Is My Idea Publishable?

Mayumi Nakagawa, MD, PhD
Professor of Pathology
University of Arkansas for Medical Sciences
Who Plans the Faculty Development Seminar Series?

Women’s Faculty Development Caucus: Mentoring Committee

Faculty Development Seminar Series

Quarterly Networking Events

Mentoring Program
Disclosures

None
Are Your Ideas Publishable?

- Almost always
- Most of the time
- Some of the time
- Rarely
- Never
Learning to Write: Why So Difficult?
Learning to Write: Why So Difficult?
Learning to Write: Why So Difficult?
Fields I Publish In

- Human Papillomavirus (HPV) Immunology
  - Cell-mediated immune responses in natural infection
  - HPV therapeutic vaccine development

- Transfusion Medicine
  - Various clinical issues
Outline

- Basics to consider
- How to overcome writer’s block
- What should you do if your paper is rejected?
- How to publish case reports
- Does impact factor matter?
Basics to Consider

- Is your idea novel?
- Is your idea of interest to the readers of the journal?
- Will you be able to make your point?
Is your idea novel?

- Do a literature search to see whether a paper has been published reporting the same or similar topic.
- Talk to your colleagues in the field.
"Distribution of Human Papillomavirus (HPV) Types and Anti-HPV T-Cell Immune Responses Among Different Racial/Ethnic Groups in Central Arkansas" Submitted to *Infectious Diseases in Obstetrics and Gynecology*

Recommendation

Reject

Comments

The authors present a cross-sectional study of the HPV type prevalence and CMI responses in women in Central Arkansas. The women were being followed for a recent history of untreated abnormal Pap smear. The authors present HPV type data that is not unlike other populations presented in other much larger studies from a colposcopy-type population. Some of these larger trials have been run through IARC or registries/tracking studies outside the US.

Other concerns:
1) There are concerns with regards to the interpretation and cutpoints of the elispot assays. Many prior human studies of CMI or elispot assays being used to look for anti-HPV T-cell responses have not correlated T-cell responses with clinical diseases. In fact there is no ‘standard’. Could this be the explanation as to why there were no differences across groups?
2) Lines 58-62 the eligibility appears shortened. Were there restrictions on other things that can greatly affect HPV persistence and CMI responses such as type of Pap? Age? Prior abnormalities or treatment? HLA? Smoking? Sexual history? Chlamydia history? (and many more)
3) How do you define regressors or persistors?
4) How is this information new to the literature? HPV type prevalence appears to look like any colpo population across the world.
“Distribution of Human Papillomavirus (HPV) Types and Anti-HPV T-Cell Immune Responses Among Different Racial/Ethnic Groups in Central Arkansas” Submitted to *Infectious Diseases in Obstetrics and Gynecology*

**Remedy**

- Submit to a journal for which characterization of this population would be novel and of interest
  - The Journal of The Arkansas Medical Society
“Distribution of Human Papillomavirus (HPV) Types and Anti-HPV T-Cell Immune Responses Among Different Racial/Ethnic Groups in Central Arkansas” Submitted to The Journal of The Arkansas Medical Society

 Resolution

 Accepted without revision 😊
Is your idea of interest to the readers of the journal?

0 Read instructions to authors
0 Look at topics of published articles
Your paper referenced above has been reviewed at the Editorial level. Based on its priority at the Editorial level, it is considered highly unlikely to achieve a priority score that could lead to its acceptance for publication in Clinical Lymphoma, Myeloma & Leukemia. We receive many more manuscripts than we can publish, and we regret to inform you that we find that this manuscript does not have sufficient relevance for our journal.
“Autologous Graft Versus Host Disease: An Emerging Complication in Patients with Multiple Myeloma” submitted to *Clinical Lymphoma Myeloma & Leukemia*

**Remedy**

Resubmitted to *Biology of Blood Marrow Transplantation* which published another paper on autologous graft versus host disease
"A Novel Human Papillomavirus Type 16 E6 52-62 CD4 T-Cell Epitope Restricted by the HLA-DR11 Molecule" submitted to *Infectious Diseases in Obstetrics and Gynecology*

Subject Appropriateness of the Manuscript
The topic of this manuscript does not fall within the scope of Infectious Diseases in Obstetrics and Gynecology

Recommendation
Publish Unaltered

Comments
This report describes identification of a novel CD4 T cell HPV 16 E6 52-62 epitope that can be used in vaccines and immunotherapies against HPV-associated malignancies. Although the work is novel and the methodology is sound, it may be more suited to a basic science journal in virology or immunology and has limited appeal to the readers of Infectious Diseases in Obstetrics and Gynecology.
“A Novel Human Papillomavirus Type 16 E6 52-62 CD4 T-Cell Epitope Restricted by the HLA-DR11 Molecule” submitted to *Infectious Diseases in Obstetrics and Gynecology*

Remedy

- Submitted to *Journal of Immunology Research* by the same publisher
Will you be able to make your point?

- Usually but not always $p < 0.05$
- Description of new phenomenon
- Safety in a Phase I clinical trial can be demonstrated descriptively by having few or no serious adverse events
Usually but not Always $P < 0.05$

T-cell proliferative response to human papillomavirus type 16 peptides: relationship to cervical intraepithelial neoplasia.

Nakagawa M¹, Stites DP, Farhat S, Judd A, Moscicki AB, Canchola AJ, Hilton JF, Palefsky JM.

Author information

Abstract

The incidence of human papillomavirus (HPV)-related cervical intraepithelial neoplasia (CIN) and cervical cancer is increased with immunodeficiency, but the role of immune response, including cell-mediated immunity, in disease prevention is not well understood. In this study, T-cell proliferative responses to six synthetic peptides with predicted immunogenic determinants from the HPV-16 E4, E6, E7, and L1 open reading frames were analyzed in 22 sexually active women with new-onset CIN and 65 sexually active women without cervical disease, characterized by cytology, colposcopy, and HPV testing. T-cell proliferative responses were demonstrated to all six HPV-16 peptides. Although not statistically significant, rates of reactivity to E6 (24-45) were higher among sexually active women without disease (26%) than among women with current CIN (7%), as was the overall number of peptides stimulating a response. Women with CIN may not respond to selected HPV antigens as well as women without disease do.
Usually but not Always $P < 0.05$

**Cytotoxic T lymphocyte responses to E6 and E7 proteins of human papillomavirus type 16: relationship to cervical intraepithelial neoplasia.**

Nakagawa M\(^1\), Stites DP, Farhat S, Sisler JR, Moss B, Kong F, Moscicki AB, Palefsky JM.

**Author information**

**Abstract**

Cytotoxic T lymphocyte (CTL) responses to the human papillomavirus (HPV) type 16 E6 and E7 proteins were measured in 20 women with known HPV and cervical disease status. CTL assays were performed after stimulation with E6 or E7 fusion proteins using autologous B lymphoblastoid cells infected with vaccinia viruses expressing E6 or E7. CTL responses to E6 and E7 were detected in 6 (75%) of 8 and 5 (56%) of 9 HPV-16-positive women without cervical intraepithelial neoplasia (CIN), respectively. Responses to E6 or E7 were each detected in only 2 (29%) of 7 HPV-16-positive women with CIN. Responses to both antigens were found in 63% of women without CIN and 14% of those with CIN. CTL responses to E6 or E7 are more commonly detectable in HPV-16-positive women without CIN than in HPV-16-positive women with CIN, suggesting that CTL response may play a role in disease protection.
Usually but not Always $P < 0.05$

“A Novel Use of a Statewide Telecolposcopy Network for Recruitment of Participants in a Phase I Clinical Trial of a Human Papillomavirus Therapeutic Vaccine”

Conclusion

The availability of a large number of potential participants from the telecolposcopy network increased recruitment to this clinical trial by 85% over other traditional means of recruitment. The telecolposcopy network is not only a means of providing a gynecological service to women who otherwise would forego care, but also a novel and valuable resource in recruiting participants for a clinical trial.

In Press, Clinical Trials: Journal of the Society for Clinical Trials 😊
Now you are ready to start writing, but

- Novel ✓
- Of interest to the readers ✓
- Can make the point ✓
"After three years of writer's block, I began writing about writer's block."

"I'm going through writer's block...

Camaraderie among all writers like thieves...

"After three years of writer's block, I began writing about writer's block."

"THE ROLE OF A WRITER IS NOT TO SAY WHAT WE ALL CAN SAY..."

"OH OH-I THINK I'VE INVENTED WRITER'S BLOCK!"

"THE MOST OF US REALLY NEED"
WHY?
WHY?

- Lack of experience
- Not knowing what the main point(s) of the paper is(are)
- Not knowing how to articulate the main point(s) of the paper
Write in this order

0 Methods
0 Results
   0 Make a list of issues that need to be discussed based on the results
0 Discussion
0 Introduction
0 Abstract
   0 A preliminary abstract can be written at any time but should be finalized at the end
What should you do if your paper is rejected?

0 You should almost always
   0 Read the reviewers’ comments
   0 Revise the paper
   0 Resubmit to another journal

0 On a rare occasion
   0 Read but ignore the reviewers’ comments
   0 Resubmit to another journal
Autologous Graft Versus Host Disease: An Emerging Complication in Patients with Multiple Myeloma” submitted to *Biology of Bone Marrow Transplantation*

Reviewers' comments:

Reviewer #1: In this manuscript, Batra and colleagues have examined patients who developed autologous graft versus host disease after undergoing transplantation for multiple myeloma. The authors compare a small cohort of patients who had the complication with a slightly larger number of patients who did not develop auto GVHD. They also performed immune phenotyping of the stem cell products to characterize T cell subsets and class I expression.

Major Points:

1. There are only 8 patients in the GVHD group and 16 in the non-GVHD group. These numbers study are too small to make any definitive statements regarding the role of prior therapies (e.g. proteasome inhibitors, Imids) in predisposing patients to auto GVHD. Furthermore, there are no data presented in Table 1 that delineate the prior induction therapies that these patients had, only the mobilization regimens are shown.

2. The mean onset of auto GVHD was quite late in this study, 29 days. Most studies have reported earlier onset coinciding with engraftment. In fact, many of these patients have feature of classical engraftment syndromes. Is there an explanation for why onset was so delayed? How long did patients have symptoms and is it possible that the diagnosis was made late?

3. The formal criteria for diagnosis of this syndrome should be explicitly stated in the methods section. Did these patients have fever along with other symptoms?

4. A recent study by Cornell and colleagues (BBMT, 2013) examined a much larger population of patients and found that prior exposure to novel immune modulatory agents was associated with a higher incidence of engraftment syndrome. This paper should be cited and discussed by the authors.

5. Was the immune profiling done from the first stem cell product in each patient since some patients may require multiple collections?

6. The relevance of the first paragraph in the Discussion is not clear. Even if Th17 cells were increased in the BM of myeloma patients, one would have to posit that these cells were preferentially mobilized in the auto GVHD group versus the non GVHD group, and it is not clear why that would occur. Also, one would predict a higher number of CD4+ T cells in the stem cell products from the auto GVHD group which was not detected.
Autologous Graft Versus Host Disease: An Emerging Complication in Patients with Multiple Myeloma” submitted to *Biology of Bone Marrow Transplantation*

0 Remedy

0 Resubmitted to *Bone Marrow Research* unaltered
0 Accepted with minor modifications 😊
CDI/456064.v1 Review Report

Subject Appropriateness of the Manuscript

The topic of this manuscript falls within the scope of Journal of Immunology Research

Recommendation

Reject (Paper is not of sufficient quality or novelty to be published in this Journal)

Comments

This manuscript describes the isolation and characterisation of a T cell recognizing an E6 epitope of HPV 16 restricted by HLA-DR11. The significance of this research is not really very clear as it accounts responses from a single patient. The reported results define what was isolated with the given methodology and cannot inform anything about disease related significance or the repertoire of the patient. The methodology is biased by the use of selected HPV 16 E6 peptides even without evidence of an HPV 16 infection in the patient. It would have been good to have the comparable sequences of HPV 39, 54 and 82 for comparison since these were detected in the CIN1. There is mention of false positive T cell clones on page 7 which suggests that the selection of clones is driven by preconceived ideas of relevance. The attempts to refine the recognized sequence and its restricting element and look for cross recognition are not wholly convincing give the relatively promiscuous binding to HLA class II. The restriction by HLA class II DR11 is not established as no blocking or account of DP genotypes is given.
"A Novel Human Papillomavirus Type 16 E6 52-62 CD4 T-Cell Epitope Restricted by the HLA-DR11 Molecule"
submitted to *Journal of Immunology Research*

0 Remedy

0 Revised one the tables to show that the HPV types the subject was infected with has no sequence homology to HPV 16

0 Changed the emphasis of the paper by revising the title

0 A Human Papillomavirus Type 16 E6 52-62 CD4 T-Cell Epitope Restricted by the HLA-DR11 Molecule Described in an Epitope Hotspot

0 Accepted without revision in MOJ Immunology 😊
How to publish case reports

0 Case report and literature review
0 Case series with a message valuable to the field
0 Case report of experimental component
How to publish case reports

Transfusion. 2004 Dec;44(12):1689-94.

Acute and transient decrease in neutrophil count in transfusion-related acute lung injury: cases at one hospital.
Nakagawa M1, Toy P.

Abstract
BACKGROUND: Transfusion-related acute lung injury (TRALI) is a rare but serious complication of blood transfusion. The syndrome is characterized by new acute lung injury developing during or within 6 hours of blood transfusion.

STUDY DESIGN AND METHODS: The study design was observational in nature.

RESULTS: All three cases of TRALI were associated with acute but transient decrease in the white blood cell (WBC) count. Implicated donors had HLA antibodies that matched the recipients' HLA antigens. The implicated units were a plateletpheresis in one case and fresh frozen plasma units in the other two. All implicated donors were multiparous women. The implicated antibody specificities were anti-HLA Class I and Class II in one case and anti-HLA Class II in the other two cases. Interestingly, patient neutrophil counts decreased by 80 to 90 percent in all three cases, including the two cases associated with HLA Class II antibodies.

CONCLUSION: An acute and transient decrease in WBC count may be a previously underrecognized feature of TRALI. A drop in the neutrophil count can occur even when the implicated antibodies have specificities to HLA Class II antigens, although they are expressed only on stimulated neutrophils. Based on the observations in these cases, it is recommended that a complete blood count and differential be obtained when TRALI is suspected. Further investigations into the mechanisms of the decrease in circulating neutrophils that is associated with infusion of HLA Class II antibody may yield new insights into the mechanism of TRALI.
Rituximab And Intermediate-Purity Plasma-Derived Factor VIII Concentrate (Koate®) As Adjuncts To Therapeutic Plasma Exchange For Thrombotic Thrombocytopenic Purpura (TTP) in patients with an ADAMTS13 Inhibitor submitted to Journal of Clinical Apheresis

Comments to the Author
The authors report a case series of three acquired TTP patients who were treated with TPE, corticosteroids, rituximab, and Koate, and eventually went into remission. Other than the novel use of Koate in the treatment of acquired TTP, the authors have not demonstrated that its use assisted in the achievement of remission in difficult-to-treat cases. Its use resulted in less plasma being used, or its use resulted in overall fewer TPE treatments and faster achievement of remission.
Rituximab And Intermediate-Purity Plasma-Derived Factor VIII Concentrate (Koate®) As Adjuncts To Therapeutic Plasma Exchange For Thrombotic Thrombocytopenic Purpura (TTP) in patients with an ADAMTS13 Inhibitor submitted to Journal of Clinical Apheresis

Remedy

- Took out the claims
- Revised as “Here we report our experience with addition of this FVIII concentrate to rituximab, corticosteroids and TPE in 3 TTP patients with an ADAMTS13 inhibitor to permit withholding TPE for 48 hours after rituximab infusion.”
Rituximab And Intermediate-Purity Plasma-Derived Factor VIII Concentrate (Koate®) As Adjuncts To Therapeutic Plasma Exchange For Thrombotic Thrombocytopenic Purpura (TTP) in patients with an ADAMTS13 Inhibitor submitted to *Journal of Clinical Apheresis*

 Resolution

 Accepted as revised 😊
How to publish case reports


A case of acquired dysfibrinogenemia in multiple myeloma treated with therapeutic plasma exchange.

Post GR¹, James L, Alapat D, Guillory V, Cottler-Fox M, Nakagawa M.

Author information

Abstract
A 70 year old Caucasian woman with IgG lambda multiple myeloma presented with uncontrollable bleeding from a bone marrow biopsy site which started days after the procedure. The patient was hyperviscous, and coagulation tests showed elevated activated partial thromboplastin time (aPTT) which was not corrected with a mixing study, elevated thrombin time and reptilase time, and possible inhibitors to Factors VIII and IX. Therapeutic plasma exchange was performed using plasma with corrections of plasma viscosity (1.6 to 1.1 centipoise) and aPTT (50 to 42.1s) observed. The bleeding was controlled, and purified IgG demonstrated dysfibrinogenemic effects of the patient's paraprotein.

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PMID: 22842111 [PubMed - indexed for MEDLINE]
Does impact factor matter?
How is impact factor calculated?

- The average number of citations received per paper published in that journal during the two prior years.

Example:

- 2014 impact factor = (# of times that all items published in 2012 and 2013 in a particular journal were cited by indexed publications during 2014)/(# of citable items published in 2012 and 2013 in the journal)
What is a good impact factor?

The Journal Citation Reports database assigned impact factors to 8,411 journals in 2012.

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Does high impact factor = quality?

Validity of the impact factor of journals as a measure of randomized controlled trial quality.
Barbui C1, Cipriani A, Malvini L, Tansella M.

Author information
1Department of Medicine and Public Health, Section of Psychiatry and Clinical Psychology, University of Verona, Policlinico G.B. Rossi, 37134 Verona, Italy. corrado.barbui@univr.it

Abstract
OBJECTIVE: To assess whether the impact factor, a measure of the frequency with which journal articles are cited in the scientific literature, is a proxy measure of the quality of articles reporting the results of randomized controlled trials.

METHOD: The quality of trials included in an ongoing Cochrane review concerned with the antidepressant fluoxetine was assessed using the Cochrane Collaboration Depression, Anxiety, and Neurosis quality assessment instrument, the Jadad scale, and the quality criterion of the Cochrane Collaboration Handbook. Journal impact factors were extracted from the Journal Citation Report.

RESULTS: A total of 131 articles reported results from 132 clinical trials comparing fluoxetine with other antidepressants. The relationship between trial quality and the impact factor of journals where these studies were published, stratified by period of publication, revealed that journals with impact factors above 4 points published only trials with above-average overall quality ratings, while journals with impact factors below 4 points published both high- and low-quality trials. The Jadad scale revealed similar quality in trials published in journals with high, medium, and low impact factors (Pearson chi(2) = 0.298, p = .861), and the quality criterion of the Cochrane Collaboration Handbook showed unclear randomization in the majority of trials and in all 15 trials published in high-impact factor journals (Pearson chi(2) = 4.678, p = .096).

CONCLUSION: The impact factor of journals is not a valid measure of randomized controlled trial quality.
THE END