In the Lion's Den:





The Manuscript Review Process and How to Survive It

Collected articles based on presentations given at a special session of the AAI Publications Committee at IMMUNOLOGY 2011[™] in San Francisco, California May 14, 2011

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In the Lion's Den: The Manuscript Review Process and How to Survive It

This collection of articles is based on presentations at an AAI Publications Committee session at IMMUNOLOGY 2011, held in San Francisco, California. The articles appeared in the *AAI Newsletter*, October/November 2011, December 2011 and January/February 2012 issues.

AAI thanks the presenters and the Publications Committee for their work in providing this resource to assist scientists in the essential process of publishing their research findings.

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I Just Clicked Submit. What Happens Next?

The first in a series of articles providing guidance to researchers on the publishing process for peer-reviewed scientific journals

Juan Carlos Zúñiga-Pflücker, Ph.D., Professor, University of Toronto Sunnybrook Research Institute

This article is the first of four based upon presentations made during an IMMUNOLOGY 2011[™] AAI Publications Committee Symposium titled **"In the Lion's Den: The Manuscript Review Process and How to Survive It."** Zúñiga-Pflücker is a former Section Editor and Associate Editor for The Journal of Immunology and a current member of the AAI Publications Committee.



Juan Carlos Zúñiga-Pflücker

I Just Clicked Submit. What Happens Next?

Is your heart racing and the excitement palpable as you click "Submit" on The Journal of Immunology (The JI) online submission site? If so, you are not alone. It's a very tense moment for everyone and for good reason. You've spent tremendous amounts of time, money, and effort in your research, and you are now eager to share your findings with your peers in the field. And you are sure your research will resonate in the broader scientific community beyond! Suddenly, though, excitement morphs into near panic as you wonder, "Did I upload the correct file, the one with the latest versions of the figures or text, the one with all the corrections and proper labels?" You check and double check yourself, verifying that all was submitted correctly. Eager anticipation is restored. But, alas, this sense of well being is short-lived, for an ominous chorus has commenced in your head: "What happens next? What will the reviewers think of my paper?"

In this article, we'll focus on the first question, the "What happens next?" That is, we'll look at the process that takes place within *The JI* from the time you submit your paper to the point that you, the Corresponding Author, receive a decision notice. (See "Corresponding Author" insert, page 30.) As in our scientific papers, I think a chart for this process may be helpful. In Figure 1, I've attempted to map the steps of *The JI* editorial process (see page 29).



For the second question, the one regarding reviewers' opinions, I advise you to seek comfort and guidance from the sages at your local hangout — your favorite bar, pub, or café.

The Editorial Structure

The JI makes use of a three-tiered editorial structure established to ensure that all full-length submissions are considered by more than one person and given a fair review. In addition to the AAI professional staff of Ph.D.s at *The JI*, there are fifty two Section Editors, ten Deputy Editors, and one Editor in Chief. The Section Editor is typically a scientist working in the same or closely related field as the author, while the Deputy Editor, who covers broader areas for *The JI* and deals with several subspecialties, is likely to be familiar with the general topic of the manuscript but less involved in that particular subspecialty of immunology. In 2010, *The JI* review process was supported by the generous assistance of nearly 3,700 reviewers and 123 Associate Editors (a select list of peer reviewers) engaged in reviewing nearly 4,000 papers received that year.

The Review Process

Once the manuscript is received, a member of the editorial staff confirms that the paper is structured according to *The JI* requirements and that all the necessary forms associated with the submission have been received (Step 2). If the paper does not pass this inspection, it is returned to the Corresponding Author (Step 2b). Note

that this and all other communications between the journal and the authors are conducted with the Corresponding Author. Any author whose manuscript is returned at this point should "re-"consult *The JI* "Information for Authors" guidelines available online at www.jimmunol.org/site/misc/ authorinstructions.xhtml.

Once the paper is properly organized and all necessary forms have been received by The Journal, the manuscript is assigned a Deputy Editor and a Section Editor. At this point, the staff Ph.D.s at *The II* compile a list of potential reviewers to be forwarded to the Section Editor with the manuscript. The Section Editor reads over the paper and assigns a rank order to the list of potential reviewers. The Section Editor may also add names or veto suggested potential reviewers. These reviewers are your peers, highly regarded scientists who, because they are working within the same field, are deemed capable of offering a substantive and insightful review of the work.

The JI staff next contact potential reviewers in the order provided by the Section Editor until at least two reviewers are secured. Reviewers are given a two-week window for providing their review of the manuscript.

Once two reviews are received (Step 7), the Section Editor reads over the manuscript again and assesses the reviews. The Section Editor is also able to consider reviewers' insights forwarded in comments made directly to the editors but not shared with the Corresponding Author. When I was a Section Editor. I found these comments extremely valuable, for they typically provided clarity on points at issue. At this juncture, if conflicting reviews are received, the Section Editor will provide a third review or seek a third reviewer's opinion. Finally, with the benefit of reviewers' comments to the Corresponding Author and those exchanged among editors, the Section Editor re-examines the manuscript and formulates a recommendation to be forwarded to the Deputy

Figure 1-The Journal of Immunology Review Process from Submission to Decision



Editor. The Deputy Editor looks over the manuscript, reads the reviews, and considers the Section Editor's recommendation before making a decision on the manuscript. The staff then send the decision letter to the Corresponding Author.

The JI does not use a triage system. That is, *The JI* does not reject or accept manuscripts without sending them for the complete peer review process. Although this lengthy process may seem onerous to an author, it provides the kind of transparency and instructive feedback that is especially important for a journal published by a professional society. (Note that a different process applies to papers submitted to the "Cutting Edge" section of The Journal. Because a dedicated editor, also an active scientist, assesses the manuscripts submitted to this section prior to soliciting reviewers' comments, these papers may be declined without the benefit of a full review. However, any manuscript rejected from the "Cutting Edge" section, either with or without

review, may be resubmitted as a full-length manuscript without any prejudice from its rejection as Cutting Edge.)

Four Potential Outcomes

There are four potential outcomes of the review process (Step 9). A paper can be accepted outright (Step 9a), a rare and wonderful outcome. (Upon this most marvelous occurrence, you are well advised to revisit your local hangout to take back all that you said about the dearth of insight and understanding you had anticipated from your peers.) Bear in mind, however, that over 50 percent of manuscripts submitted to The JI are deemed unready or, in fact, unsuitable for publication and are rejected. (See parenthetical comment above, but replace "take back" with "restate!")

Two other potential outcomes are less clear-cut, and both trigger further editorial and/or peer review. The manuscript may be accepted pending minor revisions (Step 9c).

Continued next page

That is, no new experiments or major work is required, but clarifications, corrections, or other minor changes are all that must be addressed. (Again, this calls for another visit to the local hangout, for this outcome is also greeted with much joy!) Following resubmission, the Section Editor looks over the authors' revisions and makes a recommendation to the Deputy Editor.

Alternatively, the manuscript may be returned to the authors for major revisions (Step 9d), as the work requires further experiments or major alterations before being reconsidered for publication by The JI. This decision is not made lightly. Careful consideration is given to whether the reviewers' comments and recommendations are reasonable and would, in fact, substantially improve the publication prospects for the paper. Authors of manuscripts that are returned for revisions are given a firm deadline (nine months from date of return) for requested revisions, and the Corresponding Author is given no assurances that the paper will be accepted upon resubmission.

After the authors have completed major revisions and the manuscript has been resubmitted, the Section Editor reads over the Corresponding Author's letter, which should outline point-by-point the changes made to the paper. Most revised papers are sent back to the initial reviewers for re-review. The Section Editor may recommend whether both or only one of the reviewers needs to see the revised manuscript, but it is the Deputy Editor who ultimately decides who should see the revised submission. In rare circumstances. the Section Editor alone handles the re-review. As before, the Section Editor makes a recommendation to the Deputy Editor (Step 13), who then makes a decision on the manuscript (Step14), and again the same four outcomes are possible.

If accepted, the manuscript goes to the publisher. If the acceptance is contingent upon minor revisions, the manuscript, as before, is returned to the authors. This is a common outcome. In the re-review, the reviewers and/or the editors may believe that not all the points were properly addressed by the authors, that further clarification must be requested, or that issues initially missed during the first review must now be addressed.

In a less common outcome, the manuscript is returned for major revisions a second time. This is a very rare occurrence since all major issues should have been addressed during the

The Corresponding Author

- The Corresponding Author is responsible for the content of the submitted work.
- The submission system allows someone other than the Corresponding Author to submit the manuscript (Ms), but once the "Submit" button is clicked, all correspondence about the Ms will be done only with the Corresponding Author.
- If the Ms fails Initial QC and is returned to the Corresponding Author's account to be fixed, the accompanying e-mail goes only to the Corresponding Author.
- The Corresponding Author is responsible for submitting all necessary forms to the journal.
- The Corresponding Author is responsible for paying any fees to the journal.
- Only the Corresponding Author can see the status of the Ms during the review process; office staff cannot give access to other authors to see the Ms status.
- The Corresponding Author is responsible for making newly described reagents available after the Ms is published.

initial revision. Any outstanding issues are likely either minor issues (Step 15c) or issues previously identified but not fully addressed. Issues that prove to be insurmountable lead to a rejection (Step 15b).

The fact that more than 50 percent of papers submitted to *The JI* are rejected following the initial review or after the re-review phase may strike you as a dispiriting statistic. It shouldn't. Perhaps it's cold comfort, but a rejection from *The JI* should be regarded as a learning experience. After all, it comes after a manuscript has been fully reviewed and carefully considered. The comments that authors receive from peers in the field offer critical insights for improving eventual publication prospects for the paper.

Remember, all authors are filled with anxiety as they await word from the editors. The top-of-mind question for all is why the review process must take so (fill in with your favorite expletive) long. The urge to contact the journal starts nearly as soon as the paper is submitted. Know, though, that The JI process from manuscript submission to a decision is about thirty-five days. This is an average time, and some decisions may take longer. The JI staff makes every effort to keep the time to a decision as short as possible, sending overdue reminders to reviewers. (That's likely you, at some time, or your peers!) Finally, following acceptance, the average time before the paper appears on the website as a fully formatted and proofed article is about 4.9 weeks.

So, sit back and relax. Or, as is more likely the case, continue performing your experiments and pursuing the funding to sustain them. Take comfort in knowing that your paper and the work it details will be uniquely recognized and handled by a dedicated team of editors and reviewers. After all, *The Journal of Immunology* is your society's journal, and the editors and reviewers look forward to seeing your work bear its proud imprimatur.

Making It Easier for the Reviewer

The second in a series of articles providing guidance to researchers on the publishing process for peer-reviewed scientific journals.

Melissa A. Brown, Professor, Department of Microbiology and Immunology, Northwestern University Feinberg School of Medicine

This article is the second of four based upon presentations made during an IMMUNOLOGY 2011[™] AAI Publications Committee Symposium titled In the Lion's Den: The Manuscript Review Process and How to Survive It. Brown is currently a member of the AAI Publications Committee, having formerly served as a section editor for The Journal of Immunology.

Reviewers: The Final Obstacle before Publication of Your Important Work

You have been working for some time on a most interesting project and have just finished a set of key experiments. It is clear that you now have all the makings of a good, maybe even great, story. The data are sound and will fill in critical gaps in our understanding of some previously confounding immunological process. You are ready to write a manuscript that describes



Melissa Brown

collaborations, seminar presentations at home or at a distant site, time to attend seminars, as well as writing one's own grants and papers. All this before we can try to claim some time for our personal lives.

Given all these demands, why do so many people provide such a valuable service to those of us who aspire to publish? Most reviewers believe they have a responsibility to contribute to the publication of good science. Peer review, albeit imperfect, provides the

foundation that assures the veracity of reported findings. Although reviewers are unpaid advocates of publishing good science, there are some perks for the reviewer, too. Reading about new findings before they are ready and available for general consumption is often exciting. Of course, serving as a reviewer is also an important addition to one's curriculum vitae, especially for those who are anticipating promotion.

Although you have spent a great deal of time on your story and know it intimately, remember that it is new to the reviewer. (One hopes!) Spell it out as clearly as you can. No reviewer wants to have to try to read your mind while wading through a confusing maze of data and prose. If a reviewer must spend too much time just trying to understand what you are trying to say or trying to locate Figure 2, you are immediately at a disadvantage. If, however, you invest time in a crafting a clear, easy-toread manuscript, you will set the stage for a more favorable review. This is a case where everyone benefits, especially you.

Below, I review some simple principles you'll wish to consider when writing a manuscript. If these are taken to heart, your manuscript will most certainly be one that is a joy to read.

The Abstract: First Impressions Are Important!

Once a paper is published, the abstract serves a very important function for readers who are scanning the literature for studies relevant to their own work. The abstract should convey the key points of your paper, enabling the reader to assess its relevance to their own areas of interest and determine whether they should read on. For reviewers, however, the abstract serves a different purpose. This short summary of the study makes the first — and often indelible — impression. The abstract should

your findings. When finally published and the data are disseminated to other scientists, this work will make an important contribution to the field. Only one thing stands between you and publication: The reviewers!

Whether you are in the middle of writing or are just beginning, some insight into the mind of the reviewer (or at least this reviewer) can enhance your chances of a favorable review. Some of this insight is just common sense, but some may not be so obvious. I can't guarantee that this information is the ticket to acceptance (After all, inherent to science careers are the endless questioning and challenges, criticisms and rejections), but I can guarantee that the reviewer will have a more favorable overall impression of your manuscript as he/she goes through it. This more benign impression can't hurt your chances for a thoughtful, considered, and fair review. Even if there is no immediate "accept" decision, the comments, whether you agree with them or not, are always useful and provide insight into how others perceive your work and interpretations. If taken into serious consideration, these comments can guide your revisions and lead to an improved manuscript, one that is ready for public consumption.

Who Reviews Manuscripts and Why Would Anyone Do This for Free?

There are many reasons a person agrees to review a manuscript, but it is a certainty that those of us who volunteer are not doing so to fill empty time. Reviewers, like you, have all too many demands on their time. All of us are already extremely busy, for as you know, a scientist's work never really ends. Then, there's all the juggling of responsibilities of teaching, administration of a department or laboratory, service on grant review panels, student and post-doctoral fellow mentoring, clearly convey the importance of the study in the field. If the reviewers get that point, though they must read on, they will be more enthusiastic about doing so.

A good abstract will include the following:

- A brief historical context and rationale for the work,
- An enumeration of the important unanswered questions in the area,
- A summary of the key findings in the study that address one or more of these questions, and
- The author's opinion regarding the importance of these findings.

And, yes, all of these points must be addressed within the confines of word-count limitations. While, at first, the word count can seem an obstacle, in fact, the word limit is your friend because it enforces use of simple, concise prose.

Figures: A Picture Really Is Worth a Thousand Words.

Figures are the visual depiction of your results and are arguably the most important component of the manuscript. If your figures are clear, the data will be easier to understand. Good clear figures give the reviewer a more favorable impression and increase the chances of a more positive review. Because your data are the centerpiece and foundation of the manuscript, you would do well to prepare the figures first. That practice will allow you to see what you have in its almost final form and decide whether the data sufficiently support a complete, logical, and convincing story.

Good figure preparation should incorporate the following:

1. Each figure, even if in multiple parts, should make just one clear point.

Don't try to get too fancy and make things complicated.





This figure combines too many distinct findings. If divided into two parts as above left, each concept can be considered and evaluated independently.

2. A figure should be a freestanding entity. The layout and labeling of the figures should ensure that your results are understandable, independent of any description in the text. A good figure will provide sufficient information to enable the reader to grasp most of what was done and the conclusions of the experiment(s) without having to consult the legend or the results description. Of course, details will have to be filled in, but the gist of the results should be conveyed in the labeled pictures alone.



3. Figures should contain a balance between primary data and graphical representations of compiled data from multiple experiments if appropriate (e.g., graphs). This balance is particularly important when one shows results of flow cytometry analyses, which can be very subjective. The inclusion of actual flow cytometric analyses plots is absolutely necessary, not just graphs of the compiled data. In these cases, an example of gating strategies should also be shown. Reviewers look for these to more easily evaluate the veracity of the conclusions.



4. Make sure that the figures have clear, legible labels. The font sizes must be easily readable when reduced for publication. You may be young and bright eyed with 20/20 vision, but many seasoned reviewers are at the age when not only has their thymus started its significant involution, but they also have presbyopia. Unnecessary difficulty reading small print will not make a reviewer happy. Symbols and/or distinct line styles (dashed, dotted, continuous) should also be large enough to distinguish different data groups from one another.

The examples on the bottom row are labeled with a font that is too small, and the bottom right figure has symbols and lines that are hard to distinguish. Consequently, it is almost impossible to determine which group was treated with antibody.

5. Be sure the font sizes, labels and graph styles are consistent.

This composite figure has legends formatted in two different ways. Fonts are also different styles and sizes. Be consistent.



Continued on next page

6. Number your figures in the text when you refer to them and on the figure you submit. (e.g., Figure 6, Brown et al.) A surprising number of authors forget to do this and frustrate reviewers trying to find what figure is being discussed.



7. Arrange figure panels symmetrically.



- **8. Submit high resolution figures.** The reviewer may see fuzzy figures as a sign of haste and sloppiness, both in the lab and at the computer.
- **9. Limit the amount of supplemental data included.** Don't overwhelm the reviewer! Put in only what is necessary.
- **10. The figure legends should describe the point of the figure.** Legends should recapitulate key points of the experiments to make the figure understandable. But legends should not repeat all of the detail included in the Materials & Methods section. This section, by contrast, should be comprehensive enough to allow the reader to repeat the experiments.

Introduction: You Have Great Rationale for This Study, So Tell Us!

Here, you can elaborate on the historical context and unanswered questions in your area of study. This section should establish the rationale for the current study. Use key original references, not just reviews.

The Results Section: The Verbal Description to Back Up Your Figure Presentation.

Arrange the figures and describe your data in a way to tell the story logically, not necessarily chronologically. This means the order may not reflect how the project was originally conceived.

Be concise and do not repeat the Materials & Methods or include discussion items in the results.

The Discussion: Show Your Scholarship!

This is your chance to integrate your results with findings of others in the field. You can discuss discrepancies with other studies here as well. Do not repeat a lengthy description of the results in the discussion section. Merely summarize key findings and discuss how they add to the understanding of the system you are studying. More words are almost never better. Keep your text simple and clear.

Some Final Thoughts:

- The title should inform the reader of the gist of the paper. "Studies of..." is too vague. Try something like "T cell production of IL-4 requires...in vivo"
- Make sure your statistical analyses are appropriate. Get help from someone who does this for a living if you need to do so.
- Pay attention to details. The reviewer is taking his/her time to read your paper. If you convey an attitude of haste and inattention to detail, you render yourself a disservice. Although reviewers can forgive and look beyond a certain level of imperfection, attention to the principles outlined here will signal your respect for their efforts and increase your chance of a good outcome.

Acknowledgements: Thanks to Pam Fink, Paul Love, and Cathy Nagler who provided great ideas.

(Figure 7 in this article first appeared in Dos and Don'ts for Writing a Scientific Manuscript by Pam Fink, AAI Newsletter, *February 2010, page 22.*)

It's Not Personal! Pointers for Responding to Reviewers

The third in a series of articles providing guidance to researchers on the publishing process for peer-reviewed scientific journals

Peter E. Jensen, Professor and Chair, Department of Pathology, University of Utah

This article is one in a series based upon presentations made during an IMMUNOLOGY 2011[™] AAI Publications Committee Symposium titled In the Lion's Den: The Manuscript Review Process and How to Survive It. Jensen is currently a deputy editor for The Journal of Immunology.

As scientists, we communicate our findings and discoveries primarily through the publication of peerreviewed manuscripts. The peerreview process helps to validate our results and conclusions, a first step in the process through which our studies influence the broader scientific thinking. We all invest a tremendous amount of work and expense in generating the data for each manuscript. And



Peter Jensen

we put significant effort into writing and preparing each manuscript for submission.

Our publications are critical to our prospects for obtaining jobs, keeping them, earning promotions, and gaining funding. Findings that are not published or read have no impact.

Given the importance to our careers of our every submission, I'll offer here some of my own personal views on how to approach the manuscript review process and respond to the critique in the most constructive way. That is to say, in such a way that you can enhance your chances for successful publication. My comments are tailored for *The Journal of Immunology (The JI)*, but the principles can be applied generally to any peer-reviewed journal.

The Editor's Letter

Journals generally use standard wording to communicate the initial editorial decision. The typical range of decisions includes the terms "accept," "minor revision," "major revision," and "reject." I'll briefly re-trace the path of a manuscript en route to a decision, as was discussed earlier in this series in "I Just Clicked Submit. What Happens Next?" by Juan Carlos Zúñiga-Pflücker (*AAI Newsletter*, October/ November 2011, pages 28–30). I'll attempt also to describe what I believe to be constructive responses to each decision you may receive.

A decision by a journal to **accept** an initial submission is wonderful but rare. Upon acceptance, you simply follow the instructions for reviewing galley proofs, paying page charges, consenting to copyright transfers, and other steps in the production process. Be prompt and thorough in each step taken. You don't want to tempt fate by causing delays in the process.

An outright **rejection** generally indicates that your paper will never be acceptable for publication in this particular journal. You should consider using the accompanying critique to help guide a major revision for submission to another journal. The study may be considered too preliminary, poorly performed, poorly presented, or it may need too many experiments to complete a convincing story. The reviewer may question whether his/her journal was the appropriate one for the study. For instance, a reviewer for *The JI* may ask whether the work is really a study in immunology.

Keep in mind, also, that reviewers and/or editors may reject a study they consider insufficiently novel, significant, or interesting. For example, a study might demonstrate for the first time the role of specific cytokines or transcription factors in a particular animal model of organ-specific inflammatory disease. However, the findings might be considered to be entirely predictable based on previous studies with other models of inflammatory disease.

No doubt, you'll entertain the impulse to rebut the reviewer's decision to reject your manuscript, and you'll want to send a letter to the editor-in-chief requesting reconsideration. You should, however, consider sending such a rebuttal letter only if you believe that a serious scientific error has occurred during the review process.

If important new data have been obtained since the original submission and decision, they may be incorporated into the rebuttal with the implication that the new data will address the major criticism. Note, though, that if the new data change the manuscript substantially, it is generally best to submit a new manuscript. The overall success rate for rebuttals is very low.

Success is more likely for someone receiving a journal editor's letter indicating a **"minor-revision"** decision. Such a letter generally includes a statement such as "The manuscript is acceptable for publication in *The Journal of Immunology* contingent upon revision." This

Continued on next page

response often means that little or no additional experimental data will be required, and if additional data are required, the reviewer anticipates the data will be relatively easy to obtain. This decision is good news, but the authors still must address each point in the critique and make expected modifications to the manuscript. Note that no guarantee has been made that the paper will be accepted for publication.

By contrast, a **"major-revision"** decision by a journal probably includes wording such as "Although the subject matter of your paper is of interest, a number of concerns were raised by the reviewers. While these concerns preclude publication of this manuscript in its current form, you are invited to resubmit an appropriately revised manuscript that addresses the reviewers' concerns." A successful revision in this situation will generally require important additional data and significant revisions to the manuscript.

The Critique

The JI asks its reviewers and section editors to evaluate manuscripts on the basis of originality, scope, clarity, and significance of the manuscript. Weakness in any one of these areas can lead to a rejection.

Other factors commonly leading to a decision to reject include reviewers' assessment that the work is too descriptive or that it lacks any statement of a clear hypothesis, mechanistic insight, or precise implications of the study for the field of immunology.

Novelty may be an issue. The paper may have been given a low score for a lack of originality or unique significance. If so, you may receive comments such as "This work has been done before," or "Just another cell type," or "Two recent studies support very similar conclusions." These comments provide a very clear indication of why the paper was rejected. If you are offered a chance for revision, you will need to add novel data or make a convincing case for the originality and significance of your results.

The reviewers may conclude that the work is premature for publication. The experimental design or analysis may be considered faulty. Critical results may be viewed as being weak or unconvincing. Data may be poorly presented, unclear, labeled incorrectly, or lacking statistical analysis. (For excellent guidance on the presentation of data, see "Making It Easier for the Reviewer," by Melissa Brown, *AAI Newsletter*, December 2011, pages 27–30.)

Even if reviewers consider the topic to hold potential for adding significantly to the body of knowledge in the field, any weaknesses they've identified in the data or conclusions must be satisfactorily addressed before they can recommend publication.

Formulating a Plan

If you are invited to revise and resubmit your manuscript, be sure to take the time to carefully evaluate the reviews and formulate an action plan. As a first step, carefully read the critique. Then put it aside and wait a few days before reading it again. Doing so gives you time to let your initial emotions subside and approach the critique objectively. Next, make a list of the specific points made by each reviewer. Remember, it is not helpful to assume that a negative critique is the consequence of bias or any lack of expertise on the part of the reviewer. If the reviewer has misunderstood your results or line of reasoning, focus on ways to improve the clarity of your presentation in the manuscript rather than the competency of the reviewer.

Next, outline the issues. If you get the impression that the novelty or significance is in question, draft a point-bypoint response to the critique to indicate what additional experiments are feasible and which are not. Identify what points can be addressed by argument alone as you edit the manuscript or add additional references. Consider whether you are being told that there are flaws in your logic or design and/or your controls are inappropriate and unconvincing. Are there concerns cited relating to over-interpretation or reagent validation or are divergent points of view expressed in your paper?

Ask colleagues and co-authors to read the reviews and weigh in with their opinions. Decide whether you can resubmit and what would be needed to have a reasonable chance of success. In some situations, you may decide that it is not practical to try to satisfy major concerns raised in the critique. You may conclude that you would be better off repackaging the paper for another journal. If, however, you decide to re-submit, you will need to formulate a plan to perform any required additional experiments, obtain additional information requested by the reviewers, and revise the manuscript appropriately. If clarity of your writing or language is an issue, get help from colleagues or even engage a professional copy editor.



If the reviews are highly divergent, don't assume that the favorable review will be weighed more heavily than the unfavorable one. You may conclude that a reviewer is uninformed or has negative biases, but you should still take the review seriously. Even a relatively positive review may not be as positive as it seems. Reviewers often provide confidential comments to the editors that are less "gentle" than their comments to the authors. In addition, the narrative reviews do not always reflect the ranking scores provided by the reviewers. That said, know that you can respond only to the comments that you have received. A good-faith effort to respond objectively to each point raised in the critique greatly boosts one's chances for acceptance of a revised manuscript.

Emotions and Professionalism

It's only natural to react emotionally to criticism. Be advised, though, not to let your emotions show as you begin to write the point-by-point response and cover letter that will accompany your resubmission! Reviewers have emotions, too, and they are also subject to the temptation to react poorly to comments questioning their expertise, intentions, or objectivity. You will not win favor if you state that "Reviewer #1 obviously has little expertise in the field," or "This reviewer clearly delegated the task to a first-year graduate student."

Even a less "snarky" response can seem arrogant if not carefully phrased. Avoid such dismissive remarks as "The reviewer appears not to have read the manuscript, as these points were clearly addressed in the original paper," or "We were surprised that the reviewer had such a difficult time understanding this point."

You will benefit from a professional and respectful tone. A politic response might read, "We thank the reviewer for her constructive comment. We have clarified our reasoning in the revised manuscript with changes in the Results section on p. 14," or "The reviewer's concerns are understandable. We provide additional data in Fig. 5 of the revised manuscript that strengthen this conclusion." There's merit in the proverb "You catch more flies with honey than with vinegar!"

Resubmission

Once you have obtained the additional required data and information defined by your outline of the critique, you can finalize the point-by-point response and the manuscript revision. In composing the point-by-point response, separate out each point of each review in quotation marks and write the corresponding response below each point.

Keep your responses brief and clear. Be sure to note where changes have been made in the manuscript. Don't make the reviewer have to search for the changes. Address issues with additional data whenever possible. It is often easier to perform additional experiments than to waste time and effort on verbal arguments. Fix flaws in design, validate reagents, add controls, and employ alternative approaches as necessary to strengthen the manuscript. If novelty is an issue, consolidate the original figures and provide new data. If your work contrasts with published studies, your data need to be particularly strong and convincing!

Don't risk seeming to "cherry pick" your revisions. Be sure to address all issues identified by the reviewers. Don't ignore any comments raised in the reviews.

Take great care in the creation of your figures. In your use of statistics, be sure to choose the right statistical tool. Immunologists vary considerably in their expertise with statistics. If you don't know what approach to use, get help from someone with more expertise. You may also consult "The Appropriate Use of Statistics in the Biological Sciences," by Pamela A. Shaw, in the AAI publication *Scientific Publishing: Dos and Don'ts for Authors and Reviewers*, available for downloading at www.aai.org/ About/Publications/Additional/Docs/AAI_Dos_Donts.pdf. Again, see "Making It Easier for the Reviewer," by Melissa Brown, *AAI Newsletter*, December 2011, pages 27–30. In her article, she offers very specific guidelines for creating figures.

Consider validating your results in vivo if feasible. In general, results with primary cells are better than results with transformed cell lines. The most convincing results often come from validation studies in animal models. For example, one might demonstrate that a specific signaling molecule is required for differentiation of a particular subset of T cells in tissue culture assays. The physiological role of this signaling molecule would be more firmly established by showing an effect of blocking the molecule during T cell differentiation induced in an in vivo model in animals. In vivo results can greatly increase the perceived biological significance of the findings.

Finally, you should prepare a cover letter that includes your point-by-point response and a concise summary of the ways the revised manuscript has been strengthened. Again, ask a colleague to read your cover letter to help you confirm the thoroughness and clarity of your response.

In the End

Peer review is qualitative, imperfect, and, because we are human, sometimes biased. But it is the best system that we have! As painful as it can be, the process generally results in the publication of improved manuscripts. As an author responding to a review, remember that you are also occasionally a reviewer. When you review, remember that you are often the author. Civility and respect should prevail in each of your roles.

Be assured, all of us at some point have papers rejected. What's most important is to move forward, stronger for having dealt constructively with the critiques we've received and confident that we are better prepared for our next submission. Take heart!



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