins throughout

- a) Applicant's Training
- b) Research background
- c) Career Goals

Theme - how this TL1 training program and training afforded by the mentoring team will specifically enhance your career development in CTR

This essay will be somewhat redundant with your Personal Statement from biosketch. However, don't cut/paste. Make these unique. Reviewers will read these very carefully.

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Suggestions for Personal Essay Writing in the TL1 application:

- Follow all directions
- Dot your **PERSONAL ESSAYS** with scientific facts, findings, interests, goals, etc.
- “Speak” to the reviewer; “Sell” your idea; Be compelling!!
- Write in the 1st person but don't be “folksy” or overly casual
- Reflect on your **personal experiences in science** and where this TL1 award will lead you professionally
- Make a case for your **personal career path** - describe what you hope will be your **contribution to the field**
- Don't simply walk us through your biosketch (we just read that)
- Pay attention to aesthetics/layout – **NO TYPOS, NO GRAMMATICAL ERRORS**

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TL1 Personal Statement instructions

- a) **Describe your training to date**
 - ▶ Draw attention to any special technical or clinical skills
 - ▶ Does not have to be related to the proposed project
- b) **Describe any research background**
 - ▶ In any discipline; share what you've done research-wise
 - ▶ Highlight exciting findings / skills
 - ▶ If you don't have any research background to speak of, be brief (and don't worry).
- c) **Describe your career goals**
 - ▶ in clear, concrete terms

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c) Describe your Career Goals

- ▶ How has what you've studied to date has led you to where you are now
- ▶ Consistent themes or issues – challenges in the science that intrigue you, why, what will you do to solve these problems
- ▶ Change in path, discipline - explain
- ▶ **Justify the TL1 award** - How will it help you develop and advance your career - where will you go with this award and 5 years hence scientifically speaking.
- ▶ Identify exactly what your training goals are, for example:
 1. Epidemiology of TB/HIV coinfection
 2. Advanced cohort study methodology
 3. Molecular epidemiology
 4. Bioinformatics
 5. Spatial transcriptomics

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c) Describe your Career Goals (continued)

- ▶ Tell us about your Training Plan
- ▶ What will be the elements of your Training Plan
 - ▶ MSCR – Master of Science in Clinical Research (30 credits, thesis, grant proposal)
 - ◻ highly recommended for medical students, residents, fellows, those who have had limited didactic research training
 - ▶ CPTS – Certificate Program in Translational Science (16 credits, grant proposal) – common option for PhD students
 - ▶ Menu Option – 5 required courses plus electives based on personalized training pathway (no required credit minimum outside the 5 required courses)
 - MSCR/CPTS 593 Research Ethics (required by NIH) [1 credit]
 - MSCR/CPTS 594 Scientific and Grant Writing [2 credits]
 - MSCR/CPTS 761 Introduction to Clinical and Translational Science [2 credits]
 - MSCR/CPTS 591 Community Engagement and Health Equity [1 credit]
 - MSCR 592 Clinical and Translational Science Colloquium [1 credit]
 - Electives (based on applicant's needs—can be at any of the Georgia CTSA institutions or workshops, etc.)
- If you select this option, describe in detail your plan and why you've chosen this option

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What are the Reviewers Looking for?

- ▶ **What** new scientific skills / techniques / areas will you learn?
- ▶ **Who** is spearheading your training and looking out for your career development (i.e., name the mentor / lab)?
- ▶ **How** will the new training support your ability to carry out the proposed research aims?
- ▶ All this can be very concrete and specific; **write in the 1st person** to make this flow nicely

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Selecting a Primary Mentor for Mentored Research Training

- ▶ Lead mentor should be an established investigator with current federal funding
 - ▶ NIH, AHRQ, CDC, PCORI, etc. or R01 equivalent)
 - ▶ Co-mentors do not have to meet similar requirements
- ▶ If you are uncertain about the suitability of your lead mentor, it is advised that you run this by the TL1 leadership
 - ▶ VASILIKI "VAS" MICHPOULOS, PHD, MSCR; VMICHOP@EMORY.EDU
 - ▶ HENRY BLUMBERG, MD; HBLUMBE@EMORY.EDU
 - ▶ JAMES D LAUDERDALE, PHD; JDLAUDER@UGA.EDU
 - ▶ GIANLUCA TOSINI, PHD; GTOSINI@MSM.EDU
- ▶ Review the Mentor tab at the TL1 website
<https://georgiactsa.org/training/tl1.html>

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Research and Training Plan for the TL1 Application



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Writing up the Research section (6 pages total)

This consists of two parts:

1. **Specific Aims** (~1 page, traditional style / presentation for your discipline; study other examples and your mentor's work)
2. **Research Plan** (~5 pages, see instructions)
 - ▶ Significance
 - ▶ Innovation
 - ▶ Approach

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NIH Specific Aims page

→ **Master Plan for your application**

- See examples of Specific Aims pages on Dropbox (I will share with you)
- Typically, 1 page in length (maximum allowed)
- **Encapsulation of the entire proposal – sets the stage for how compelling, exciting and feasible is your work**
- Presentation style for this 1 page reflects the style used in your field of work – standard, stereotyped presentation style
 - Introductory section establishing public health relevance and scientific rationale
 - How this project exemplifies clinical and/or translational research
 - Followed by listing of the research objectives/tasks/overarching scientific questions
 - Sometimes followed by a summary of 'what is the value of this work to the field'

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An excellent Specific Aims page:

- Favorably disposes the reader for the rest of the application
- Augers well for your qualifications, your grant writing and your research skills
- Conveys excitement and importance while using a very logical, compelling and articulate presentation
- Becomes the “**master plan**” for the rest of your research plan
- This section of a grant is the **#1 most important section** to the reviewers and to your research

#1

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Specific Aims instructions from the NIH grant proposal guidelines

- State concisely the **goals** of the proposed research and summarize the **expected outcome(s)**, including the **impact** that the results of the proposed research will exert on the research field(s) involved.
- List succinctly the **specific objectives** of the research proposed, e.g.,
 - to test a stated hypothesis,
 - create a novel design,
 - solve a specific problem,
 - challenge an existing paradigm or clinical practice,
 - address a critical barrier to progress in the field, or
 - develop new technology.
- Specific Aims page cannot exceed one page.

Words in **RED** are all good words to use in a Specific Aims section

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RESOURCES for writing the SPECIFIC AIMS page



- Look at others’ Specific Aims pages
- See my Dropbox site
- Google “how do I write an NIH F31” (or F32)
- NIH Specific Aims writing support
 - <https://www.niaid.nih.gov/grants-contracts/draft-specific-aims>
- Writing an NIH F31 proposal
 - <https://www.niaid.nih.gov/grants-contracts/three-new-f31-sample-applications>
- Northwestern University CLIMB writing program
 - <https://www.northwestern.edu/climb/resources/written-communication/nih-grant-and-dissertation-proposals.html>

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Structure: According to Russell and Morrison (2018) (see my Dropbox folder)

1. Introductory paragraph will contain a **high impact opening sentence** that “immediately establishes the relevance of the proposal to human health”
2. **Current knowledge**
3. **Gap in the knowledge** base and/or unmet need, i.e., what is the clinical problem
4. **What/Why/Who** – long-term goal, objective of this application, and central hypothesis and how it is formulated
5. **Listing of the Specific Aims**

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Each Aim should yield interesting findings

- You should be able to test hypotheses (or conduct the research) for each aim regardless of the outcome of the other aims
- Being able to conduct Aims 2 and 3 cannot be dependent on an anticipated outcome from Aim 1
 - Unless, you have strong preliminary data for what you anticipate you will find in Aim 1 (i.e., Aim 1 is a replication of previous work)
- The work proposed can be achieved in the 1-2 year time allotted (depends on how long you will be a TL1)
 - How will you substantiate this?
 - Preliminary data, past experience, timeline?

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Example of Specific Aims using the term “Objectives”

Objectives
Objectives of the proposed study include:

Objective 1. To estimate prevalence of latent tuberculosis infection among HIV positive individuals in Georgia, using two IFN-g assays (T.SPOT-TB and QuantiFERON Gold in Tube) and tuberculin skin test.

Objective 2. To examine factors associated with concordance and discordance between the three tests to be utilized.

- a) To assess impact of degree of immunosuppression (by CD4 count) on performance of IFN-g assays and TST
- b) To assess influence of co-infection with hepatitis C virus on the performance of IFN-g assays and TST.

Objective 3. To determine predictors of latent tuberculosis infection among HIV positive individuals

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KL2 (funded) Specific Aims:

Aim 1: To develop an electronic decision support tool to communicate estimated risks of poor health outcomes for dialysis vs. kidney transplantation. There are three objectives for this aim:

- 1) To develop and validate predictive models for 3-year mortality for three treatment options: a) dialysis, b) deceased donor (DD) transplant, and c) living donor (LD) transplant.
- 2) To develop and validate predictive models for length of stay for 1) dialysis, b) DD transplant and c) LD transplant.
- 3) To translate these predictive models into a decision support tool (i.e. iPad App).

Aim 2: To determine the feasibility of implementing the decision support tool among a metro-Atlanta dialysis patient population. Our primary objective of this feasibility study is to gather preliminary data to inform a future, randomized study of the tool in a metro-Atlanta dialysis population to improve outcomes.

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Example of Inter-dependent Aims

To test our hypotheses, we propose the following **3 Specific Aims:**

Aim 1. To determine if patients with chronic renal failure (CRF) have an exaggerated sympathetic response during exercise.

Aim 2. Test a pilot therapy of BH4 for patients with an exaggerated sympathetic response during exercise.

Aim 3. In patients with a good treatment response to therapy, determine if there is improvement in resting and exercise-induced sympathetic over-activity, endothelial dysfunction, and oxidative stress.

Consider:

- *Why are these aims inter-dependent?*
- *Is this a good strategy?*

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.... Introductory para here

To investigate these associations, I propose to work with a multidisciplinary team with expertise in nutrition, endocrinology, metabolomics, and the gut microbiome to examine a dataset from the National Institute of Health’s (NIH) Metabolomics Workbench, which contains metabolic profiling of >100 participants enrolled in the Prospective Registry (PRISM) in IBD study at Massachusetts General Hospital. We will test the following aims and hypotheses:

Aim 1: To investigate the associations of fecal level of 5-MIAA with Crohn’s disease in humans.

Hypothesis: Higher fecal 5-MIAA will be associated with fewer diagnoses of Crohn’s disease.

We will conduct targeted analysis of the fecal metabolome database from a cross sectional cohort of individuals enrolled in PRISM (N=102 selected individuals; CD (N=68), non-IBD (N=34) controls) by quantitating the levels of 5-MIAA in relation to CD. CD was diagnosed using standard endoscopic, radiographic, and histologic criteria.

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K23 (funded)

AIM 1: To determine the pharmacokinetics of levofloxacin (LEV) and capreomycin (CAP) in patients with MDR-TB including the examination of drug levels in plasma, pulmonary tissue, and tuberculous cavity lung among patients undergoing adjunctive surgical therapy.

Hypotheses: LEV and CM levels will be lower inside tuberculous cavity lesions compared to plasma, and non-cavity lung samples. Utilizing a cohort of MDR-TB patients undergoing adjunctive surgery and an innovative microdialysis method we will be the first group to assess SLD levels among various compartments including within pulmonary cavities, the site of the highest concentration of *Mycobacterium tuberculosis* (MTB).

Training will include coursework in pharmacology, learning the technique of microdialysis, and practical experience in pharmacology research.

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Specific Aims (1 page)

- ▶ Do you have too many aims?
- ▶ Are they logically interrelated?
- ▶ Are subsequent aims dependent on successful outcome of preceding aims? (bad idea)
- ▶ Do they belong in the same proposal?
- ▶ *Most proposals are overly ambitious.*
- ▶ *You can weave in mentions of your Training Opportunity on the Specific Aims page for a training grant*

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RESEARCH Plan (~5 pages)

a) **Significance**

- Typically, a series of paragraphs, often organized by subheaders

b) **Innovation**

- Often this is a series of terse statements or small paragraphs that make a specific point that supports innovation, novelty, important groundbreaking techniques, first time to do something, etc.
- Can be a bulleted list

c) **Approach**

- A highly formatted 'recipe-like' presentation of methodology

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SIGNIFICANCE

- ▶ Explain the **importance of the problem** or **critical barrier to progress** in the field that the proposed project addresses.
- ▶ Explain how the proposed project will **improve** scientific knowledge, technical capability, and/or clinical practice in one or more broad fields.
- ▶ Describe how the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field **will be changed if the proposed aims are achieved**.

THIS SHOULD NOT BE A LITERATURE REVIEW

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Organization for Significance section:

(example #1)

SIGNIFICANCE

Critical Barriers to Eye Examination in the Emergency Department

Technical Improvements to the Fundusoscopic Exam

Telemedicine in Neuro-ophthalmology of the Future

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RESEARCH STRATEGY *(example #2)*

A. Significance

A.1. Kidney Disease is a substantial public health problem in the Southeastern US. Kidney transplantation is the optimal treatment for ESRD patients

A.2. Racial disparities exist in access to optimal treatment for ESRD patients.

A.3. AA ESRD patients are less likely to be informed of kidney transplantation.

A.4. Patients who are most at risk for poor outcomes have the greatest difficulty in accessing health information.

A.5. Critically important treatment decisions are often made without evidence-based information about a patient's prognosis.

A.6. Shared decision making through decision support tools can increase patient involvement in the health care decision making process, leading to better health outcomes.

Important Preliminary Data might go HERE

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Innovation

- Explain how the application **challenges and seeks to shift** current research or clinical practice paradigms.
- Describe any **novel** theoretical concepts, approaches or methodologies, instrumentation or interventions to be developed or used, and any **advantage** over existing methodologies, instrumentation, or interventions.
- Explain any **refinements, improvements, or new applications** of theoretical concepts, approaches or methodologies, instrumentation, or interventions.

- WORDS IN RED ARE GREAT GRANT WRITING WORDS

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INNOVATION

- 1) Research questions and hypotheses that have never been clinically tested:
- 2) Studying a unique patient population:
- 3) Utilizing advanced technologies in an innovative fashion:

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Innovation (KL2)

Figure 2. Clinical and Translational Framework for Research

The diagram illustrates a three-step process: 1. Predictive Model Development (ROC Curve) - Aim 1; 2. Refine Patient Education iPad Application - Aim 2; 3. Translate to a Clinical Setting - K01. The ROC curve shows a curve above the diagonal line, indicating good predictive performance.

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APPROACH

- Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project.
 - Describe plans to address **weaknesses in the rigor of the prior research** that serves as the key support for the proposed project.
 - Describe the **experimental design and methods** proposed and how they will achieve robust and unbiased results.
 - Unless addressed separately in the **Resource Sharing Plan**, include how the data will be collected, analyzed, and interpreted, as well as any resource sharing plans as appropriate.
 - Resources and tools for rigorous experimental design can be found at the **Enhancing Reproducibility through Rigor and Transparency website**.

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APPROACH (continued)

- For trials that randomize groups or deliver interventions to groups, describe how your methods for analysis and **sample size** are appropriate for your plans for participant assignment and intervention delivery.
 - These methods can include a group- or cluster randomized trial or an individually randomized group-treatment trial.
 - Additional information is available at the **Research Methods Resources webpage**.
- Discuss **potential problems, alternative strategies, and benchmarks** for success anticipated to achieve the aims.
- If the project is in the early stages of development, describe any strategy to establish **feasibility**, and address the management of any high risk aspects of the proposed work

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APPROACH (continued)

- Explain how relevant **biological variables, such as sex**, are factored into research designs and analyses for studies in vertebrate animals and humans.
 - For example, strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex.
 - Refer to the **NIH Guide Notice on Sex as a Biological Variable in NIH-funded Research** for additional information.
- Point out any procedures, situations, or materials that may be **hazardous** to personnel and the precautions to be exercised.
 - A full discussion on the use of select agents should appear in the **Select Agent Research** attachment below.
- If research on Human Embryonic Stem Cells (hESCs) is proposed but an approved cell line from the NIH hESC Registry cannot be chosen, provide a strong justification for why an appropriate cell line cannot be chosen from the registry at this time.

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Rigor and Reproducibility including **Sex as a Biological Variable (SABV)**

► Required discussion of this issue in all NIH grants including the KL2/K12/TL1

The screenshot shows the NIH website page for 'NIH Policy on Sex as a Biological Variable'. It features a search bar, navigation links, and a main heading. The text on the page discusses the importance of including women in clinical research and the impact of sex on health outcomes.

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APPROACH (many options for organizing this)

- Use subheaders to make this section very clear*
- Be generous in using 'white space', indenting, stylized text*

- Overview of research design
- Methods (for each aim)
 - Analyses and Expected Results
 - Limitations/Anticipated Problems
 - Alternative Approaches
- Timeline
- Future Directions

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Study good examples


- ▶ Read any kind of grant application from your mentor's lab
- ▶ Study my examples on Dropbox
- ▶ Review F31 and F32 examples
 - ▶ Examples from UAB: <https://www.uab.edu/cts/research-commons/grant-help/proposal-development/grant-library/nih-grant-f-series-samples>
 - ▶ Examples posted by NIAID: <https://www.niaid.nih.gov/grants-contracts/three-new-f31-sample-applications>
 - ▶ Lots of interesting info on Google
- ▶ Look at F31 and F32 examples of abstracts on NIH RePORTER
 - ▶ <https://projectreporter.nih.gov/reporter.cfm>

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Grant Writing

DOs

DON'Ts



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Terms/phrases to avoid

Expressions with no clear limits	Words of personal judgment	Causal colorful language	Use with caution as transitions but never as fillers
a lot	assuredly	agree to disagree	in effect
fairly	beautiful	bottom line	indeed
really	luckily	brute force	basically
slightly	obviously	few and far between	in terms of
sort of	sadly	okay	it goes without saying
	fortuitous	sketchy	
	intriguing	tip of the iceberg	

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Can you deconstruct a paragraph?

Distracting	Useful
<ul style="list-style-type: none"> • Tangent – material that is not directly related • Digression – going off in a different direction than the topic • Fluff/filler <div style="border: 2px solid orange; padding: 2px; margin: 5px;"> <p>e.g., As part of this research, we plan to fulfill our mission of recruiting the maximum number of patients possible.</p> </div> • Vague • Emotional/Jargon/Colloquial • Passive/indirect • Redundant 	<ul style="list-style-type: none"> • Opening/introductory statement or lead statement • Factual support • Examples of the focal point • Supporting data/findings <div style="border: 2px solid orange; padding: 2px; margin: 5px;"> <p>e.g., We will enroll 10 patients per week which will be feasible based on the current census of more than 100 emergency room visits/week.</p> </div> • Implications of the facts presented • Transition • Summary statement • Header/Subheader

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Reviewers' Concerns and Criticisms of the Research Plan

Is the research design complete?

For example, if you are comparing 3 out of 4 cells of a 2x2 design, why are you omitting the 4th cell?

- Do not leave anything to the imagination.

Group 1: *Stroke Pts who are Smokers*

Group 2: *Stroke Pts who are non smokers*

Group 3: *MI Pts who are Smokers*

?? *MI Pts who are non smokers*

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Research Plan

Level of Detail in Methods

1. Treatment of data
 - Raw data, transformed/scaled data
 - Collapsed by group
 - Confounds to the data

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Research Plan

2. Well-specified, operationally defined variables and outcomes; what are they and how will they be obtained?
 - Demographics
 - Biomarkers
 - Correlates of depression
 - Immune functioning

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Research Plan

3. Description of Experiments
 - Consistency of level of detail from one experiment to the next
 - General Methods section can save you space
 - Know your agents, your clinical interventions, your high tech procedures. Are there alternatives that you should mention? Have you thoroughly described them?

"It is clear that the applicant is not completely familiar with the drug interactions that follow the combined administration of substance x and substance y in patients with diabetic neuropathy."

80

Research Plan

4. Use of scientific terminology
 - Controversial terms vs. well-accepted terms
 - Are there philosophical "camps" in this scientific community? Are you considering all sides of the issue fairly?
5. Theoretical framework
 - Is this customary for your field?
6. Theoretical context
 - Is your idea supported by the research design and methodology proposed?
 - Are you using the best model/organism/ procedures for the research question proposed?
 - Substantiate all this

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Sources of Data

1. Most 1-2 year proposals will leverage existing data
 - ▶ Banked biospecimens
 - ▶ Access an available dataset or registry
 - ▶ Piggy-back on ongoing enrollment in a clinical trial
2. Be sure reviewers have all the information they need to evaluate the integrity of your sources of data
 - ▶ Data collection methods
 - ▶ Sampling techniques
 - ▶ Reproducibility and validity of assays
 - ▶ Representativeness of subjects
 - ▶ Previous publications with these data

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Human Subjects

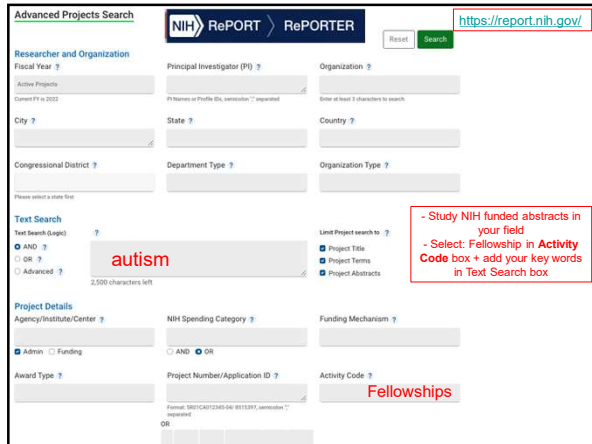
- ▶ Using an existing dataset
 - ▶ How much information should you provide?
- ▶ Why are you proposing the population you've chosen?
- ▶ Is this the best organism for this research question and have you defended this adequately?
- ▶ Relevance to state of the research - omitting children, omitting males or females
- ▶ Availability and likelihood of getting data from these subjects, tissue, animals, etc.
- ▶ Do you have enough subjects in your study?
 - ▶ Statistical implications - sample size calculation and power analysis – is this necessary for this kind of research?

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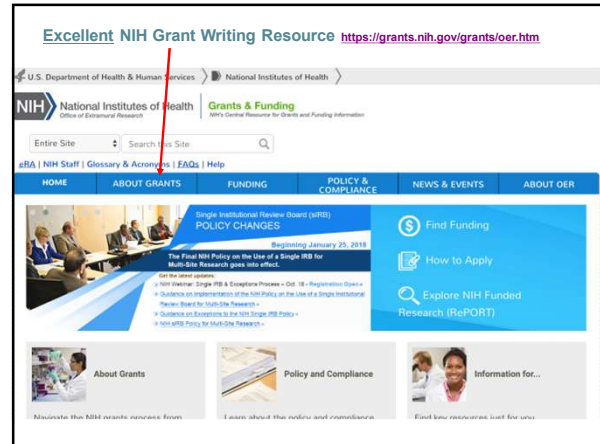
RESOURCES



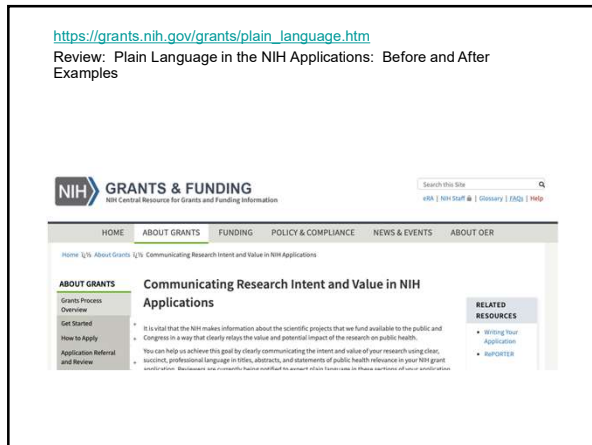
84



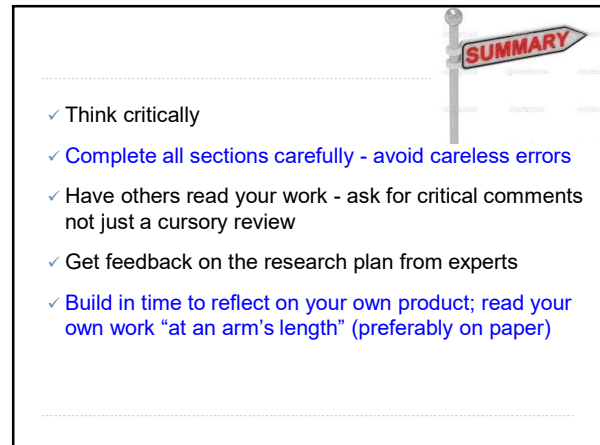
85



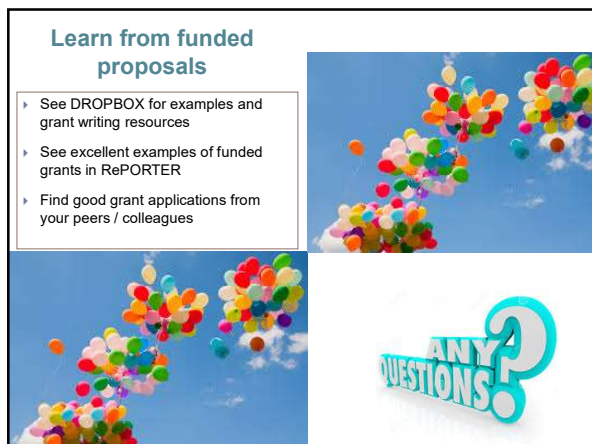
86



87



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