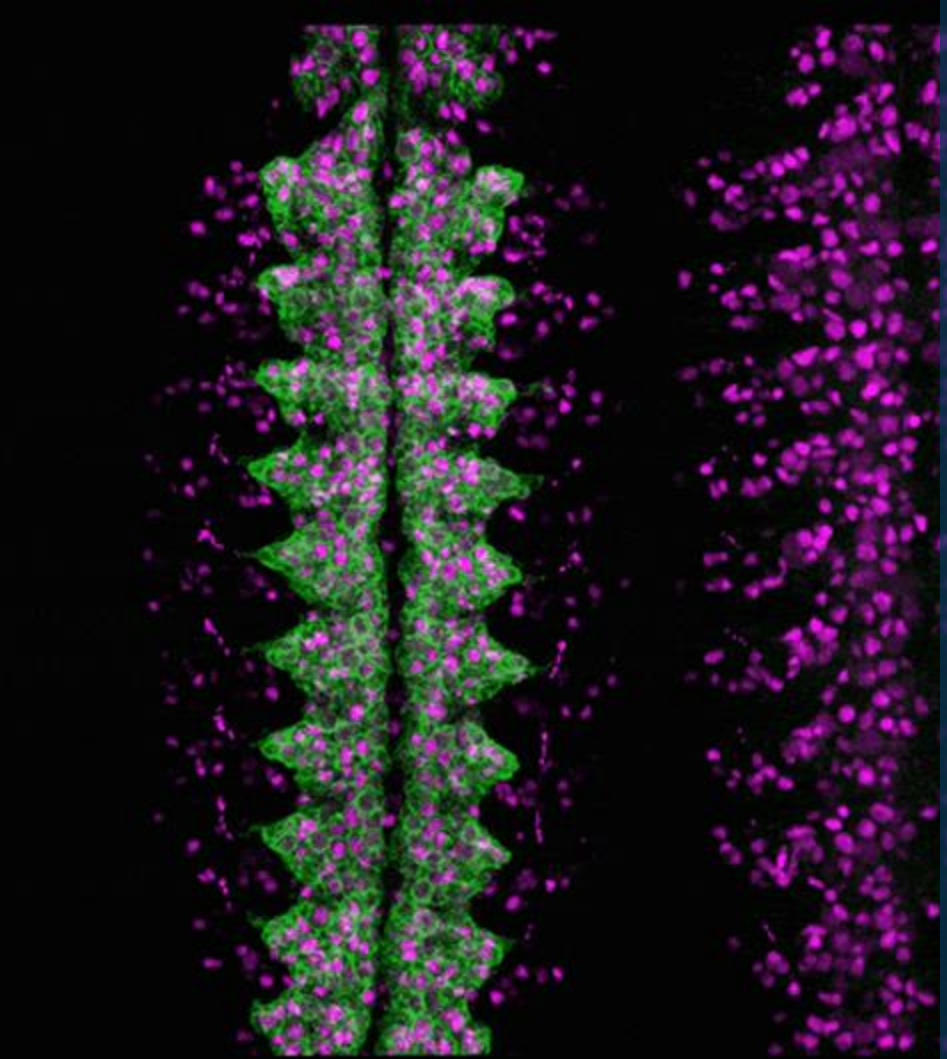


Photo credit: Tanguy Lucas/Kohwi Lab

COLUMBIA | Zuckerman Institute

Crafting Compelling Research Proposals as a New PI

Viktoriya Zhuravleva, Ph.D.
Associate Director, Strategic Research Development
Zuckerman Institute, Columbia University

Grant proposals feel like …

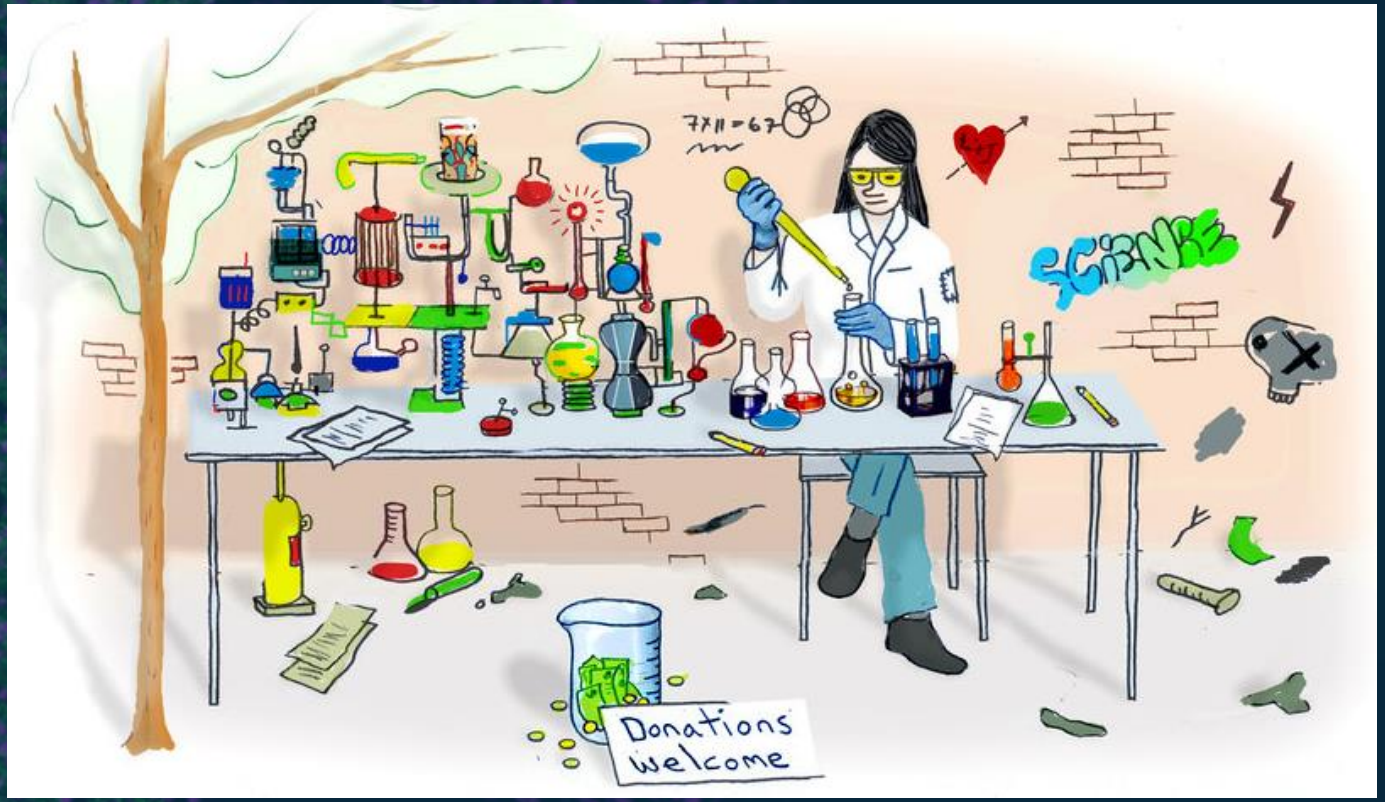


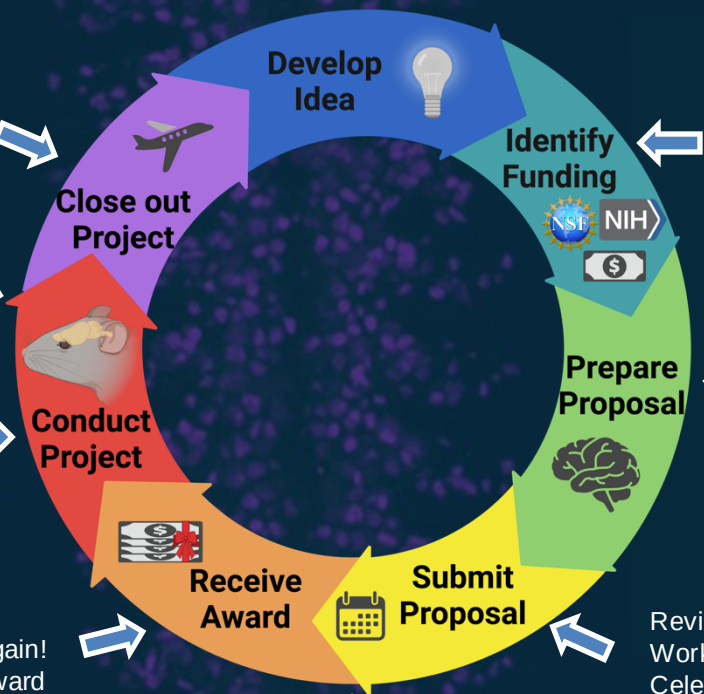
Image from JOVE: Scientific Research Funding: 10 Grant Application Sources Worth Your Time

Grant proposals are actually like …

Photo by Adam Rose/ABC

Grant life cycle

What you are doing



Setting up collaborations
Collecting feasibility data

Identifying fitting funding opportunities
Reaching out to program officers

Managing your time wisely
Thinking deeply about future work
Still collecting preliminary data (probably)
Writing (a lot)
Getting peer/mentor feedback
Working with offices at your institution

Reviewing your application
Working with appropriate offices at your institution
Celebrating
Resting

Checking your score / application outcome
Looking over reviewer comments + strategizing resubmission
Reaching out to program officer for clarity

Celebrate again!
Work with institutional offices to set up award
Hire your personnel!

Do the fun science part!
Write and publish work
Prepare annual progress reports
Keep track of finances w/institution
Plan for more grant proposals

In final 2 years of your grant, plan the renewal and/or other grants

Final progress report

What you are doing

Setting up collaborations
Collecting feasibility data

Identifying fitting funding opportunities
Reaching out to program officers

Managing your time wisely
Thinking deeply about future work
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Final progress report

Overview

1. Developing your idea
2. Tailoring your idea to the funding opportunity
3. Planning, planning, planning (and executing)
4. Crash course on NIH and NSF grant components
5. Tips for good proposal writing
6. Keeping your mind on the future

Developing your idea / sales pitch

- What makes your idea or question exciting?
- What makes you the best scientist/lab to carry out this work?
- What preliminary data do you have?
- What publications are coming out soon (from your lab)?
- What are different directions you can take your idea?
- What research projects can your lab work on simultaneously? (Mind the overlap)
- Who can you collaborate with?

Tailoring your idea to funding opportunity

"Off the rack" = might be fine, but not a great fit

- Reusing what you wrote before
- Not paying attention to the review criteria
- Not doing your research on who the reviewers might be, who the scientific board is, etc.
- Waiting until the last minute to prepare = not enough time to tailor your proposal

"Tailored" = made to fit a particular person/funder

- You *can* reuse what you wrote before
- Paying attention to the review criteria
- Doing your research on who the reviewers might be, who the scientific board is, etc.
- Giving yourself plenty of time to tweak everything to fit the funding opportunity

Tailoring your idea to funding opportunity

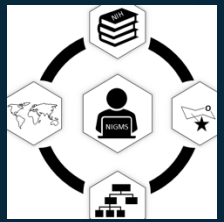
Do your research:

- What type of funder and grant is it?
  - Federal funder that is looking for specific projects that meet their priorities
  - Foundation looking to fund promising “big picture ideas”
  - Foundation that funds the person, not the project
  - Seed grant to fund high-risk, high-reward projects
  - Institutional small grants

- Read through the instructions!
  - What are the required components (take note of page/word limits)
  - What are the review criteria?
  - Budget info: How many years? What is the budget amount? Do they expect you to include special things like teaching initiatives? This will help you develop the right **scope** for your project

Contact them!

- Ask them about your project’s fit for their program
- Do you need an eligibility extension, and can you make a case for one?



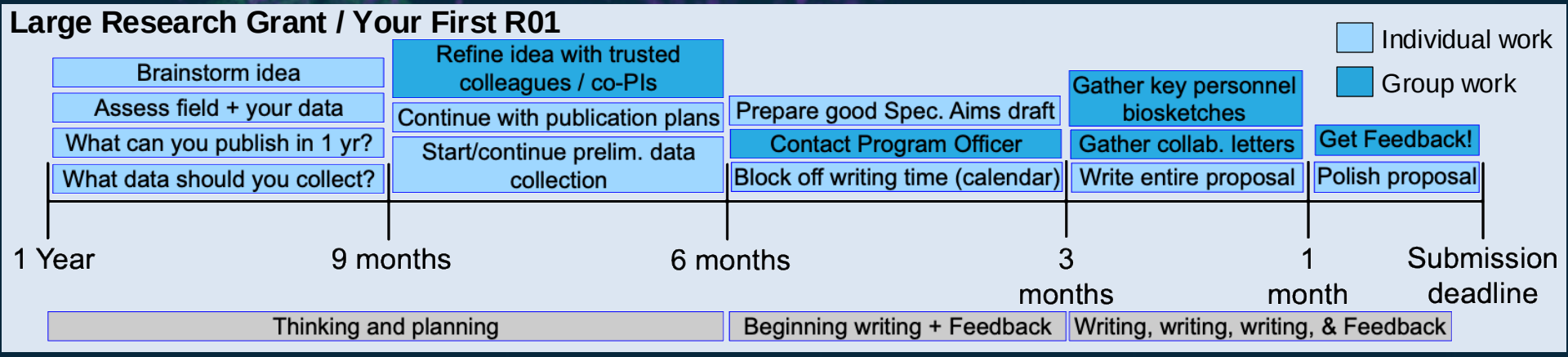
Planning, planning, planning

"If You Fail to Plan, You Are Planning to Fail"
- Benjamin Franklin

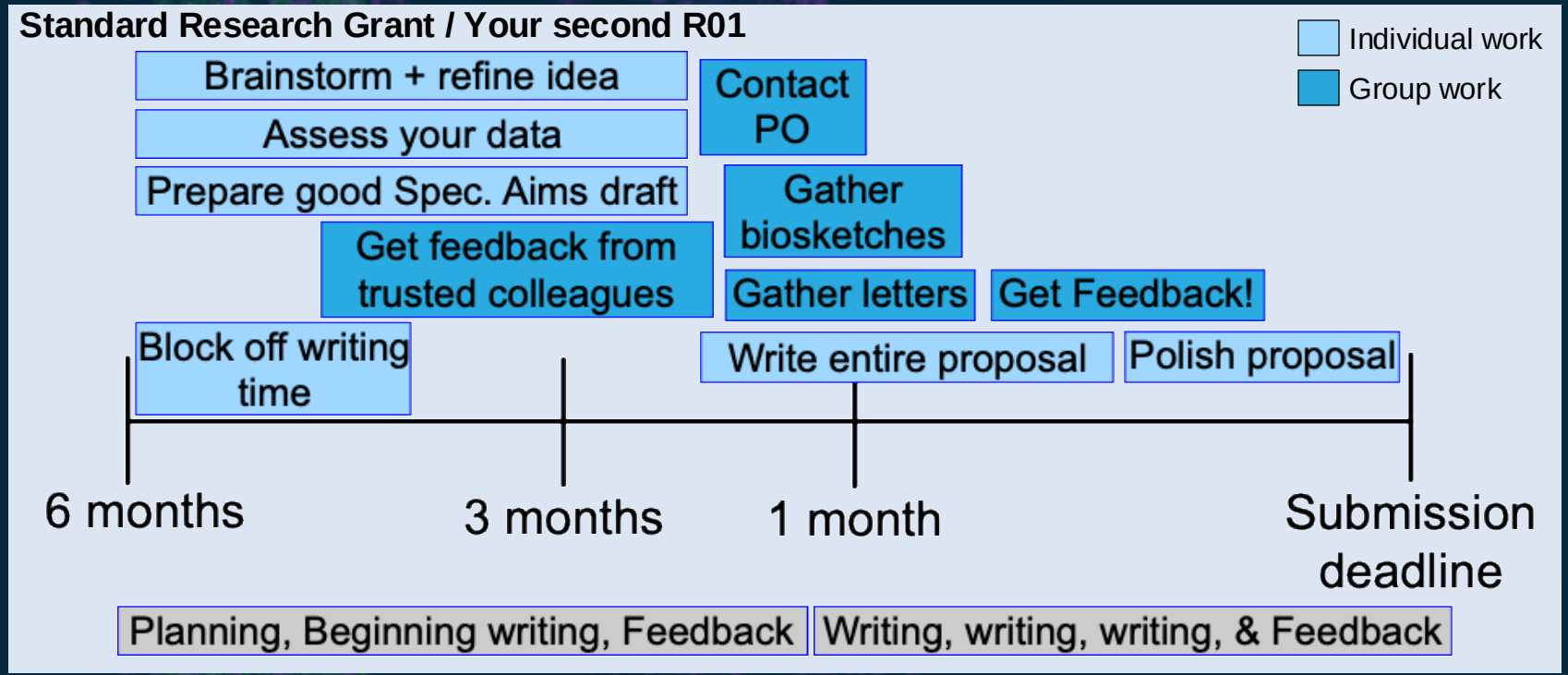
Managing your time wisely

KNOW YOURSELF

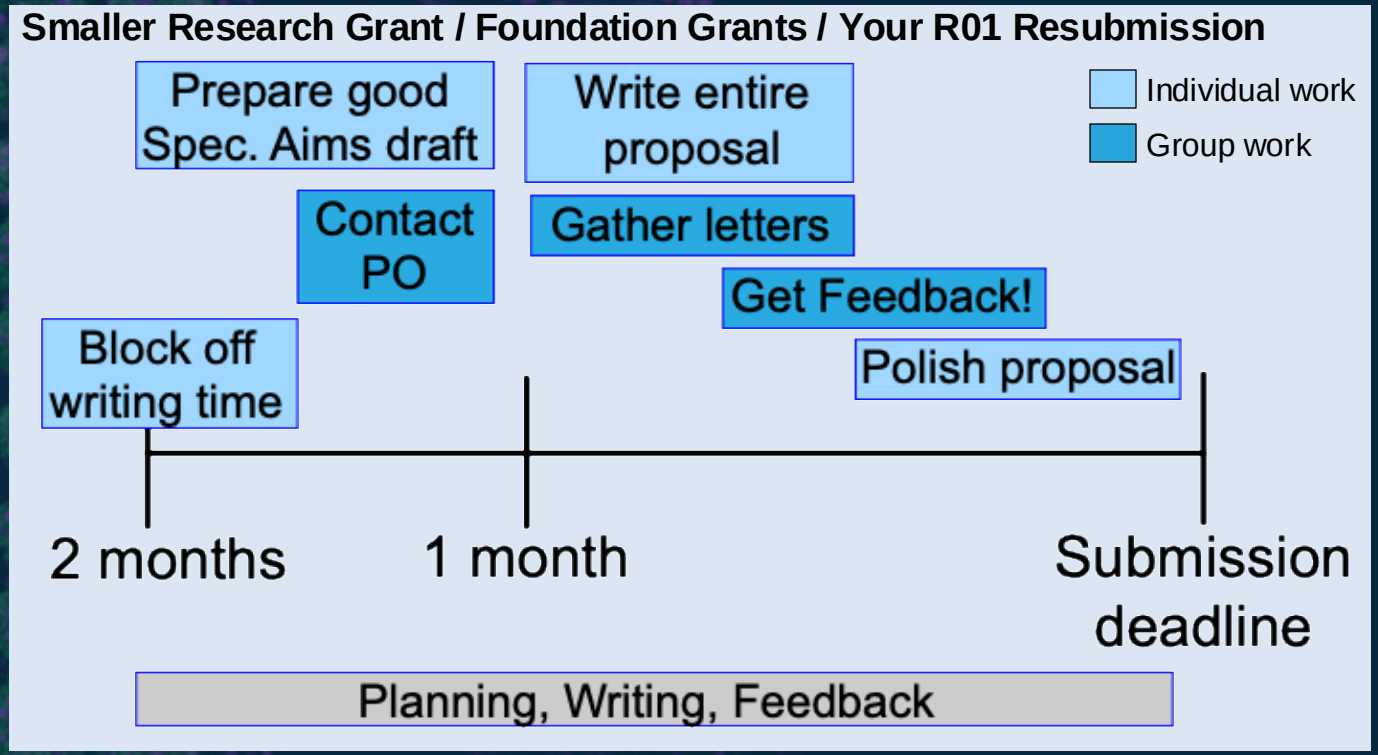
- Do you work better when you write a little every day?
- Or do you know that you aren't going to touch this until the day before the deadline? (Don't plan anything for submission day!)
- Make a *realistic* writing plan
  - Include planning what you will write about, doing more research/reading
  - Leave time for peer/mentor feedback
  - Have you already written something similar before that you can reuse and edit?



Suggested Writing Timeline



Suggested Writing Timeline



Leveraging your support network

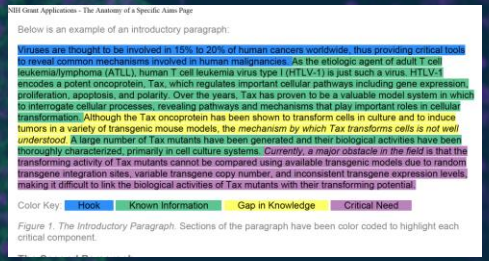
You have people to support you!

- Figure out who is there to help:
  - Departmental grants team: What is their role?
  - Colleagues/mentors: Is there anyone willing to share their previous application or advice?
  - Colleagues/mentors: Who is willing to peer review your work? (Arrange with them in advance!)

- Ask your trainees for data that you will use
  - You don't have to do everything yourself + this is a learning opportunity for the trainee

- Available resources – at your institution, online, etc.
  - What are resources you need/will use for writing?
  - Can you find examples of this type of proposal online?

Peer writing groups or workshops at your institution?



NIH Grant Applications - The Anatomy of a Specific Aims Page

Below is an example of an introductory paragraph:

Viruses are thought to be involved in 15% to 20% of human cancers worldwide, thus providing critical tools to reveal common mechanisms involved in human malignancies. As the etiologic agent of adult T cell leukemia/lymphoma (ATLL), human T cell leukemia virus type I (HTLV-1) is just such a virus. HTLV-1 encodes a potent oncoprotein, Tax, which regulates important cellular pathways including gene expression, proliferation, apoptosis, and polarity. Over the years, Tax has proven to be a valuable model system in which to interrogate cellular processes, revealing pathways and mechanisms that play important roles in cellular transformation. Although the Tax oncoprotein has been shown to transform cells in culture and to induce tumors in a variety of transgenic mouse models, the *mechanism by which Tax transforms cells is not well understood*. A large number of Tax mutants have been generated and their biological activities have been thoroughly characterized, primarily in cell culture systems. *Currently, a major obstacle in the field* is that the transforming activity of Tax mutants cannot be compared using available transgenic models due to random transgene integration sites, variable transgene copy number, and inconsistent transgene expression levels, making it difficult to link the biological activities of Tax mutants with their transforming potential.

Color Key: Hook | Known Information | Gap in Knowledge | Critical Need

Figure 1. The Introductory Paragraph. Sections of the paragraph have been color coded to highlight each critical component.

BioScience Writers: Anatomy of a Specific Aims page

Sample Applications and Documents

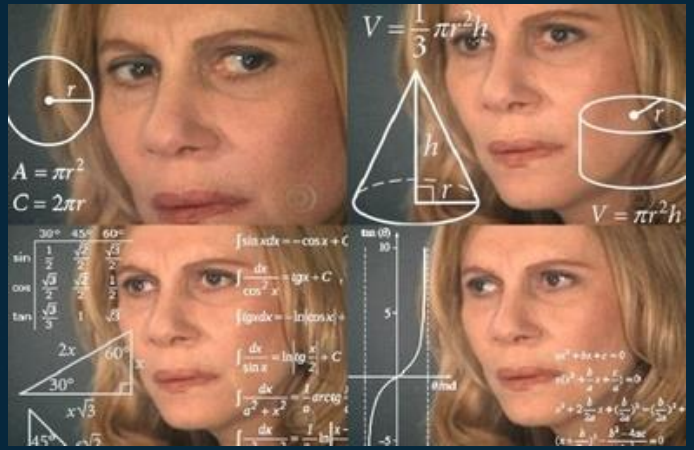
https://grants.nih.gov/grants-process/write-application/samples-applications-and-documents

Collecting data

How much data do I need?

- Varies by grant type (for smaller, private foundation grants, you don't need much)
- Goal: feasibility data for most of the techniques that you propose to use
- If your idea is risky, your preliminary data should also support your hypothesis
- Remember to add schematics as figures
- IMPORTANT: Still write your proposal, leaving space for the data to be added later.

  Don't wait until you have the perfect data to start preparing your proposal (it is rare for everything to line up perfectly anyway)



Scientists calculating how much data they need before submitting an R01

Example of caution: NIH R01 vs R21

Characteristic	Parent R21	Parent R01
Purpose	To introduce novel scientific ideas, model systems, tools, agents, targets, and technologies that have the potential to substantially advance biomedical research.	To support a discrete, specified, circumscribed project...in an area representing the investigator's specific interest and competencies, based on NIH's mission.
Duration	Up to 2 years.	Up to 5 years.
Budget	Up to $275,000 in direct costs over 2 years. At most $200,000 for any year.	No limit (But note that applicants must request Division permission to submit grants with budgets of $500,000 or higher for any year of the grant. Check our Big Grants webpage and Big Grants SOP.)
Preliminary data	Not required.	Required.
Participation	For a list of participating institutes and centers (ICs), check the parent R21 announcements on our Funding Opportunities page.	Most NIH ICs. For a list of participating ICs, check the parent R01 announcements on our Funding Opportunities page.
New Investigator benefits	Not Applicable	Higher payline than established PIs.
Renewals Allowed	No	Yes

NIH R21

What I ordered:
"Preliminary data not required"

What I got:
"Preliminary data are not required for the exploratory/developmental grant (R21) or small grant (R03) mechanisms. However, we've seen that most R21 applicants include preliminary data, and those who do typically enjoy greater success rates."

https://www.nidcd.nih.gov/funding/sample-grant-applications

human tongue and oral cavity has been reported[55-60] most recently in type II taste cells bearing GPCRs for sweet, bitter and umami stimuli and near taste buds in post-mortem circumvallate papillae and fungiform biopsies[61]. In the latter study, replicating SARS-CoV-2 was detected in type II taste cells in fungiform papillae and taste stem cell proliferation was decreased by viral infection in patient biopsies. This study, while small, suggests that direct infection of type II taste cells could explain deficits in sweet, bitter and umami taste stimuli while indirect mechanisms could impact salt and sour taste perception[61]. ACE2, TMPRSS2 and furin expression in human taste cell cultures have also been reported[56].

Whether rodent taste buds express ACE2 is currently less clear. *Ace2* was only detected in a small subset of mouse type III taste cells and lingual epithelial cells using RNA-Seq[62]. Preliminary data mining from public databases indicated more widespread *Ace2* expression in subsets of mouse type II, III and LGR-5+ taste stem cells[63]. A type I cell database was not available[63]. Though a minor part of the publication, *Ace2* was also demonstrated in mouse taste buds and non-taste epithelium[64]. ACE2 and TMPRSS immunoreactivity was reported in rat taste buds though not localized to specific types[65]. Tmprss2 was not detected in type II or III taste cells in other analyses[63].

Preliminary results. We demonstrate robust immunoreactivity for ACE2 (Fig. 2) and TMPRSS2 (Fig. 3) in K8+ taste cells from C57BL/6J mice. ACE2 and TMPRSS2 staining largely overlaps with K8, expressed by mature taste cells[66], indicating widespread expression in anterior and posterior lingual taste buds. We verified our results using lung as a positive control for ACE2 (Fig. 2C) and TMPRSS2 (Fig. 3C)[67,68]. Minimal staining was observed in negative control sections in which primary antibody was omitted (Fig. 2 and 3). Compared to lung, *Ace2* mRNA expression levels are elevated in the CV papillae and anterior lingual epithelium containing fungiform taste buds (Fig. 2D). *Tmprss2* expression levels are similar in lung, CV and anterior lingual epithelium (Fig. 3D). The reason for the difference between preliminary results and RNA-seq studies[62,63] is unclear. In Aim 1 we resolve this discrepancy with a new reporter mouse to identify even weakly-positive and transiently-expressing *Ace2*+ cells.

To facilitate the identification of *Ace2*-expressing cells and the functional study of ACE2 in the taste tissue, we have been creating in the C57BL/6J background the following three novel *Ace2* mouse models

Fig. 2 Robust ACE2 expression in mouse taste buds. ACE2 expression (green) in (**A**) circumvallate (CV) and (**B**) fungiform (FG) taste buds labeled with the taste cell marker keratin (K)8 (red). CV taste buds in white squares are shown at higher magnification on the right. ACE2 antibody was omitted in negative control sections and laser settings matched to within-assay positive tissues. (**C**) Lung positive tissue control and nega ive staining control. Results are representative of n=3-4 mice in assays performed ≥3x. (**D**) *Ace2* mRNA expression in CV papillae, anterior lingual epithelium containing fungiform taste buds and lingual mucosa. Transcript levels are expressed relative to lung which was set as 1 (n=3 mice/tissue).

Fig. 3 TMPRSS2 expression in mouse taste buds. TMPRSS2 is expressed in K8+ taste buds in (**A**) CV and (**B**) FG papilla and TMPRSS2-omitted negative control. Positive and negative staining is also shown in (**C**) lung. Results are representative of n=3-4 mice in assays performed 3x. (**E**) Tmprss2 mRNA expression levels in the CV and anterior lingual epithelium were similar to those in lung which was set as 1 (n=3 mice / tissue).

(Fig. 4 and Table 1): (1) *Ace2-P2A-CreERT2* (*Ace2*^{CE}) knock-in mice: a tamoxifen-inducible CreERT2 (CE) fusion protein is inserted in-frame to the C-terminus of endogenous ACE2, an approach that we have recently used to create *Gfi1*^{GCE} mice[69].

The self-cleaving P2A peptide allows the co-expression of CE from the endogenous *Ace2* locus without disrupting ACE2 expression and function. In Aim 1, we will use this *Ace2*^{CE} strain to activate reporter gene expression in *Ace2*-expressing cells and determine the taste cell types and primary taste structures potentially targeted by SARS-CoV-2. (2) *Ace2* conditional knockout (*Ace2*^{tmF}) mice: Exon 4 is floxed by loxP and can be deleted by Cre recombinase to cause a shift in reading-frame and the inactivation of *Ace2*. This strain allows study of *Ace2* function in tissue/cell type-specific fashion; and (3) Humanized *Ace2* knock-in (h*Ace2*-KI) mice: Human *Ace2* and SV40 polyadenylation sequences are knocked in the first *Ace2* coding exon (exon 2) and in-frame with the translation initiation Met codon at mouse *Ace2* locus. Thus, hACE2 expression is driven by the mouse endogenous *Ace2* promoter and should recapitulate the expression of endogenous ACE2. *Ace2*^{tmF} and h*Ace2*-KI mice will be used for neurophysiological studies in Aim 2. Currently, we have successfully generated germline-transmitted

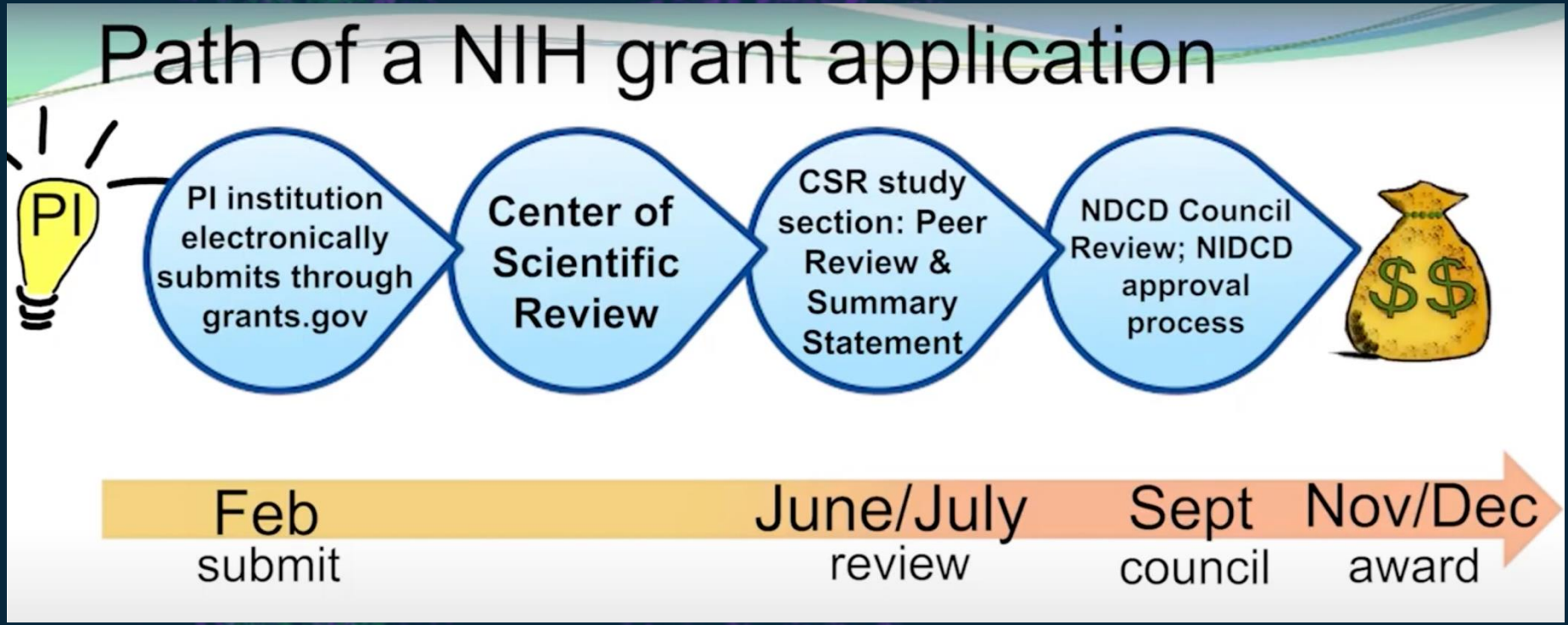
Fig. 4 Generation of novel *Ace2* mice. (**A**) h*Ace2-KI* targeting strategy and PCR genotyping confirmation of *Ace2-KI* heterozygotes. (**B**) *Ace2*^{tmF} targeting strategy and PCR genotyping confirmation of *Ace2*^{tmF} mice. (**C**) *Ace2*^{CE} targeting strategy and lineage tracing of *Ace2*-expressing cells by tamoxifen-inducible CE and Rosa26-tdTomato reporter gene. Arrowheads and arrows indicate WT and targeted *Ace2* PCR fragments, respectively.


NIH Grants Crash-Course

NIH Review Process

NIDCD = National Institute on Deafness and Other Communication Disorders

Process is the same for any Institute



NIDCD New Investigator Workshop: The Grant Application Process --https://youtu.be/47ot47nEyQg

NIH Review Process: Peer review

Overall Impact or Criterion Strength	Score	Descriptor
High	1	Exceptional
	2	Outstanding
	3	Excellent
Medium	4	Very Good
	5	Good
	6	Satisfactory
Low	7	Fair
	8	Marginal
	9	Poor

Other Designations for Final Outcome	
AB	Abstention
CF	Conflict of Interest
DF	Deferred
ND	Not Discussed
NP	Not Present
NR	Not Recommended for Further Consideration

Score-driving components

- **Factor 1 : Importance of the Research**
  - Significance, Innovation
  - Scored 1 - 9
- **Factor 2 : Rigor and Feasibility**
  - Approach (also includes Inclusion and Clinical Trial (CT) Study Timeline)
  - Scored 1 - 9
- **Factor 3 : Expertise and Resources**
  - Investigators, Environment
  - Evaluated as appropriate or gaps identified; gaps require explanation
  - Considered in overall impact; no individual score

Components that may affect score

Revised Additional Review Criteria

- Human Subject Protections (for HS and CT)
- Vertebrate Animal Protections
- Biohazards
- Resubmission/Renewal/Revisions

Components that don't affect score

- Authentication of Key Biological and/or Chemical Resources
- Budget and Period of Support

https://grants.nih.gov/policy-and-compliance/policy-topics/peer-review/simplifying-review/framework

NIH Review Criteria

Factor 1. Importance of the Research

Significance

Evaluate the importance of the proposed research in the context of current scientific challenges and opportunities, either for advancing knowledge within the field, or more broadly. Assess whether the application addresses an important gap in knowledge in the field, would solve a critical problem, or create a valuable conceptual or technical advance.

Evaluate the rationale for undertaking the study, the rigor of the scientific background for the work (e.g., prior literature and/or preliminary data) and whether the scientific background justifies the proposed study.

Innovation

Evaluate the extent to which innovation influences the importance of undertaking the proposed research. Note that while technical or conceptual innovation can influence the importance of the proposed research, a project that is not applying novel concepts or approaches may be of critical importance for the field.

Evaluate whether the proposed work applies novel concepts, methods or technologies or uses existing concepts, methods, technologies in novel ways, to enhance the overall impact of the project.

https://grants.nih.gov/policy-and-compliance/policy-topics/peer-review/simplifying-review/framework

NIH Review Criteria

Factor 2. Rigor and Feasibility

Approach

Evaluate the scientific quality of the proposed work. Evaluate the likelihood that compelling, reproducible findings will result (rigor) and assess whether the proposed studies can be done well and within the timeframes proposed (feasibility).

Rigor:

- Evaluate the potential to produce unbiased, reproducible, robust data.
- Evaluate the rigor of experimental design and whether appropriate controls are in place.
- Evaluate whether the sample size is sufficient and well-justified.
- Assess the quality of the plans for analysis, interpretation, and reporting of results.
- Evaluate whether the investigators presented adequate plans to address relevant biological variables, such as sex or age, in the design, analysis, and reporting.

For applications involving human subjects or vertebrate animals, also evaluate:

- The rigor of the intervention or study manipulation (if applicable to the study design).
- Whether outcome variables are justified.
- Whether the results will be generalizable or, in the case of a rare disease/special group, relevant to the particular subgroup.
- Whether the sample is appropriate and sufficiently diverse to address the proposed question(s).

NIH Review Criteria

Factor 2. Rigor and Feasibility

Feasibility:

- Evaluate whether the proposed approach is sound and achievable, including plans to address problems or new challenges that emerge in the work. For proposed studies in which feasibility may be less certain, evaluate whether the uncertainty is balanced by the potential for major advances.
- For applications involving human subjects, including clinical trials, evaluate the adequacy and feasibility of the plan to recruit and retain an appropriately diverse population of participants. Additionally, evaluate the likelihood of successfully achieving the proposed enrollment based on age, racial, ethnic, and sex/gender categories.
- For clinical trial applications, evaluate whether the study timeline and milestones are feasible.

https://grants.nih.gov/policy-and-compliance/policy-topics/peer-review/simplifying-review/framework

NIH Review Criteria

Factor 3. Expertise and Resources

Investigator(s)

- Evaluate whether the investigator(s) have demonstrated background, training, and expertise, as appropriate for their career stage, to conduct the proposed work.
- For Multiple Principal Investigator (MPI) applications, assess the quality of the leadership plan to facilitate coordination and collaboration.

Environment

- Evaluate whether the institutional resources are appropriate to ensure the successful execution of the proposed work.

https://grants.nih.gov/policy-and-compliance/policy-topics/peer-review/simplifying-review/framework

SUMMARY STATEMENT

PROGRAM CONTACT: [redacted] (Privileged Communication) *Release Date:* 12/19/2019
Revised Date:

Application Number: 1 R01 DC018745-01

Principal Investigator

LOMVARDAS, STAVROS

Applicant Organization: COLUMBIA UNIVERSITY HEALTH SCIENCES

Review Group: ZRG1 IFCN-U (02)
Center for Scientific Review Special Emphasis Panel
Member Conflict: Sleep, Movement, Mood and Olfaction

Meeting Date: 11/19/2019 *RFA/PA:* PA19-056
Council: JAN 2020 *PCC:* CS04
Requested Start: 04/01/2020

Project Title: Principles of zonal olfactory receptor gene expression

SRG Action: Impact Score:13 Percentile:1 #
Next Steps: Visit https://grants.nih.gov/grants/next_steps.htm
Human Subjects: 10-No human subjects involved
Animal Subjects: 30-Vertebrate animals involved - no SRG concerns noted

Project Year	Direct Costs Requested	Estimated Total Cost
1	[redacted]	[redacted]
2		
3		
4		
5		
TOTAL	[redacted]	[redacted]

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the **COMMITTEE BUDGET RECOMMENDATIONS** section.

1R01DC018745-01 Lomvardas, Stavros

RESUME AND SUMMARY OF DISCUSSION: This is an R01 application from an established investigator seeking to elucidate the mechanisms underlying the zonal expression patterns of specific olfactory receptor (OR) genes in the olfactory epithelium. The investigator will use an array of state-of-the-art tools, including Cut and Run, to establish the genomic targets of different transcription factors, HiC, deep sequencing, and 11 different mouse lines, as well as CRISPR/dCas9 approaches, to parse the epigenetic role of NFI transcription factors and examine the influence of the zonal repressive mark H3K79me3 to explicate their collective critical contributions to zonal OR expression. During the discussion, there was considerable excitement for this application. The panelists remarked on the many strengths of the application, including the powerful, innovative techniques that will be applied to the research goals, the high value of the research goals for the field, the convincing, high quality preliminary data, and the "gorgeous" experiments proposed. Further, the panelists commented on the superb investigative team. Only two weaknesses were raised by the panelists: (i) whether the proposed full conditional knockout of three independently segregating alleles, using an independent inducible driver, would yield artifacts affecting interpretation, and (ii) a concern over whether the number of replicates were sufficient for the proposed analyses and interpretations, particularly with respect to sex as a biological variable. Overall, however, these weaknesses did not significantly affect the study section's enthusiasm for this exceptional, high impact application that was considered likely to advance fundamentally our understanding of the mechanisms by which activating and repressive interchromosomal interactions incorporate feedback signals to regulate selective zonal transcription of a particular OR in the olfactory epithelium.

DESCRIPTION (provided by applicant): The monogenic, monoallelic, and seemingly stochastic transcriptional choice of one out of > 1000 olfactory receptor (OR) genes remained elusive for decades after the discovery of the largest mammalian gene family. However, in the past few years we obtained significant understanding on the molecular underpinnings of this enigmatic gene regulatory process. Specifically, we showed that OR gene clusters become heterochromatic at the early stages of olfactory sensory neuron (OSN) differentiation and then they aggregate in distinct nuclear compartments that assure their stable repression. As a result of this interchromosomal convergence, intergenic OR enhancers (known as Greek Islands) that are found in most OR gene clusters come in close nuclear proximity and form a multi-chromosomal super-enhancer that in each OSN associates with the transcriptionally active OR allele. The formation of the Greek Island hub is dependent upon the recruitment of the adaptor protein Ldb1, which is essential for the stable interchromosomal interactions between Greek Islands and for OR transcription. This intricate network of activating and repressive interchromosomal interactions, together with a feedback signal elicited by the expression of the chosen OR, likely generate the regulatory framework for transcriptional singularity. However, what remains

CRITIQUE 1

Significance: 1
Investigator(s): 1
Innovation: 1
Approach: 1
Environment: 1

Overall Impact: The experimental program addressed by this application is focused on how olfactory sensory neurons express different odorant receptors in different regions of the olfactory epithelium. Recent studies, largely from the Principal Investigator's laboratory, have elucidated a complex multi enhancer complex that activates transcription from singular OR loci, followed by a feedback mechanism that helps to keep all other OR loci silent. In this application very promising preliminary studies suggest that the transcription factors NFIA, B, and X contribute to both the selective expression of olfactory epithelium Zone 5 ORs and the repression of Zone 2 and 3 ORs. The Aims of this application are designed to better understand NFIs' roles in zonal OR expression. A triple deletion of all three NFIs perturbs zonal OR expression. In Aim 1, each NFI will be tested individually for its ability to perturb expression through loss of function experiments, and its sufficiency for perturbation through gain of function experiments. This is worthwhile as different NFI factors may have specialized roles. Aim 2 addresses the mechanisms through which NFIs regulate zonal OR expression. In one series of experiments their direct binding sites will be probed using a method named 'cut and run'. In a second series of experiments interchromosomal contacts will be assayed using HiC in normal and NSI mutant OSNs collected from specific zones of the epithelium. One potential outcome is that zone appropriate OR to OR enhancer contacts will be detected, and that these will be disrupted in some of the knockout animals produced in Aim1. In a third series of experiments a candidate suppressive epigenetic mark, H3K79me3, will be tested for its contribution to zonal OR expression with an OSN knockout of the enzyme that produces it, and by determining whether any of the NFIs contribute to its deposition in zones that would otherwise be available for OR expression.

This is an outstanding application in every way. The biological problem it addresses is fundamental to understanding olfactory system function, it builds upon the seminal contributions the Principal Investigator has already made towards understanding OR gene expression, its preliminary findings are extensive, informative and provide a strong basis for the proposed experiments, and the experimental approach is innovative, powerful, and will almost certainly yield exciting results.

1. Significance
Strengths

- Understanding the mechanisms of the zonal expression patterns of specific OR genes in the olfactory epithelium is fundamental to understanding the development and function of the system. This is largely unexplored territory and an advance would have the potential to be of more general developmental interest.

Weaknesses

- None noted.

Protections for Human Subjects
Not Applicable (No Human Subjects)

Vertebrate Animals
Acceptable

Biohazards
Acceptable (No Biohazards)

Budget and Period of Support
Recommend as Requested

CRITIQUE 2

Significance: 2
Investigator(s): 1
Innovation: 2
Approach: 2
Environment: 1

Overall Impact: The intellectual formulation of this application places the details of transcriptional regulation of zonally restricted odorant receptor expression into a very clear and compelling biological framework. The identification of a family of transcription factors, the NFIs, that may be key determinants of expression of multiple genes within a single zone provides a starting point to discern several mechanistic dimensions of patterned gene expression. Some concern is raised by the multi-allelic/ conditional recombination approaches necessary to test some of the hypotheses and the potential for low yield from these experiments and also genetic artifacts that reflect the technique but nevertheless influence execution and interpretation of the data. One wishes that the Principal Investigator had dealt more with this technical issue.

1. Significance
Strengths

- This application considers the mechanism and biological significance of zone restricted expression of odorant receptors based upon its transcriptional and chromosomal regulation and its expression as an example of patterned gene expression.
- The application places the problem of odorant receptor gene expression, and by extension coordinated expression of multiple genes in a distinct domain, in the appropriate context—how chromatin confirmation/architecture may or may not regulate this critical feature of morphogenesis and tissue architecture.

Weaknesses

- The application focuses on the mechanism of transcriptional control for patterning, but does not discuss whether the experiments and potential results address issues of the functional/ behavioral consequences of this developmental/cellular regulation.

2. Investigator(s)

NIH grant components: R01

Component	What is it?	Page limit	Who should prepare?
Title	Proposal title (public if funded)	200 characters	You
Summary/Abstract	Proposal abstract (public if funded)	30 lines of text	You
Project narrative	Public health relevance of the proposal (public if funded)	3 sentences	You
Specific Aims	1-page description of the research project	1 page	You
Research Strategy	Full description of the research project	12 pages	You
Bibliography/References	References that support your research project; those used in the research strategy or any other place in your application	Unlimited	You
Facilities & Other Resources	Describes your lab, the scientific environment of your institution, relevant core facilities available to you; biohazards	Unlimited	You + institutional information (work with grants office/find online)
Equipment	List and/or brief description of major equipment available in your lab	Unlimited	You

NIH grant components: R01

Component	What is it?	Page limit	Who should prepare?
Resource Sharing Plan (if applicable)	Describes plans for sharing model organisms and/or research tools with the broader scientific community	Unlimited	You
Data Management and Sharing Plan	Describes the types of data that will be generated; the tools, software, or code needed to process the data; standards; and the repository where data will be made publicly available	2 pages (recommended)	You
Biosketches	A 5-page description of you as an investigator. The personal statement should be tailored to each application.	5 pages (per key personnel)	You + each person prepares their own biosketch
Letters of support	Each letter specifies what that collaborator, consultant, or other significant contributor will do for the project	~1-2 pages per letter (suggested)	Collaborators/consultants must sign the letter
Vertebrate animals (if applicable)	Describes procedures, justification for using that type of animal, and interventions against pain and distress;	Unlimited	You

NIH grant components: R01

Component	What is it?	Page limit	Who should prepare?
Use of human specimens or data (if applicable)	Provides an explanation for any use of human specimens and/or data not considered to be human subjects research. Importantly, this page specifies why the data is not considered human subjects research (who has access to identifying data?)	Unlimited	You
Human subjects forms (if applicable)	Information about human subjects, clinical, or clinical trials research, including study population characteristics, protection and monitoring plans, and a protocol synopsis. ● Inclusion of Individuals Across the Lifespan ● Inclusion of Women and Minorities ● Recruitment and retention plan ● Study Timeline (Optional for non-clinical trial studies) ● Inclusion Enrollment Report (table) ● Protection of human subjects		
Authentication of key biological and/or chemical resources (if applicable)	Briefly describes methods to ensure the identity and validity of key biological and/or chemical resources used in the proposed studies	1 page (suggested)	You

NIH grant components: R01

Component	What is it?	Page limit	Who should prepare?
Detailed budget	Costs requested for the proposed project. Must be specified for each appropriate cost category, e.g., personnel, equipment, supplies, and other expenses, and not exceed the maximum direct costs allowed for the project type (always check NOFO)	Entered in portal	You + grants team
Budget justification	Provides the additional information requested in each budget category and any other information the applicant wishes to submit to support the budget request. If you have a quote(s), you may include it here. The following/ budget categories must be justified, where applicable: equipment, travel, participant/trainee support, and other direct cost categories.	Unlimited	You

Other potential NIH grant components

Component	What is it?	Page limit	Who should prepare?
Multiple PD/PI Leadership plan (for proposals with multiple PIs)	A rationale for choosing a multiple PD/PI approach, the governance and organizational structure of the leadership team, communication plans, conflict resolution.	Unlimited	You + other PI(s)
Foreign justification (required if there are international collaborators, PIs, etc)	Describe special resources or characteristics of the research project (e.g., human subjects, animals, disease, equipment, and techniques), including the reasons why the facilities or other aspects of the proposed project are more appropriate than a domestic setting.	Unlimited	You + international collaborator(s)
Consortium justification	If any PIs or collaborators are at another institution, you must have sub-award to that institution (the money will be sent there after it is received by your home institution). Explain the programmatic, fiscal, and administrative arrangements to be made between the applicant organization and the consortium organization(s).	Unlimited	You
Introduction (for resubmissions only)	Summarizes substantial additions, deletions, and changes to the application and responds to the issues and criticism raised in the summary statement	1 page	You
Progress report publication list (for renewals only)	Attach a report of publications, manuscripts accepted for publication, patents, and other items resulting from last funding cycle.	Unlimited	You


NSF Grants Crash-Course

NSF Review Process

Individual or Panel review, usually a mix of both

Individual:
- Excellent
- Very Good
- Good
- Fair
- Poor

Panel:
- Outstanding
- High
- Medium
- Low
- Not Competitive

NSF's merit review process determines which research has the greatest potential - https://youtu.be/WMoGdIEgy5o

NSF Review Process

Panel Summary:
A study of naturally occurring granitic melts of high-grade metamorphic rocks designed to understand the mechanisms of melt production, transfer and emplacement. Results will be useful in improving our understanding of melting processes of continental crust by observing small-scale macroscopic features in the field.

Intellectual Merit
Advancing knowledge

This study will consist of detailed, outcrop-scale field and geochemical studies utilizing teams of undergraduate students to map, measure, sample, and carry out analyses. This is a topic about which much is assumed, but about which little is known. The PIs have developed an important method by which field and geochemical data can be used to address leucosome/granite relationships. The pnael rated this RUI proposals very highly. The research plan is well constructed and carefully planned.

Creative and Original

These types of observations have been made for more than a century, but what is original is the attempt to match the macro-scopic observations with geochemical constraints.

Broader Impacts
Advance discovery while promoting teaching?

There will be intensive involvement of undergraduates which is carefully thought out and well-organized. The project will be a very enriching learning experience for undergraduates in the basics of field intensive research.

Summary: The panel recommends support for this proposal, if funds are available.

Panel Recommendation: Fund If Possible

https://faculty.buffalostate.edu/solargs/solar/NSF-EAR0510726/EAR0510726reviews.html

Reviewer #2 **Very Good**

REVIEW:

What is the intellectual merit of the proposed activity?

This proposal addresses a number of fundamental problems for our understanding of the linkages between melt generation, collection, and ascent. The PIs propose to attack these problems through numerous detailed field, petrographic, and geochemical studies of migmatites and potentially associated plutons at critical localities in the Central Maine metamorphic belt. The field studies will focus on the geometries of migmatites and related(?) plutons, and will be integrated with the petrographic, geochemical, and geochronological research. Much of the research will be carried out by undergraduate students under the close supervision of the PIs.

The proposal has a number of strengths. It raises important questions about migmatites and the flow of melt. Solar and Tomascak are well qualified to carry out the research and have a solid track record of publishing their data. They combine expertise in field-oriented structure and metamorphic petrology (Solar) with isotope geochemistry (Tomascak). Both have worked extensively on the migmatites and plutons of the central Maine metamorphic belt.

Despite these strong points, I have several concerns with the proposal.
1. This project builds on the earlier work of the PIs (particularly Solar's Ph.D. thesis) with Mike Brown at the University of Maryland. This research has led to numerous quality papers on the interrelationships of migmatites, plutons, and deformation in the region. From the proposal, it is not clear to me that the planned research will involve new avenues of inquiry, but rather will continue the same types of study of a larger area. Thus, it will probably lead to a better understanding of this specific migmatite belt, but it is less likely to result in any significant new insights into some of the fundamental questions on migmatites raised in the proposal.

2. The ages of migmatite leucosome crystallization versus pluton crystallization are critical for interpretations of melt collection, etc., as pointed out by the PIs. It is not clear that the PIs will be able to provide sufficiently precise geochronological data to test several of the major questions addressed in the proposal. Leucogranites are commonly difficult to date because of inheritance, and it would have been helpful if the PIs had more fully explored this and other issues in the proposal. The isotope lab at Syracuse is of high quality, but it is not clear that the PI will be able to devote the type of effort needed (CL imaging, numerous single grain fractions, etc.) to get the necessary age precision. A letter of support from Sampson (Syracuse) on the use of the lab was alluded to in the proposal, but I could not find it on fastlane.

3. I have concerns that the outcrops and topographic relief are not of sufficient quality to answer some of the questions posed by the PIs on the 3-D geometry of melt bodies. The stream exposures worked on by Solar are sufficient for some studies, but their lateral continuity and the relief are perhaps too limited.

The budget is very reasonable. I'd encourage the PIs to ask for buyout money to enable them to have more time to supervise the students.

What are the broader impacts of the proposed activity?

The strength of this proposal is the undergraduate research component. The PIs, and particularly Solar, have an exemplary record of mentoring undergraduate students on meaningful research projects. This is particularly noteworthy because Buffalo State is a commuter campus where it is commonly difficult for students to be involved in any activities beyond their course work and especially independent research. The PIs have also provided an unusually thorough plan for the undergraduate projects and have nicely displayed how the different student research projects will be integrated.

Summary Statement

This proposal focuses on important issues in melt generation, collection and flow in migmatites and will involve numerous undergraduate students in research. My overall rating is "very good", which I would break down into "good" for the intellectual merit and "excellent" for the broader impact.

NSF Merit Review Criteria

Intellectual Merit

The potential for the proposed project to advance knowledge and understanding within its own field or across different fields.

What is the potential for the proposed activity to:

- Advance knowledge and understanding within its own field or across different fields (Intellectual Merit);
- To what extent do the proposed activities suggest and explore creative, original, or potentially transformative concepts?
- Is the plan for carrying out the proposed activities well-reasoned, well-organized, and based on a sound rationale? Does the plan incorporate a mechanism to assess success?
- How well qualified is the individual, team, or organization to conduct the proposed activities?
- Are there adequate resources available to the PI (either at the home organization or through collaborations) to carry out the proposed activities?

NSF Merit Review Criteria

Broader Impacts

The potential for the proposed project to benefit society and contribute to the achievement of specific, desired societal outcomes.

- What is the potential for the proposed activity to benefit society or advance desired societal outcomes?
- To what extent do the proposed activities suggest and explore creative, original or potentially transformative concepts?
- Is the plan for carrying out the proposed activities well-reasoned, well-organized and based on sound rationale? Does the plan incorporate a mechanism to assess success?
- How well qualified is the individual, team or institution to conduct the proposed activities?
- Are there adequate resources available to the principal investigator (either at the home institution or through collaborations) to carry out the proposed activities?

Your project's broader impact activities don't need to be a separate add-on to your research. Your project can have broader impacts through:

- Your research activities.
- Activities directly related to your research.
- Activities that are supported by, but complementary to, your research activities.

NSF Broader Impacts

Suggested areas provided by NSF include, but are not limited to:

- Full participation of women, persons with disabilities, and underrepresented minorities in science, technology, engineering, and mathematics (STEM)
- Improved STEM education and educator development at any level
- Increased public scientific literacy and public engagement with science and technology
- Improved well-being of individuals in society
- Development of a diverse, globally competitive STEM workforce
- Increased partnerships between academia, industry, and others
- Improved national security
- Increased economic competitiveness of the U.S.
- Use of science and technology to inform public policy
- Enhanced infrastructure for research and education

ARIS
Advancing Research Impact in Society

Tools to help you develop broader impacts: https://researchinsociety.org/broader-impacts/
Broader Impacts wizard: https://aris.marine.rutgers.edu/wizard/intro.php

NSF grant components: research grants

Component	What is it?	Page limit	Who should prepare?
Cover sheet	NSF Unit of consideration Proposal title (public if funded)		You
Project summary	Summary of the proposed project; consists of an overview, a statement on the intellectual merit, and a statement on the broader impacts of the proposed activity.	1 page	You
Project description	Full description of the research project; should include intellectual merit AND broader impacts sections	15 pages	You
References Cited	Full references cited	Unlimited	You
Facilities, Equipment, & Other Resources	Describes your lab (including major equipment), the scientific environment of your institution, relevant core facilities available to you; biohazards	Unlimited	You + institutional information (work with grants office/find online)
Biosketches	Biosketch prepared using SciENcv; Includes: Identifying Information, Organization and Location, Professional Preparation, Appointments and Positions - Reverse chronological order by start date, Products, Certification	Unlimited	You + each person prepares and certifies their own biosketch

NSF grant components: research grants

Component	What is it?	Page limit	Who should prepare?
Synergistic activities	A list of up to five distinct examples that demonstrate the broader impact of your professional and scholarly activities, focusing on the creation, integration and transfer of knowledge.	1 page	You
Current and Pending Support	Current and pending other grant support. Can be produced using SciENcv	Unlimited	You
Budget	Costs requested for the proposed project. Must be specified for each appropriate cost category, e.g., personnel, equipment, supplies, and other expenses, and not exceed the maximum direct costs allowed for the project type (always check NOFO)	Entered in portal	You + grants team
Budget justification	The budget justification must be no more than five pages per proposal. The amounts for each budget line item requested must be documented and justified in the budget justification	5 pages	You
Letters of collaboration	Letters of collaboration should be limited to stating the intent to collaborate and should not contain endorsements or evaluation of the proposed project.	1 page per letter	Must be signed by collaborators
Mentoring plan	A description of the mentoring activities that will be provided for postdocs and/or grad students.	1 page	You

NSF grant components: research grants

Component	What is it?	Page limit	Who should prepare?
Data management and sharing plan	Types of data, standards to be used, policies for access and sharing, plans for archiving data, samples, and other research products.	2 pages	You
Collaborators & Other Affiliations	Information regarding collaborators and other affiliations (COA) must be separately provided for each individual identified as a senior/key person on the project.	Unlimited	You

Tips for good grant writing

Most importantly …

To be a good writer, you do not need to have special talents or wait for creativity to strike. A writer is someone who writes consistently.

<u>Writing is a 3-step process:</u>

1. Planning (what you will write *and when*)
2. Writing (even if you think it's garbage)
3. Editing (for clarity *and* content)

Try not to take it personally if your proposal isn't funded. <u>Revise and resubmit</u>.

Proposal writing: non-negotiables

Address the review criteria (consider your audience)

Remember that this is like a sales pitch for your excellent idea!

Significance + Background (research proposal)

- What is your project about? Focus ONLY on the main theme.
- Why is your idea important? (In the context of the field)
- What gap in scientific knowledge will your work fill?
  - Get to the main point quickly!
  - Make your broad overarching goal obvious within the first paragraph or two
- Keep it linear! Include only the background information that the reader absolutely needs to know.

Significance

Pattern formation is a fascinating phenomenon that governs fundamental developmental processes in plants and animals, vertebrates and invertebrates[7-9]. From the classic theoretical predictions on the chemical basis of morphogenesis[10] to the seminal demonstration of the genetic control of segmentation in drosophila[11,12]; and from the elucidation of motor neuron pool identity along the spinal cord axes[13] to the explanation of photoreceptor patterning in invertebrate omatidia[14], developmental biologists have made strides in understanding various forms of patterning. However, patterning in the main olfactory epithelium (MOE), as manifested by the zonal expression of olfactory receptor (OR) genes[5,6], remains intractable. This constitutes a glaring gap of knowledge for sensory biology for two main reasons: First, we cannot fully comprehend how an OR is chosen if we do not decipher why this choice is restricted to a zonal OR repertoire. The realization that OR gene choice is influenced by the position of an OSN begs the fundamental question: what mechanisms impose deterministic restrictions to an otherwise stochastic process? This question becomes even more pressing upon our recent discovery that OR gene choice is mediated by a multi-chromosomal enhancer hub that interacts in *trans* with the active OR allele, regardless of the zonal identity of the chosen OR[15,16]. Therefore, determining how this zonally invariant enhancer hub exhibits differential affinity for distinct OR combinations along the 5 zones, may provide valuable insight into the mechanism of OR choice itself.

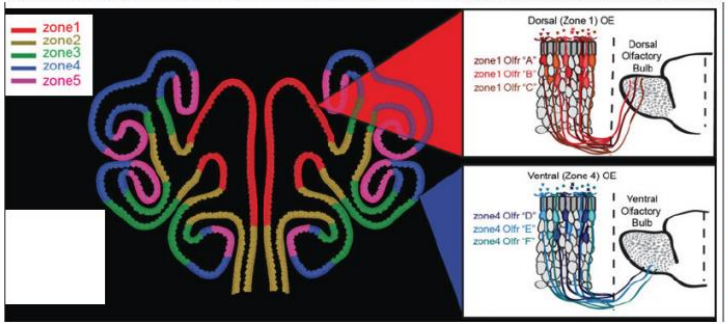


Figure1: The 5 major zones of OR gene expression. Coronal MOE section depicting the 5 zones (left) and the projections of zonal OSNs to the olfactory bulb.

Second, without knowing the regulatory mechanism that orchestrate zonal OR expression, we cannot address the biological significance of this expression pattern. The conservation of zonal OR expression in most vertebrates suggests that spatial restrictions of OR gene choice is selected through evolution. The fact that zonal coordinates are preserved in the olfactory bulb raises possible implications in olfactory perception[17]. For example, there is evidence that dorsal glomeruli receiving input from zone I respond to odors associated with innate fear responses[18]. Thus, although most odorants lack strong innate valance[19,20] and activate dispersed glomeruli[21], zonal boundaries may influence odor perception. Even if zonal OR expression is not contributing to odor perception, it may have different functional roles. For example, zonal restrictions may facilitate axon fasciculation and convergence of like axons

Proposal writing: non-negotiables

Significance + Background (research proposal)

- What work have you/your lab done along this main theme?

Significance

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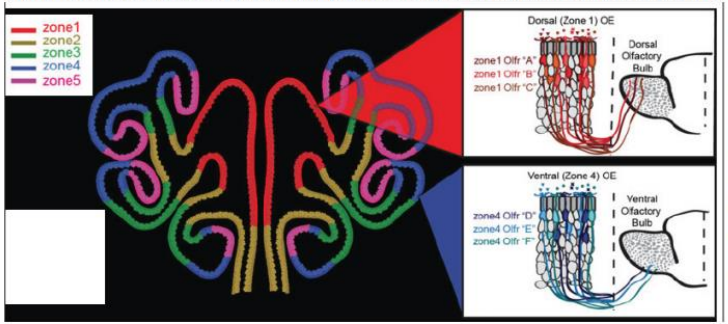

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Proposal writing: non-negotiables

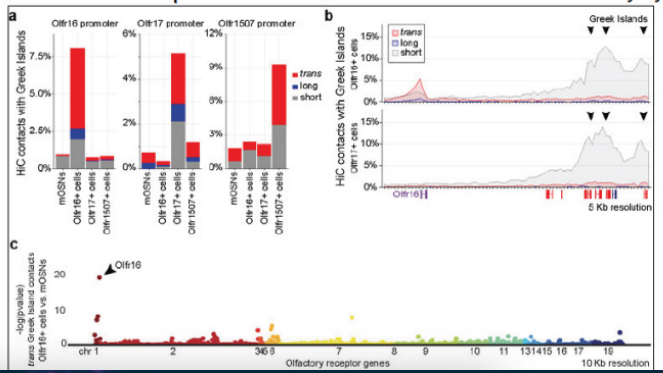
Significance + Background (research proposal)

- What work have you/your lab done along this main theme?
- If successful, what will this project contribute to the field?

simultaneously with the activating enhancer hub, violating the "one receptor per neuron rule". Therefore, our work is creating the foundation for a future experimental interrogation of the role of zones in olfactory coding, OSN targeting, and singular OR choice.

In addition to its importance for olfaction, this project has general significance for developmental biology and for the emerging field of nuclear architecture. The role of long-range and *trans* genomic interactions in developmental patterning is starting to be appreciated in numerous fields. In developing cardiomyocytes, a multi-chromosomal gene hub coordinates the alternative splicing of cardiomyocyte-specific genes[22], promoting cardiogenesis. Further, photoreceptor gene choice in flies[23], Th1/Th2 lymphocyte differentiation in mice[24], and X-chromosome inactivation in humans[25,26] are orchestrated by interchromosomal contacts, highlighting the diversity of cell specification processes and organisms utilizing this mechanism. Super-enhancers (SEs) tend to form interchromosomal compartments, likely promoting transcriptional

robbustness[27,28]. SPRITE, an alternative to HiC, revealed multi-chromosomal interactions organized by nuclear RNA speckles[29], and similarly, the non-coding RNA Firre promotes interchromosomal interactions[30,31]. In the case of human antiviral responses, multi-chromosomal transcription factor "repositories" appear essential for the activation of INFβ[32,33]. Multi-chromosomal interactions are also used by trypanosome[34] and plasmodium[35,36] during the process of antigenic variation[34,37]. Therefore, deciphering mechanisms that regulate the formation of interchromosomal interactions across the axes of the MOE will have general impact in understanding 3D genome organization, especially since NFI proteins regulate a plethora of developmental processes[38-44].



Finally, there is potential translational significance of our proposal. Recent experiments revealed the feasibility of cell transplantation experiments in

Proposal writing: non-negotiables

Significance + Background (research proposal)

- What work have you/your lab done along this main theme?
- If successful, what will this project contribute to the field?

Innovation (research proposal)

- How is your proposal innovative technically and conceptually?
  - Conceptual innovation: What novel concepts are being tested in the proposal? How will the findings from the proposal advance the field?
  - Technical innovation: What novel techniques are developed for this proposal? How will they advance the rest of the field? And/Or what established techniques are used in new ways for the project?

Innovation

Our proposal is conceptually and technically innovative. On the conceptual front we tackle a problem that has not been solved in any model organism, thus, by default, we break new ground. The correlation between formation of zone-dependent interchromosomal interactions in OSN progenitors and zonal transcriptional restrictions in mature OSNs (mOSNs) suggests that we uncovered a completely novel mechanism for establishing epigenetic memory during developmental patterning. In this note, this is the first demonstration that interchromosomal interactions can be subject to deterministic spatial restrictions that change along the dorso-ventral axis of an organ in a reproducible and stereotypic fashion. Until now such super long range genomic interactions were considered highly variable and appropriate only for stochastic transcriptional outcomes[48]. Moreover, this is the first ever demonstration of a role of NFI proteins in the regulation of nuclear architecture and in establishing epigenetic memory, opening new routes for the study of these protein at the context of cell type specification. Finally, gradients of H3K79me3 along developmental axes represent a completely novel finding, adding a new potential function of this histone modification in patterning.

From the technical standpoint we utilize cutting edge genomic approaches, such as *in situ* HiC and Cut&Run[49], which are applied in zonally dissected, FAC-sorted populations from mice carrying numerous genetically modified alleles. To our knowledge, we are the first to combine these state-of-the-art genomic approaches with sophisticated and complex genetics in any model organism. Thus, we approach an elusive and fundamental biological problem with a multi-disciplinary approach that deploys state of the art techniques and is poised to produce novel regulatory principles with general impact in developmental biology.

Proposal writing: non-negotiables

Investigator and Environment (usually captured in other components besides the research proposal)

- Provide evidence that you are the best investigator for this work
  - Use your past work (that the proposal builds off of) to showcase that you do impactful and rigorous work
  - Emphasize your accomplishments throughout your career (awards, papers, grants, etc)
- Highlight what an excellent environment you are in for carrying out the work

A. Personal Statement

My research program aims to understand the molecular mechanisms that generate the astounding diveristy of cell types that characterise the mammalian nervous system. As a model system for our studies we use the olfactory system and the study of the epigenetic mechanisms regulating olfactory receptor (OR) gene choice. OR genes compose the largest mammalian gene family consisted of >1000 members. These genes are expressed in a a mutually exclusive fashion, in such a way, that only one OR allele is expressed in each olfactory sensory neuron. In our effort to understand this extreme mode of stochastic gene expression we uncovered novel genetic and epigenetic principles that are likely deployed by other neuronal populations. For example, we previously showed that OR translation activates the unfolded protein response pathway (UPR) toward the generation of a feedback signal that prevents the expression of other OR alleles by silencing Lsd1. Moreover, we showed that the singularity of OR gene choice is orchestrated by an intricate network of interchromosomal interactions that culminates in the formation of a singular, multienhancer complex over the transcriptionally active OR. Our published work clearly indicates our expertise in genetics, epigenetics, nuclear architecture, gene regulation and developmental biology to lead a project seeking to decipher the zonal gene expression of olfactory receptor genes and the molecular mechanisms that recruit a single OR allele to the mult-enhancer hub. My move from UCSF to Columbia in the end of 2014 posed significant delays to our research progress due to issue related to the mouse house of our interim space at the main campus at Columbia University. Due to technical problems at the vivarium we had limited mouse space that drastically delayed our genetic experiments. Importantly, due to delays in the completion of the Jerome L. Green Science building we spent 3 years instead of 6 months at this interim space. Since our move to the new state-of-the-art science building we have expanded our colony and accelarated our productivity (one manuscript accepted in Nature, one in Cell and one in eLife in 2019 and three other manuscripts in preparatoin)

1. Clowney E.J., LeGross M.A., Mosley C.M., Clowney F.G., Markenskoff-Papadimitriou E.C., Myllys M., Barnea G., Larabell C.A. and **Lomvardas, S.** (2012). Nuclear aggregation of olfactory receptor genes regulates their monogenic expression. *Cell*, 151(4), 724-737. PMCID: PMC3659163.
2. Lyons, B.D., Allen, W.E., Goh, T., Tsai, L., Barnea, G. & **Lomvardas, S.** (2013). An epigenetic trap stabilizes singular olfactory receptor expression. *Cell*, 154(2), 325-336. PMCID: PMC3929589.

3. Markenscoff-Papadimitriou, E.C., Allen, W.E., Colquitt, B.M., Goh, T., Monahan, K., Murphy, K.K., Mosley, C.P., Ahituv, N., & **Lomvardas S.** (2014). Enhancer interaction networks as a means of singular olfactory receptor expression. *Cell*, 159(3), 543-557. PMCID: PMC4243057.
4. Monahan, K., Horta A., and **Lomvardas S** (2019). Lhx2/Ldb1-mediated trans interactions regulate olfactory

Research proposal: basic components

Address the review criteria (consider your audience)

Approach (Aims) (research proposal)

- Rationale (short reminders of the things you said in significance/background)

- How will you carry out this work?
  - Why are you doing the experiment (“In order to determine …”)
  - How will you do the experiment and what will you measure (“I will use … to measure…”)
  - Which groups are you comparing (“to compare … between …”)
  - What will this mean/what new information will the experiment reveal (“This will reveal how/whether/if …”)

- Expected results and what they would mean (ideally, bring everything back to your overarching hypothesis)

- Include potential challenges and alternative approaches
  - Limitations: consider—if everything goes perfectly, what piece of the puzzle would you still not figure out?
  - Potential challenges: for difficult techniques, what are realistic challenges you may encounter, and what is one alternative approach you could use to get around those challenges?

- Preliminary data can go at the beginning of the approach, or it can be included within the aims

Research proposal: non-negotiables

Rigor!!! (research proposal)

- Rigor of prior research on which the proposal is based (should be showcased throughout proposal)
  - If there are weaknesses in the prior research, state how you will address them/not repeat them

- **Sample sizes**: what are they, and how did you arrive at those numbers?
  - If possible, use a power analysis. State what you used to estimate effect sizes in the power analysis (preliminary data? Published data?)

- **Sex as a biological variable**: Are you using both sexes? Why or why not? Make sure to collect, analyze, and report data disaggregated by sex (if possible). Are your studies powered to detect sex differences?

- **Statistical analyses/computations**: What statistical tests or analyses are you going to be using? Make sure that these are appropriate for your work.

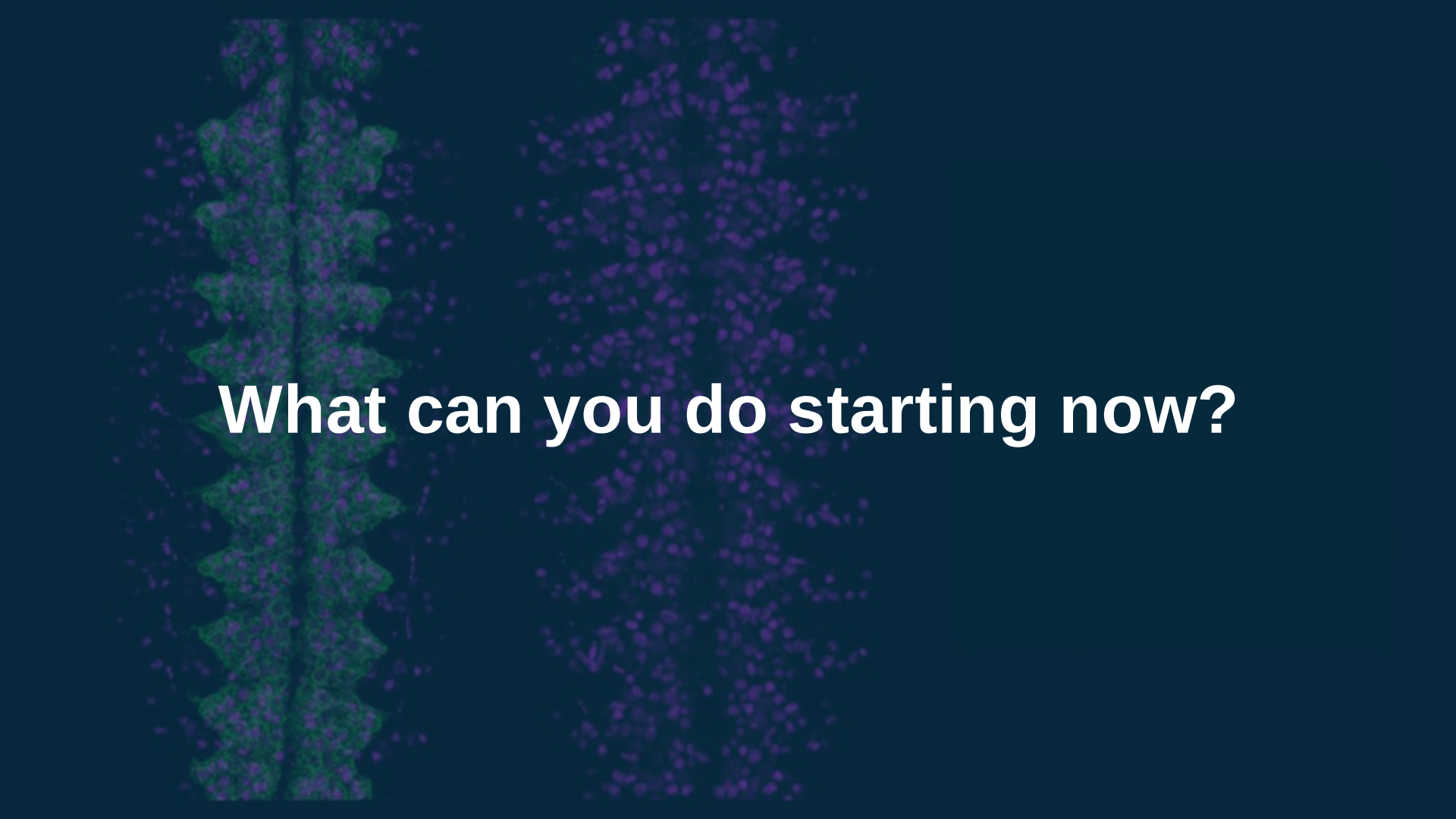
- Blinding, etc.


Keeping your mind on the future

Keep in mind …

Fellowships and Awards for trainees

- Your grad students and postdocs are also eligible for fellowships– consider the effort required from you for helping them apply vs. the benefit of having their salary (partially) covered
  - Consider overlap for federal (NIH/NSF) grants. Trainees' applications cannot be copy-cat of your proposals.
  - Once they write one version, they can often reuse it for many fellowship applications (can only accept one)


What can you do starting now?

Writing skills to develop

Individual writing skills
- Clear, concise, linear scientific story-telling
- Using first-person “active” language (“We will [use what technique] to [measure/compare what]”)
- Cut out unnecessary phrasing (“Prior research has shown that …” can be just the factual statement with citations)

Group work
- Share your work with others for constructive criticism
- Develop a support system for your applications
- Help others with their writing (this will make you a better editor for your own work and for your trainees)
- Once you are a PI: Serving as a reviewer

Resources
- Coursera (free) – Writing in the Sciences by Dr. Kristin Sainani: https://www.coursera.org/learn/sciwrite
- VP&S Grant Writing Resources: https://research.columbia.edu/nih-grants-workshop-series-recordings
- Bioscience Writers knowledge articles: https://www.biosciencewriters.com/EditingArticleLibrary.aspx
- ZI Research Development Website: https://research-development.zuckermaninstitute.columbia.edu/

Grants/Awards you can apply for now

NIH K01 or K08 (US citizens/permanent residents)

NIH K99/R00 (postdocs within their first 48 months of training)

Brain & Behavior Research Foundation NARSAD Young Investigator (can be held concurrently with a fellowship)

NIH R03, R21 (as co-I or co-PI with your faculty mentor)

Warren Alpert Distinguished Scholar Awards (internal application in September/October)

Simons Foundation Fellows-to-Faculty Award (for those from under-represented groups within specific areas of research)

Practice good writing skills when you write your manuscripts

Job applications