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EDITORIAL

Thirty-two steps for getting your R01: advice to early career investigators

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Certainly, one of the biggest challenges in pursuing a research-oriented academic career is being awarded your first large grant, an R01, from the National Institutes of Health. In general, domestic or foreign, public or private, non-profit or for-profit organizations are eligible to receive NIH grants. One does not need to be a US citizen or permanent resident to apply for an R01. So, for the purposes of giving advice on how to obtain an R01, this advice can be used by the international readership of Pediatric Research. Even those who have obtained a K award will find the transition to an R award daunting. In a recent comment, Good et al observe the limited achievement of NIH independent R funding by pediatric K award recipients.[1] And not much has changed in supporting this transition since 2018 when Alan Jobe wrote in his commentary "the academic pyramid to a successful career in pediatric research is in tatters".[2] Thus we are writing this editorial so that early career investigators may have a better chance of obtaining independent funding. Co-author Ben Gaston, a reasonably successful and well-funded pediatric researcher—who also has been on a number of NIH study sections—once offered the following advice to a junior faculty member who was starting to write an R01. Here, we offer it more generally to the pediatric research community.

1. At least a year ahead of the deadline, decide on the novel, clinically relevant question you would like to answer. Spend a week or two in PubMed, looking at everything that has been published. Decide how you can advance the science beyond what has been published. Look at the data differently: don't just buy the conventional wisdom. Begin to formulate an overall aim that is novel, relevant and do-able. Dream big. If you don't have a big vision, or if you are writing an incremental grant primarily to advance your career, stop. Begin again when you are inspired by the question.
2. Choose your optimal target study section. Find out who on it works in your focus area. Collect and read their papers.
3. Draft aims and sub-aims. Make sure that they are significant and innovative; things you are passionate about. Make sure that they are things that you have shown you can do (in your T or K grant, or just in your training or faculty position in general). If you are a mid-level faculty member who has a big idea and some data, that's even better than being a junior faculty member who is writing a grant because he/she is required to.
4. If you haven't shown you can do an aim you think is important (innovative, significant and vital to the overall project), do the experiments and publish a paper on the results before you go any farther; or find a collaborator who definitely can do it. Find the best person, not the nicest person. Not necessarily a mentor at this point (this is an R): a collaborator.
5. Don't write for the sake of writing. Have a specific idea in mind. But don't share the idea too broadly… you could dilute your focus implementing collaborators' ideas.
6. Harshly criticize each aim and sub-aim. Do you have expertise? Do you have any evidence it will work? Is your rationale elegant, scientifically? Do you have the equipment and facilities needed? Have you published in the field? Are there weaknesses in your preliminary data? Can you can begin to show clinical relevance? Do you have a long-term plan? Are your aims mechanistic and focused, or diffuse hand-waving? Is your point of focus credible? Do you have strong data to support the mechanism? Is your aim based on a statistically answerable questions? Will you have the power fully to answer the question? Are you in the right cell type? Do you need an animal model, or will humans do? Do you have a correlate or validation in humans?
7. Ask yourself if specific members of your study section reviewers will have an issue with an aim. Be particularly harsh.
8. Change your aims or sub-aims. Be sure each is really strongly in an area of your (and your collaborators') published expertise, that the rationale and mechanisms are based on data everyone will buy, that you have addressed experimentally or (for a MINORITY of weaknesses) that you have considered the weaknesses and have a plan to address them (note that these latter weaknesses CANNOT be show-stoppers… the Aim needs to be able to proceed if the weakness cannot be overcome… otherwise, change the aim). Then go back and be sure they are clinically relevant.
9. Start doing additional specific experiments that you are proposing to support the aims. Start the experiments needed. You will already have been doing some of them, but there will be new ones.
10. Go back to PubMed. See who has already done each of the experiments you propose. Spend a week or so on this. You may find that most of the experiments you propose have already been done in some fashion. What are the loose ends from these studies? The unanswered questions of clinical relevance? Often, the people who did the experiments were thinking about the problem differently than you are thinking about it. How do their data fit your paradigms in ways you were not considering?
11. Change your aims and sub-aims based on the re-review of the literature.
12. Repeat steps 6–9.
13. Look at your new preliminary data. Some of the experiments will have given you data different from what you proposed that they would.
14. Change your aims based on your new results.
15. Repeat aims 6–9 based on your new data and Aims, and re-consider the literature.

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16. Learn new techniques and get collaborators to plug any gaps. For example, single cell analysis, big data analyses, advanced microscopy, clinical studies, etc.
17. Go back again and be sure that each of your aims and sub-aims is innovative (has not been thought of before in the way that you are thinking of it), is significant, is supported by very focused data (either published or your own) and is something you and your collaborators (mostly you) can accomplish with your skills and resources.
18. Change your aims to address any weaknesses identified in step 17.
19. Make sure all the aims follow logically from one another, but that there are no show-stoppers (something that would mean that there was no point in doing a specific follow-on Aim if the experiment did not work). Also make sure your aims represent realistically five years of work, not two or ten.
20. Change your aims based on 19, then repeat step 15.
21. Draw an easy to understand schematic for your Aims.
22. Now you are ready to start writing the grant. It will flow pretty easily at this point. If it does not, I highly recommend Anne Lamott's book, "Bird by Bird", with regard to getting started with your first draft.[3] In the first draft, perfectionism can be you enemy. Get something on paper. Though the Aims page will have taken a year, the first draft of the rest will take a few weeks. All other pieces… worry about them last. Even though your office of sponsored research will be bugging you, don't do anything else at this point except getting the science right. Then, the rest will be easy and won't need to be changed.
23. While all this is going on, get all the papers you can published. Balance. If you have time for a high impact paper, great. But if you just need to show that you can do/have done something, get it out quickly. When you write methods, you can then just cite your paper, not write out all the details (you only have 12 pages).
24. Remember under the research design section: for each sub-Aim, have: hypothesis; rationale; design; statistical analysis; anticipated results and interpretation; and potential pitfalls, problems and solutions. This section is a tedious slog but important. This is where points are most commonly lost at study section. Find help with the stats/power analyses.
25. Be sure ALL the references are included, especially from relevant groups on the study section. It's not possible to be over-referenced. But just be sure the references don't show that your work is irrelevant, already done, or impossible. If you now discover a paper that suggests any of these problems, go back to step 11 and start over. I'm not kidding.
26. In your next time through the grant, pay tremendous attention to detail. Especially time course, dose response, negative and positive controls, etc. Include all of this in your preliminary data explanations to show that you pay close attention to these things.
27. Then go back and be sure you are making no assumptions about what the reviewers will understand. Assume the reviewers have very little background relevant to the details of your grant (remember, I'm one of them sometimes). Lead them by the hand through the science, especially on the Aims page. Also, have no abbreviations (or very few abbreviations) on the Aims page. No clinical jargon (that you might use on rounds): the grant will be evaluated by scientists. Minimal scientific jargon: the grant will be evaluated by clinicians.
28. Make really high-quality, comprehensive figures for preliminary data and schematics.
29. When you are done, this will be about 20–25 pages. Shorten it to 12 (13 with the aims) by getting rid of adjectives (especially self-congratulatory ones) and statements like, "… we are one of the best at…." Get rid of jargon and redundancies. Don't change direction (using terms such as but, however, on the other hand, etc.) more than once per paragraph. Reorganize paragraphs and sections to be sure they are tight. Don't ramble or prate. Let the data be your adjectives; and let the reviewer decide whether you are really the best in the world. Turn every sentence into beautiful, clear, concise poetry. Make sure each paragraph makes a clear point, and follows in logical sequence. Go over it again and again, making everything shorter, but with the same meaning. Don't leave out any facts or data… but cut theory and opinion and adjectives to a minimum. Brevity.
30. Get input from other people, especially collaborators. All criticisms are valid, even if the reader misses the point entirely. If your colleagues miss the point, the reviewers (really unfamiliar with your subject matter, remember) will probably miss the point as well. Simplify.
31. While this is going on, publish more papers and do the extra bits. Of the extra bits, the most important are: the biosketches, the abstract (something brief that all the members can read), the budget justification, the budget, the protections for humans and animals, and the planned enrollment. Be sure there are no internal inconsistencies. The Facilities and Resources can be important as well. All the various documents should be professional-looking. Administrative help is invaluable, but spend a day looking through all this stuff to make sure that it is not sloppy.
32. Read the grant harshly. Don't be afraid to cut and re-arrange if, in the end, something doesn't make sense. It's OK to move to a later grant deadline.

Good luck!

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REFERENCES

1. Good, M., McElroy, StevenJ., Berger, JenniferN., Moore, DanielJ. & Wynn, JamesL. Limited achievement of NIH research independence by pediatric K award recipients. *Pediatr. Res.* **84**, 479–480 (2018).
2. Jobe, AlanH. Commentary on "Limited achievement of NIH research independence by K award recipients". *Pediatr. Res.* **84**, 481–482 (2018).
3. Lamott A. Bird by bird: some instructions on writing and life. Second edition. (New York: Anchor Books, 2019).

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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