WRITING GRANTS: BEYOND THE SCIENCE

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DISCLOSURES

Michelle Kahlenberg: Consulting for Novartis

Alexis Ogdie: Consulting for Novartis, Pfizer, Takeda; Grant from Pfizer (co-investigator), Grants from Celegene, Abbvie, and Pfizer (on behalf of GRAPPA)

OBJECTIVE

Grant writing is not just about the specific aims and the science!

Our objective is to walk through the pieces that no one talks about and to give tips on how to approach them.

PROJECT NARRATIVE

The Project Narrative is the section of the grant application where the applicant should talk about the relevance of the proposed research project to public health. The information should be:

Succinct (no more than 2-3 sentences long)

In plain language understandable by a general, lay audience

PROJECT SUMMARY

The most important piece after your specific aims

- It is what all the other people who score your grant but don't read it will look at during study section.

Limit length to 30 lines or less of text

Include the project's broad, long-term objectives and specific aims

Include a description of the research design and methods for achieving the stated goals

Do NOT include proprietary or confidential information, or trade secrets. *This will be publicly available if the project is funded.*

Write in plain language, so even a non-scientist can understand the importance of the project

BIOSKETCH

Standard form in NIH format

- http://grants.nih.gov/grants/forms/biosketch.htm

The most important pieces are your personal statement and contributions to science

Personal Statement:

- Should be unique to each application
- This is your chance to summarize and sell you and your application.
- Why are YOU the one for the job?

"Briefly describe why you are well-suited for your role(s) in the project described in this application. The relevant factors may include aspects of your training; your previous experimental work on this specific topic or related topics; your technical expertise; your collaborators or scientific environment; and your past performance in this or related fields (you may mention specific contributions to science that are not included in Section C). Also, you may identify up to four peer reviewed publications that specifically highlight your experience and qualifications for this project. If you wish to explain impediments to your past productivity, you may include a description of factors such as family care responsibilities, illness, disability, and active duty military service"

http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-032.html

CONTRIBUTIONS TO SCIENCE

Briefly describe up to five of your most significant contributions to science.

- Indicate the historical background that frames the scientific problem; the central finding(s); the influence of the finding(s) on the progress of science; and your specific role in the described work.

Reference up to four peer-reviewed publications or other non-publication research products (can include audio or video products; patents; data and research materials; databases; educational aids or curricula; instruments or equipment; models; protocols; and software or netware) that are relevant to the described contribution.

- **No longer than one half page including figures and citations**.

Provide a **URL to a full list of your published work** as found in a publicly available digital database such as SciENcv or My Bibliography, which are maintained by the US National Library of Medicine.

CONTRIBUTIONS TO SCIENCE

Example:

- Linked altered inflammasome biology with the development of systemic lupus erythematosus (SLE) and its vascular complications. My work has demonstrated that the inflammasome is upregulated in lupus nephritis and that overexpression of IL-18 by inflammasome activation in endothelial cells contributes to endothelial dysfunction and the elevated risk of cardiovascular disease in SLE. Further, we have shown that macrophage production of IL-18 and IL-1β is hyperactivated in SLE and this can be induced by neutrophils extracellular traps (NETs) leading to a vicious cycle of cytokine production which can further induce NET formation. Importantly, we have also utlized murine models to demonstrate that the central inflammasome enzyme, caspase-1, is required for IgG autoantibody development and lupus nephritis. This work has demonstrated an essential role for the inflammasome in SLE and identifies this complex as a potential target for further therapeutic development.
  - **Kahlenberg JM**, Thacker SG, Berthier CC, Cohen CD, Kretzler M, Kaplan MJ. Inflammasome activation of IL-18 results in endothelial progenitor cell dysfunction in systemic lupus erythematosus. J Immunol. 2011 Dec 1;187(11):6143-56. PubMed PMID: 22058412; PubMed Central PMCID: PMC3221936.
  - **Kahlenberg JM**, Carmona-Rivera C, Smith CK, Kaplan MJ. Neutrophil extracellular trap-associated protein activation of the NLRP3 inflammasome is enhanced in lupus macrophages. J Immunol. 2013 Feb 1;190(3):1217-26. PubMed PMID: 23267025; PubMed Central PMCID: PMC3552129.
  - **Kahlenberg JM**, Yalavarthi S, Zhao W, Hodgin JB, Reed TJ, Tsuji NM, Kaplan MJ. An essential role of caspase 1 in the induction of murine lupus and its associated vascular damage. Arthritis Rheumatol. 2014 Jan;66(1):152-62. PubMed PMID: 24449582; PubMed Central PMCID: PMC4135431.
  - Morse M, Clark KL, **Kahlenberg JM**. Caspase-1 is required for maintenance of marginal zone B cells in pristane-induced lupus. Lupus. 2016 Jan;25(1):81-7. PubMed PMID: 26405027

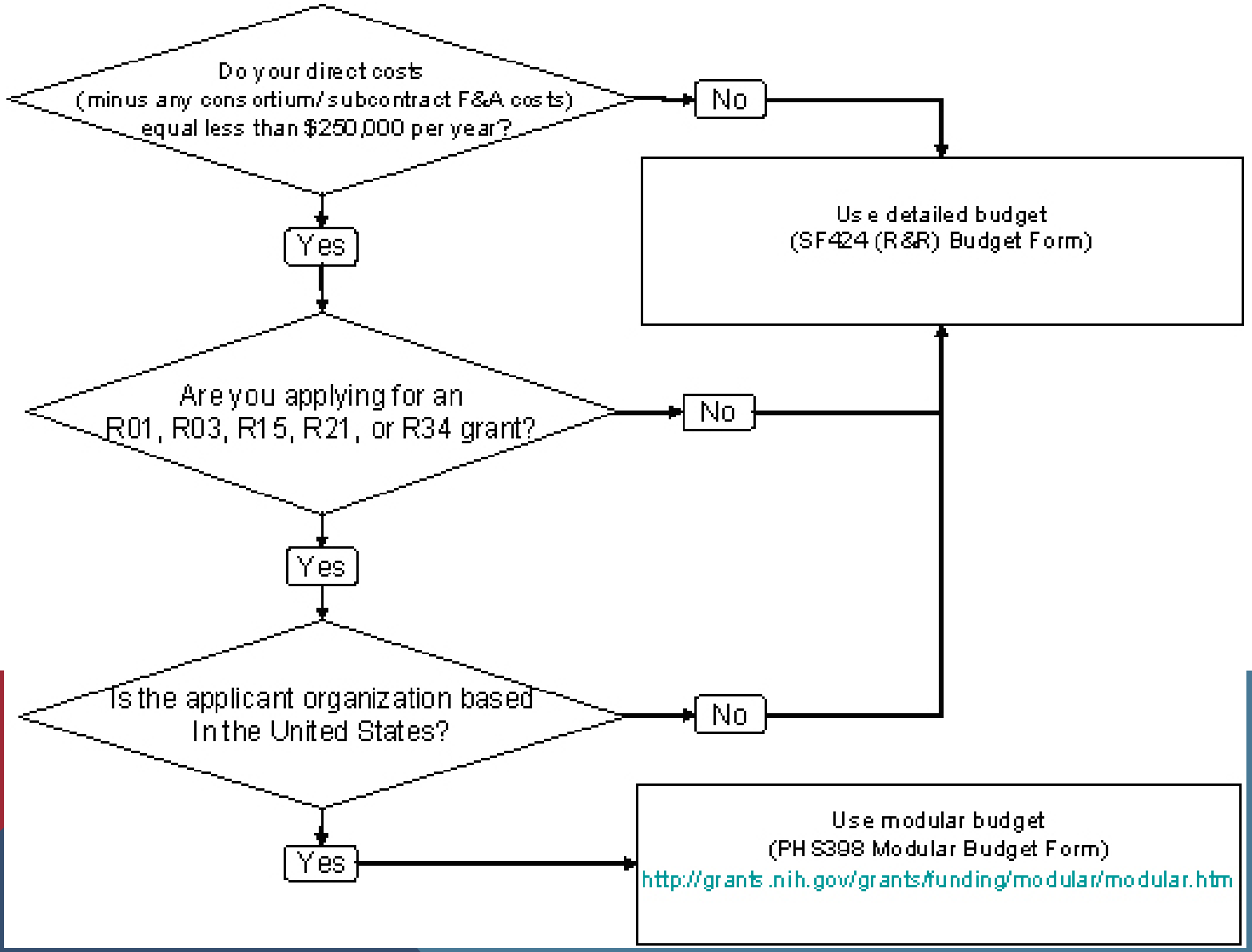
BIOSKETCH

You’re not only in charge of YOUR biosketch, but also everyone on your team!

Give people plenty of time to get them to you.

Review them in detail and make them specific (especially the personal statement) to your application (sending back to them for approval of course).

BUDGETS


Do your direct costs
(minus any consortium/subcontract F&A costs)
equal less than $250,000 per year?
No
Yes
Use detailed budget
(SF424 (R&R) Budget Form)
Are you applying for an
R01, R03, R15, R21, or R34 grant?
No
Yes
Is the applicant organization based
In the United States?
No
Yes
Use modular budget
(PHS398 Modular Budget Form)
http://grants.nih.gov/grants/funding/modular/modular.htm

MODULAR BUDGET JUSTIFICATION

A modular budget justification should include:

- *Personnel Justification:* The Personnel Justification should include the name, role, and number of person-months devoted to this project for every person on the project. Do not include salary and fringe benefit rate in the justification, but keep in mind the legislatively mandated salary cap when calculating your budget. [When preparing a modular budget, you are instructed to use the current cap when determining the appropriate number of modules.]

Consortium Justification: **If you have a consortium/subcontract, include the total costs (direct costs plus F&A costs), rounded to the nearest $1,000, for each consortium/subcontract. Additionally, any personnel should include their roles and person months; if the consortium is foreign, that should be stated as well.**

Additional Narrative Justification: **Additional justification should include explanations for any variations in the number of modules requested annually. Also, this section should describe any direct costs that were excluded from the total direct costs (such as equipment, tuition remission) and any work being conducted off-site, especially if it involves a foreign study site or an off-site F&A rate.**

http://grants.nih.gov/grants/how-to-apply-application-guide/format-and-write/develop-your-budget.htm

DETAILED BUDGET JUSTIFICATION

Personnel:

- Effort in CM
- Senior/Key Personnel are from your institution
- Other Personnel (lab technician)

Equipment (>$5,000), Travel (list destination, who is going and anticipated costs), Trainee costs

Other

- Materials and supplies
- Animal Costs
  - Give per diem rates, breeding rates, purchase costs
- Publication Costs
- Consultant Services (charge a fixed rate for services)
- Computer Services
- Alterations/Renovations
- Patient Costs
- Tuition for graduate students

USE THE BUDGET JUSTIFICATION

Give more detail about collaborators/mentors and why they are a perfect fit

Outline what each person will do and how much effort they will contribute

Alexis Ogdie-Beatty, MD, MSCE, Principal Investigator, University of Pennsylvania (25% effort)
Dr. Ogdie is a rheumatologist and epidemiologist with expertise in psoriatic arthritis, use of large databases, and application of biostatistical methods for pharmacoepidemiology studies including use of complex multivariable models. Dr. Ogdie's responsibilities will include:

- Coordinate all aspects of the project
- Create analytic datasets from clinical trials data and perform data analyses for Aim 2
- Work with Dr. Troxel and the BAC statistician to derive, test, and validate the simulation models
- Work with BAC to perform simulation modeling as outlined in Aim 2
- Meet twice monthly with Dr. Troxel
- Meet twice monthly with BAC statistician
- Conduct monthly phone meetings and twice yearly in person meetings adjacent to ACR and GRAPPA with the study investigators.
- Draft manuscripts and revise with the help of the co-investigators
- Work with study investigators to design future studies based on the simulation results
- Submit manuscripts and subsequent grant applications
- Submit annual reports to the RRF

FACILITIES FOR BASIC SCIENCE LABS

Environment

Institutional Commitment to the Success of the Investigator

- This is a must for ESI applicant
- Discuss start-up funds and resources available for faculty development and enhancement of the intellectual environment

Core facilities

- Transgenic and KO mouse cores, sequencing, flow cytometry, microscopy, histology, luminex, etc.

Clinical facilities if relevant

Computing resources (software, support, etch)

Office space/Lab space

FACILITIES FOR CLINICAL STUDIES

Clinical sites: this is a place to give more detail about where you will recruit patients and your collaborators

For Career Development Awards, this is where you can include more detail about conference series, additional training, etc.

Think about all of the potentially supportive cores or other resources that will support your development as an investigator (and/or development of future collaborations).

- e.g. CTSA, pilot grant programs, faculty development programs, local grant writing programs/work groups
- For each item, write WHY it's important to you. Don't just list.

EQUIPMENT

List the equipment available to you to demonstrate you have the resources available to complete your research. Most people take the strategy to list anything that may be even slightly relevant.

EQUIPMENT

Currently available in Dr. Kahlenberg's lab

2 humidified CO2 tissue culture incubators, two biological safety cabinets, a low speed refrigerated centrifuge, 2 microcentrifuges, two refrigerators, two -20 freezer, two -80°C freezers, a liquid N2 cell storage container, two microscopes, one inverted microscope for tissue culture, protein and DNA electrophoresis apparatus, a gradient PCR machine, an imaging system for chemiluminescence, fluorescence and chromogenic labels, electro-transfer apparatus, pH meter, water baths, rockers, a spectrophotometer, and UV transilluminator.

Common equipment in adjacent laboratories includes high speed and ultra centrifuges, gamma counter and beta counter, cold room, nano-drop for DNA and RNA measurements, FPLC, and a plate reader with microscope capabilities. The laboratory has been approved as an OSEH biosafety level II containment facility.

Available through Core Facilities

The *Microscopy Core* includes a Noran Confocal Laser Scanning Imaging System, Flurescence Resonance Energy Transfer (FRET) System, the MetaMorph Imaging System, Zeiss-Attofluor Fluorescence Digital Imaging System, CSMZ-U Zoom 1:10 Light Microscope, 2 Workstations, Kodak Digital Scient 8650 PS and Tektronix Phase 550 Printers. The *Flow Cytometry Core* has several machines including MoFlo Astrios (6 lasers and biosafety cabinet for sorting), ImagestreamX MarkII (4 lasers), Cyan (3 lasers), and MACSQuant 2 (3 lasers). The *Affymetrix and Microarray Core Group* offers an Agilent 2100 BioAnalyzer to assess RNA quality, the Affymetrix Gene Chip System with the Affymetrix scanner 3000 7G, and an ABI 7900HT real time PCR instrument. *The Bioinformatics Core* is aligned closely with the Microarray core and provides assistance with data analysis for genome resequencing, ChIP-Seq transcription factor analysis, RNA-Seq analysis, de novo assembly, metagenomic sequencing, and gene set enrichment analysis. Additionally they facilitate custom-designed analysis. The *Experimental Radiation Core* offers an orthovoltage irradiator to perform moderate dose rate gamma irradiation to cell cultures, tissue specimens or animals.

HUMAN SUBJECTS DOCUMENTS

Protection of Human Subjects

Inclusion of Women and Minorities

Inclusion of Children

Target Enrollment

Notes since 2019:

The Inclusion of Women, Children, and Minorities is now a single document and you must not only address the patients that will be enrolled but also how you will take subgroups into account in the analysis. Include “sex as a biological variable” in the main grant.

Additionally, in Forms E, there are MANY documents now as a part of the Human Subjects portion. You complete a checklist to see which ones you need to include. There are also fields that are directly entered into ERA commons and not separate documents.

PROTECTION OF HUMAN SUBJECTS

Think of this like the IRB protocol.

You will cut and paste parts of your grant (or IRB) into the specific subheadings.

This may be an opportunity to include additional figures that show where and how people are recruited as well as additional logistics.

Make it easy to read. There's no page limit so consider using bullet points, tables, etc

PROTECTION OF HUMAN SUBJECTS

Risks to Human Subjects

- Human Subjects Involvement, Characteristics and Design
  - Recruitment and Retention
  - Special vulnerable populations
- Sources of Materials
- Potential Risks

Adequacy of Protection Against Risks

- Recruitment and Informed Consent
- Protection Against Risk

Potential Benefits of Proposed Research to Human Subjects

Importance of the Knowledge to be Gained

WOMEN AND MINORITIES

What percentage of the enrolled patients will be women? What percentage will be minorities?

Is this reflect of the disease? Why or why not? (If no, rationalize why it needs to be done this way.)

This can be very short

PROTECTION OF CHILDREN

Are children included? (now <18 years old)

If yes, why?

How will they be protected?

INCLUSION OF CHILDREN

The specific aims of this study include determining early disease activity of psoriatic arthritis (PsA). PsA is a subtype of JIA, which is by definition a pediatric disease with onset at or before age 18. Therefore, the study involves children and adolescents. All children and adolescents between 6 and 21 years of age who fulfill ILAR criteria for PsA, or receive a dermatologist-confirmed diagnosis of psoriasis, and are cognitively capable of participating will be invited to enroll in the study. Children are members of a special class. Fully informed, written consent will be obtained from the parent(s) or legal guardian(s). In addition, age-appropriate informed assent will be obtained from the subjects themselves. The Children's Hospital of Philadelphia is a healthcare institution devoted to pediatric care. The research team is skilled in pediatric and young adult studies and will make every effort to make the experience enjoyable, as well as scientifically and methodologically sound.

VERTEBRATE ANIMALS

Requirements

If live vertebrate animals are to be used, federal policy requires applicants to address the following criteria:

1. **Description of Procedures.** Provide a concise description of the proposed procedures to be used that involve vertebrate animals in the work outlined in the Research Strategy section. Identify the species, strains, ages, sex and total number of animals by species to be used in the proposed work. If dogs or cats are proposed, provide the source of the animals.
2. **Justifications.** Provide justification that the species are appropriate for the proposed research. Explain why the research goals cannot be accomplished using an alternative model (e.g., computational, human, invertebrate, in vitro).
3. **Minimization of Pain and Distress.** Describe the interventions including analgesia, anesthesia, sedation, palliative care and humane endpoints to minimize discomfort, distress, pain and injury.
4. **Euthanasia.** State whether the method of euthanasia is consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals. If not, describe the method and provide a scientific justification. Note, for applications with due dates on or after May 25, 2016, the method of euthanasia is eliminated from the VAS and is addressed in the FORMS-D Cover Page Supplement or PHS Fellowship Supplemental forms.

VERTEBRATE ANIMALS

Checklist

Performance sites:

__ If the applicant's institution is not where animal work will be performed, are all collaborative performance sites identified?

__ If more than one performance site is planned, are descriptions of animal use addressing the required criteria provided for each site?

1. **Describe the animals and their proposed use. Address the following for all species to be used:**
   - __ Species
   - __ Strains
   - __ Ages
   - __ Sex
   - __ Total number of animals by species to be used
   - __ Concise, complete description of proposed procedures (i.e., sufficient information for evaluation)
   - __ Source, only if dogs or cats are proposed
2. **Provide justifications for:**
   - __ Choice of species
   - __ Why research goals cannot be accomplished using an alternative model (e.g., computational, human, invertebrate, in vitro)
3. **Describe interventions to minimize discomfort, distress, pain and injury. Examples of the kinds of items that may be appropriate to include are:**
   - __ Circumstances relevant to the proposed work, when animals may experience discomfort, distress, pain or injury
   - __ Procedures to alleviate discomfort, distress, pain or injury
   - __ Identify (by name or class) any tranquilizers, analgesics, anesthetics and other treatments (e.g., antibiotics) and describe their use
   - __ Provisions for palliative care or housing that may be necessary after experimental procedures
   - __ Plans for post-surgical care, if survival surgeries are proposed
   - __ Indicators for humane experimental endpoints, if relevant
4. **State if method of euthanasia is consistent with AVMA Guidelines. If method does not follow the guidelines:**
   - __ Describe the method of euthanasia
   - __ Provide a scientific justification

   Note, for applications with due dates on or after May 25, 2016, the method of euthanasia is eliminated from the VAS and is addressed in the FORMS-D Cover Page Supplement or PHS Fellowship Supplemental forms.

http://grants.nih.gov/grants/olaw/vaschecklist.pdf

AUTHENTICATION OF KEY RESOURCES

State, in one page or less, how you will authenticate key resources, including the frequency, as needed for your proposed research

Key biological and/or chemical resources may or may not be generated with NIH funds and: 1) may differ from laboratory to laboratory or over time; 2) may have qualities and/or qualifications that could influence the research data; and 3) are integral to the proposed research. These include, but are not limited to, cell lines, specialty chemicals, antibodies, and other biologics

Standard laboratory reagents that are not expected to vary do not need to be included in the plan. Examples are buffers and other common biologicals or chemicals.

Purchased or established resources may have been authenticated prior to receipt, and the vendor may have included a specification sheet with the product. If the authentication data provided by the vendor meets your needs in terms of how the product will be used, this may be mentioned this in the plan, but you should also include a plan to independently verify the identity and activity of the product before use.

Currently NOT scored, but may be in the future.

https://nexus.od.nih.gov/all/2016/01/29/authentication-of-key-biological-andor-chemical-resources-in-nih-grant-applications/

SUMMARY

Each document is important

Use the Space!

Project Narrative and Summary are particularly important because most people who vote on your application will read it (or at least glance at it).