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Preparing for and taking your candidacy exam

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(Chair of NGP candidacy exam committee, 2021-2024)

Major steps for advancing to candidacy

- **Generate a compelling F31-type research proposal**
  - addresses an interesting scientific question
  - has a strong, testable hypothesis
  - employs logical, related but independent steps (aims) to address that question
  - makes use of rigorous experimental approaches to answer the question
  - feasible, not too narrow but also not over-ambitious

- **Seek constructive feedback (fellow students, postdocs, faculty)**

- **Present your proposal to your candidacy exam committee and address any comments/questions**

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

Before you petition….

- Form an advisory committee
- Ideally hold two (but at least one) advisory committee meetings
- Take required Neuroscience core courses (Molecular and Cellular Neuroscience, Systems Neuroscience), Biostatistics, and (if possible) Graduate Neuroanatomy
- Complete online ethics module, Scientific Writing course by the end of summer term of 2nd year.
- Use the scientific writing course to develop a solid first draft of your proposal
- Neuroscience electives do **not** need to be completed prior to your candidacy exam.

Getting approval from your advisory committee (end of year 2)

- Get approval from your mentor(s) and your advisory committee to petition for candidacy (preferably during an advisory committee meeting). **Important: to obtain approval, you don't need preliminary data for your proposal!**

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

- Keep in mind: Your advisory committee will (usually) not make specific comments on the aims page of your proposal. To get their feedback, best to set up individual meetings.

Candidacy exam - Complete timeline

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

2. Send me your current specific aims page. The two of us will then form your candidacy exam committee (next slide)

3. Submit your aims page and the signed candidacy petition forms to Academic Standards by the **first Wednesday** of the month. Deadline to submit your petition is August 31 of your 2nd year (2020 or later). Following approval….

4. Schedule your oral exam at a minimum of 6 weeks following approval, but not later than the end of the same semester

5. Send your final proposal to the CE committee two weeks before your exam

Candidacy exam committee

Neuroscience Program candidacy exam committee

Michael Beierlein (Chair) - Cellular, Systems

Jian Hu - Molecular, Cellular

Scott Lane - Systems, Behavioral

Pierre McCrea - Molecular, Cellular

Consuelo Walss-Bass - Molecular, Behavioral

Sheng Zhang - Molecular, Cellular

- Your committee (total of 5) consists of the chair, 1-3 members of standing committee, and 1-3 faculty of your choice (who have expertise in your proposed research). One "outside" member should have a non-overlapping research focus.
- 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.

Writing your proposal

Format: NIH F31 fellowship proposal

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. Includes Significance, Innovation (optional), and Approach sections

c. Bibliography – not included in the page limits.

Specific aims

- Aims should be related, but NOT interdependent

- Each aim should have its own sub-hypothesis which leads to specific predictions for the outlined experiment(s)

- Try to avoid entirely descriptive aims
  - strong proposals seek to determine 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

  Aim 1: Determine activation of cortical microglia following TBI
  Aim 2: Determine activation of cortical microglia during AD

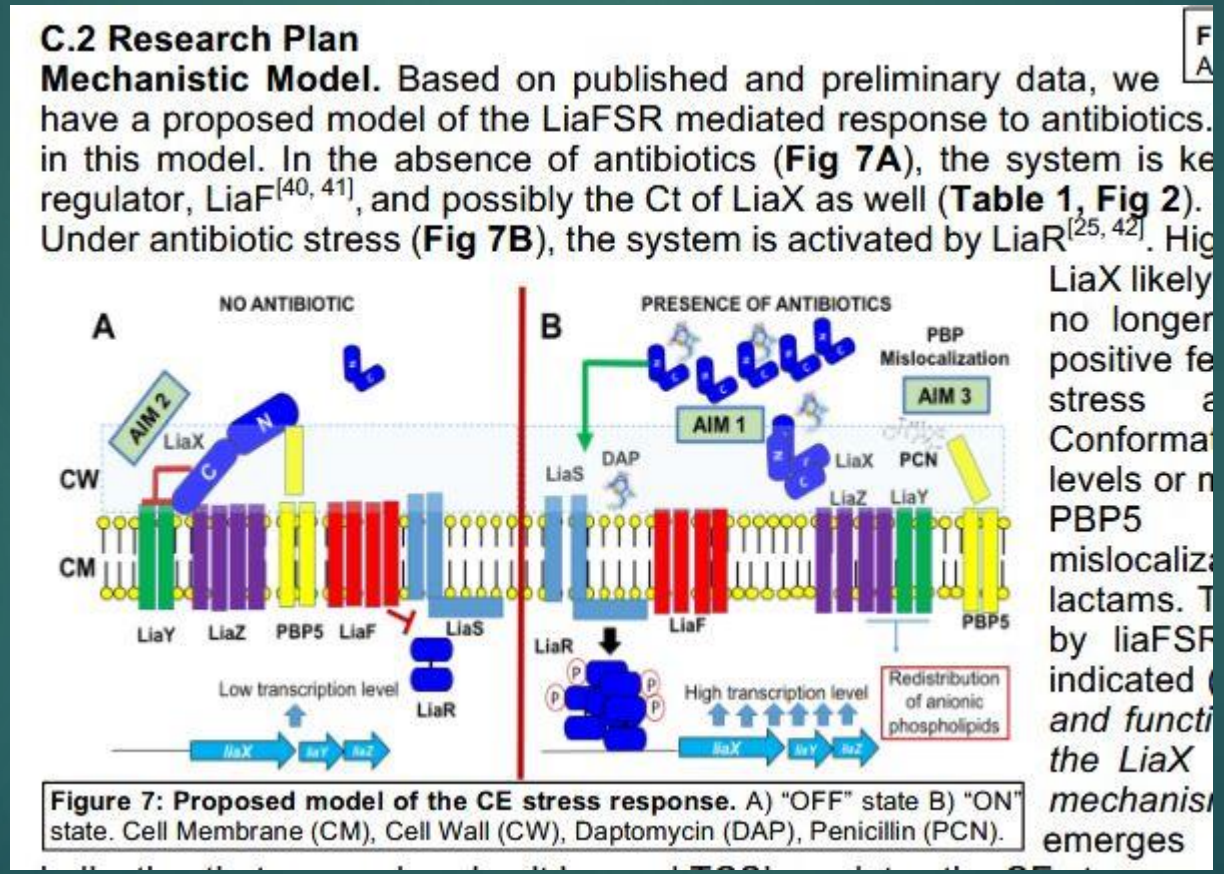
  You can modify your aims anytime, up until you submit your final proposal to your CE committee.

Your overall hypothesis should be

- testable/falsifiable
- clear and simple
- 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)

Example: Projections from the orbitofrontal cortex to the basolateral amygdala control the encoding of reward value.

Generate schematics to illustrate hypotheses, experimental procedures, expected experimental outcomes etc.



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 LiaX likely no longer positive fe stress a Conforma levels or n PBP5 mislocaliz lactams. T by liaFSR indicated *and functi the LiaX mechanis* emerges

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).

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

Research strategy (6 pages)

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)

2. Innovation (optional) – concise summary of novel ideas, technical innovations, model systems, etc. that make your project unique (0.5 pages max).

3. Approach – detailed description of experimental strategies, including the underlying rationale, your methods, and expected outcomes. Discuss potential pitfalls and alternative approaches. Each aim should be separate.

Approach & experimental design

- must be feasible (but - unlike F31 – you can propose approaches not employed in your lab)
- make sure your experiments test your hypothesis
- if possible, employ multiple methods to address the same question from different angles. Don't propose a correlational analysis for a hypothesis that requires a causal analysis.
- **describe preliminary data (can be from you, your lab, or simulated) and expected results**
- include controls and if necessary, validations of novel techniques
- carefully think through your statistical analyses

Generate schematics to illustrate hypotheses, experimental procedures, expected experimental outcomes etc.

vides essential stromal support. This also contributes an immune system with granulocytes, macrophages and dendritic cells that is only lacking in mature T-aftment (23). Athymic nude mice grouped into 4 arms containing 5 mice each

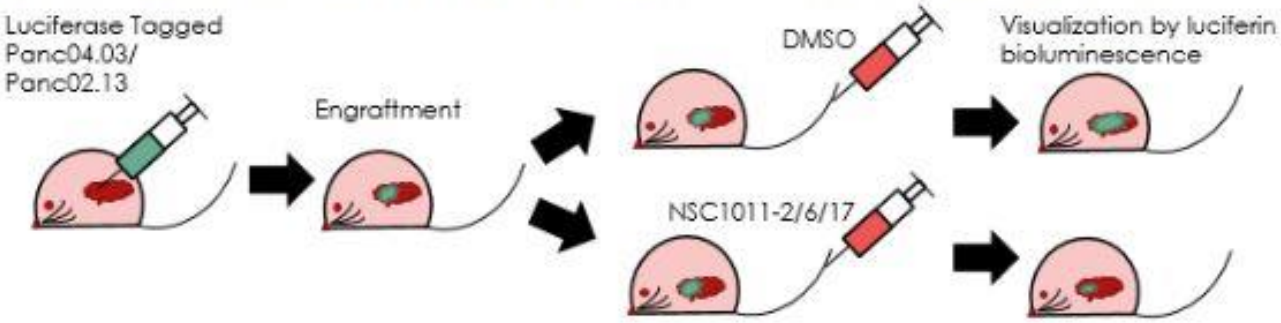


Figure 4: Schematic for animal studies. Athymic nude mice will be injected orthotopically with luciferase tagged PDAC cells. Once the cells have engrafted, the mouse models will be treated with the RCE1 inhibitor which was most effective *in vitro*. Tumor burden and metastasis will be tracked by luciferin bioluminescence every 7 days.

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every 24 hours (Figure 4). Survival will be assessed as well as tumor burden luciferin bioluminescence every 7 days for 120 days. Animal studies will be

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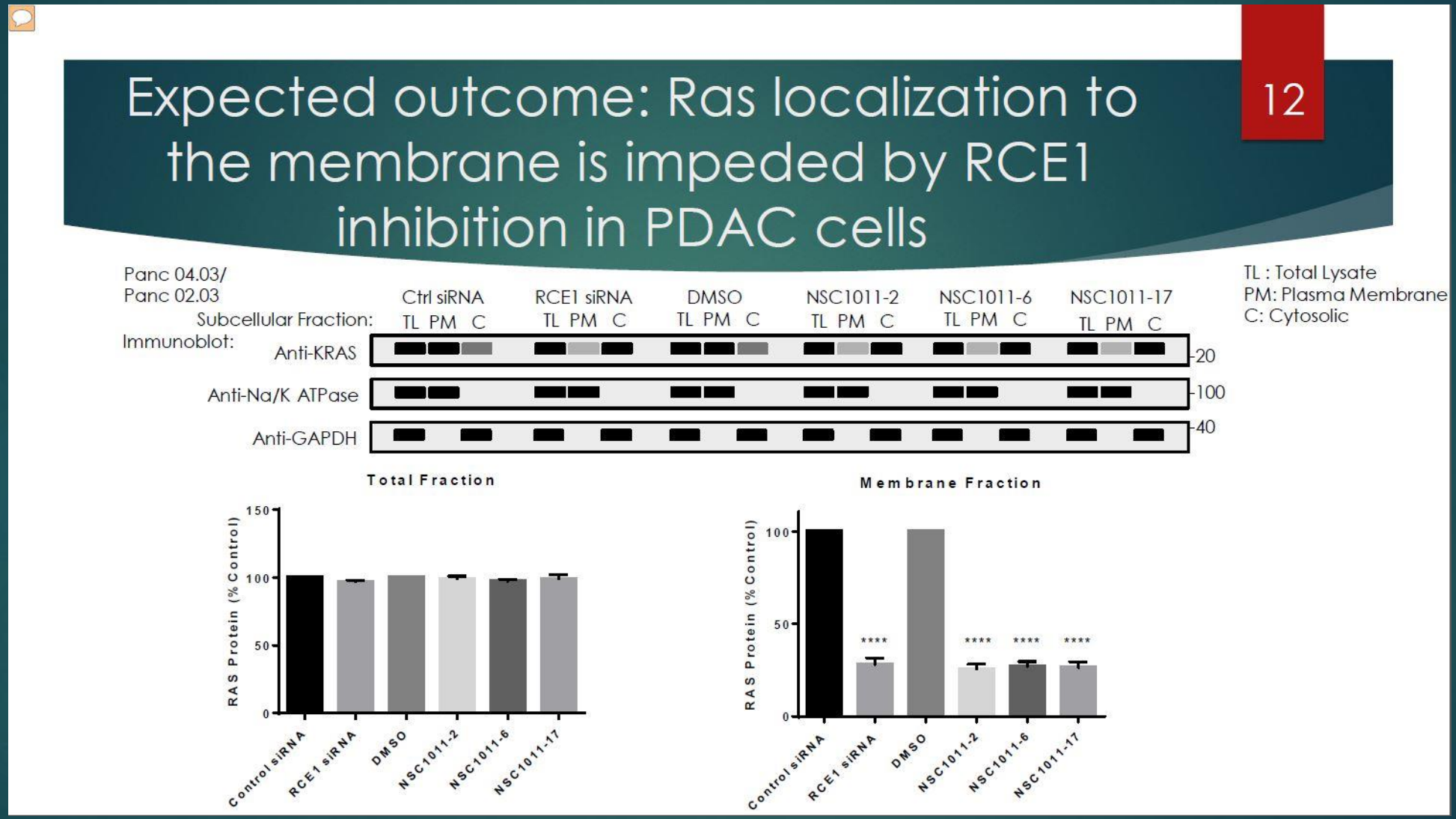
Generate schematics to illustrate hypotheses, expected experimental outcomes etc.



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Oral presentation

Prepare a presentation about 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. Briefly explain how you will approach them experimentally.
c. Research Strategy. Explain in detail the experimental approach(es) for each aim. Carefully describe expected results.

Oral presentation

Make extensive use of figures/schematics to illustrate

- Background
- Hypotheses
- Experimental strategy
- Expected outcomes (-> “preliminary data”)

Most questions from your committee will relate to…

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
5. Details of 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 proposal weaknesses

Problems with Significance

- Neither significant nor exciting new research (i.e., will not advance science)
- Lack of compelling rationale
- Incremental and low impact research

Problems with Experimental Approach

- Too much unnecessary experimental detail (e.g. buffer concentrations)
- Not enough relevant detail on experimental design
- No "preliminary data" to establish feasibility of each aim
- Lack of appropriate controls
- Not directly testing hypothesis
- Too much correlative or descriptive data
- Inadequate consideration of power
- Experiments not directed towards mechanisms
- No consideration of alternative models or hypotheses
- No consideration of potential pitfalls
- No data interpretation

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
c. **Re-take exam:** Significant 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!!**

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 (ideally, schedule a mock exam)

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