

Session 5: The Synthesis of Progress II. Moving the Bar with Compelling Discussion Sessions

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Elements to Include in the Discussion

- Recap the study's major findings (not data)
- Interpret the meaning of the findings, especially in the context of their importance
- Discuss your findings in the context of similar studies
- Suggest alternative interpretations or explanations to discuss the findings?
- State the limitations of the study
- Clearly state how the results will lead to stimulate further research

Structure of the Discussion

Opening 1. Restate major finding and how it led to conclusion

or

Opening 2. Re-orient reader to the "big-picture" perspective.

Opening 1: Restate Major Finding...immediately link to the "hook"

Discussion.

"During infection of the gastric mucosa, *H. pylori* modulate the properties of host cells and tissues to generate a more suitable niche for colonization and persistence. In this study, we demonstrated *H. pylori*-dependent modification of the abundant and important nuclear protein PARP-1. However, contrary to our original hypothesis, PARP-1 is not mono-ADP-ribosylated by the action of an *H. pylori* toxin or effector. Rather, PARP-1 undergoes automodification with PAR as a result of *H. pylori*-mediated activation of the intrinsic poly(ADP-ribosylation) activity of PARP-1. PARP-1 activation by a bacterial factor in a cell-free system has not been previously reported."

Opening 2: Begin by re-orienting reader to the "big-picture" perspective.

Discussion

"By modulating important properties of eukaryotic cells, many toxins remodel the host environment to create a suitable niche for pathogenic organisms to colonize and persist during infection [14]. Many of the most potent toxins act upon intracellular targets. As the first step in cellular entry, intracellular-acting toxins bind to one or more plasma membrane surface receptors [7]. Notably, cells lacking toxin receptors are generally resistant to intoxication, underscoring the importance of the toxin-receptor complex [14].

Our results indicate that the important plasma membrane sphingolipid, SM, functions as a receptor for VacA....."

Structure of the Discussion

Use each major point within the results as a paragraph topic

- only one topic per paragraph
- first sentence

Use each major point within the results as a paragraph topic

Result

These results indicated that longer acyl chain SM promotes a Cdc42-dependent uptake mechanism, as previously described for VacA (Gauthier *et al.*, 2005), and suggests that plasma membrane SM influences the mechanism by which VacA taken up from the cell surface.

Discussion

"A potential mechanistic role for SM in Cdc42-dependent pinocytosis was previously suggested by studies demonstrating that depletion of SM from the surface of Chinese hamster ovary (CHO) cells using SMase C inhibited the targeting of Cdc42 to membrane rafts within the plasma membrane required for the uptake of the fluid phase marker dextran (Cheng *et al.*, 2006). Supplementation of SMase C pretreated CHO cells with exogenous SM, but not ceramide, monosialoganglioside GM3, or lactosylceramide, restored cellular uptake of dextran and plasma membrane targeting of Cdc42 (Cheng *et al.*, 2006). Although we did not investigate SM-dependent Cdc42 membrane recruitment within VacA-intoxicated cells, we speculate that SM may target VacA to membrane rafts containing the effector molecules required for uptake of the toxin by the Cdc42-dependent pathway."

Structure of the Discussion: Data in the Discussion?

Conventional Wisdom: NO!!

Unconventional wisdom (??):
Sometimes

Structure of the Discussion: Providing the Teaser...

Result: H. pylori infection activates PARP-1

Discussion:

"...recent work has expanded the physiologic functions of PARP-1, and it is now clear that this important protein is involved in many disease pathologies, including cancer (7, 8). Interestingly, PARP-1 synthesized PAR was recently identified as an important trigger of apoptosis, which is a hallmark of H. pylori infection (1, 20). PARP-1 generated PAR exits the nucleus and induces the release of mitochondria-associated apoptosis inducing factor (AIF), which, in turn, translocates into the nucleus and promotes caspase-independent apoptosis (21, 22). Notably, H. pylori infection was recently demonstrated to induce the release of AIF from mitochondria (23, 24). While beginning to explore the consequences of H. pylori PARP-1 activation, we validated that H. pylori 26695 infection of AGS cells with H. pylori 26695 resulted in the release of AIF from mitochondria (Fig. S3). However, H. pylori-mediated AIF release was significantly inhibited in the presence of the PARP-1 inhibitor, 3-AB (Fig. S3). These results suggest the possibility, which is currently being investigated, that one consequence of H. pylori-mediated PARP-1 activation may be the induction of apoptosis via the PAR-mediated release of AIF from mitochondria."

Structure of the Discussion: How long should a Discussion be?

It depends....

Our goal is usually 2-4 double-spaced Arial 11 font....

...Translates to approximately 0.5 – 1.0 printed pages

....be concise!!!

Common Mistakes – How to avoid bumps, pitfalls, and fatal errors

- Strict recapitulation of the results
- Inflation of the importance of the findings
- Failure to clearly communicate the strength of advance to the field
- Failure to clearly communicate why the results should be of interest to the broader readership
- "Me too, me too!"
- Failure to capture the "common thread" – too many tangential issues for a coherent story
- Where's it all going?
- Entering the "Twilight Zone" - Unwarranted speculation
- The "bully pulpit"
- Drawing conclusions that are not supported by the data!!!!!!

When to combine Results and Discussion

1. When each figure or table requires extensive explanation and comparison to previous work to interpret the data
2. When having a discussion is a liability...
 - not enough context to provide a compelling stand-alone discussion
 - too much recapitulation

Strategies for making your discussion work for you

- Painting the Sistine Chapel – get your audience to “see” the big picture
- Stirring the pot - Identify a point of disagreement or “controversy” that your paper addresses
- The big hook – how to “win over” your audience
 - How can your results potentially advance your audience’s work?
 - How do your results provide new opportunities for your reading audience?
- Plugging the holes: “Yes, we thought of that...”
- Advancing the field
 - Include a figure of an updated model
- Be a visionary – where does the future lay?
- Write powerfully – be crisp and concise

How to write beautiful discussions?

Write often – be a practitioner...

...but get feedback from many sources