PREPARING FOR AND TAKING YOUR CANDIDACY EXAM

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Major goals for advancing to candidacy

- **Generate a F31-style research proposal, ideally based on your thesis project**
  Actively seek out and incorporate feedback (from your fellow students, postdocs, faculty, including your PI)

- **Present your proposal to your candidacy exam committee (20 min) and address any comments/questions (~90 min)**

- **Optional but strongly recommended: Submit your (revised) proposal to NIH or other funding agency**

Before you petition for candidacy….

- Form an advisory committee

- Hold two (but at least one) advisory committee meetings

- Take required Neuroscience core courses (Molecular and Cellular Neuroscience, Systems Neuroscience) and Biostatistics

- Use the scientific writing course to develop a solid first draft of your proposal. Ideally, your main scientific goals are clear before you take the course.

- Neuroscience electives do **not** need to be completed prior to candidacy.

Getting the green light from your advisory committee (end of year 2)

- Get approval from your mentor(s) and your advisory committee to petition for candidacy. Ideally, use your 2nd committee meeting to announce your intention. **Important: to obtain approval, you don't need (significant) preliminary data!**

- Write a specific aims page (NIH style), either based on or related to your thesis research (**on-topic**), or on a completely unrelated topic that neither you nor your lab have ever worked on (**off-topic**).

- Your advisory committee will (usually) not make comments on your specific aims. To get feedback, best to set up individual meetings.

Candidacy exam - Complete timeline

1. Get approval from your mentor/advisory committee for your petition.

2. Send your specific aims page to CE committee chair, who will then generate your candidacy exam committee with you. Please do not contact potential committee members on your own.

3. Submit your aims page and the signed candidacy petition forms to Academic Standards Com. (ASC) by the **first Wednesday** of the month. Deadline to submit your petition is August 31 of your 2nd year (but you can ask for an extension).

4. Schedule your exam at a minimum of 6 weeks following ASC approval, but not later than the end of the same semester. **Be conservative and give yourself enough time to finalize your proposal.**

5. Send your final proposal to your CE committee two weeks before your exam. Note that you can change your SAs until you submit your proposal.

Selecting your candidacy exam committee

Members of standing committee, as of Sep. 2024 (year denotes end of term)

Sheng Zhang (Chair, 2027) – Molecular & Cellular, Translational

Fabricio Do Monte (2026) – Systems & Cognitive

Kristin Eckel-Mahan (2026) – Molecular & Cellular

Gabriel Fries (2026) - Molecular & Cellular, Translational

Qingchun Tong (2027) – Systems & Cognitive

- Your committee (total of 5) consists of the current chair, some members of the standing committee, and other faculty of your choice. Include one "outside" member (not necessarily outside NGP) who has a non-overlapping research focus. Your PI can't be a member (or even be present for the exam).

- Expertise is important! Consider including members from your advisory committee (2 max), and/or non-GSBS faculty

- MD/PhD students: Include a member of the MD/PhD committee

- Students with a secondary area of concentration: Include a faculty of the program of secondary focus.

Your proposal

- Written entirely by you
- addresses an interesting scientific question/gap in knowledge
- contains a novel & testable hypothesis
- employs logical, related but independent steps (aims) to address that question
- makes use of rigorous experimental approaches
- feasible, not too narrow but also not overambitious

Format: NIH F31 fellowship proposal   ("1+6")

a. Specific Aims – 1 page limit. Concisely state goals and summarize expected impact of the research. **Clearly-defined** aims with **explicit hypotheses to be tested**.

b. Research Strategy – 6 page limit (not more, but also not less). Includes Significance (max. 1 page), Innovation (1/3 page, optional), and Approach sections.

c. Bibliography – not included in the page limits.

Your overall hypothesis should be

- specific/directional
- well rooted in the literature (but not incremental)
- **directly tested by your aims**
- feasible to test within a reasonable timeframe
- devoid of any conditional (may, might, could)
- visualized as a schematic (in significance section)

Example:

Social deprivation controls molecular and cellular properties of hippocampal astrocytes
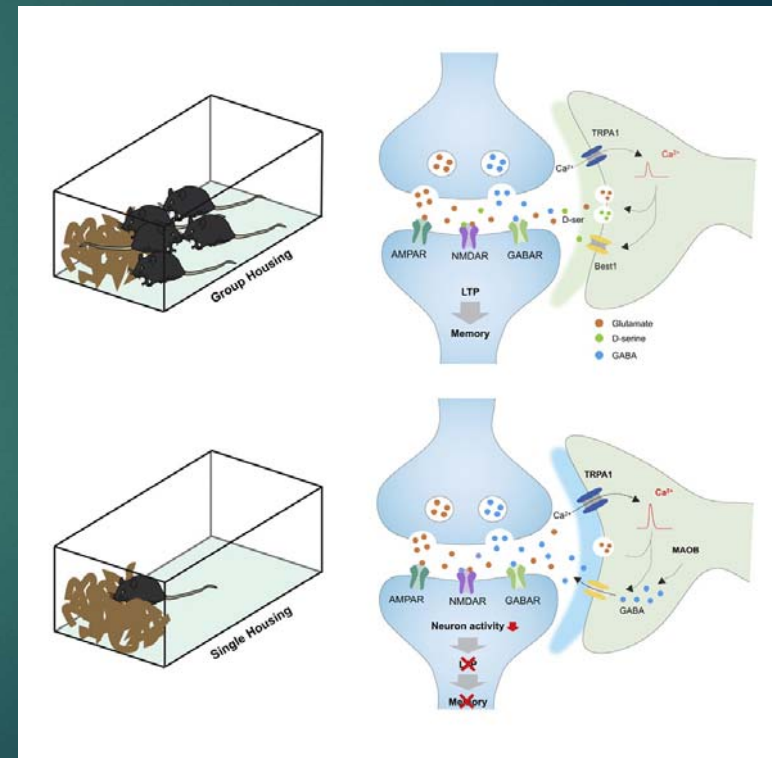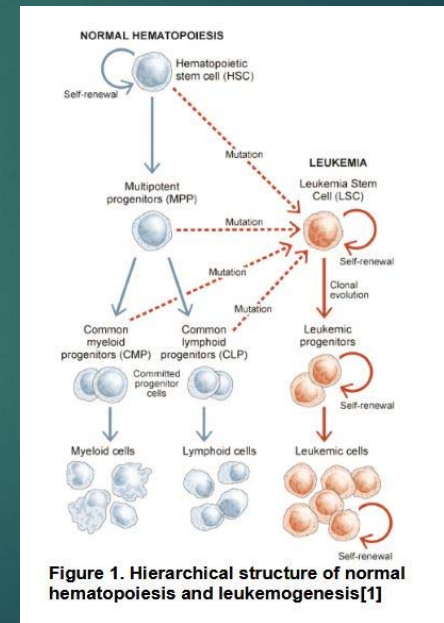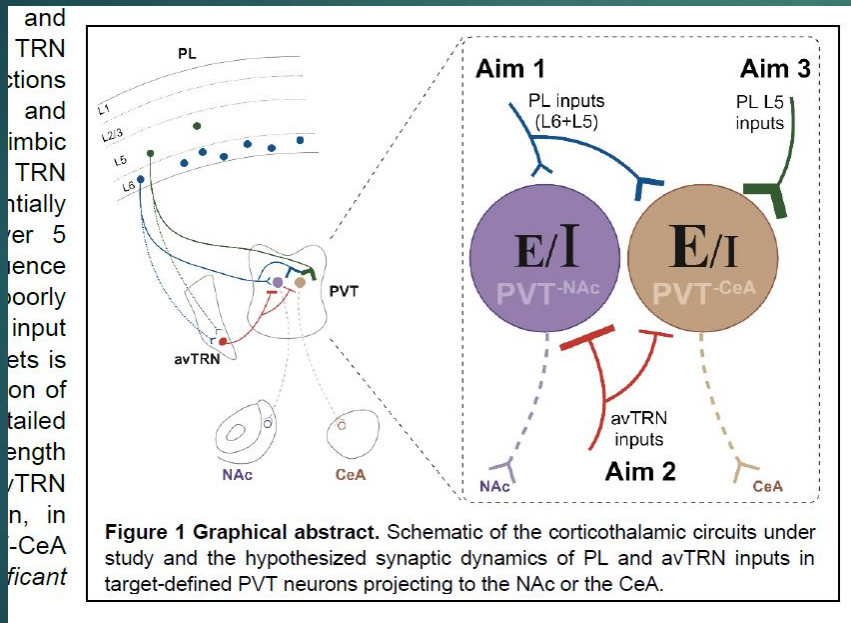
Specific aims

- Aims should be related, but NOT interdependent

- Ideally, each aim should have its own sub-hypothesis, leading to specific predictions for the outlined experiment(s)

- Try to avoid entirely descriptive aims
    - If possible, include aims seeking causal relationships and/or mechanisms. If necessary, add a (sub)-aim addressing a mechanistic question, even if you/your lab does not employ the relevant approaches

- Avoid redundant aims e.g.
  Aim 1: Determine activation of cortical microglia following TBI
  Aim 2: Determine activation of cortical microglia during AD

Research strategy

1. Significance – broader context of your proposal, explain what gap in knowledge you will fill and how this will move the field forward (1 page max, including graphical abstract/hypothesis). Extend on and validate your specific aims. Use this section to raise excitement!!

Figure 1 Graphical abstract. Schematic of the corticothalamic circuits under study and the hypothesized synaptic dynamics of PL and avTRN inputs in target-defined PVT neurons projecting to the NAc or the CeA.

Figure 1. Hierarchical structure of normal hematopoiesis and leukemogenesis[1]

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https://gsbs.uth.edu/academics/candidacy-exam

Research strategy

2. <u>Innovation</u> (optional) – concise summary of novel ideas, technical innovations, model systems, etc. that make your project unique (1/3 pages max).

3. <u>Approach</u>
   General intro (optional): more specific background information, gap in knowledge, and rational for your hypothesis. Describe the approach you will take and why it's a good approach

   Aim 1:
       Background/Rationale/Hypothesis
       Experimental procedures
       Predictions
       Alternative strategies
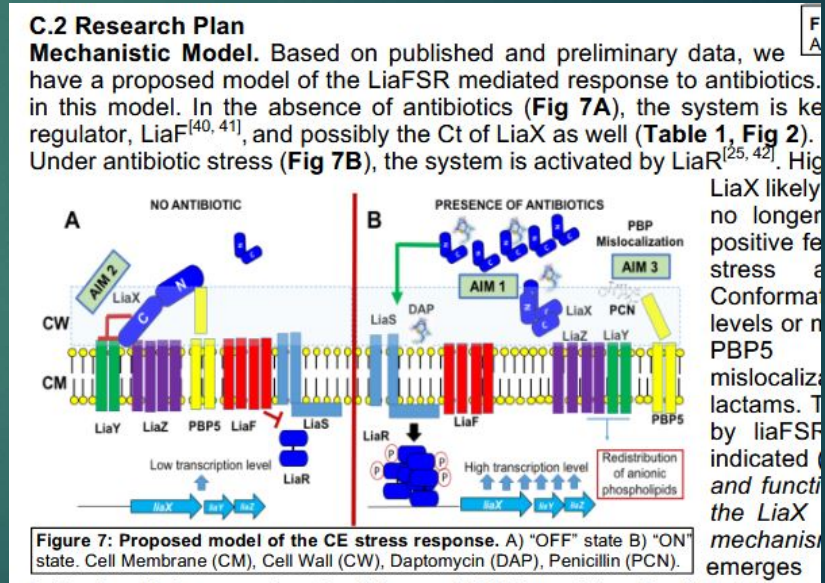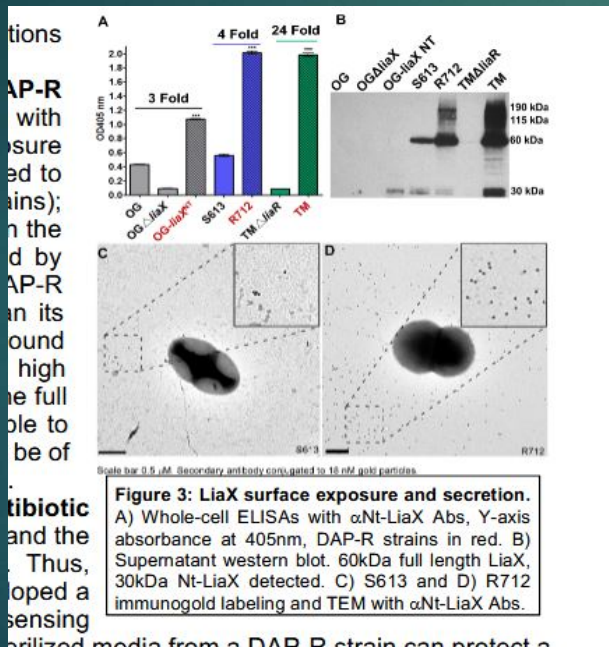
   Repeat for the other aims…

Approach

- must be feasible (but - unlike F31 – you can propose experiments not employed in your lab).

  Ideally, use multiple methods to address the same question from different angles.

- **make sure your proposed experiments test your hypotheses**

- **outline expected outcomes (need to directly address hypotheses)**

- include controls and if necessary, validations of novel techniques

- Consider the statistical analyses you will employ (can be short but should be there)

- Outline potential pitfalls & alternative strategies

  -> should not highlight fatal flaws in your experimental design!

Approach

Include preliminary data / models /experimental timelines throughout your approach section

Figure 3: LiaX surface exposure and secretion.
A) Whole-cell ELISAs with αNt-LiaX Abs, Y-axis absorbance at 405nm, DAP-R strains in red. B) Supernatant western blot. 60kDa full length LiaX, 30kDa Nt-LiaX detected. C) S613 and D) R712 immunogold labeling and TEM with αNt-LiaX Abs.

C.2 Research Plan
Mechanistic Model. Based on published and preliminary data, we have a proposed model of the LiaFSR mediated response to antibiotics. in this model. In the absence of antibiotics (**Fig 7A**), the system is ke regulator, LiaF[40, 41], and possibly the Ct of LiaX as well (**Table 1, Fig 2**). Under antibiotic stress (**Fig 7B**), the system is activated by LiaR[25, 42]. Hig

Figure 7: Proposed model of the CE stress response. A) "OFF" state B) "ON" state. Cell Membrane (CM), Cell Wall (CW), Daptomycin (DAP), Penicillin (PCN).

Oral presentation

Prepare a presentation of your proposal ~ 20 minutes long (20-25 slides).

a. Significance/Background. Frame your project within the work in the field and identify gaps in knowledge that your project will fill.

b. Specific Aims (same as your written proposal). Clearly state your aims and your hypotheses. Explain how you will approach them experimentally.

c. Research Strategy. Explain the experimental approach(es) for each aim. **Carefully describe predicted outcomes**
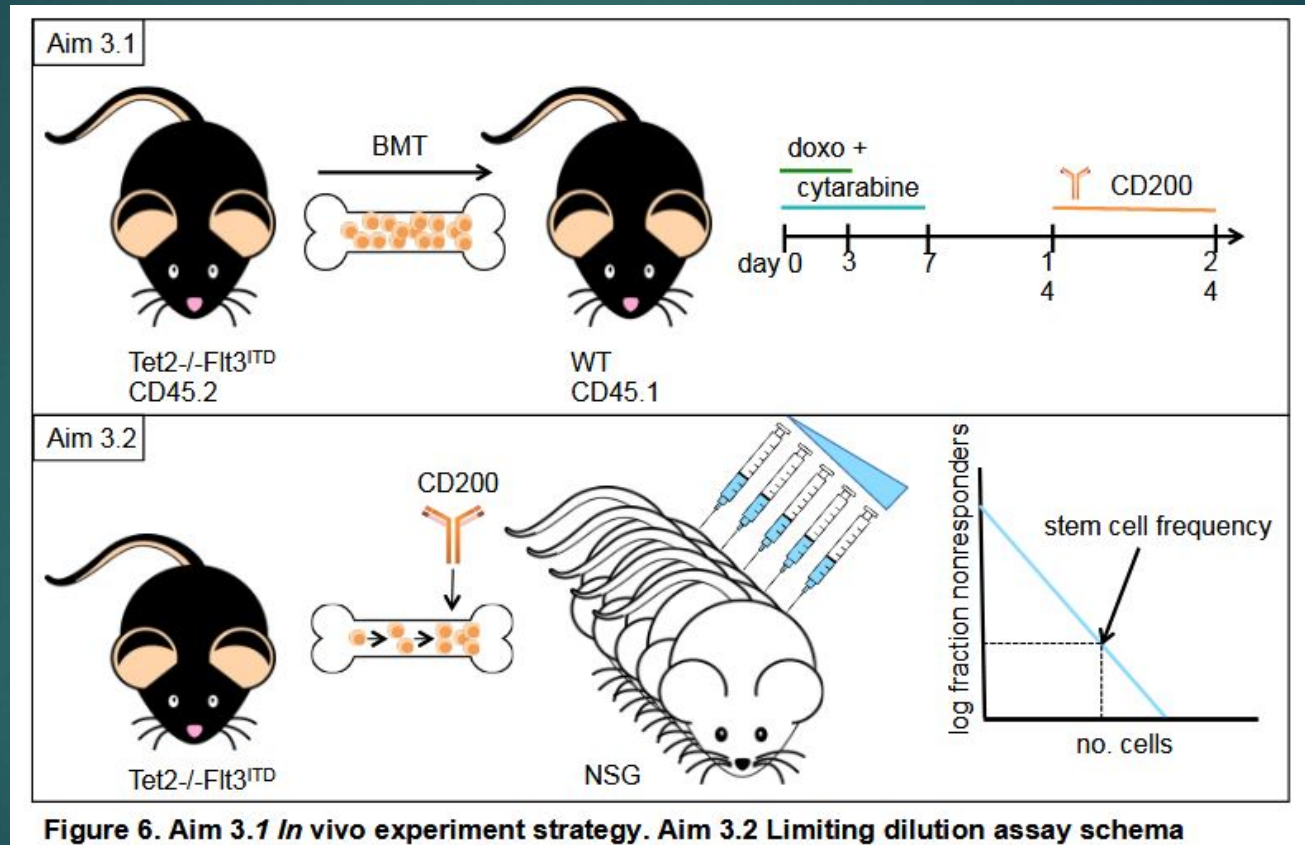
Oral presentation

Make extensive use of figures/schematics to illustrate
- Background
- Hypotheses
- Experimental strategy
- preliminary data/expected outcomes

Schematics (to illustrate hypotheses, strategies, outcomes) in both the proposal and the presentation **should be generated by you**. Showing figures/schematics from other sources should be the exception.

Generate schematics to illustrate background, hypotheses, experimental procedures, or expected experimental outcomes.

Figure 6. Aim 3.1 *In vivo* experiment strategy. Aim 3.2 Limiting dilution assay schema

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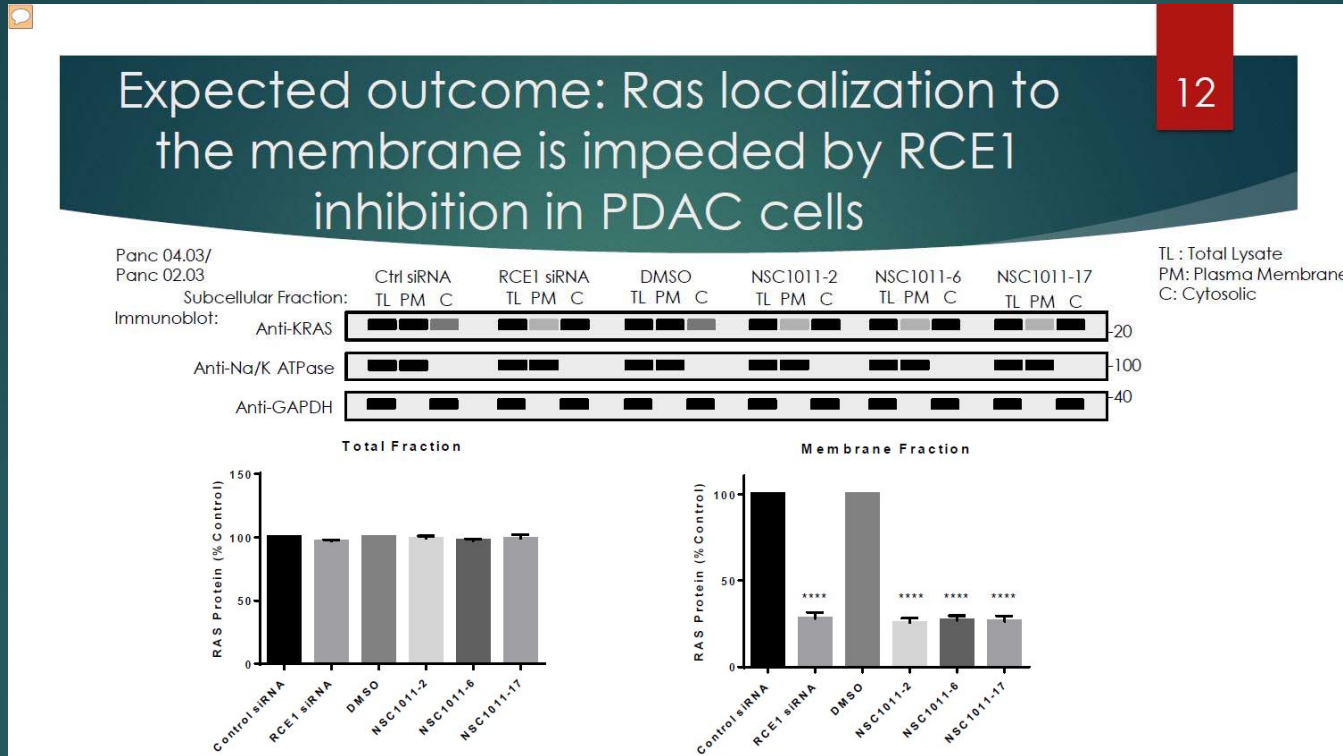
Important: data/outcomes can be simulated but make a note and don't use these "data" in your F31 ☺

Show preliminary data and expected outcomes, but limit showing results

Preliminary data
- demonstrate feasibility
- demonstrate rigorous science
- highlight variability/noisiness, which informs statistics to be used, n's needed

Expected outcomes
- final (simulated) summary for each aim/sub-aim "if everything goes according to plan"
- needs to address your (sub)hypothesis!!!

Results
- show productivity but distract from the points above. Even if you are almost done with a sub-aim, consider showing fake predicted outcome, rather than your results

Most questions from your committee will be on…

1. Biological and/or theoretical concepts/background related to your proposal

2. Scope and Significance ("Why is this an important problem?")

3. Rationale ("Why did you pick transcription factor x, and not y?")

4. Scientific methods/approaches, and why you chose them

5. Experimental outcomes (raw data, analyses, statistics)

6. Pitfalls, alternative strategies (including those that might be more appropriate but not used in your lab)

Most common weaknesses

Problems with Significance
- Neither significant nor exciting new research (i.e., will not advance science)
- Too incremental
- Lack of compelling rationale (**Why** is this important)

Problems with Experimental Approach
- Too much unnecessary experimental detail (e.g. buffer concentrations)
- Not enough description of experimental design, including appropriate controls
- Experiments are not directly testing hypothesis

- **Too much emphasis on your existing results**
- **No expected outcomes for each aim/sub-aim**

- No consideration of potential pitfalls or alternative models/hypotheses
- Inadequate consideration of statistics and/or power analysis

Possible outcomes

a. **Unconditional Pass:** Most likely outcome. You are done ☺.

b. **Conditional Pass:** The committee has identified some issues and will ask you to remedy them, e.g. with a revision of your proposal, a chalk talk, or a appropriate class

c. **Re-take exam:** Major issues with your proposal **and** your oral exam

Re-take exam (if necessary, after 3-6 months):

a. Unconditional Pass

b. Fail. **Has never happened in the NGP!!**

Your exam outcome is not a grade and has no impact on e.g. your chances to obtain an F31, GSBS awards etc.

Seek constructive feedback

- **On:**
  1. Your specific aims (can be modified even after approval!)
  2. Your research proposal (has to be written by you, but feedback - even if detailed - is perfectly ok)
  3. Your presentation (practice with your non-lab classmates)

- **From:**
  1. Your lab members
  2. Fellow students
  3. Faculty, including your advisor

A lot of info was taken from this very helpful primer
https://wassumlab.psych.ucla.edu/wp-content/uploads/sites/4/2019/12/How-to-write-a-strong-NRSA-b.pdf