

2011 ASBMB Student Centered Education in the Molecular Life Sciences II

From Proposal to Publication: Writing and Critical Thinking Skills

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Planning and conducting research for PUI or Graduate Faculty is always challenging with a constant competition for time. This workshop will focus on effective approaches to experimental design and writing manuscripts from grant to paper submission. Workshop leaders will describe how to think about research in terms of a hypothesis driven publication that will aid in planning the types of research experiments and controls necessary to focus the efforts of undergraduates at PUI's. Differences in strategies effective in R1 institutions involving both graduate students and undergraduates will also be discussed. The workshop will address effective mechanisms for approaching writing each section of a manuscript and focus on how journal editors view PUI submitted manuscripts. Challenges more typical of research-intensive environment will also be addressed. Despite significant differences in approach, there are basic common features of well-written manuscripts that are common to both groups. Ultimately the significance of the science and clarity of the presentation are the driving factors in acceptance of manuscripts for publication. The workshop will include small group work analyzing manuscripts for structure and key sentences. Attendees are encouraged to bring a draft of their work to share and analyze with a small group.

Writing is easy. All you do is stare at a blank sheet of paper until drops of blood form on your forehead.

Gene Fowler

Brilliance has an obligation not only to create but also to communicate.

J.R. Platt

The trouble with most of us is that we would rather be ruined by praise than saved by criticism.

Norman Vincent Peale

Planning and Designing Experiments for Publication – be efficient or be unpublished:

- Avoid fishing experiments early. Each paper should answer one big and two or so smaller questions. Be hypothesis driven.
- Review current literature early – don't wait because you are busy. Papers for PUI's can take a while to finish... stay ahead of the game and keep up with the relevant publications as you go.
- Existing grants can be used to write papers but often are not in shape for papers. Instead think of how a grant can be turned into one, two or three papers. The first paper may not be one aim, but parts of several. I often look at a grant as NIH paper I, NIH paper II. The second paper is typically plan-able by the grant but any follow up papers are pretty esoteric.
- Be efficient early in your planning process. Plan each experiment as a figure – Using hypothesis/paper's main question, sketch out each figure BEFORE the experiments are started. After the big question may have driven a few cool experiments it is time to get things in "paper order". Think of a, if this is true then what should the data look like... format for each figure. This will help design the individual experiment and a good way to carefully consider what controls need to be included in the experiment. This philosophy will keep you from going down side trails. "side trails" can be followed up later or part of another project.
 - *Think of it as if you are a lawyer arguing a case... you present the witnesses (experiments) to the jury in the most clear and logical order -- one that tells a story. This is not necessarily the order in which you originally interviewed them.*
- Be efficient – Know when to cut bait or fish. Is the technique not working, is the experiment need to change to answer the question, is it the "bench hands" or is the hypothesis wrong? How many times does one expt need to be repeated?
- Controls, controls, controls... PUI faculty often will be asked to do more than a more famous R1 PI. Plan ahead of time. Control expts are great positive experiences for new research students!
- Be efficient in your student's time – consider using a team approach to a paper. Each student or student team could work on one or two connected figures; all put together will form a paper.
- Make students do repeats, create publishable quality figures, including statistical analysis and figure legends.
- Post the figures in the lab in order of the paper – helps motivate and keep things on track. Create the title page and outline of figures.
- Carve out time to write – wait until summer? Don't wait until all the expts are over. Two-hour blocks can be effective when making small goals in your writing.
- Organize pertinent papers – electronically, piles on the desk or folder. This will help when writing.
- Be disciplined – use those times when students aren't around. Put up signs to not feed the bear. Protect your time.

Proofreading and Revising Your Manuscript.

- Ask (pay) non-disciplinary scholars to proofread your manuscript after you have written the first draft. Have them critique the paper for:
 - clarity
 - organization
 - incorrect grammar
 - simple and concise descriptions/definitions of key terminology
 - convoluted or run-on sentences
 - paragraphs that are too long and contain too many ideas
- Ask disciplinary scholars to proofread your manuscript after you have written the second draft. Have them critique the paper for:
 - clarity and organization
 - relevant and descriptive figures, equations, schemes, and tables
 - proper use of scientific jargon
 - proper use of tense
 - relevant and current references
- Use the key sentence method for proofreading and revising.
 - A key sentence articulates the main point, claim or idea of a paragraph or a larger text. Strong key sentences enable the author to write with clarity and organization.
 - The **thesis of the paper** should be described in a key sentence that is underscored/supported throughout the article.
 - Each paragraph should contain a key sentence. In scientific writing the key sentence is often the first sentence in the paragraph, but it need not be. The key sentence should (1) express the topic of the paragraph (2) be central to the paragraph such that all other sentences provide the necessary details, descriptions, and proofs to support it, and (3) be noteworthy and concise.
- Provide the proofreaders with a list of specific questions that you would like them to answer regarding the text. For example:
 - Is Equation 1 sufficiently descriptive of the general reaction described?
 - Is my definition of _____ and the parameters affecting it clear?
 - Have I provided enough detail for someone else to reproduce the synthesis of ___ in the experimental section?

Organizing and writing your manuscript:

- Determine appropriate journal, read instructions to authors and get two or three examples from same journal of similar papers to use as templates.
- Tell a good story – be complete but concise.
- Sectional organization – write figures first (should already be done)! Then write easiest – Figures and the methods. Work on results then discussion. Don't do the introduction until you know what to introduce.
- Follow a cadence or algorithm for each section. Keep the flow going, wordsmith later.
- **Start** with your initial hypothesis then layout the figures.
- **Next** consider your hypothesis as a story.
 - Use the figures and the hypothesis to determine one, two or three summary statements; questions your studies will answer. The hypothesis and summary statements should organize each section of the manuscript. These are the take home message or question your paper answers.
 - Use short sentences which use cause and effect words (necessary, influence, predict, causes) to generate your summary sentences.
 - Get your story to an elevator speech and stick to the point throughout the manuscript.
- **Figures:** Work on details for publishable quality figures– too specific for this presentation.
 - Include rough drafts of legends. Use summary statements for headers of each figure legend to help organize the thoughts.
 - Arrange the figures in order to tell the best story not always chronologically.
 - Creating and arranging the figures first helps to determine what is needed. Spread out the figures on a poster or the wall. Review the figures (feedback) and determine if they are in the right order for your story. Analyze if there are too many or unnecessary figures?
 - Present work in a manner which best tells the story – analogy for papers is that you are a lawyer arguing a case... present the witnesses (experiments) to the jury in the most clear and logical order -- one that tells a story. This is not necessarily the order in which you originally interviewed them.
- **Methods:** Pay attention to the Journal's style guide (wrong style can irritate reviewers). Methods must have enough details to allow someone to repeat the experiments.
 - Organize in order of figures/results section. Written in past tense with a passive voice, avoid first person.

- Often looked at much more closely by editors and reviewers than one might imagine. This section should allow reviewers and readers a clear way to understand how the studies were conducted.
- Include relevant information on animal and human studies (IRB/UACUC) how subjects were included or excluded.
- Less information on materials is included than 15 – 20 years ago, but don't forget specific specialized reagents, antibodies, oligo reagents...
- Avoid referencing methods that are references themselves.
- Create the section in small segments in a logical order – use subheadings.
- **Results:** This section is used to 1) report results and present how this data supports the hypothesis.
 - Written in past tense with summarizing data in present verb tense. Avoid discussing the findings.
 - Organize the results in the same order as materials section for clear reading – may even use same basic topic sentences or subheadings as in figure legends.
 - There is a very straightforward rhythm to the results section. Use the algorithm: because of this (earlier study, data presented in the MS or other's work) we asked this question (sub-hypothesis). To do this we did this... experiment. Follow with description of results with final comment.

As constitutive activation of Erk-MAP kinase has been implicated with upregulation of uPAR in several human tumour types (Hoshino and Kohno, 2000), we investigated whether p42/44 Erk-MAP kinase activity plays a role in the regulation of uPAR expression in HCT116 cells. In vitro kinase assay, specific for p42/44 MAP kinase activity, showed approximately two-fold higher MAP kinase activity in WT and mock-transfected HCT116 cell lines compared to A/S cell line (Table 2). British Journal of Cancer (2003) 89, 374 – 384.

Alternative regioisomers 3-chloro-2-aminopyridine and 2-chloro-3-aminopyridine and the more reactive 4-amino-3-bromopyridine also did not couple with borolane 5 beyond 3% yield under these conditions. To eliminate the possibility that ethoxyvinylborolane 5 cannot couple or decomposes under these conditions, it was tested in a reaction with 4-chloroaniline 7, previously shown to couple efficiently with a range of borolanes.(21) This reaction was successful, giving 52% product (entry 1, Table 2). J. Org. Chem., 2010, 75 (1), pp 11–15

- Key transition phrases between data groups include... “Having shown... we next examined / determined, these results suggest that...” Read through accepted MS in the journal you plan to publish in to identify key results words that do not interpret. Examples include: associated, correlated, significantly, apparent, ... having these phrases and words will greatly speed up the writing process.
- **Discussion:** Often the hardest section to write during the school year. The purpose of this section is to answer the key questions from the hypothesis, fit the findings with existing knowledge, and convince the reader/reviewer with the approach and limitations of the results.
 - Written in present tense and is often written in the active voice.
 - Start with a paragraph reviewing main thrust of results – highlighting only the most key points. Keep in mind the summary statements. Clearly write how this study answered these questions and the degree that the described work advances the state of knowledge. Finish the initial paragraph with a clear statement indicting the significance of the MS. This paragraph should only be a few sentences long.
 - Identify the main results from each section of the results and figures – then add in causality. i.e. find a mechanism to explain/interpret the results.
 - Do not overstate the significance or novelty. Use terms and phrases such as: “probably”, “is likely”, “one possible interpretation is...” to avoid sweeping or overly enthusiastic conclusions.
 - Discussion words (different from results words): those that infer mechanistic causes and effects from data presented in the results section: “influences, sufficient, necessary, associated can be used if needed to soften if the link between cause and effect are less clear.
 - Overall flow of discussion: opening paragraph, explain results, indicate originality and importance of study, discuss unexplained or expected findings and how findings concur with others.
 - Concluding paragraph: restate logical conclusions and why the study is relevant. Then add how further studies could further your work or substantiate the findings of the MS.
- **Introduction:** Write this last as your understanding of where the paper is going will have matured at this point. Also there is no need to introduce what is not discussed.
 - Past tense for much of the introduction. When discussing established facts, switch to present tense.
 - Introduction answers three questions: 1) what is the big picture or question, 2) what is the specific question, 3) what don't we know/how will this study help?
 - A clear statement of the hypothesis and main questions early in the introduction will help focus the reader's attention.
 - Start with a summary of the subject and literature to provide reviewer enough information to understand the main points of the results and discussion, how these points expand the body of understanding and to allow the reviewer to better understand how the work is worth publishing.

- Second illustrate and introduce what is unknown or problematic. Identify gaps and disclose similar studies to those presented in the MS.
- Close with a clear declarative paragraph of the problem you have answered. Remember your hypothesis and summary questions when writing this paragraph. Include a simple summary of the most important finding(s) of the paper. "...in the current study, we demonstrate that...", "the purpose of this study was...", or "this study was undertaken to..."
- Review your introduction when finished. Does each sentence contribute to the summary statement described above? If not, delete.
- **Abstract:** Simple statements. (mixed tense)
 - First sentence is the question asked with one or two sentences on background if word limit allows (present tense).
 - Research approach to answer the question (past tense).
 - Most significant findings (past tense).
 - Answer the question posed in the beginning of the abstract (present tense).
 - If space allows – include a speculation of the implication of the study.
- **Title:** Now – write the title for the manuscript. Incorporate a positive statement from the summary statement found at the end of the discussion and introduction.
- **Hypothesis and Data Review:** As you get to the summary statements, finish the figures, complete the results section work through the discussion and create the final conclusion paragraph, review the data to see if the data, results and discussion all point to the main hypothesis. Does this story still match your summary statements? Review and revise to keep a clear story. This is especially important for when a MS is written in the middle of many distractions a semester will bring.

Exercises on Proofreading and Revising Papers Using Key Sentences

The paper journey – what happens to your manuscript after submission (*The details will vary from one journal/publisher to another and also differ when Academic editors are the ones running the process*):

- The paper is read by an editor and often discussed by a team of editors (in general many of the decision points below are often done in consultation with a team although this varies).
- It is then either:
 - Sent out for review to 2-4 experts chosen by the editors (many journals welcome suggestions for reviewers and respect exclusions)
 - Returned to the authors with an explanation as to why the editor feels it is not likely to be a strong candidate for publication
- Role of the Reviewer:
 - Provide expert advice on technical merits and conceptual advance of the manuscript
 - Provide fair and constructive feedback on how the paper can be improved
- When the reviews are returned, the editor evaluates the reviewers' comments in much the same way she evaluated the original manuscript. Editors may weigh in with their own opinion as necessary
- The editor decides how to proceed, often in consultation with a team. She will either:
 - decline the paper,
 - invite the authors to resubmit the work after revision, or
 - accept the paper in its current form

Note: the ultimate decision is not a simple tally of "fors" and "againsts". Often reviewers don't agree and the Editor must decide which advice to follow.

- The editor writes a letter to the authors, conveying the decision and the rationale behind it; and including the reviewers' comments.
- At most journals, authors who have been invited to resubmit will be asked to provide a detailed point-by-point response to the reviewers' comments outlining how they have addressed them. It is also a good idea to include in the letter a short description of any additional data in the manuscript. This enables the editor and the reviewers to easily assess the new data.
- The resubmitted paper is then evaluated by the editors and may undergo another round of review before the final decision is made – usually to decline or accept the paper but sometimes the authors are asked for a second round of revisions (typically not extensive).

Editor's tips

1. When reviewing a MS to accept or decline for publication, what things do you look for? What kinds of science do you find particularly exciting?

- Following are questions editors typically ask when evaluating a paper:
 - Scope: Does it fall within the scope of the journal? Who will be most interested in the work? A paper on a topic that falls well outside the scope of a journal will almost certainly be rejected no matter how good the work (e.g. a study of 3D tissue development submitted to a molecular biology journal).
 - Significance: How does it fit with other papers published on this topic? Does it pose (and answer) questions that are important to the field? Does it move our understanding of the field forward?
 - Logic: Are the experiments logically designed? Do they directly test an experimental hypothesis or are they merely consistent with it?
 - Technical Quality: Although the technical evaluation is mostly done by the reviewers, the editor does check that the experiments are performed reasonably.
- Have the authors presented a reasonable question or goal.
- Have the authors performed the appropriate experiments to address this question. Did they try and see if they could get the same answer using two or more distinct experimental approaches?
- Does the data address the original question and support the conclusions drawn [If not, the authors should perhaps rethink the question].
- Do the authors give appropriate credit to other investigators?
- Have the authors cluttered the manuscript with tangential experiments or attempted to stretch the significance by piggybacking a provocative, but incomplete and preliminary experiment, upon the core study.
- Is there sufficient information provided so that a person can determine how the experiments were performed and know the source of any key clones, cell lines, antibodies, etc.
- See if there are clear reasons why they did the research. See if they state clearly what they found. Look for true novelty. Look for reproducibility of findings and proof thereof. Make sure that any conclusions are fully supported by the data.
- As far as excitement goes, something off the beaten path. There is way too much "Me too" science out there
- In my opinion, state of the art science is the most exciting part of reading a manuscript. After reading a good manuscript, you say something like, how come I didnt think of it or what a great idea, etc. This does not mean other type of science is not important or interesting to read. For example, a new method to do a synthesis better, a new analytical tool, mechanistic insights, a new computational work which could lead to better design of an experiment etc. The type of science you read and like also depends on what type of manuscript it is: full paper, review, communication or a note. The type of science reported will be different and hence the reading interest or excitement. The emphasis of these categories varies with disciplines: chemistry, biochemistry, molecular biology, etc.
- An example of my own science which when carried out more than 10 years ago was fundamental in nature and curiosity driven. So when doing it an writing the paper, it was interesting but not very exciting. Last year, a Pharma company used our method to make two tons of a potential drug candidate. So the work became useful. If the reviewer in late nineties was of the opinion that the paper was not exciting and worthy of publication, we wouldnt have the present outcome. So when reviewing a manuscript, one needs to take a broader view and not get too hung up on asking for the state of the art science all the time.

2. What kinds of science do you find should not be published?

- I don't think there are any specific kinds of science that should not be published but papers in which the experiments do not provide insights into the questions posed – either because of poor design or poor technical quality – ordinarily do not fare well in the review process.
- Superficial, phenomenological studies. Information should go into a database. Investigations should be published in peer-reviewed journals.
- Decline anything that is trivial or superficial. Decline anything that is hyped, exaggerated or emotional i.e. attacks other authors.

3. Outside of obvious readability, how important is writing style when you review manuscripts?

- The writing style itself is not that important but clarity is key. Poor English is often not the main reason for a badly written paper: lack of focus and logical flow are more often the problem Flow and organization are key. While it is wonderful if the author is a terrific wordsmith, what really matters is putting things together in a logical manner.
- Following are some general guidelines:
 - Place the work in context. What important question does the paper address?
 - Restrict it to one main message.
 - Show your paper to colleagues outside the field. Can they understand the points you are trying to make and do they find your presentation persuasive?
 - Clearly distinguish between what you can conclude and what you can only suggest – limit the amount of speculation.
- Try to be explicit in stating the goal of the research described – a question to be answered, a quantity to be measured, a protein to be isolated.

- Present only those experiments germane to the goal or question, don't litter the manuscript with descriptions of the blind alleys you encountered before hit in the right path. Quantity cannot make up for quality. In fact, it often backfires by confusing the reader.
- Present the experiments in the order that makes the most sense, not necessarily in the order in which they were done.
- In presenting results, don't jump directly to interpretation. Tell me what information was produced and then tell me what you think it means. So instead of saying that "all cells were viable", tell me the outcome, "more than 95% of the cells excluded trypan blue, indicating that the cultures were viable". Do not tell me that the K_d for substrate is X when what you determined was a K_m unless you can support this with substantiation that the enzyme follows an equilibrium mechanism!
- Keep your story clean and focused, the introduction and discussion clear and concise.
- Use clear, consistent nomenclature. Label figures and tables clearly and write clear and complete legends. Don't make me jump back and forth looking for stuff.
- Must be clear and not confusing. Not too wordy. Should just not cite the author's work, but recognize the work of others. Must know the relevant literature.
- Writing style is important. The first paragraph should state a hypothesis for the work and state why it is important. Describe what is known and how your work answers the hypothesis.
- One does get annoyed with bad grammar, a lot of spelling mistakes, etc. With the outstanding word processing available now, there is no reason to have misspelled words. Although I won't reject a paper for poor grammar or spelling mistakes, it does turn you off. So take good care in proofing your manuscript before sending it to the editor. Use simple declarative sentences, Don't hype your science. Reviewers can easily recognize quality of the science presented.

4. What are the most obvious problems you find when declining submitted manuscripts?

- Phenomenological, descriptive work packaged as critical, incisive investigation. It is possible to generate a lot of data about something without ever performing an experiment that addresses the authors' working hypothesis in a direct, critical fashion. Unless you risk being proven wrong, you cannot convince me that you are right in the scientific sense of the concept. Too many people consciously or unconsciously seem to avoid having their favorite hypothesis placed at risk, and hence end up including every experiment with the exception of the "right one".
- Lack of key controls. You'd be surprised how many people submit papers describing new enzyme assays in which they failed to determine the dependence of the assay's output on the quantity of analyte present, substrate concentration, incubation time, etc.
- Failure to follow up the inferences drawn from one type of approach with a second and more appropriate approach. Whatever function a bioinformatics analysis suggests for a protein, until you do an assay showing that it possesses the requisite activity that function remains putative. [I remember seeing a paper several times where the authors claimed to have identified a new subfamily of phosphohydrolases that were distinct from other known subfamilies. However, in response to my request that they check for phosphohydrolase activity with pNPP, they replied that this was not necessary because the protein was so similar in sequence to homologs outside the alleged new subfamily that had been tested. They didn't seem to blink at eye at their self-contradiction – that this new subfamily was important because it might have distinct functional properties, but were so similar to others that activity could be taken for granted].
- I have yet to encounter a paper in which a scientist was able to convincingly and compellingly determine a catalytic mechanism or other structure-function relationship at amino acid resolution using genetics alone.
- Trying to make something look more original or novel than is warranted by giving it a new name / acronym to render it more difficult to discover other published work.
- No clear message. Methods not good or poorly described so work can't be confirmed. Data inconsistent or don't support conclusions
- Poorly crafted. The stated hypothesis does not agree with the results. Data missing and or poorly analyzed. Supporting information in not good shape.

5. How much weight do you place on who the PI is or if they are a PUI faculty when considering manuscripts.

- I don't think I have ever thought about whether an author is PUI faculty. On a related note, however, I and all the other editors I knew did go to several scientific meetings each year, and it is definitely easier to evaluate a paper if we had recently heard a discussion of the general scientific topic or a presentation of the work itself (either as a talk or in a poster). So I would say that taking advantage of any opportunity to present your work in public is important – even if the editor wasn't at the meeting/seminar, one of the reviewers might have been
- I will admit that I do not expect PUI faculty to have access to the same research infrastructure as R1 faculty. So I am less demanding regarding scope or technical virtuosity. However, I remain equally demanding that the experiments presented are appropriate in nature, logical and rigorous in approach, and well controlled. The questions addressed may not always be as "hot" or as "grand in scale", but the data has still got to back up the conclusions.
- I don't care who the author is or where the work was done.
- Not much. Some high profile PIs don't seem to supervise their groups very well, or assist much with manuscript preparation.
- Very little. With the international aspect of publishing these days, lot of times you don't have any clue as to where the place is and I still review the paper as a normal one. So if the school is a PUI, it doesn't matter.

6. What are the things you have found yourself wishing you found or did not find in manuscripts?

- A professional and scholarly discussion of the existing literature is important - particularly when you are presenting results that differ from or even contradict previous work. I found it frustrating when very closely related references were missing (I always did a literature search when evaluating a paper) but just as frustrating when related work was cited but discussed in a dismissive or unprofessional manner. Both of these tend to distract the reader - editor or reviewer - from the work you're trying to present. First and foremost, whatever your favorite acronym, please start out by listing all of the published names/acronyms to help me get oriented.
- I get very perturbed at people who try to work a lot of speculation into the discussion in order to be able to claim that they somehow thought of it first. This is an egotistical and arrogant practice that is profoundly unscientific. Science is about proof.
- Use superlatives sparingly.
- Don't make mountains out of molehills. Claims such as this is the first time that this enzyme has been characterized in a salamander caught by a left-handed graduate student just doesn't cut it, or that you wish to settle the raging controversy over whether the pKa of histidine 1511 is 6.23 or 6.31 are counterproductive. Some questions may be simple or not particularly glamorous, but that does not mean they are not worth investigating. But these exaggerations actually diminish stature.
- Keep the introduction to two pages or less double spaced. Keep the discussion to four pages or less. Get to the heart of the matter; don't bury your core message under a mass of ancillary materials.
- Faked data or data taken from someone else's work or from previous publications by the author.
- Clear figures illustrating pathways or models, intelligible to a general audience.
- Sometimes the science will be very good but poorly presented and you end up asking for major revisions or reject. In those cases, you do your best to help the authors, and many times, time crunch doesn't let you help the authors. I usually do not want to do a second review of a paper I had previously reviewed. I wish to read different science than what I had seen before.
- I also do not like to see over interpretation or stating ones work is better than what it is (be humble) but also dont undersell your science.
- I like a well laid out manuscript: A question posed, experiments to answer the question, and discussion.

7. Can you tell us anything else that undergrad faculty should know when writing and submitting manuscripts.

- Clear, simple, direct generally works best -- especially when selling the significance of the problem being addressed. If the experimental work is good, it will elevate the question in away no superlatives or distant connection to cancer ever could.
- Don't apologize for not having a million dollar mass spec. The power of an experiment comes from the rationale underlying its design, not the expense or newness of the equipment used.
- Ask a scientist from a different field to critically read the manuscript for advice on intelligibility and whether the nature and significance of the scientific advance is clear to a general audience.
- One of the most important thing about submitting manuscripts is placing ones science in the proper context. That is, how important is the work being presented? What would be the readership? Are we breaking new ground, etc. If the answer is yes to all the above, then craft a manuscript in the best possible manner and submit it to the best journal, a journal with high impact factor, etc. Suggest reviewers who are experts in the field, even if you think they may be competing with you. We do have a tiered structure for journals. For example, nature, cell, science, PNAS, JACS are first tier. To get an article published in these journals, the science has to be super good. If the work is not suitable for the top tiered ones, pick a journal which is appropriate for the work. Second and third tiered journals are not bad. Publishing one article in a highly reputed journal is a big accomplishment regardless of where you are (PUI or not). If one is not able to publish in a top tiered journal because of the quality of the work, see if you can improve the science and make it worthy (say takes one more year because you need to strengthen the work). In my opinion it is worth waiting.
- Also, do not submit average science to the best journals. This turns off the reviewers and it they are less likely to give you a break the next time.
- Overall, there is always a journal which is appropriate for the work one does. So choose the one which fits best. Self evaluation of the quality of ones work is important and writing a good manuscript helps you sell your science easier.
- Before submission:
 - A concise, edited cover letter setting out the main points of the paper can be very helpful. Tell the editors what YOU find most interesting about the work. Use the opportunity to convey why the paper is important for the field and the readership of the journal.
- When you receive the reviews:
 - Read the decision letter and reviews carefully.
 - Focus on the scientific issues.
 - If the reviews or editorial evaluation cite legitimate limitations or lack of sufficient general interest or if the reviewers' recommendation is unanimous, it is usually best to submit the manuscript to another journal.
 - If the reviewers and/or the editors have misunderstood a key aspect of the paper, it is sometimes possible to email the editor about the possibility of reconsideration with a brief explanation of the relevant points and how you plan to address them.
 - ABOVE ALL: Do not respond immediately. You won't have thoroughly considered all the issues or carefully drafted your response. Wait at least a day.

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