



# National Institutes of Health National Research Service Award

(Kirschstein Fellowship: F30, F31, F32)

## Information Session

December 12, 2018

### *Presenters:*

**Dr. Jim Slauch** - Professor of Microbiology & Director of the Medical Scholars Program

**Dr. Sayeepriyadarshini Anakk** - Associate Professor, Molecular & Integrative Physiology

**Hanna Erickson** - NRSA Fellow & MD/PhD Student, Molecular & Integrative Physiology

# NIH/NRSA/Kirschstein F30, F31, F32 Pre- and Postdoctoral Fellowships -Nuts and Bolts-

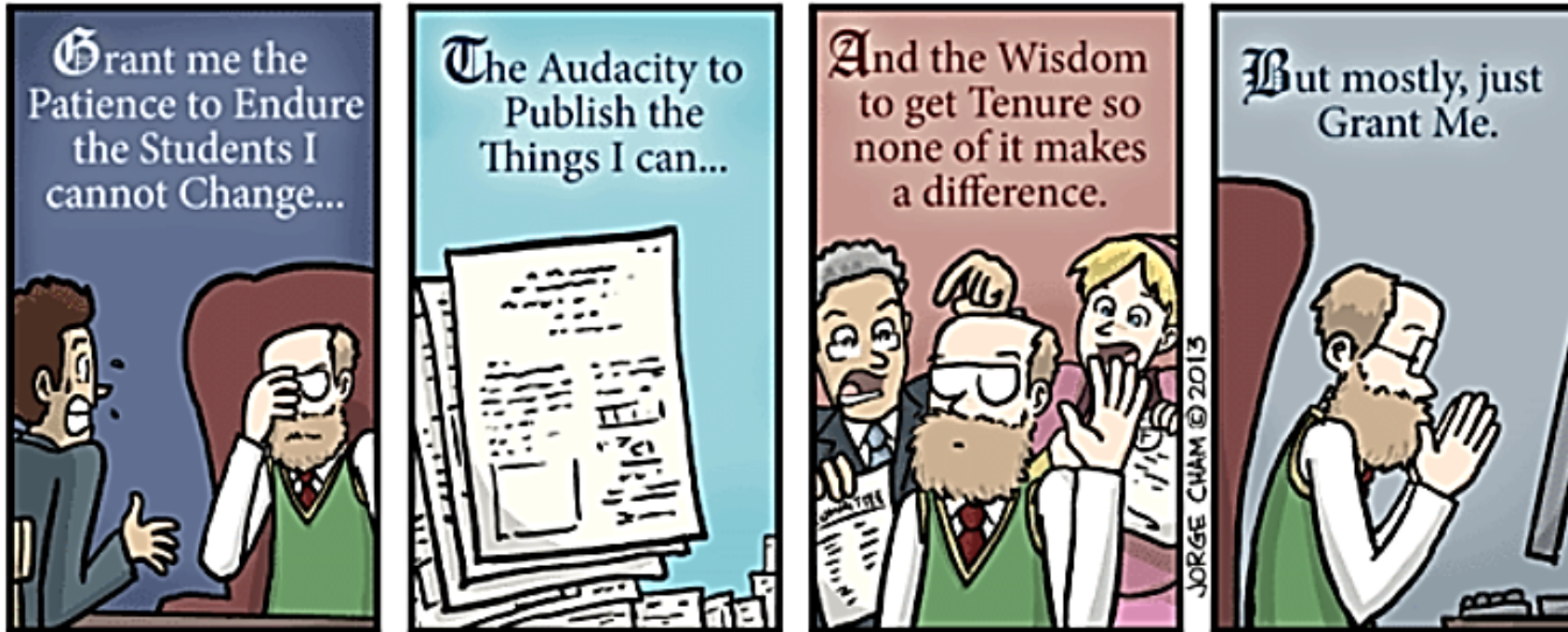
**James M. Slauch**

Dept of Microbiology

Medical Scholars Program

December 12, 2018

## A Professor's Prayer



# What are we talking about?

- Individual fellowships from the National Institutes of Health
- Who's eligible?
  - Must be a US citizen or permanent resident (at the time of the award)
- Predocs: 5 Years
- MD/PhDs: 6 years including some Med school after PhD.
  - Must apply within 48 months of joining the program
- Postdocs: 3 years
- Years funded by other NIH training grants are subtracted

# How to Start

- Give yourself plenty of time ~6 weeks
  - More if your project involves animals or humans

<b>Submission</b>			
<b>F30 F31 F32</b>	April 8	August 8	December 8
<b>Scientific Merit Review</b>	June - July	Oct - Nov	Feb - March
<b>Advisory Council Review</b>	Aug or Oct	Jan	May
<b>Earliest Project Start Date</b>	Sept or Dec	April	July

# Program Announcements

[http://grants.nih.gov/grants/guide/search\\_results.htm?scope=pa](http://grants.nih.gov/grants/guide/search_results.htm?scope=pa)

- Can be confusing
- F31s
  - PA-18-671 Individual PhD Fellowships
  - PA-18-666 PhD or MD/ PhD Fellowships for under-represented minority or disabled students
- F30s
  - PA-18-673 MD/PhD Fellowships (for institutions w/o MSTPs)
- F32s
  - PA-18-670 Postdoctoral Fellowships
  - PA-12-261 AHRQ – Healthcare research and quality



# How to Start

- Read the Program Announcement CAREFULLY
- Why different PAs?
  - “F” specific directions
  - Institute-specific rules
  - Not all Institutes participate in each PA
- Download the Application Instructions; NEW FORMS as of Jan 2018 (E vs D)
  - For all grants: <https://grants.nih.gov/grants/how-to-apply-application-guide.html>
  - Fellowship (F) Instructions: **<https://grants.nih.gov/grants/how-to-apply-application-guide/forms-e/fellowship-forms-e.pdf>**
  - Read it carefully
- The PA trumps the general instructions

# How to Start

- Contact your “Grants Administrator” in your Dept
  - Talk to your thesis advisor – who do they go to when filling out an NIH grant?
- The Grants Administrator should download the application package and fill out all the detailed stuff
- F Kiosk -  
<https://researchtraining.nih.gov/programs/fellowships>

# Register in the eRA Commons

- All PIs (that's you) need to interact with the NIH via the “eRACommons”
- Go to the OSP website
  - <http://sponsoredprograms.illinois.edu/sponsors/national-institutes-health>
  - Under “Help” at the bottom, click on “Create an eRACommons account”
    - You will need:
      - UIN
      - First & Last Name
      - Date of birth
      - Email



# The Application

- The application is a fancy PDF file

<a href="#">View Burden Statement</a>		OMB Number: 4040-0001 Expiration Date: 10/31/2019	
<b>APPLICATION FOR FEDERAL ASSISTANCE SF 424 (R&amp;R)</b>		<b>3. DATE RECEIVED BY STATE</b>	<b>State Application Identifier</b>
<b>1. TYPE OF SUBMISSION</b>		<b>4. a. Federal Identifier</b>	
<input type="checkbox"/> Pre-application <input type="checkbox"/> Application <input type="checkbox"/> Changed/Corrected Application		<b>b. Agency Routing Identifier</b>	
<b>2. DATE SUBMITTED</b>	<b>Applicant Identifier</b>	<b>c. Previous Grants.gov Tracking ID</b>	
<b>5. APPLICANT INFORMATION</b>			
		<b>Organizational DUNS:</b>	
Legal Name:			
Department:		Division:	
Street1:			
Street2:			
City:		County / Parish:	
State:		Province:	
Country:		ZIP / Postal Code:	
USA: UNITED STATES			
Person to be contacted on matters involving this application			
Prefix:	First Name:	Middle Name:	
Last Name:	Suffix:		
Position/Title:			
Street1:			
Street2:			
City:		County / Parish:	
State:		Province:	
Country:		ZIP / Postal Code:	
USA: UNITED STATES			
Phone Number:		Fax Number:	

# The Application

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<a href="#">View Burden Statement</a>	
APPLICATION FOR FEDERAL ASSISTANCE <b>SF 424 (R&amp;R)</b>	
<b>1. TYPE OF SUBMISSION</b>	
<input type="checkbox"/> Pre-application <input type="checkbox"/> Application <input type="checkbox"/> Changed/Corrected Application	
<b>2. DATE SUBMITTED</b>	<b>Applicant Identifier</b>
<input type="text"/>	<input type="text"/>

There are lots of  
directions for each  
item

## 1. Type of Submission

This field is required. Check one of the "Type of Submission" boxes:

### Pre-application:

The pre-application option is not used by NIH or other PHS agencies unless specifically noted in a funding opportunity announcement (FOA).

### Application:

An "Application" is a request for financial support of a project or activity submitted on specified forms and in accordance with NIH instructions. (See NIH [Types of Applications](#) for an explanation of the types of applications).

### Changed/Corrected Application:

Check this box if you are correcting either system validation errors or application assembly problems that occurred during the submission process. Changed/corrected applications must be submitted before the application due date.

When you submit a changed/corrected application, follow these guidelines:

- After submission of an application, there is a two-day application viewing window. Prior to the due date, you may submit a changed/corrected application. Submitting a changed/corrected application will replace the previous submission and remove the previous submission from consideration.
- If you check the "Changed/Corrected Application" box, then "Field 4.c Previous Grants.gov Tracking ID" is required.
- Do not use the "Changed/Corrected Application" box to denote a resubmission application. Resubmission applications will be indicated in "Field 8. Type of Application." See NIH Glossary for the definition of [Resubmission](#).

# The Application

- Some info is entered directly – the important stuff is uploaded

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## R&R Other Project Information Form

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### RESEARCH & RELATED Other Project Information

OMB Number: 4040-0001  
Expiration Date: 10/31/2019

1. Are Human Subjects Involved?

☒ Yes ☐ No

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ☐ Yes ☐ No

If yes, check appropriate exemption number. ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8

If no, is the IRB review Pending? ☐ Yes ☐ No

IRB Approval Date:

Human Subject Assurance Number:

2. Are Vertebrate Animals Used?

☒ Yes ☐ No

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ☐ Yes ☐ No

IACUC Approval Date:

Animal Welfare Assurance Number:

3. Is proprietary/privileged information included in the application?

☒ Yes ☐ No

4.a. Does this Project Have an Actual or Potential Impact - positive or negative - on the environment?

☒ Yes ☐ No

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed?

☐ Yes ☐ No

# The Application

- Some info is entered directly – the important stuff is uploaded

<b>Fellowship Applicant Section</b>				
2. * Applicant's Background and Goals for Fellowship Training	<div></div>	<a href="#">Add Attachment</a>	<a href="#">Delete Attachment</a>	<a href="#">View Attachment</a>
<b>Research Training Plan Section</b>				
3. * Specific Aims	<div></div>	<a href="#">Add Attachment</a>	<a href="#">Delete Attachment</a>	<a href="#">View Attachment</a>
4. * Research Strategy	<div></div>	<a href="#">Add Attachment</a>	<a href="#">Delete Attachment</a>	<a href="#">View Attachment</a>
5. * Respective Contributions	<div></div>	<a href="#">Add Attachment</a>	<a href="#">Delete Attachment</a>	<a href="#">View Attachment</a>
6. * Selection of Sponsor and Institution	<div></div>	<a href="#">Add Attachment</a>	<a href="#">Delete Attachment</a>	<a href="#">View Attachment</a>
7. Progress Report Publication List (for Renewal applications)	<div></div>	<a href="#">Add Attachment</a>	<a href="#">Delete Attachment</a>	<a href="#">View Attachment</a>
8. * Training in the Responsible Conduct of Research	<div></div>	<a href="#">Add Attachment</a>	<a href="#">Delete Attachment</a>	<a href="#">View Attachment</a>

Note that even boxes that are not yellow may be “required”

# Format Everything Correctly

- Follow the directions: <https://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/format-attachments.htm>
- PMCID MUST be included on any reference from “Senior Personnel” both in the reference section and biosketchs
- Do NOT put page numbers on the PDFs you create, but do put titles
- 11 pt Arial, Georgia, Helvetica, or Palatino Linotype

# Letters of Recommendation

- Ask for your letters at least three weeks in advance (a month's notice is better).
- Provide your letter writers with a resume as well as a summary of your research interests/specific aims. They don't need to see the proposal per se.
- The LORs are submitted electronically. Follow the instruction in the "Application Guide".
- You are allowed 3-5 LORs – NOT your advisor or co-advisor.

# Letters of Recommendation

- Send an email to each letter writer.
- Thank you for agreeing to write me a letter of recommendation for my NRSA application. The due date for my application is [August 8]. The letter must be submitted via the eRA Commons at:  
<https://commons.era.nih.gov/commons/reference/submitRefereeInformation.jsp>
- The additional information you need is:
  - PI Commons User ID: [Your Commons ID]
  - PI Last Name: [Your last name]
  - Funding Opportunity Announcement Number: [The appropriate PA number, eg, PA-18-671]
- Provide instructions:
  - <https://grants.nih.gov/sites/default/files/instructions-for-fellowship-referees.docx>



# Stipend and Tuition Projection

- Your grant administrator will provide a projection of tuition and fees for the next five to six years. This will differ depending on your graduate program.
- You will also need to show this table to the Graduate College Fellowship Office. Note that this projection is your best estimate and you are not limited by what you say here. The Univ actually bills the NIH later based on real costs.

## Budget Section

All Fellowship Applicants:

25. \* Tuition and Fees:

☐ None Requested

☐ Funds Requested:

Year 1

Year 2

Year 3

Year 4

Year 5

Year 6 (when applicable)

**Total Funds Requested:**

# Choose a Study Section

- <http://public.csr.nih.gov/StudySections/Fellowship/Pages/default.aspx>

Study Section ▲	Study Section Description	Scientific Review Officer
F01A	Fellowships: Brain Disorders and Related Neurosciences	Dr. Vilen Movsesyan
F01B	Fellowships: Learning and Memory, Language, Communication and Related Neurosciences	Dr. Susan Gillmor
F02A	Fellowships: Behavioral Neuroscience	Dr. Mei Qin
F02B	Fellowships: Sensory and Motor Neurosciences, Cognition and Perception	Dr. Sharon Low
F03A	Fellowships: Neurodevelopment, Synaptic Plasticity and Neurodegeneration	Dr. Mary Schueler
F03B	Fellowships: Biophysical, Physiological, Pharmacological and Bioengineering Neuroscience	Dr. Sussan Paydar
F04A	Fellowships: Chemistry, Biochemistry and Biophysics A	Dr. Mike Radtke
F04B	Fellowships: Chemistry, Biochemistry and Biophysics B	Dr. Sudha Veeraraghavan
F05-D	Fellowships: Cell Biology, Developmental Biology, and Bioengineering	Dr. Alexander Gubin

Etc....

[View Burden Statement](#)

## PHS Assignment Request Form

OMB Number: 0925-0001

Expiration Date: 3/31/2020

Funding Opportunity Number:

Funding Opportunity Title:

### Awarding Component Assignment Request *(optional)*

If you have a preference for an awarding component (e.g., NIH Institute/Center) assignment, use the link below to identify the appropriate short abbreviation and enter it below. All requests will be considered; however, assignment requests cannot always be honored.

Awarding Components: [https://grants.nih.gov/grants/phs\\_assignment\\_information.htm#AwardingComponents](https://grants.nih.gov/grants/phs_assignment_information.htm#AwardingComponents)

	First Choice	Second Choice	Third Choice
Assign to Awarding Component:	<input type="text"/>	<input type="text"/>	<input type="text"/>
Do Not Assign to Awarding Component:	<input type="text"/>	<input type="text"/>	<input type="text"/>

### Study Section Assignment Request *(optional)*

If you have a preference for study section assignment, use the link below to identify the appropriate study section (e.g., NIH Scientific Review Group or Special Emphasis Panel) and enter it below. Remove all hyphens, parentheses, and spaces. All requests will be considered; however, assignment requests cannot always be honored.

Study Sections: [https://grants.nih.gov/grants/phs\\_assignment\\_information.htm#StudySection](https://grants.nih.gov/grants/phs_assignment_information.htm#StudySection)

	First Choice	Second Choice	Third Choice
Assign to Study Section: <i>Only 20 characters allowed</i>	<input type="text"/>	<input type="text"/>	<input type="text"/>
Do Not Assign to Study Section: <i>Only 20 characters allowed</i>	<input type="text"/>	<input type="text"/>	<input type="text"/>

## COVER LETTER

Application title:

Really cool stuff that you should fund

Funding Opportunity:

PA-18-671 Ruth L. Kirschstein National Research Service Award (NRSA)  
Individual Predoctoral Fellowship (Parent F31)

Letters of recommendation will be sent from:

Sayeepriyadarshini Anakk  
Dept of Molecular and Integrative Physiology  
University of Illinois

Albert Einstein  
Institute for Advanced Study  
Princeton University

Also fill out the “Assignment  
Request Form”

Thank you,

Jane Doe, PI

# Get Feedback

- Your advisor!
- Others: Fellow students, post-docs, committee members...
- After your advisor has signed off on it:
  - Ken Vickery – Grad College

# Application Sign-Off

- Several university officials must sign off on your application
- You must allow sufficient time for each of these entities to act.
- These individuals are not competent to judge the actual proposal. So although you need a “complete” application to get signatures, you can continue to make minor edits to the proposal and upload new PDF files into the master PDF UNTIL it is time to send it to OSP. (I THINK this is true, but the process has gone online recently.)
- Your Grants Administrator will help with the university form
- For fellowship applications, the Grad College Fellowship Office also needs to sign off. This is not explicitly listed on the transmittal form; rather this is an “other signature if required.”
- Submit completed application that has been reviewed by the appropriate offices (with help from your Grants Administrator) to OSP (at least 48 hours in advance).

# Other Important Points

- This is a “training grant”. The NIH training record of your thesis advisor matters.
- Ideally, your advisor is:
  - Tenured
  - NIH Funded
  - Has successful PhDs out in the world doing good
- If not, fear not
  - Seek out a “co-advisor” that meets the above criteria



Good Luck!

# **CONTENT FOR F30/F31/F32 NRSA APPLICATIONS**

**Sayeepriyadarshini Anakk and Hanna Erickson**  
Department of Molecular and Integrative Physiology  
December 12, 2018

# CHOOSE AN NIH INSTITUTION

Preparing an application is a **very significant investment of time** by you AND your advisor. Need to be aware of this in determining probability of success. Make sure you **fit the mission** of the institution.

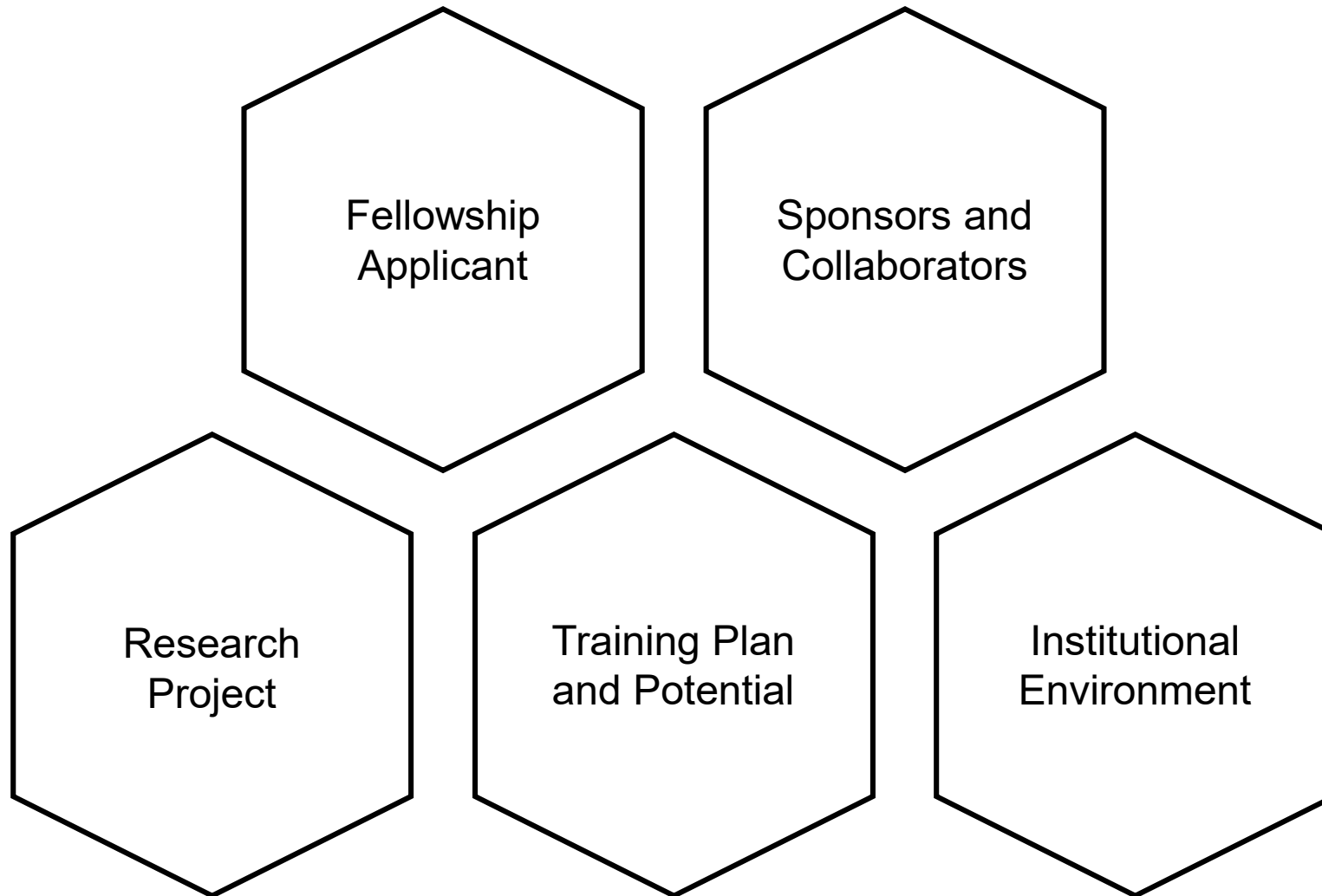
**MSP website:** <https://www.med.illinois.edu/MSP/Students/Fellowships/>

**F30 - PA-18-668** <https://grants.nih.gov/grants/guide/pa-files/PA-18-668.html>

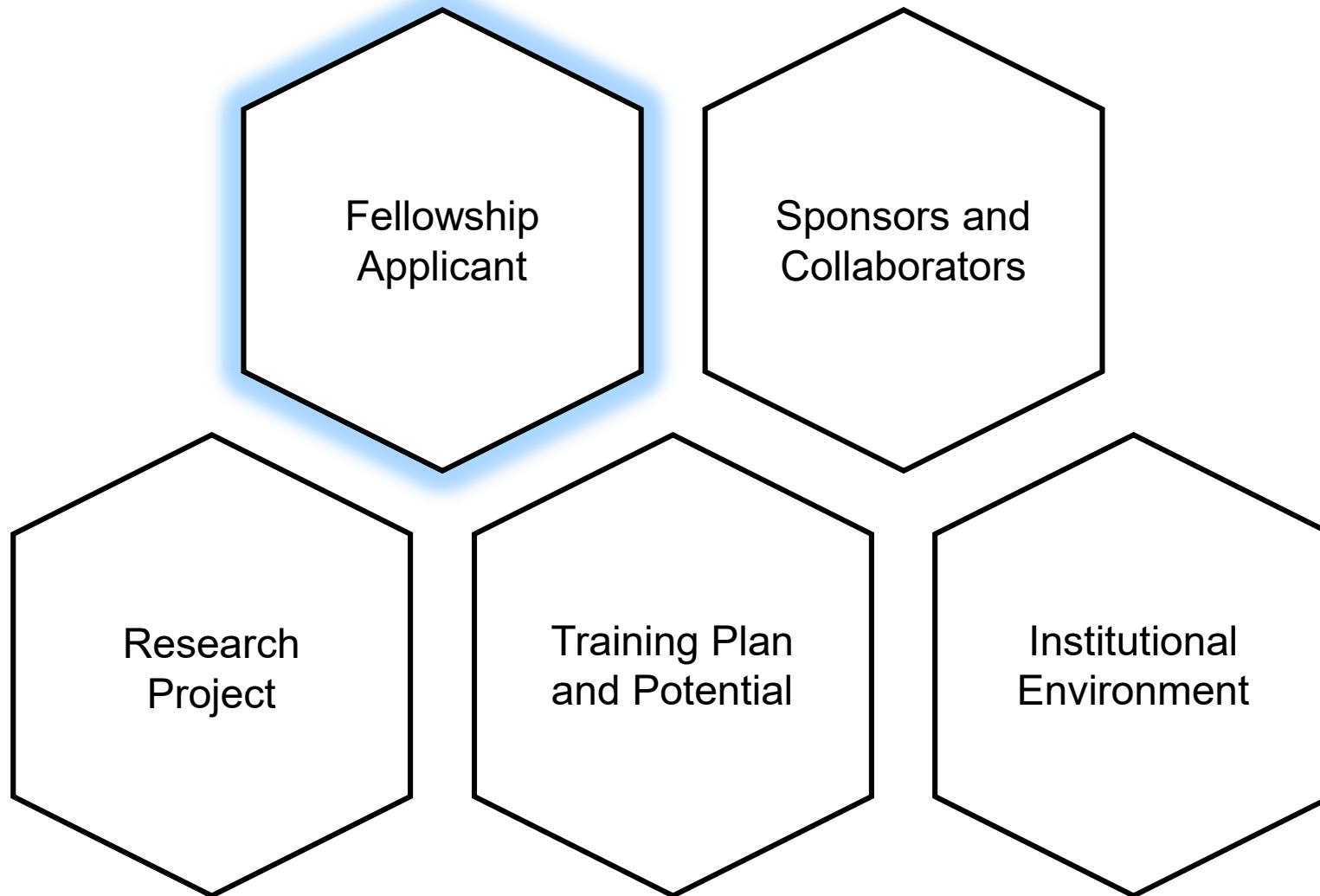
Participating Institutes:

- National Cancer Institute (NCI)
- National Eye Institute (NEI)
- National Heart, Lung, and Blood Institute (NHLBI)
- National Human Genome Research Institute (NHGRI)
- National Institute on Aging (NIA)
- National Institute on Alcohol Abuse and Alcoholism (NIAAA)
- National Institute of Allergy and Infectious Diseases (NIAID)
- *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD)
- National Institute on Deafness and Other Communication Disorders (NIDCD)
- National Institute of Dental and Craniofacial Research (NIDCR)
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)
- National Institute on Drug Abuse (NIDA)
- National Institute of Environmental Health Sciences (NIEHS)
- National Institute of Mental Health (NIMH)
- National Institute on Minority Health and Health Disparities (NIMHD)
- National Center for Complementary and Integrative Health (NCCIH)

# CORE REVIEW CRITERIA



# CORE REVIEW CRITERIA



# FELLOWSHIP APPLICANT

Important to provide evidence for your potential/alignment with institute mission and explicitly state how this fellowship will help you improve/achieve your goals.

## Relevant documents:

- **Applicant's Biosketch**
- Applicant's Background and Goals for Fellowship Training
  - **Doctoral Dissertation and Other Research**
- Sponsor and Co-Sponsor Statement
  - **Applicant's Qualifications and Potential for a Research Career**
- **Letters of Reference**

# APPLICANT BIOSKETCH

Use NIH biosketch format: <https://grants.nih.gov/grants/forms/biosketch.htm>

Personal Statement	Career goals consistent with the mission of the institution
Academic Credentials	Grades, productivity, quality of undergraduate institution* *May be disadvantage to be at same school
Demonstrated Scientific Accomplishment	Publications, Presentations (Authorship on peer-reviewed paper is useful but not essential.)
Past Funding	Graduate fellowship, slot on NIH training grant, undergraduate research fellowship/grant



# PERSONAL STATEMENT

## *Applicant Biosketch*

I am an aspiring physician-scientist focused on becoming a **leader in the field of hepatobiliary cancers**. I want to address the gaps in liver cancer prevention and treatment from both the bench and the bedside by leading an active research laboratory, managing patient care, and using my expertise to impact others through leadership, research, and teaching. Physician-scientists are uniquely trained to integrate these roles, and with the NRSA fellowship, I will be able to strengthen my skills and gain expertise necessary for this career.

My utmost goal is that my research and clinical interests will be mutually beneficial. While I will develop strong research skills during my PhD training, **it is essential that I learn to apply these skills to the clinic** and be able to maneuver my research based on my clinical findings. Thus, receiving NRSA support for my medical school years will be imperative to **foster my development into a physician-scientist**. The College of Medicine provides a number of hands-on clinical training opportunities to **facilitate this training** and allots 20 weeks for electives and/or research during M4 for students to pursue specific interests. By performing clinical and basic research during this time, I will be able to combine my knowledge from my PhD and medical training and establish myself as a clinician-investigator.

# POSITIONS AND HONORS

## *Applicant Biosketch*

ACTIVITY/ OCCUPATION	BEGINNING DATE (mm/yy)	ENDING DATE (mm/yy)	FIELD	INSTITUTION/ COMPANY	SUPERVISOR/ EMPLOYER
Hospital Volunteer	06/06	08/13	Medicine	University of Minnesota Medical Center	Mrs. Sarah Blanchette
Vice President	07/17	Present	Leadership	American Physician Scientists Association	Ms. Jillian Liu

### **Academic and Professional Honors:**

2008 Junior Volunteer Scholarship, University of Minnesota Medical Center  
2017 Graduate Teacher Certificate, Center for Innovation in Teaching

### **Memberships in Professional Societies:**

American Association for the Study of Liver Disease

# CONTRIBUTIONS TO SCIENCE

## *Applicant Biosketch*

### **1. IQGAP1 coordinates nutritional signaling and contributes toward liver cancer**

IQGAP1 is a scaffolding protein that is largely known for its role in cell-cell adhesion, motility, and proliferation. However, its role in regulating metabolism has not been studied. **I discovered that** hepatic IQGAP1 expression is induced by fasting and is essential for adaptation to nutritional ketosis. Loss of IQGAP1 results in impaired PPAR $\alpha$  activation, which is consistent with the elevated mTORC1 levels observed. This is interesting because IQGAP1 expression and mTORC1 activity have both independently been found to be elevated in HCC, but our data indicates that they are inversely related in healthy liver tissue. This work was initiated by a technician in the laboratory, Karen Wendt, who began a fasting study to teach me how to work with mice and do controlled metabolic studies. I then performed follow up experiments under the guidance of Dr. Anakk and was responsible for identifying the reciprocal IQGAP1-mTORC1 regulation.

- a. Erickson H, Anakk S. IQGAP1-mTORC1 interaction coordinates fat metabolism. Oral presentation at Central Society for Clinical and Translational Research Meeting. 2017 Apr 21; Chicago, IL.
- b. Erickson H, Wendt K, Anakk S. IQGAP1-mTORC1 interaction coordinates fat metabolism. Oral presentation at American Association for the Study of Liver Diseases Liver Meeting. 2016 Nov 14; Boston, MA.
- c. Erickson H, Wendt K, Anakk S. Bridging the (IQ)GAP between liver metabolism and cancer. Oral Presentation: Beckman Institute Graduate Student Seminar Series. 2016 Feb 10; Champaign, IL.
- d. Erickson H, Wendt K, Anakk S. Role of scaffolding protein IQGAP1 in fat metabolism. Poster Presentation at Cold Spring Harbor Laboratory Metabolic Signaling & Disease: From Cell to Organism Meeting. 2015 August 12; Cold Spring Harbor, NY.

# SCHOLASTIC PERFORMANCE

## *Applicant Biosketch*

YEAR	SCIENCE COURSE TITLE	GRADE	YEAR	<u>OTHER</u> COURSE TITLE	GRADE
UNIVERSITY OF MINNESOTA UNDERGRADUATE CLASSES					
2009	Organic Chemistry I	B+	2009	American Government and Politics	B+

UNIVERSITY OF ILLINOIS GRADUATE CLASSES			UNIVERSITY OF ILLINOIS MEDICAL CLASSES		
2013	Advanced Biochemistry	A-	2013-2014	Clinical Practice Preceptorship	S

M1 courses are graded O (Outstanding), S (Satisfactory), and U (Unsatisfactory). Seminars, Research Ethics, and Clinical Practice Preceptorship are graded S (Satisfactory) and U (Unsatisfactory)	
STANDARDIZED EXAM SCORES	
Graduate Requirement Exam (GRE)	<b>QUANTITATIVE:</b> 168 (96 percentile) <b>VERBAL:</b> 163 (91 percentile) <b>WRITING:</b> 5.5 (97 percentile)
Medical College Admissions Test (MCAT)	<b>TOTAL SCORE:</b> 35 (93.8-95.7 percentile) <b>PHYSICAL SCIENCES:</b> 13 (95.3-97.3 percentile) <b>BIOLOGICAL SCIENCES:</b> 11 (77.1-88.8 percentile) <b>VERBAL REASONING:</b> 11 (83.5-95.4 percentile)

# DOCTORAL DISSERTATION AND GOALS FOR FELLOWSHIP TRAINING

## *Applicant's Background and Goals for Fellowship Training – Part 1*

- Describe previous research experience
  - Questions asked, techniques used, major findings
- Include only substantial research experience (not ones that didn't yield a presentation/publication)

*August 2011 – August 2013*

**Project:** Synthesis and Analysis of Deoxyguanosine-Cisplatin-Cysteine Cross-links

**Advisor:** Dr. Natalia Tretyakova, Ph.D., Professor, Department of Medicinal Chemistry, University of Minnesota – Twin Cities, Minneapolis, MN

**Role:** Undergraduate Research Assistant

Cross-linking agents have long been used as anti-cancer therapeutics, with numerous side effects. The goal of Dr. Tretyakova's laboratory is to understand the exact mechanism by which these drugs work and how cells respond to this damage...

# **APPLICANT'S QUALIFICATIONS AND POTENTIAL FOR A RESEARCH CAREER**

*Sponsor and Co-Sponsor Statement – Part 5*

- Written from the perspective of the sponsor/co-sponsor.
- Highlights the unique accomplishments/abilities of the applicant

# LETTERS OF REFERENCE

Should be **excellent** (“enthusiastic support”).

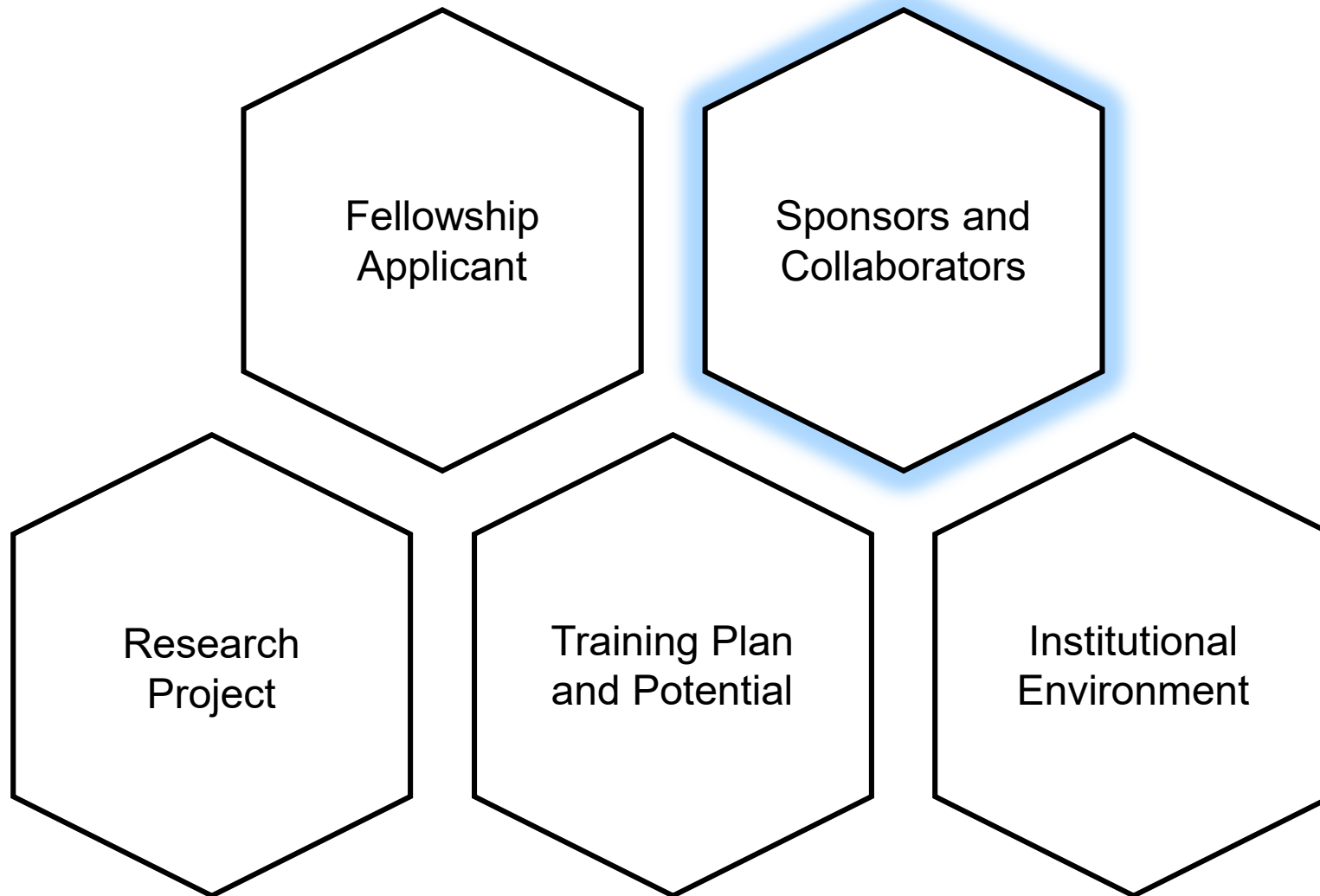
Reach out to LOR writers 1-2 months in advance. Provide biosketch and specific aims page.

Who to select:

- Previous research mentors (undergraduate, masters, etc.)
- Thesis committee members
- Collaborators



# CORE REVIEW CRITERIA



# SPONSORS AND COLLABORATORS

Important to show that you have established adequate support that will be able to help you achieve your research and training goals (financially and otherwise).

## Relevant documents:

- **Sponsor's and/or Co-Sponsor's Biosketch**
- Sponsor and Co-Sponsor Statement
  - **Research Support Available for this Project**
  - **Sponsor's/Co-Sponsor's Previous Fellows/Trainees**
  - **Number of Trainees to be Supervised during Fellowship**
- **Selection of Sponsor and Institution**

# KEY SPONSOR CRITERIA

\$\$\$	Grants and funding, ideally covering the entire length of the fellowship
Productivity	Publications, publications, and more publications Expertise in relevant research area
Mentoring Record	Successful previous and current fellows and trainees, mentoring awards

# PICKING A CO-SPONSOR

Fill a gap:

Since Dr. Anakk is a new faculty member, Hanna will receive additional mentoring from Dr. Katzenellenbogen (co-sponsor), which will tremendously boost her development as a scientist. Dr. Katzenellenbogen is a renowned expert in the field of nuclear receptor signaling and **cancer biology** and has an **extensive track record** as a highly successful investigator and mentor.

Her laboratory is also adept at evaluating tumor promotion and progression. This **overlaps with Hanna's long-term interest**, so having Dr. Katzenellenbogen as her co-sponsor will benefit Hanna as she proposes to determine the role for IQGAP1 in tumor progression and metastasis proposed in Aim 2.

Define relationship:

Both laboratories are proximal within the department, which will facilitate collaborations and mentoring. Dr. Katzenellenbogen will separately **meet with Hanna for an hour every month** to review her progress and provide advice on her science, feedback on research presentations, and suggestions on how to best achieve her career objectives.

# COLLABORATORS AND LETTERS OF SUPPORT

## Benefits:

- Provide evidence of additional methodology that they are experts in and that you would benefit from
- Additional mentoring opportunities, e.g. if they are in a career path that you would like to follow such as medicine or industry
- Evidence of opportunity for additional training in another setting

## Collaborators vs. Letters of Support

- Collaborators need to provide **letter of support** and **biosketch**
- Letters of Support can come from research core or department to show that resources are available to perform experiments/training

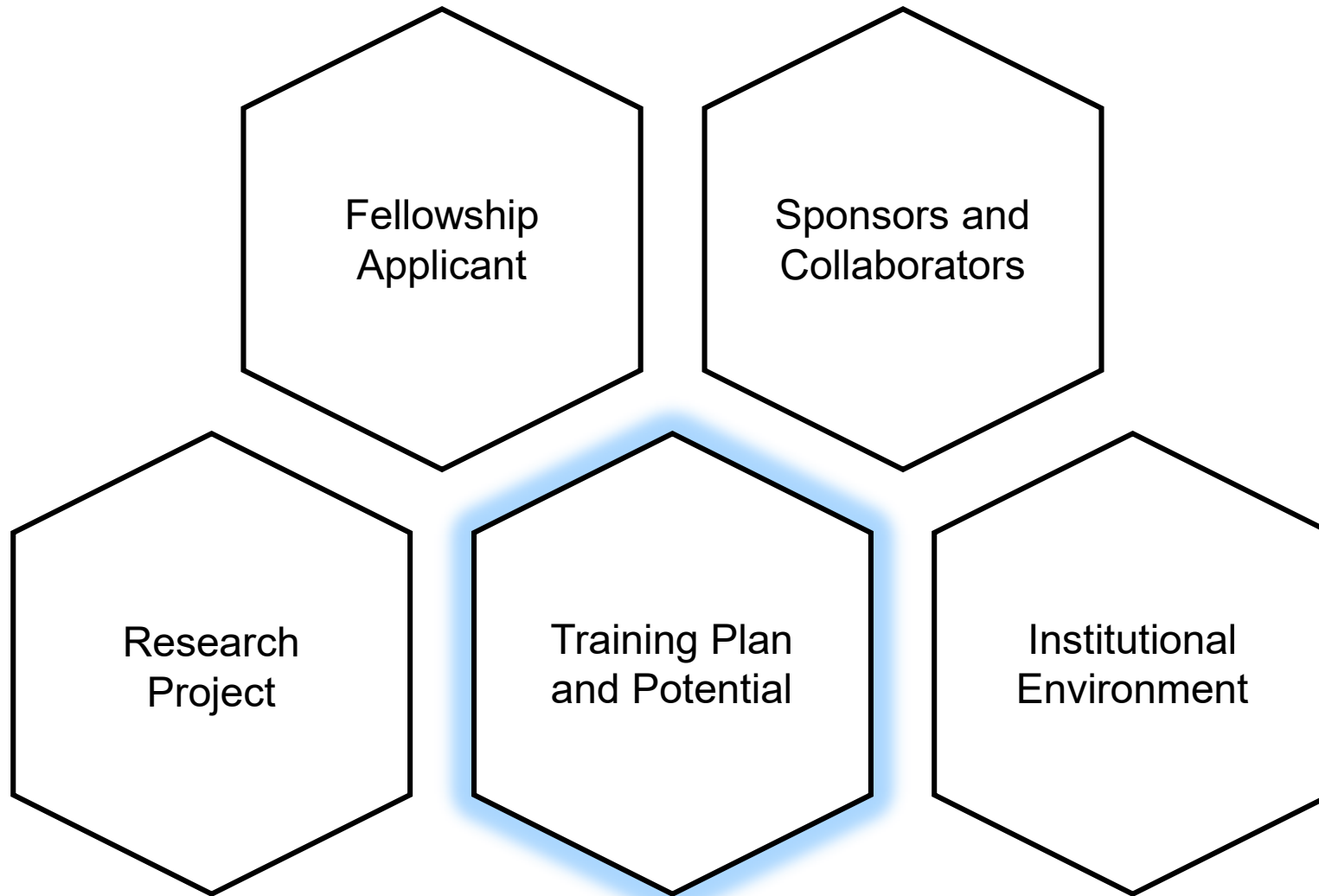
# SELECTION OF SPONSOR (AND INSTITUTION)

I chose Dr. Anakk as my sponsor and Ph.D. advisor for a number of reasons. First, she is a **successful scientist** and completed her postdoctoral training in the laboratory of Dr. David Moore at Baylor College of Medicine who is a leader in the field of nuclear receptor signaling. Dr. Anakk has a **strong background in studying liver physiology** and using transgenic mice, and she **has studied bile acid signaling for over a decade...**

As a faculty member of the College of Medicine and School of Molecular and Cellular Biology at UIUC, she has **demonstrated commitment** to my medical education and graduate training. She is also a faculty member of the Division of Nutrition Sciences and an affiliate of the Beckman Institute, which provides me **access to resources** that will enhance my training in tumor biology and metabolism.

Since Dr. Anakk is a new advisor, I additionally chose Dr. Benita Katzenellenbogen as my co-sponsor because of her **extensive experience with mentoring students**. She is a nationally recognized scientist with **decades of experience studying hormonal signaling and cancer**. Notably, she has trained over 90 pre-doctoral and post-doctoral students in her laboratory. She is also a prolific author, with 340 papers. Thus, her decades of experience will be an **excellent complement to Dr. Anakk** as she will be able to advise me on my research, career development, and writing skills.

# CORE REVIEW CRITERIA



# TRAINING PLAN AND POTENTIAL

Need to have a training plan that is **specific** to your career goals and current skills. Must **go beyond** basic requirements for degree.

## Relevant documents:

- Applicant's Background and Goals for Fellowship Training
  - **Training Goals and Objectives**
  - **Activities Planned Under This Award**
- Sponsor and Co-Sponsor Statement
  - **Training Plan**



# TRAINING GOALS AND OBJECTIVES

## *Applicant's Background and Goals for Fellowship Training – Part 2*

Connect to your career goals:

My overall career goal is to become an **academic physician-scientist** who is a leader in the clinical management and study of **hepatobiliary cancers**.

State where this falls along your training path:

Following my completion of the MD/PhD program, I plan to train in an internal medicine **physician-scientist residency program** in either gastroenterology or oncology. I **specifically** identified these programs since they provide physician-scientists protected research time and a mentorship committee for the entirety of the program. This training will help me obtain expertise in the biological and clinical manifestations of hepatobiliary cancer and **enable me to acquire a tenure-track faculty position** at a major research university where I will have access to all the necessary tools to successfully establish myself as an independent investigator.

# TRAINING GOALS AND OBJECTIVES

## *Applicant's Background and Goals for Fellowship Training – Part 2*

Specify how training will benefit you in individual categories such as:

- Research training
- Courses and seminars
- Conferences
- Publications
- Leadership and teaching
- Clinical training
- Grant writing

\*Adjust categories to fit your research goals

**Courses and Seminars** – So far in my Ph.D. studies, my focus has been to establish a strong knowledge base in liver physiology with an emphasis on bile acid and metabolic signaling. In preparation for my tumor studies, I will take coursework in exercise oncology and cancer biology to **appreciate diverse perspectives**. With the support of this fellowship, I will additionally take two biochemical nutrition courses to build a broad foundation in metabolic signaling that will help me become a **versatile researcher**.

# ACTIVITIES PLANNED UNDER THIS AWARD

## *Applicant's Background and Goals for Fellowship Training – Part 3*

Detailed plan for each year and timeline for entire award

- Explain structure of your program and where you currently are
- Include when each Aim will be accomplished and all courses, professional development, and training activities are planned
- Name specific research techniques you will learn and how you will learn them (i.e. training courses, collaborations)
- List specific professional development opportunities.

My first year in the Anakk lab was dedicated to learning techniques, breeding mice for experiments, and contributing to grant proposals. The next two years have been primarily dedicated to advancing my project in which I have identified a role for the scaffolding protein IQGAP1 in regulating ketogenesis and mTORC1 activation... These [proposed] time-consuming experiments have been **carefully planned** so that I would utilize my upcoming 2 years of graduate school to gain as much expertise as I can to become a **cancer biologist with a focus on metabolism**.

# ACTIVITIES PLANNED UNDER THIS AWARD

## *Applicant's Background and Goals for Fellowship Training – Part 3*

Year	Program Benchmarks	Research (%)	Coursework (%)	Clinical (%)	Professional Development (%)
1	Defend dissertation.	85%	10%	0%	5%
2	M2 coursework. Take STEP 1.	20%	75%	0%	5%
3	M3 clinical clerkships. Take STEP 2.	20%	0%	75%	5%
4	M4 clinical clerkships. Apply to residency	25%	0%	70%	5%

Aim	2017-2018	Fall 2018	Spring 2019	Summer 2019
1a. Determine which pathways are involved in <i>lqgap1</i> regulation	X	X		
1b. Examine the relative contribution of transcription and translation		X		
1c. Define the role of FXR in regulating <i>lqgap1</i> transcription			X	X
1d. Determine the tissue-axis responsible for regulating hepatic <i>lqgap1</i> expression		X	X	
2a. Initiation of tumorigenesis in mice	X	X		
2b. Characterization of tumors		X	X	X
2c. Examine the effect of IQGAP1 in cell motility			X	X

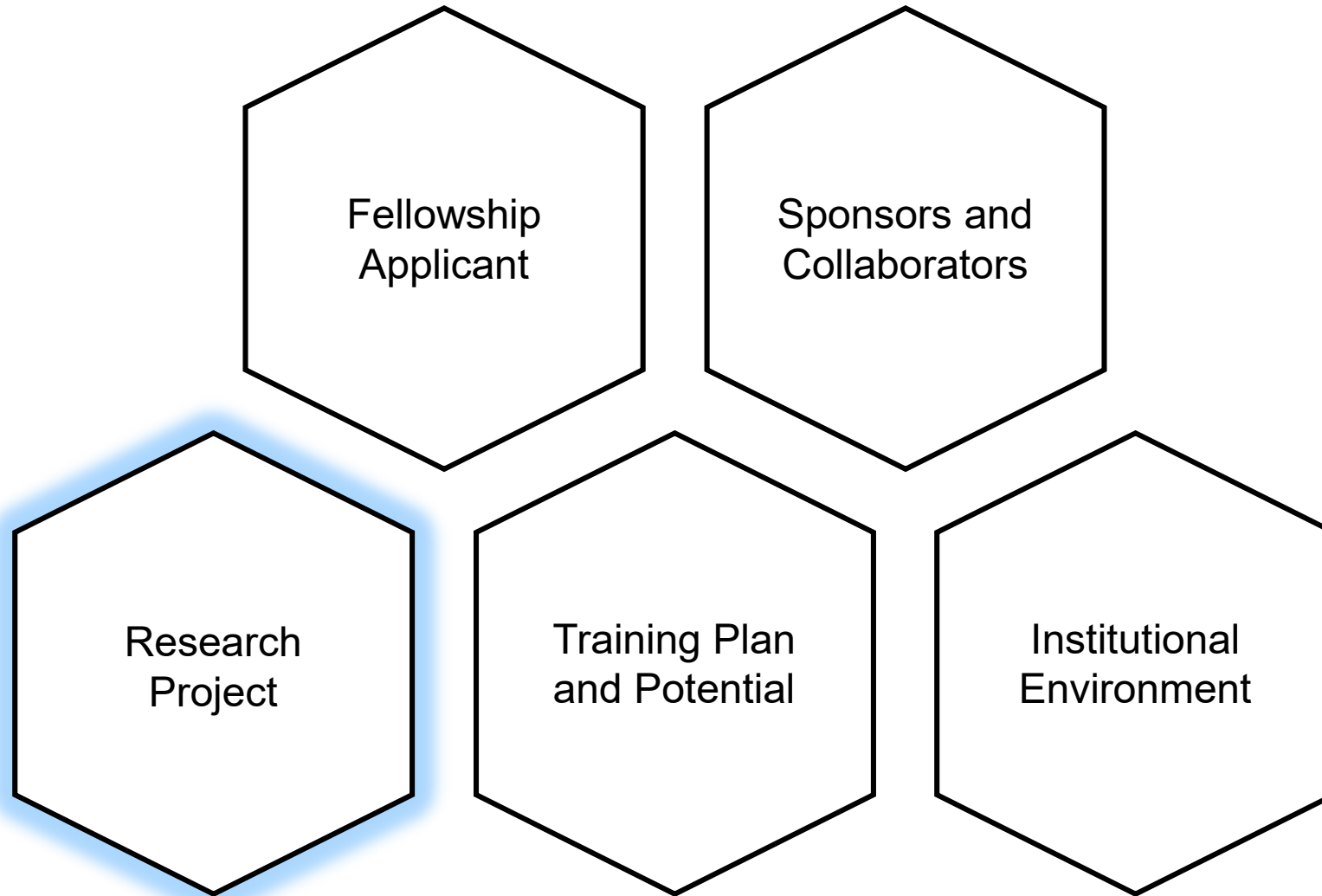
# TRAINING PLAN

## *Sponsor and Co-Sponsor Statement – Part 3*

Similar to “Training Goals and Objectives” and “Activities Planned Under this Award” but from sponsor/co-sponsor’s perspective.

- **Seminars and courses** – taken and planned, find unique things tailored to your career trajectory
- **Research training** – technical and intellectual skills learned/to learn, critical analysis, grant writing, presentation skills, mentorship skills, interaction with scientific community
- **Mentoring** – how often will you meet with your sponsor and collaborators, what you will glean from these meetings, other support available (i.e. committee members, program directors)
- **Scientific presentations and publications** – attended and planned

# CORE REVIEW CRITERIA



# RESEARCH PROJECT

Needs to be feasible in the available timeline, well-designed, and complementary to existing skill set and career goals.

## Relevant documents:

- **Specific Aims**
- **Research Strategy**
- **Project Summary**
- **Project Narrative**
- **Responsible Conduct of Research**
- **Vertebrate Animals\***
- **Human Subjects\***
- **Resource Sharing Plan**

# SPECIFIC AIMS

Should include:

- **Disease your research addresses and its impact on human health** (prevalence, cost, morbidity)
- **What is NOT known:** e.g. mechanisms of biological processes that impact the disease; how to design targeted therapeutic
- **Research question/hypothesis**
- **Brief summary of preliminary data:** how it fits into the question and what is known
- **Specific Aims:** experimental design to test hypothesis (1-3, should be complementary but independent)



# SPECIFIC AIMS

Example:

**IQGAP1 and Hepatic Tumorigenesis:** *The overall goal of this proposal is to (i) define IQGAP1's role in promoting hepatic tumorigenesis and (ii) identify the mechanism(s) that regulate IQGAP1 expression in hepatocytes.* Hepatocellular carcinoma (HCC), the major form of liver cancer, is the fourth most common cancer in the world and the second most lethal cancer... The Anakk laboratory identified that bile acids (BA) promote hepatic tumorigenesis... this... was found to be dependent on the scaffolding protein IQGAP1... However, the signals that induce IQGAP1 expression are completely unknown. *We hypothesize that BA-induced IQGAP1 expression is sufficient to promote hepatic tumorigenesis...*

**Specific Aim 1:** Identify the mechanism by which BAs regulate *lqgap1* expression.

**Specific Aim 2:** Determine whether IQGAP1 is required to promote hepatic tumorigenesis.

**Overall impact:** This work will be the first to provide an understanding of IQGAP1 regulation and its role in promoting hepatic tumorigenesis in the presence and absence of BAs. These studies will determine if IQGAP1 can act as a therapeutic target for HCC and identify mechanisms for controlling its expression and function.

# RESEARCH STRATEGY

Background and significance:

- What is the major question?
- What is the relevance to human health?
- What will be accomplished if aims are achieved?
- How will these studies change the field?
- How is this approach innovative?

Preliminary studies:

- Detailed explanation of how your data address the research question and lead to hypothesis

Research approach:

- Expand on aims
- Overview, rationale, and design of each aim (include statistical analysis)
- “Expected Results” and “Potential Pitfalls and Alternative Approaches”

# RESEARCH STRATEGY

## Formatting

- Break up sections with headings
- Use bold, italics, underlining to emphasize points
- Don't fill up all the available space
- Leave blank lines between sections if you can
- A picture is worth a thousand words

Your advisor/sponsor should provide advice and examples of previous grants

### Research Strategy

#### Significance

As the second leading cause of cancer-associated death worldwide, liver cancer is a major public health concern (2). Over the last decade, the incidence of liver cancer in the United States has steadily increased an average of 2.7% annually (NCI). This is consistent with the association between liver disease, a major risk factor for liver cancer, and the growing obesity epidemic (27, 28). In fact, the American Liver Foundation estimates that liver disease currently affects 1 in 10 Americans. Strikingly, over 80% of patients with liver cancer die within five years of diagnosis, which makes liver cancer one of the most fatal cancers in the United States (NCI). Yet, few effective treatments exist that extend the survival of patients diagnosed with hepatocellular carcinoma (HCC), the major form of primary liver cancer. The current treatment options include surgical resection (29), liver transplantation (30), and Sorafenib (31), a receptor tyrosine kinase inhibitor. However, the efficacy of these treatments is limited by patient eligibility based on stage of disease and availability of compatible donors. This clearly underscores the necessity for identifying novel therapeutic targets for the treatment of HCC.

Bile acids (BAs) are cholesterol derivatives that are essential for dietary lipid absorption, become elevated in diseased livers, and are known tumor promoters (14-16, 32). Over the past two decades, they have become recognized as signaling molecules (12), regulating their own synthesis (33). BAs bind to and activate the nuclear receptor farnesoid X receptor (FXR), which results in negative feedback to tightly control BA levels. But, how they signal to promote cancer is not fully understood. Dr. Anakk's previous work demonstrated that mice with chronically elevated bile acid levels are predisposed to develop liver adenomas and carcinomas (1, 34). In this context, BAs activated Yes-associated protein (YAP), a potent promoter of proliferation via induction of the scaffolding protein IQ motif-containing GTPase Activating Protein 1 (IQGAP1). Consistently, mice lacking IQGAP1 were refractory to BA-induced proliferation, indicating a role for IQGAP1 in mediating BA-induced proliferation.

While multiple IQGAP isoforms have been identified in mammals, IQGAP1 is the best characterized and the only ubiquitously expressed isoform (35). In mice, hepatic IQGAP1 expression is high during development and decreases in quiescent liver but becomes re-expressed in disease states (36). For example, IQGAP1 is upregulated in many cancers, and its overexpression often correlates with a poor clinical outcome (7-10, 37). IQGAP2 is also expressed in the liver but functions as a tumor suppressor. In fact, IQGAP2 expression decreases in HCC (38). Loss of IQGAP2 leads to spontaneous development of HCC, which is abrogated upon concurrent loss of IQGAP1, suggesting that IQGAP1 is required for HCC development in *Iqgap2<sup>-/-</sup>* mice (18). These data raise two key questions about IQGAP1's role in neoplasia: (i) How is hepatic IQGAP1 regulated? and (ii) Is IQGAP1 required for BA-induced tumorigenesis? (figure 1). This proposal is designed to answer these questions and to investigate whether modulating IQGAP1 is a feasible therapeutic option for HCC.

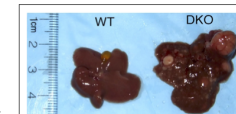
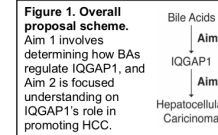
#### Innovation

Not applicable for fellowship applications.

#### Approach

##### Preliminary Data to the Proposed Research

My Ph.D. mentor, Dr. Anakk, serendipitously discovered that concurrent loss of *Fxr* and *Shp* from the whole body (DKO mice) synergistically elevated BA levels beyond that of single *Fxr<sup>-/-</sup>* and *Shp<sup>-/-</sup>* mice resulting in juvenile-onset cholestasis (34). Despite being maintained on the tumor-resistant C57BL/6 background, these mice developed large liver adenomas by 12 months (figure 2) that progressed to HCC by 15-17 months (1). Excitingly, these observations are consistent with the development of HCC in human patients who suffer from chronic BA overload (39). Furthermore, the DKO mice showed activation of YAP, and the DKO tumors macroscopically mirrored mice with enhanced YAP activation (40-47). Importantly, this activation of YAP was shown to be dependent on the expression of the scaffolding protein IQGAP1 (1). IQGAP1 is an evolutionarily conserved protein originally identified by its calmodulin-binding IQ motifs and GTPase Activating Protein (GAP) homology



**Figure 2. BA overload promotes HCC and robustly upregulates IQGAP1.** 12-month old DKO mice show well-developed adenomas. Published. (1)

# PROJECT SUMMARY AND NARRATIVE

## **Project Summary (30 lines)**

- Significance of project and relevance to human health
- Brief description of what is known about the question you are addressing
- How your proposal will address unknown aspects and connect to human health
- This is published on a public NIH database

## **Project Narrative (3 sentences)**

- Very brief description of question you are addressing
- What results from your proposal will add to knowledge about particular disease or question
- Lay person should be able to understand

# RESPONSIBLE CONDUCT OF RESEARCH

NIH requires that fellows have received training in the responsible conduct of research (RCR).

- Explain how you will fulfill this requirement
- If you have or plan to take the MCB ethics course requirement, outline topics covered and how they were covered (texts read, exercises, etc.) and time spent on these activities
  - Format
  - Subject Matter
  - Faculty Participation
  - Duration of Instruction
  - Frequency of Instruction
- List any other possible ethics courses, workshops or ethics discussions or mentorship with sponsors

# STUDY SUBJECTS

If you're proposing to use either **Vertebrate Animals** or **Human Subjects**, you are required to complete the respective section.

Get info on this from your sponsor. You should be covered under their protocols.

Will need to provide justification for sample size (use power analysis).

# RESOURCE SHARING PLAN; RESPECTIVE CONTRIBUTIONS

## Resource Sharing Plan (1 page)

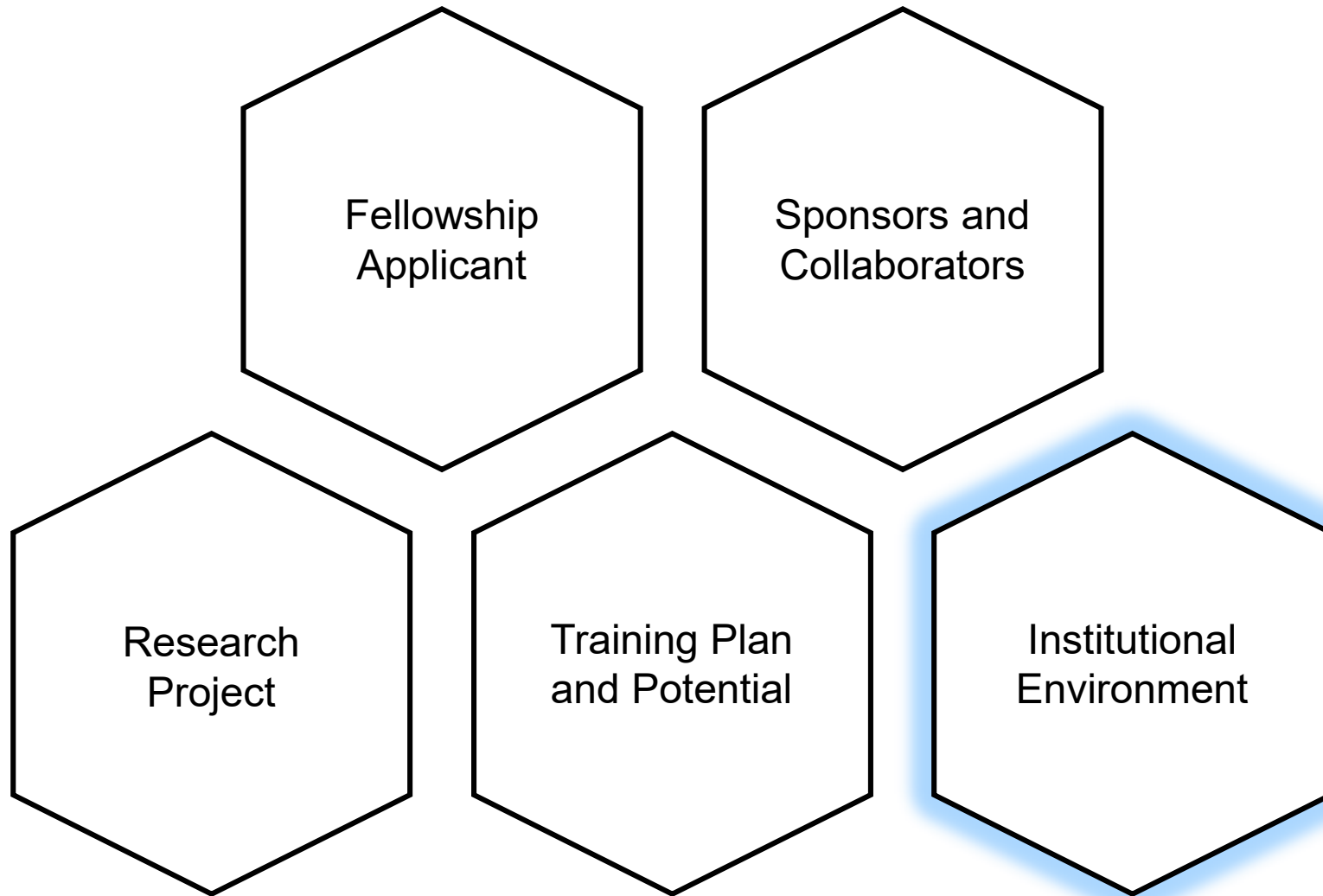
Must adhere to NIH Grants Policy on Sharing Research Resources

- **Data Sharing Plan** – important to share data with the public (present at meetings, publish promptly), make protocols of our procedures available by request
- **Sharing Model Organisms** – available after publication
- **Genome-wide Association Studies** – available after publication

## Respective Contributions (1 page)

- Delineate applicant role in obtaining preliminary data generated for proposal vs. data from others
- Applicant role in preparing grant application

# CORE REVIEW CRITERIA





# INSTITUTIONAL ENVIRONMENT

Should have all of the required resources and support to complete proposed research and training.

## Relevant documents:

- **Selection of Sponsor and Institution**
- **Description of Institutional Environment and Commitment to Training**
- **Facilities & Other Resources**
- **Equipment**
- **Sponsor and Co-Sponsor Statement**
  - **Environment**
  - **Research Facilities**

# SELECTION OF (SPONSOR AND) INSTITUTION

- Prestige and reputation of university and applicant's affiliated program
- How selection of university/program fits into applicant's research interest and training plan for future career

The University of Illinois at Urbana-Champaign (UIUC) is a **highly ranked institution** with a unique environment to foster innovation and creativity. I was drawn to UIUC because of its Medical Scholars Program (MSP) that takes advantage of the rich culture of collaboration at the university to provide a **multidisciplinary, research-focused program** for its MD/PhD students.

One **particularly unique aspect** of the MSP that appealed to me is its non-traditional structure that provides freedom for its diverse student population to create a training plan that best fits their interests and goals.

# DESCRIPTION OF INSTITUTIONAL ENVIRONMENT AND COMMITMENT TO TRAINING

- Describe the facilities and resources available for research
- Document a strong research program
- List intellectual interactions available (seminars, presentations, lab meetings, courses, journal clubs)
- Facilities and resources for career enhancement
- For F30/F31, describe the program (structure, milestones, courses, teaching, average time to degree, how students are monitored)
- For F30, describe clinical activities during graduate years and research activities during clinical years

# FACILITIES & OTHER RESOURCES; EQUIPMENT

## Facilities & Other Resources (1 page)

Describe the scientific environment, especially what is unique

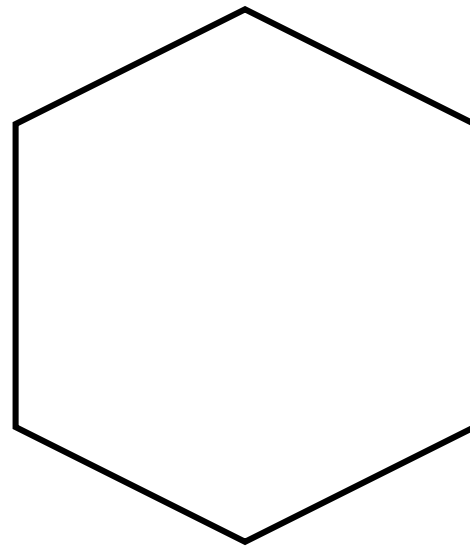
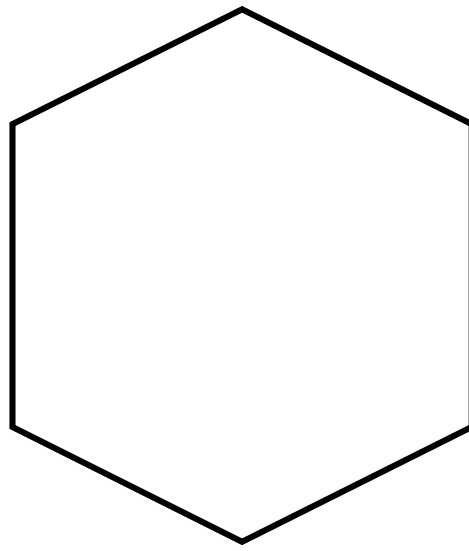
- **Institutional support:** animal care and use, trainee travel grants
- **Physical resources:** core facilities
- **Personnel resources:** collaborators, collegiality (MCBees)

## Equipment (1 page)

List (in outline form) the equipment available to you during your training and where it is located

- **Common lab facilities:** list all *common* equipment including microscopes and data processing equipment
- **Core facilities:** histology, sequencing, flow cytometry

\*Your advisor probably has “boiler plate” documents for these.



**QUESTIONS?**

