NIH Fellowship Info Session 2

June 16th, 2021

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Yinghui Mao, PhD (Assistant Dean of Graduate Affairs, Associate Professor of Pathology and Cell Biology)
Anna Cetnerowski, MPA (Senior Director, Grants Management Service)
Becky Spurr (Program Coordinator, MD-PhD Program)
Stefanie Makinson, PhD (Grant & Research Development Associate)
NIH Fellowship Info Session 2 Agenda

- Sign-in
- Fellowship Review Criteria
- NIH Review Process
- Applicant Background
- Specific Aims
- Research Strategy
- Timeline
Fellowship review criteria cont.

1. Fellowship Applicant
   - High-quality research & academic track-record
   - Potential to develop as an independent & productive researcher in biomedical, behavioral or clinical science
     - Evaluated via Biosketch, Applicant Background, Letters of Reference, what your sponsors say about you

2. Sponsor/mentors, collaborators & consultants
   - Sponsor’s qualifications (including grant support) and mentoring track record
   - Good match between research interests of applicant and sponsor?
   - Sponsor should demonstrate an understanding, ability & commitment to meet your training needs
   - Collaborators need complementary expertise & previous experience in training fellows
     - Evaluated via Biosketches, Sponsor Statement(s), and Letters of Support
Fellowship review criteria cont.

3. Research Plan

- Significant scientific & technical merit?
- Is the research plan relevant to the applicant’s training plan & career goals?
- Individualized and supervised experiences that will develop research skills needed for the applicant’s independent & productive research career?
- Is the training plan consistent with the candidate’s stage of research development

➢ Evaluated via the Research Training Plan (primarily) with consideration given to other attachments: Respective Contributions, Vertebrate Animals, Authentication of Key Reagents, Human Subjects attachments etc.
Fellowship review criteria cont.

4. Training Potential

- Does the proposed training provide a sound foundation for a productive research career?
- Does the training provide both individualized & supervised experiences that will develop research skills needed for applicant’s career?
- Do they propose to learn a new area or techniques?

➢ Evaluated in the Applicant Goals/Planned Activities section, Responsible Conduct of Research, Respective Contributions
Fellowship review criteria cont.

5. Institutional Environment & Commitment to Training

- Quality of training environment & commitment of the institution (Columbia, your graduate program, your department)

- Appropriate facilities, resources (e.g., equipment space) & training opportunities (e.g., seminars, coursework)?

  Evaluated via Facilities & Other Resources, Institutional Environment & Commitment to Training, Selection of Sponsor and Institution
Fellowship review criteria

The applicant receives an overall impact/merit score (what matters) as well as five areas that are also scored.

**Overall impact/merit (scale = 10–90)**

- “the likelihood that the fellowship will enhance the candidate’s potential for, and commitment to, a productive independent scientific research career in a health-related field”

- The five scorable areas as well as additional review criteria are considered in this score.
  - Scorable areas (scale = 1 - 9):
    1. Fellowship Applicant
    2. Sponsors, Collaborators, and Consultants
    3. Research Training Plan
    4. Training Potential
    5. Institutional Environment & Commitment to Training

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<tr>
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<th>Reviewer 1</th>
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<tr>
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<td>Sponsors, Collaborators, and Consultants</td>
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<td>Research Training Plan</td>
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<td>Training Potential</td>
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<tr>
<td>Institutional Environment &amp; Commitment to Training</td>
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• Additional review criteria: Protection for Human Subjects; Inclusion of Women, Minorities, and Across the Lifespan; Vertebrate Animals; Biohazards; Resubmissions
The Three Ps of NIH Funding

Priority score

The scale is 1–9. The SRO averages the three impact scores from the reviewers and the top 50% are discussed during the meeting and the bottom 50% are not discussed. After the grant is discussed, each study section member votes for a score that is between the 3 reviewers. The scores are averaged and the final score (overall impact score) is multiplied by ten to be expressed on a 10–90 scale.

<table>
<thead>
<tr>
<th>Score</th>
<th>Descriptor</th>
<th>Additional Guidance on Strengths/Weaknesses</th>
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<tbody>
<tr>
<td>1</td>
<td>Exceptional</td>
<td>Exceptionally strong with essentially no weaknesses</td>
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<tr>
<td>2</td>
<td>Outstanding</td>
<td>Extremely strong with negligible weaknesses</td>
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<tr>
<td>3</td>
<td>Excellent</td>
<td>Very strong with only some minor weaknesses</td>
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<tr>
<td>4</td>
<td>Very Good</td>
<td>Strong but with numerous minor weaknesses</td>
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<td>5</td>
<td>Good</td>
<td>Strong but with at least one moderate weakness</td>
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<tr>
<td>6</td>
<td>Satisfactory</td>
<td>Some strengths but also some moderate weaknesses</td>
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<tr>
<td>7</td>
<td>Fair</td>
<td>Some strengths but with at least one major weakness</td>
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<tr>
<td>8</td>
<td>Marginal</td>
<td>A few strengths and a few major weaknesses</td>
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<tr>
<td>9</td>
<td>Poor</td>
<td>Very few strengths and numerous major weaknesses</td>
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Minor Weakness: An easily addressable weakness that does not substantially lessen impact
Moderate Weakness: A weakness that lessens impact
Major Weakness: A weakness that severely limits impact

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<tr>
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<td>R2 = 4</td>
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<td>R3 = 3</td>
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<tr>
<td>SRO avgs. score, ranks top 50%</td>
<td>3 (discussed)</td>
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<tr>
<td>All members of study section vote</td>
<td>2</td>
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<tr>
<td></td>
<td>4</td>
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<td>3</td>
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<tr>
<td>Impact score (avg. of scores x 10)</td>
<td>26</td>
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</table>
The Three Ps of NIH Funding

Priority score
Overall impact score on a scale of 10 – 90.

Percentile
The application is ranked against all other applications reviewed by that study section over this and the previous two review cycles.
The Three Ps of NIH Funding

Priority score

Overall impact score on a scale of 10 – 90.

Percentile

Rank of the application over three review cycles.

Pay line

Applications are compared to the IC’s pay line for a funding recommendation.

Some institutes do not have a strict pay line for F awards. Rather, they weigh priority scores, percentiles & Council’s funding priorities.

The NIH Review Process

Application submitted to Center for Scientific Review (CSR)

CSR assigns application to Study Section (IRG) & Institute/Center (IC)

SRO assigns applications to three reviewers for critiques

SRO averages reviewer scores, ranks applications

Top 50% of applications are reviewed by study section for Scientific Merit (impact score)

Application evaluated by IC council for relevance to IC’s funding priorities

Funded!

Not funded. Revise and resubmit.

Bottom 50% not discussed. Therefore, not funded. Revise and resubmit.

https://grants.nih.gov/grants/peer-review.htm
## Roster Index for Fellowship Study Sections

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<td>Dr. Vilen Movsesyan</td>
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<td>F01B</td>
<td>Fellowships: Learning and Memory, Language, Communication and Related Neurosciences</td>
<td>Dr. Jyothi Arkkath</td>
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<td>F02A</td>
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<td>Fellowships: Sensory and Motor Neurosciences, Cognition and Perception</td>
<td>Dr. Cibu Thomas</td>
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<td>F03A</td>
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<td>F03B</td>
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<td>F05-U</td>
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<td>Fellowships: Infectious Diseases and Immunology A</td>
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<td>F07C</td>
<td>Fellowships: Infectious Diseases and Immunology</td>
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<td>F08</td>
<td>Fellowships: Genes, Genomes and Genetics</td>
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<td>F10C</td>
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<td>Fellowships: HIV/AIDS Behavioral</td>
<td>Dr. Kristen Prentice</td>
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<tr>
<td>F18</td>
<td>Fellowships: Epidemiology and Population Sciences</td>
<td>Dr. Ananya Parya</td>
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[https://public.csr.nih.gov/StudySections/Fellowship](https://public.csr.nih.gov/StudySections/Fellowship)
Funding is competitive! Your proposal has to explain:

1. Why is your work so IMPORTANT that it should be funded instead of other areas of research?
   
   • Impact on human health?
   
   • How do your aims advance the field?
   
   • What is innovative about the proposed work?
Funding is competitive! Your proposal has to explain:

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2. **Why are the proposed studies the BEST approach to address they hypothesis?**
   - Contrast with alternative approaches
   - Addresses potential weaknesses
   - Establish feasibility
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2. Why are the proposed studies the BEST approach to address they hypothesis?
   • Contrast with alternative approaches
   • Addresses potential weaknesses
   • Establish feasibility

3. Why should YOU be funded to do this research?
   • You & your sponsor have the expertise to complete each aim
   • You have (or can easily get) the resources to complete your aims
   • Aims will provide training that advances your career
Applicant’s background and goals for training

- Three sections (6 pages)
  A. Doctoral Dissertation and Research Experience
  B. Training Goals and Objectives
  C. Activities Planned Under this Award
Applicant’s background and goals for training

A. Doctoral Dissertation and Research Experience

- Summarize past research experience, results, and conclusions and describe how the experience relates to the proposed fellowship.
  - If past research experience is in a different field, then note that.
  - If no research experience, then describe other scientific experiences.
  - If advanced graduate student, then include a narrative of the doctoral dissertation.

- Do not list academic courses

- Tips:
  - Use narrative form starting with your first research experience (normally, undergrad)
  - For each research experience/stage include where it occurred, with whom, what you learned, and how it set you up for the next stage (if applicable). Figure out the humble brag.
  - Also, include research products such as publications, funding, presentations at conferences, and awards. It is important that you elaborate on how the result impacted the field and led to additional questions.
  - A common weakness is low productivity so use this section to show what you’ve accomplished and explain areas of concern.
  - Could also use this section to reiterate overcoming any weaknesses in the application (e.g., poor undergrad grades)
  - 1 – 2 pages out of the 6 pages allotted.
Applicant’s background and goals for training

B. Training Goals and Objectives

• Describe overall training goals for the fellowship and how the activities proposed will help you attain those goals.

• Identify the skills, theories, conceptual approaches, etc., to be learned or enhanced during the award, including, as applicable, *expertise in rigorous research design, experimental methods, quantitative approaches, and data analysis and interpretation*, as applicable.
  
  • Can group by what you need to learn: technical skills, conceptual approaches, scientific communication, career guidance etc.
  
  • Or you can group by subject (scRNA-seq, behavioral analysis of transgenic mouse models etc.)
  
  • EVPR ReaDI program has a guide to help you.

• Discuss how the proposed research will facilitate your transition to the next career stage, if applicable.

• Normally 1 - 2 pages out of the 6 allotted.
C. Activities Planned Under this Award

- The activities planned should be individually tailored to your goals and integrated with your research project.
  - Mentors/sponsors: if you have a junior PI, include a senior co-sponsor.
  - Research/lab work.
  - Coursework (state year and semester you plan on taking the course).
  - Professional development:
    - Meetings, seminars, conferences.
    - Scientific writing (publications and grants).
    - Oral presentations.
    - Teaching.
    - IDP (Individual Development Plan).
  - Clinical activities (if applicable).
- Describe, by year, the activities that you propose to be involved in during the award.
- Provide a timeline for the training/career development activities.
- 1 – 1.5 pages.
Applicant’s background and goals for training

Reviewer comments on Training Potential

• The applicant has **substantial experience** with optogenetics and mouse behavior. Consequently, it is unclear how the proposed research will provide substantial new training.

• It is **not clear what the applicant will learn** during the training period, as she is apparently adept at the methods to be employed.

• Mr. X has **already acquired** the technical skills required for completion. Training in MATLAB is required but two years is a substantial amount of time to acquire this training.

• The applicant will be **exposed to a relatively limited number** of new research methods, i.e., electrophysiology, that he has not previously learned.

• Dedicated time toward **professional development** is lacking.

• Over two years passed between her qualifying exam in 2014 and her first thesis committee meeting in 2016. **Thesis committee meetings should be an integral part of the training plan** and occur at least yearly, if not more frequently.
Purpose of the Research Training Plan

• Present the scientific problem for investigation
• Explain the importance and relevance of the scientific topic/problem
• State and develop the hypotheses to be addressed
• Plan experiments, anticipate problems and outcomes
Organization of the Research Training Plan

- Composed of two sections
  - Specific Aims: 1 page
  - Research Strategy: 6 pages
    - Significance
    - Approach
Writing a Specific Aims Page

➢ 1 page

• Include:
  • Central hypothesis
  • Aims and goals
  • Overall results
Anatomy of a Specific Aims page

1st paragraph

State the scientific/medical problem, importance to human health, and what is needed to solve the problem and/or cure the disease.

2nd paragraph

State specifically the advances your lab has made in this field, key new results and central hypothesis.

3rd paragraph

Indicate specific aims by a numbered list; each aim should have its own hypothesis.

Some people include a 4th paragraph that discusses the impact of the work in the context of the larger field and how this award will provide you with skills to pursue an academic research career.
Specific Aims Checklist

- **First Paragraph (Why): Preamble/Introduction**
  - **What is the topic?** Write a concise, active sentence introducing the topic of the proposal. This sentence should be interesting and tell the reader the main subject of your grant.
  - **What is the gap?** Describe the gap in knowledge or unmet need that this proposal will address.

- **Second Paragraph (What):**
  - **What is the long-term goal?** The long-term goal of my research is to…
  - **What are the specific objectives for this proposal?** Describe the objective(s) of this proposal to address the unmet gap/need.
  - **What is the hypothesis?** Define your hypothesis without reference to experiments.
  - **What is the evidence for the hypothesis?** Describe literature background & preliminary data (highlights only!).
  - **What is the summary (rationale/significance)?** Write a sentence summarizing the proposal and that it will be accomplished via the following aims (optional)

- **Specific Aims (How): For each aim:**
  - Write a short descriptive title.
  - Include a brief description of activities to be performed, hypothesis to be tested, &/or outcomes predicted by the hypothesis (the aims should have clear, measurable outcomes).

- **Last paragraph (Payoff): Concluding Statements**
  - **What are the (big picture) outcomes/impact?** How this study will impact the field/move it forward and how will the fellowship help you become an independent investigator. The expected outcomes are….The broader impact is…
Specific Aims: General Tips

• Use clear language and minimize jargon and abbreviations
• Not necessary to cite references
• Don’t propose more than three aims, and two aims are fine as well
• Include a central hypothesis
• Use “I” instead of “we”
• Use strong active verbs for your aim statements

• RESOURCE: Northwestern University videos for writing an aims page as well as significance and innovation:
  https://www.northwestern.edu/climb/resources/written-communication/index.html
Specific Aims: Active Verbs

Examples of strong, Active Verbs

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<th>Attain</th>
<th>Determine</th>
<th>Identify</th>
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<td>Administer</td>
<td>Compare</td>
<td>Estimate</td>
<td>Represent</td>
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Red Flags

Explore
Describe
Characterize
Examine

https://www.nordp.org/assets/active%20vs.%20passive%20verbs.pdf
SPECIFIC AIMS: Recent advances in transcriptome-wide analyses have revealed that while the vast majority of the mammalian genome is transcribed, the approximately 1.5% that is translated into protein is dwarfed in comparison to the abundance of non-protein-coding RNAs (ncRNAs). A significant subset of these ncRNAs are long noncoding RNAs (lncRNAs), which are defined as transcripts longer than 200 nucleotides that lack protein-coding potential. LncRNAs have been implicated in processes such as dosage compensation, imprinting, pluripotency and apoptosis, and are believed to function through several mechanisms, including transcriptional regulation in cis or trans and chromatin remodeling. Discovery of these new regulatory mechanisms suggests a need to reassess biological processes in the context of a role for lncRNAs. Several studies have indicated a role for lncRNAs in the pancreas through identification of thousands of novel lncRNAs in mouse and human islets; however, the biological function of most lncRNAs is unknown. Additional evidence comes from genome-wide association studies (GWAS) showing that most susceptibility variants for Type 2 diabetes (T2D) fall outside coding genes. While this could be explained by variants impacting regulatory elements, recent studies have mapped human T2D-associated SNPs to known lncRNAs signifying a biological requirement for these transcripts in the pancreas.

To understand the lncRNA mechanisms regulating pancreas development and islet cell identity, we have conducted RNA-seq analysis of embryonic day 14.5 (e14.5) mouse pancreas and 12-week-old mouse islets. Our preliminary results have revealed several interesting novel and conserved lncRNA candidates, as well as the lncRNA Paupar (Pax6 Upstream Antisense RNA) that has been previously characterized in neuroblastoma cells. We therefore hypothesize that pancreatic lncRNAs promote proper pancreas development and β cell function through regulation of essential pancreatic genes. To test our hypotheses, we plan to pursue the following three specific aims:

**Aim 1:** Characterize the spatial, temporal, and cellular localization of pancreatic lncRNAs. **Hypothesis:** Pancreatic lncRNAs are expressed in a temporal, spatial, and cellular pattern suggestive of function. We have identified a large number of pancreatic lncRNAs. Several of these lncRNAs are located in relative proximity to known pancreatic genes. We will focus on four candidates that have high conservation in human islets, are in relative proximity to a gene required for pancreas development and/or function, and are expressed in beta cell line that will facilitate in vitro knockdown analysis. 1a) In order to test the functionality of these candidates, we will perform expression analysis in cell lines, and embryonic and adult tissue to determine the temporal, spatial, and cellular localization of each lncRNA. 1b) Functional lncRNAs are often co-expressed, or co-regulated, with a gene in relative proximity. We will therefore conduct gene expression analyses of the gene in closest proximity to a candidate lncRNA and compare it to the lncRNA expression data from Aim 1a to see if they share an expression pattern.

**Aim 2:** Determine how novel lncRNAs regulate essential pancreatic genes in vitro. **Hypothesis:** Candidate lncRNAs act as transcriptional regulators of essential pancreatic genes. 2a) We will confirm the regulatory relationship between novel lncRNAs and their associated genes by knocking down candidate lncRNAs in vitro and assaying for misregulation of associated genes. 2b) To analyze the pancreas-specific mechanism of Paupar regulation, we will knockdown Paupar in vitro and analyze misregulated genes. We will also implement a technology for identifying genome-wide RNA binding sites to show that Paupar is directly regulating pancreatic genes in trans.

**Aim 3:** Elucidate the pancreas-specific function of candidate lncRNAs. **Hypothesis:** Pancreatic lncRNAs are required for proper β cell function 3a) We will analyze the phenotype of lncRNA knockdown in vitro using both gene expression analyses and functional analyses to uncover disruption of canonical pancreas regulatory pathways. 3b) The in vivo requirement of Paupar for proper pancreas development and function will be tested by analyzing a Paupar knockout mouse. We will phenotypically characterize this mutant mouse to identify changes in RNA, protein, and the epigenetic landscape, that will solidify a mechanism of Paupar function.

This study will further our understanding of the developmental biology and gene regulatory networks of the pancreas. The experiments described will enhance our ability to create beta cells for replacement therapy and treat pancreatic diseases.
Writing a Research Strategy

- 6 pages
  - Need two components
    - Significance
    - Approach
      - Preliminary studies for New Applications

Research Training Plan weaknesses that come up

- The plan isn’t convincing
- The mixed use of “we” and “I” is confusing and may give the wrong impression of potential “lifting” parts from the sponsor’s grant
- Proofreading should be encouraged to facilitate the reading of an exciting proposal. There are numerous typographical errors in the text, including the aims page.
- Some of the figures are hard to understand and lack detailed explanation.
Writing a Research Strategy cont.

Significance section: Guidelines

- Include relevant background to understand the work and its significance
- Include relevance to human health and what the proposed research could potentially contribute
- Include key references briefly describing the current state of the field and state concisely where the “holes” are
  - NIH changed their requirements and you now need to ensure that you are including a “rigor of the prior research”. Include general strengths and weaknesses of both published and unpublished research that serves as key support for the project. Pay attention to experimental design details such as biological variables and authentication of key resources.
- For significance, make sure you include: how your research will advance the field, the knowledge gaps that the work will fill, what is unique about the work being proposed, how the work meets NIH’s mission
- Try to keep it to 1 – 1.3 pages
Significance section: Figures

• Include a figure or diagram(s) if essential for understanding your project
• If you are studying a specific molecule, include a diagram of the molecule
• If you are exploring a specific model, include a diagram of the model
• Always include a legend with each figure
Approach section

• This is your research plan

• Preliminary data

• Organize into specific aims and restate hypothesis for each aim. Some example subheaders:
  • Rationale
  • Preliminary data (if you didn’t already describe it)
  • Methods
  • Potential outcomes, problems, and follow-up experiments

• Describe experiments and controls for each section-methods can be brief

• Always include section on potential outcomes, problems, and follow-up experiments
Formatting: Don’t upset your reviewers

Font recommendations: Arial, Georgia, Helvetica, or Palatino Linotype

Font Size: 11 points or larger for general text and no less than 9 points for tables or figure legends

Spacing: No more than 15 characters per inch and not more than six lines of text per inch

Text color: No restrictions but NIH recommends black

Greek/special characters: You may use symbol font or special characters but size limitation still applies

Figures: Make sure they are legible when printed

Margins: at least half-inch (0.5”) on all sides

Page size: US Letterhead (8 ½” x 11”)
Don’t forget about these resources

BioRender
Create professional scientific figures.

https://research.ps.columbia.edu/content/grant-starter-kit
https://research.ps.columbia.edu/content/biorender
## Timeline

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<th>Weeks until deadline</th>
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<td>8 - 12</td>
<td>Determine and meet with mentors/sponsors/collaborators; Draft Specific Aims &amp; Biosketch; Contact NIH</td>
</tr>
<tr>
<td>6 - 10</td>
<td>Contact references and collaborators; Start drafting Applicant Section and Research Strategy</td>
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<tr>
<td>5 - 8</td>
<td>Work on Applicant Section and Research Strategy</td>
</tr>
<tr>
<td>4</td>
<td>Send draft of Applicant Section and Research Strategy to mentors for review; speak to grant administrator in the Pre-Award Team for to address the budget; start drafting other attachments</td>
</tr>
<tr>
<td>3</td>
<td>Incorporate feedback; remind references to submit; continue drafting other attachments</td>
</tr>
<tr>
<td>2</td>
<td>Start gathering letters, Biosketches etc.; finalize attachments and send to the Pre-Award Team; incorporate any additional feedback</td>
</tr>
<tr>
<td>1</td>
<td>All documents should be submitted to the Pre-Award Core/grant administrator. The Pre-Award Team/grant administrator will upload them into the system.</td>
</tr>
<tr>
<td>0</td>
<td>Last day to submit!! No changes after NOON (12p). Deadline by 5p (including reference letters).</td>
</tr>
</tbody>
</table>
Questions?

- Feel free to send us things to read (ps-officeforresearch@cumc.columbia.edu)
  - NIH Biosketch: 6/28/2021
  - Specific Aims: 6/28/2021
  - Applicant Section: 7/19/2021

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