F32 BOOT CAMP

From start to submission (grants due April 8, 2020)

Research Approach

Presented 14Feb2020

Required Documents

Documents	Page limit	Comments
Cover Letter	No limit	Individual fellowship applicants must include a cover letter that contains a list of referees (including name, departmental affiliation, and institution). See instructions for other required content.
Project Narrative	3 sentences	Lay language – 8th grade reading level
Abstract (project summary)	30 lines	
Specific Aims	1 pg	
Research Strategy (Significance, Approach)	6 pgs	
Bibliography and References Cited	No limit	Attached separately from research strategy
Applicant's Background and Goals for Fellowship Training	6 pgs	Contains three sections: applicant's background, goals, planned activities
Resources and Environment	No limit	But be concise and specific to your application, will contain some overlap with sponsors statement and institutional environment
Equipment	No limit	But be concise and specific to your application. If no equipment, attach sheet with 'NA'
Respective contributions	1 pg	
Selection of sponsors and institution	1 pg	
Training in Responsible Conduct of research	1 pg	
Sponsor/Co-sponsor statements	6 pgs	All info from sponsor and co-sponsor(s) must fit in this 6 pages
Letters of support from Collaborators	6 pgs total	Need one from everyone named in your application (does not include sponsor/co-sponsor)
Description of Institutional environment and commitment to training	2 pgs	
Resource Sharing Plan	No limit	Must include if you are generating model organisms or genomic data. If none, attach a sheet with 'NA'
Biographical sketch	5 pgs	Include Biosketches for key personnel (you and your sponsor/co-sponsors only). Do not include for collaborators/advisors/etc

Documents	Page limit	Comments
Optional Documents: Depending on application		
Introduction	1 pg	If this is a resubmission
Vertebrate animals	No limit	Specific instructions for content
Human subjects and clinical trials information	Multiple documents	If your proposal involves human subjects research
Select Agent Research	No limit	Include a “Select Agent Research” attachment if your proposed activities involve the use of select agents at any time during the proposed project period, either at the applicant organization or at any performance site. See SF424 for what qualifies and what to include
Applications for concurrent support	No limit	If you answer ‘Yes’ to the applications for concurrent support question, attach a description

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Research Strategy

6 pages

Organize the Research Strategy in the specified order and use the instructions provided below, unless otherwise specified in the FOA.

Start each section with the appropriate section heading – Significance, Innovation (not in F32), Approach.

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Research Strategy

Special Rules for proposals using human subjects

- Read instructions carefully

Research 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.
- 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.
- 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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Research Approach - Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project.

- Describe in enough detail that reviewers know what you are doing (and can tell that you know what you are doing)
- Potential space savers:
  - Use previous publications from the lab that describe methods
    - Make sure that it's clear that the publication is from your lab (eg …will be performed as previously described. Briefly,…)
  - Refer to preliminary data
  - Refer to previous aim if similar methods
  - Use a figure
- Don't forget the analysis plan

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Research Approach - Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.

Weaknesses in the training plan

- Not clear whether the data presented in Fig 1 are from whole brain, PFC or hippocampal synaptoneurosomes. No details given how the authors have prepared these fractions.
- The application lacks details on the identification of genotypes of PND1 pups.
- The preparation of primary cortical neurons at PND 1 will give glial contamination. Although the applicant refers to the protocol published from (the) Lab, the referred article shows preparation at E16.5.
- The application lacks details on methods.
- The rationale for selecting PAK is not well discussed.
- Not clear what new information is expected from the western blot analysis in neuronal culture lysates compared to the preliminary data from tissue extracts.
- Power analysis is not provided. N=4 for experiments in Aim 1b seems underpowered.
- In Aim 2, control and patient derived iPSCs will be used. However, no details are provided on the clinical phenotypes of patients.

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Research Approach - Describe the overall strategy, methodology, and analyses to be used to accomplish the specific aims of the project.

- Should include elements of design (timeline, groups), methods, and analysis (not just stats package, or test, but what you will compare)
- If vertebrate animals are involved – a lot of detail can go in the vertebrate animals section
- If no vertebrate animals, make sure you include info on replicates, n, etc in the approach

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Research Approach - Describe plans to address weaknesses in the rigor of the prior research that serves as the key support for the proposed project.

- This is new to the instructions – rigor is replacing premise
- NIH expects applicants to:
  - Describe (in the significance) the general strengths and weaknesses in the rigor of the prior research (both published and unpublished) that serves as the key support for the proposed project.
  - It is expected that this consideration includes attention to the rigor of the previous experimental designs, as well as the incorporation of relevant biological variables and authentication of key resources.
  - Applicants are expected to include plans to address any weaknesses or gaps identified.

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Research Approach - Describe plans to address weaknesses in the rigor of the prior research that serves as the key support for the proposed project.

- If you identified weaknesses in the prior research in your significance, make sure that you are addressing those weaknesses as part of your approach

- Check for coherence – make sure that after you write the approach, go back to the significance and make sure that you have only identified weakness that you are addressing in the approach

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Research Approach - Describe the experimental design and methods proposed and how they will achieve robust and unbiased results.

- Link to a website (https://grants.nih.gov/policy/reproducibility/index.htm) designed to assist in addressing rigor and transparency
- Resources, FAQs, blog posts

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Research Approach - Unless addressed separately in the Resource Sharing Plan attachment, include how the data will be collected, analyzed, and interpreted as well as any resource sharing plans as appropriate.

- Do not use the Resource Sharing Plan to try and save space
- Describe critical elements of data collection, analysis and interpretation in the Research Approach
- Within the 'Approach' section, use headings to ensure that the information is easy to find, e.g.
  - Rationale
  - Design
  - Methods
  - Data collection
  - Analysis and Interpretation
  - Alternative outcomes
  - Training value
  - Timeline/Milestones

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Research Approach - 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 (https://researchmethodsresources.nih.gov/)

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Research Approach - Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.

- Critical to include this:
  - Identifying problems (including less than optimal outcomes) and alternative strategies, and proposing solutions or interpretations is critical → strong foundation in research design and critical thinking

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Research Approach - Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.

Summary comments on recent F32 (scored and resubmitted)

"…The research project is **hypothesis-driven** and having **translational significance**. The **feasibility of the project is supported by the preliminary data**. Several minor to major concerns were raised. Two reviewers considered that the **scientific rationale** …**is not well-defined and the proposed approaches seem to have some conceptual deficiency**. The **potential pitfalls and alternative results are not thoughtfully discussed**. The **training potential is comprehensive with a detailed plan covering relevant technical skillsets and professional development skills, such as grantsmanship and transition grants (K99) application**. Overall, a promising applicant proposes an interesting project with several addressable issues that drove the score range. The panel reviewers expressed their moderate to high enthusiasm to the application."

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Research Approach - Discuss potential problems, alternative strategies, and benchmarks for success anticipated to achieve the aims.

Summary comments on recent F32 (scored and resubmitting)

"…The **applicant has an outstanding research experience** .... The applicant has 9 publications…Two aims are proposed. The **strength of the application is the use of a combination of mouse model and patient-derived iPSC approaches**. The **training potential is good**. The **environment is excellent**. **The major weakness of the application is the lack of experimental details**. Although a number of experiments are proposed, it is **difficult to follow the rationale, methods proposed and overall interpretation of the data**.."

No weaknesses noted in applicant, sponsor/s, training potential or environment

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Research Approach - 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.

- Acknowledge problems with feasibility or areas of high risk
- This can be included in the problems/alternative strategies
- Clearly describe the benefit of high risk aspect and provide options for mitigating risk
  - Alternative methods
  - Experts (sponsor, co-sponsor, advisors, collaborators, etc)

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Research Approach - Explain how relevant biological variables, such as sex, are factored into research designs and analyses for studies in vertebrate animals and humans.

- Sex as a biological variable will be factored into research designs, analyses, and reporting in vertebrate animal and human studies.
- Strong justification from the scientific literature, preliminary data, or other relevant considerations, must be provided for applications proposing to study only one sex.

SF424 version E. Fellowship

NIH Guide Notice on Sex as a Biological Variable in NIH-funded Research (https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-102.html)

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Preliminary Data - Include information on preliminary studies (including data collected by others in the lab), if any.

- Discuss the applicant's preliminary studies, data, and/or experience pertinent to this application.
- Depends on PA (eg NINDS says no preliminary data)
- Can provide:
  - Demonstration of novel/difficult/potentially problematic methods
  - Rationale for current studies

- Figure legends should be understandable without reading the text
  - Tell the reviewer's why you are showing them the data

- Indicate your role in generating the preliminary date
  - Data is from your lab
  - Data is from you
  - Data is from a co-sponsor/collaborator etc

F32 BOOT CAMP

Preliminary Data - Include information on preliminary studies (including data collected by others in the lab), if any. Discuss the applicant's preliminary studies, data, and/or experience pertinent to this application.

3. Research Training Plan: **Score = 3**

Strengths

- Proposal to study LRH-1 receptor agonists with defining gene regulation in human liver cell line (Aim 1).
- They have produced a human receptor agonist that is more potent than currently used one
- They have also produce a humanized LHR-1 mouse and show that it has similar activation by agonist. They will use this to test metabolic effects on gene expression, lipidomics
- Descriptions of methods on gene sequencing appear detailed

Weaknesses

- Not clear what data generated by applicant
- Adding more metabolic studies might also be informative

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Research Approach - Point out any procedures, situations, or materials that may be hazardous to personnel and the precautions to be exercised.

- These include working with vectors, hazardous or toxic compounds, human blood or tissues, etc
- A full discussion on the use of select agents should appear in the Select Agent Research attachment.
- 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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Research Approach - If you are proposing to gain clinical trial research experience (i.e., you will not be leading an independent clinical trial), briefly describe your role on the clinical trial.

- F32s can not have an independent clinical trial
- You can do human subjects research (ie working with humans, but not a trial)
- If you are working on a trial, describe your role

Research Approach

- Provide the what, why and how
  - Include enough detail to show you know what you are doing and why
  - Rationale (if not covered in the significance)
  - Outcomes
  - Analysis plan
  - Interpretation
- Acknowledge and thoughtfully discuss:
  - Alternate outcomes
  - Potential problems
  - Feasibility issues and how you will overcome

From ‘The Reviewer’s Perspective’

Research Training Plan

Is the research plan well integrated with the candidate's goals, will it expand the candidate’s conceptual understanding and is the plan of high scientific quality?

- Keep your focus on the big picture; don’t get bogged down in the experimental details. Focus more on rationale.
- Has the candidate properly considered alternative outcomes or methodologies?
- Describe why you think an aspect of the approach is a strength or a weakness. Avoid just restating the key aims or other descriptive information in the application.
- Are publishable results from the work likely? Is the amount of work proposed feasible within the timeframe requested?
- Is the work proposed sufficiently distinct from the sponsor’s funded research for the applicant’s career stage?
- Is the scope of the work proposed appropriate for the candidate’s career stage?
- Evaluate with candidate’s career stage in mind. An F31 application from a second year graduate student should be assessed differently than an F32 application from a second year post-doc.

From ‘The Reviewer’s Perspective’

Training Potential

Do the proposed research project and training plan have the potential to provide the applicant with the requisite individualized and mentored experiences that will develop his/her knowledge, research and professional skills?

- The training should be consistent with applicant’s career goals in a health-related field and help them advance to the next stage. If a specific career goal has not been chosen (for an F31), the training should be consistent with the various options.
- Is the proposed research complementary to previous training (particularly for F32)? What new research areas/skills/techniques will be learned?
- The sponsor’s training plan and applicant’s proposed activities should address any weaknesses/gaps in the applicant’s background relative to their career goal.
- The training plan and applicant activities should include non-research training appropriate to the career goals (e.g., teaching, coursework, grant-writing, presentations)