20.109 Communication Workshop 4

Research Manuscripts: structure and writing process

The Broccoli and the Hourglass

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MIT BE
BIOLOGICAL ENGINEERING

Communication Lab

Welcome back to us!

- Still interactive, so keep your cameras on!
- Ask lots of questions! We love them!
- Unmute or raise your hand with emojis.

photo: Junque 2 Jewels

What do you find makes good writing?

clear and effective

elegant and stylish
(don’t worry about that now)

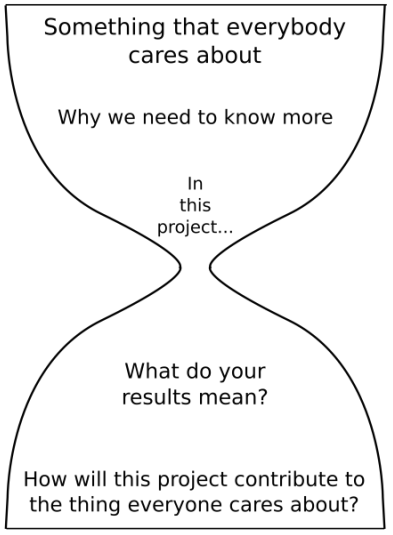
Clarity comes from ORGANIZATION

Across sections (fractal)

- sections answer different questions
- some effective redundancy
- content in parallel order (figures too)

Within sections

- go from most significant to less
- use topic sentences
- motivation, action, finding, transition



Revising is essential.

- Do not try to write this paper all at once.
- **Outline, pause, draft**, set aside for a few days
- When you get stuck: write topic sentences, work on the next section, look at examples
- Get feedback:

  peers, instructors, Comm Lab Fellows!

There is not just one way to write a successful paper.

Collect papers that you like!

Analyze what makes them especially clear & compelling.

Try using their techniques.

Writing a paper integrates topics we have already covered…

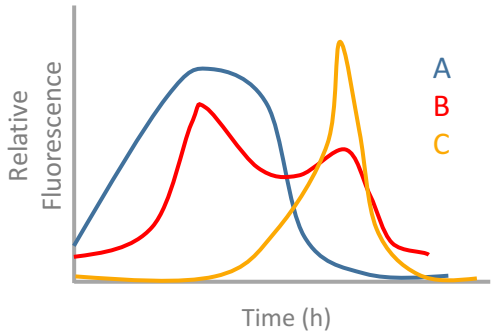
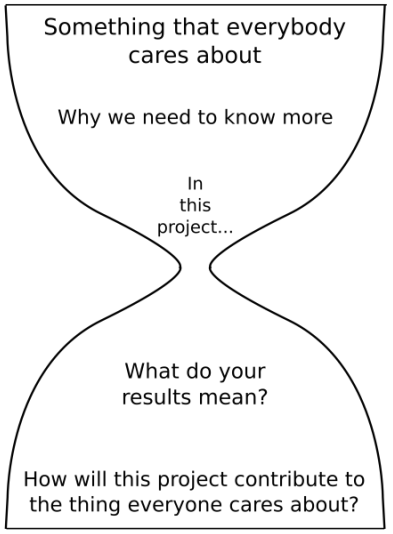


Fig. 1: A, B, and C have different dynamics under Condition X. A, B, and C were sampled using Method 1 and their fluorescence quantified with Method 2. Fluorescence data normalized to negative control.

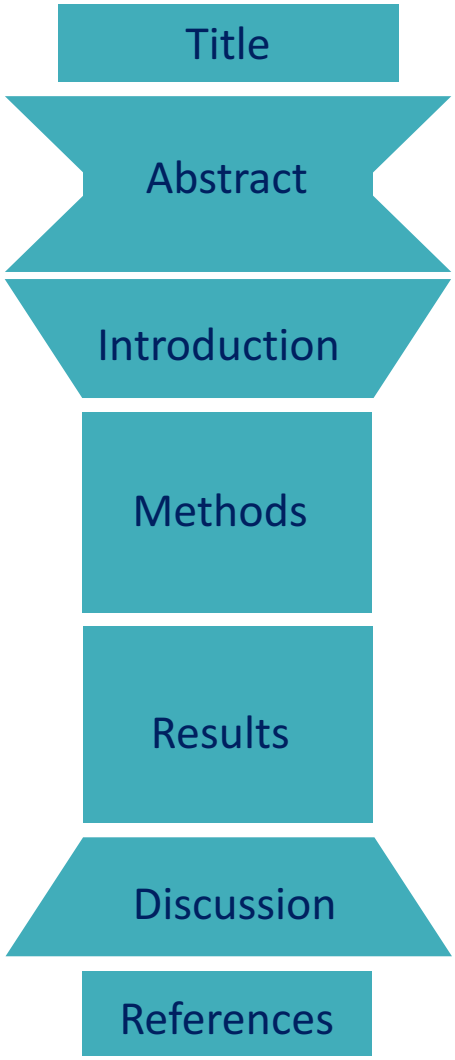
Figures & Captions



Abstracts & Titles

CHAT: What are some important tips about figures and abstracts/titles?

Sections answer different questions



What is your story?
Why should I care?

What do I need to know to understand your story?

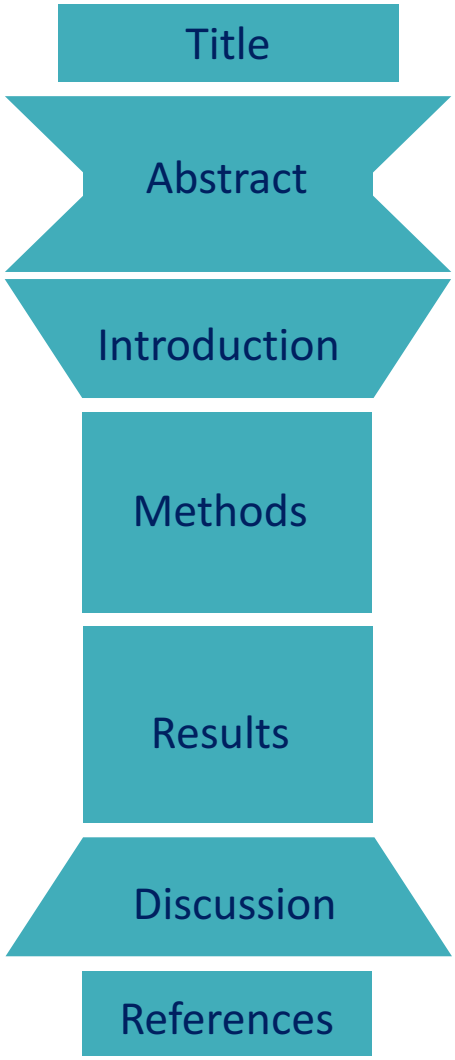
How did you do your experiments?

What did you find?

What does it mean?
Where can we go from here?

What other work is connected?

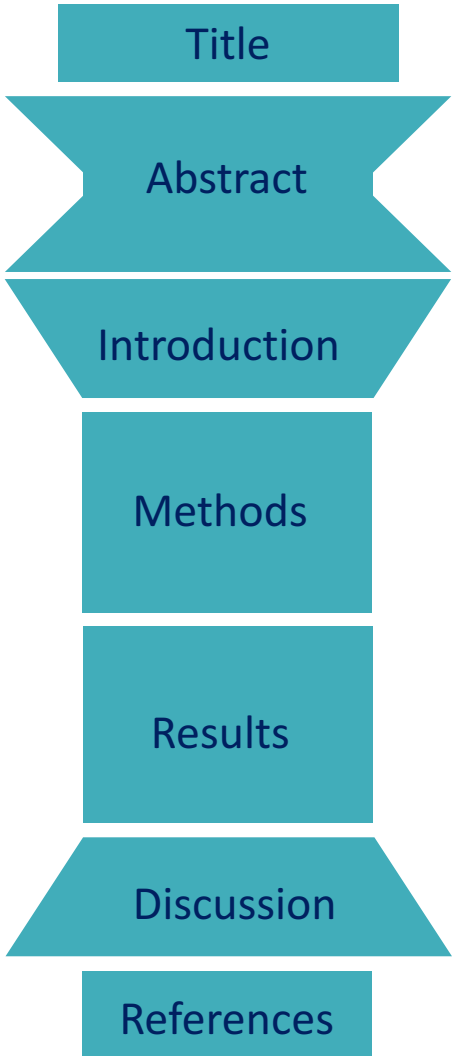
http://dbis.rwth-aachen.de/~derntl/papers/misc/



In what order do you read a paper?

In what order will you write a paper?

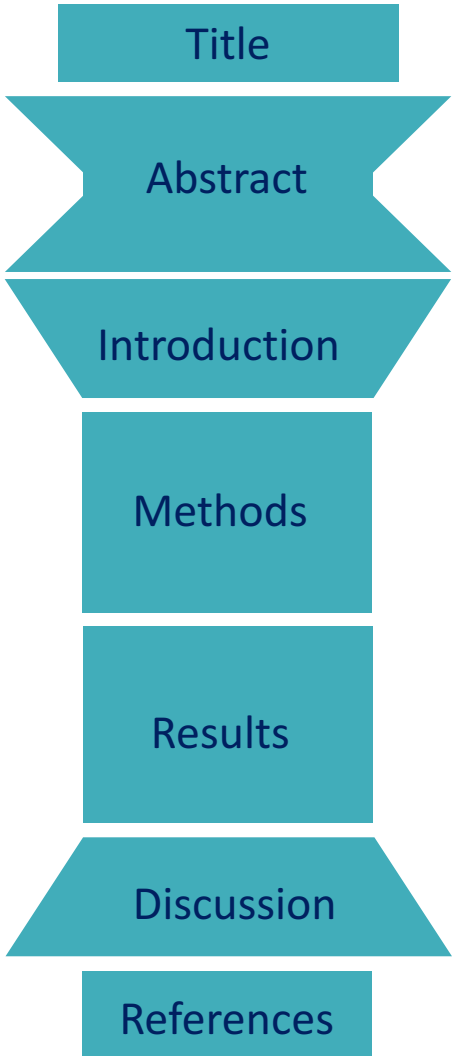
We recommend writing in this order

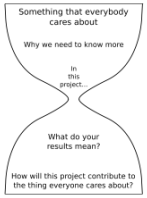


1. Figures + Captions
2. Results
3. Discussion
4. Introduction
5. Abstract
6. Title

Methods?

A paper is also fractal, building in redundancy to help guide the reader



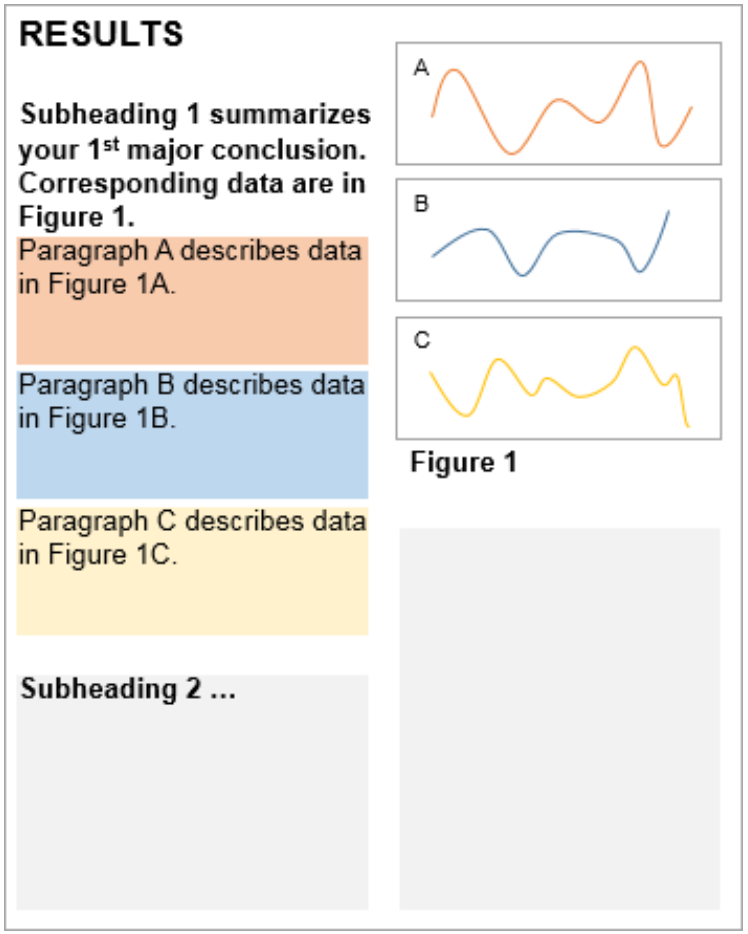


Redundancy in your paper helps your reader find the information they need.

General background	Something everyone in your audience cares about.	Introduction: beginning
Specific background	Zoom in from General Background to the thing you did.	Introduction: middle
Knowledge gap, Unknown	Question that will be answered by your research. Problem, phenomenon that is not understood.	Introduction: end
HERE WE SHOW	Conclusion, answer to the Unknown	Introduction: end Results: end Discussion: beginning
Results	Brief summary of approach + very high-level results. Common pitfall = too much Methods/Results.	Introduction (high level) Results Methods
Implication, Significance	So what? What do your results mean for the thing everyone cares about?	Discussion

Parallelism: Content goes in same order.

Data || Methods || Results || Discussion



Methods: Most technical detail

Results: Motivation for key methods you used; high-level summary of methods used to obtain results

Figure captions: high-level description of methods used

1 thought, 1 paragraph

- Topic sentence summarizes this thought
- Last sentence reiterates and/or transitions
- Go in an order that's logical for the reader
  - pro then con
  - most to least important evidence
  - chronological (careful!)
- Organized paragraphs help you and your reader

Results

What did you find?

Results = rationale + data + conclusion

Conclusion 2

Title

Paragraphs for each of the key experiments

RESULTS

Subheading 1 summarizes your 1st major conclusion. Corresponding data are in Figure 1.

Paragraph A describes data in Figure 1A.

Paragraph B describes data in Figure 1B.

Paragraph C describes data in Figure 1C.

Subheading 2 ...

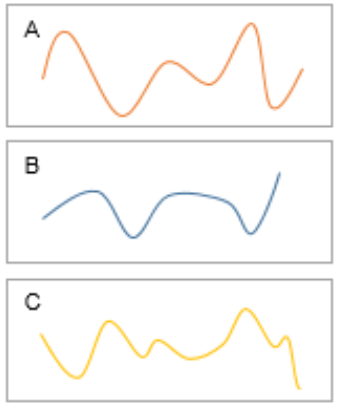


Figure 1

Results = rationale + data + conclusion

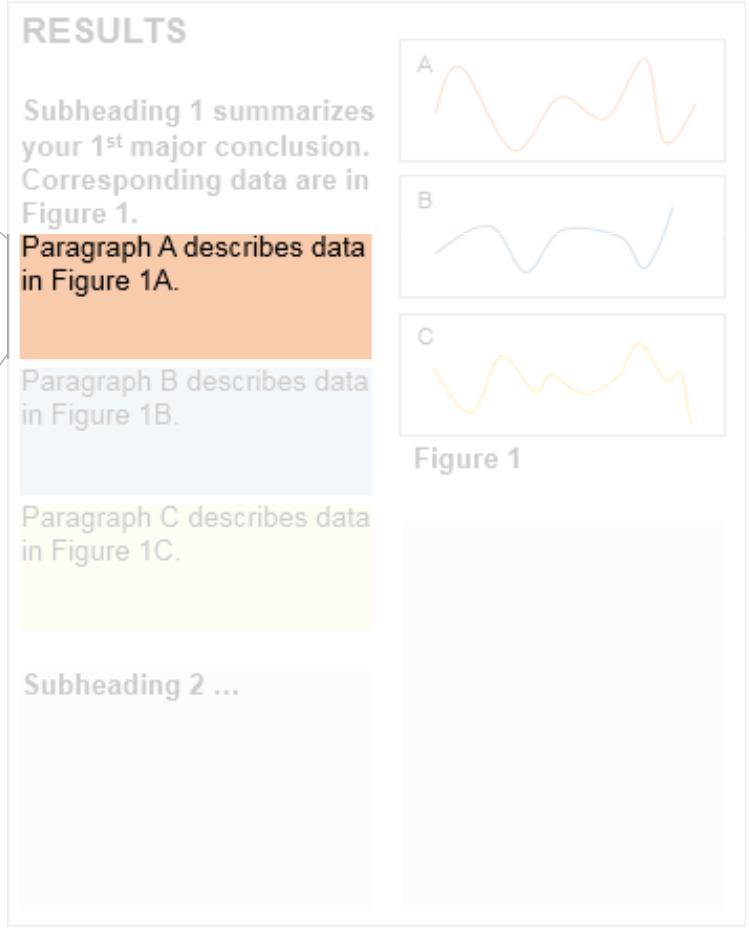
In order to determine *X*, *Y* was performed, showing *Z* major results.

Data + conclusions

- pro, then con
- most to least important
- experiment vs. control

Transition sentence

- re-summarize findings
- justify movement to next experiment or hypothesis



Results: Present minimal essential data.

Remember: MAXIMIZE signal-to-noise.

Include in your paper

- The experiment or dataset that is the **strongest proof** of your conclusion.
- Parts of your chosen dataset might contradict your main conclusion, or support one claim but not another.
- Discuss all parts of a figure in your results section.

Results: Present minimal essential data.

Include as Supplementary Info

Experiments or datasets that…

- Also support your conclusion but are not the strongest proof

  method is less validated
  data are less statistically significant
  data are less intuitive to interpret

- Were run to validate methods

- Were run to rule out alternative hypotheses

Results: Keep a sense of proportion

space spent describing an individual result $\propto$ **importance** of that result to the paper's main conclusion

Ira Herskowitz, UCSF

Results: The heading of each result section reflects the message of that figure

DDO-5936 targets a surface binding site on Hsp90 to inhibit the Hsp90-Cdc37 PPI

What do you notice about this figure title?

Fig. 2. DDO-5936 binds to a critical residue on the Hsp90-Cdc37 PPI interface.

Wang *et al*., *Sci. Adv.* 18 Sep 2019

Results: Motivating the experiment

Recently, it has been proposed that binding of CDK4/6 to Cdc37 could be blocked by their ATP competitive inhibitors (*29*).

What do you think they will do next?

Wang *et al*., *Sci. Adv.* 18 Sep 2019

Results: Briefly what was done

Recently, it has been proposed that binding of CDK4/6 to Cdc37 could be blocked by their ATP competitive inhibitors (*29*). Considering the possibility of direct inhibition effects of DDO-5936 on kinases, especially cell cycle–related kinases, we screened 20 kinases using DDO-5936.

Wang *et al.*, *Sci. Adv.* 18 Sep 2019

Results: What was FOUND: data + conclusions

Recently, it has been proposed that binding of CDK4/6 to Cdc37 could be blocked by their ATP competitive inhibitors (*29*). Considering the possibility of direct inhibition effects of DDO-5936 on kinases, especially cell cycle–related kinases, we screened 20 kinases using DDO-5936. As expected, DDO-5936 exhibited no inhibition effects on ATPase activity of the selected kinases (IC50 > 100 μM), leading to exclude the possibility of DDO-5936 as a kinase inhibitor (table S2).

Wang *et al.*, *Sci. Adv.* 18 Sep 2019

Results: Example of overall structure

In order to determine *X*, *Y* was performed, showing *Z* major results.

Data + conclusions

pro, then con
most to least important
experiment vs. control

Transition sentence

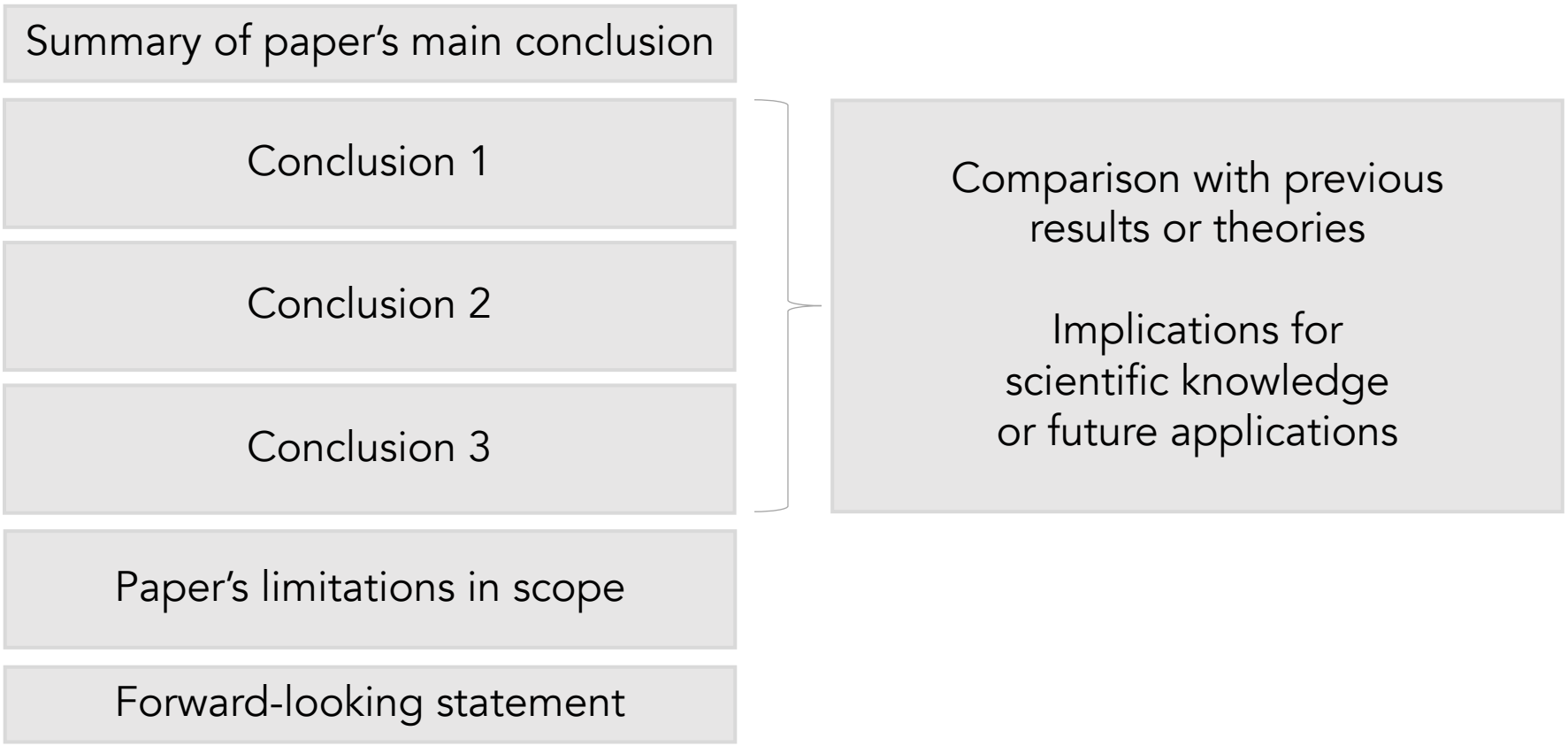
re-summarize findings
justify movement to next experiment or hypothesis

Recently, it has been proposed that binding of CDK4/6 to Cdc37 could be blocked by their ATP competitive inhibitors (*29*). Considering the possibility of direct inhibition effects of DDO-5936 on kinases, especially cell cycle–related kinases, we screened 20 kinases using DDO-5936. As expected, DDO-5936 exhibited no inhibition effects on ATPase activity of the selected kinases (IC50 > 100 μM), leading to exclude the possibility of DDO-5936 as a kinase inhibitor (table S2).

Discussion

What does it all mean?

Speculation and interpretation belongs in Discussion, not Results.



The Discussion should start with a summary of the main message/conclusion

Summary of paper's main conclusion

1 or 2 sentences

Reiterate your "here we show"

To obtain a full view of the Hsp90 chaperone system, we focused on the global regulation process, which indicated a key role of multichaperone Hsp90 complexes formed with different cochaperones by diverse PPIs.

A successful Discussion answers questions for both experts and non-experts.

Comparison with previous results or theories	*How do you account for results that contradict the rest of the field? How does it connect with other work?*
Scientific or engineering implications	*How will this work impact the field or people or the world?* No more than 1 degree of speculation
Paper's limitations in scope	*How do you explain confusing or complicated results?*

Discussion builds from the results

Comparisons?
Implications?
Limitations?

Particular phrases that would not be in other sections?

Differences in language?

The Hsp90-Cdc37 complex might be an attractive target because it meets the following criteria: (i) Cdc37 is expressed more in cancer cells than in normal cells to provide a potential therapeutic window;

…

indicating a potential specific modulation mechanism to avoid unnecessary toxicity.

Discussion often ends with a look at the future

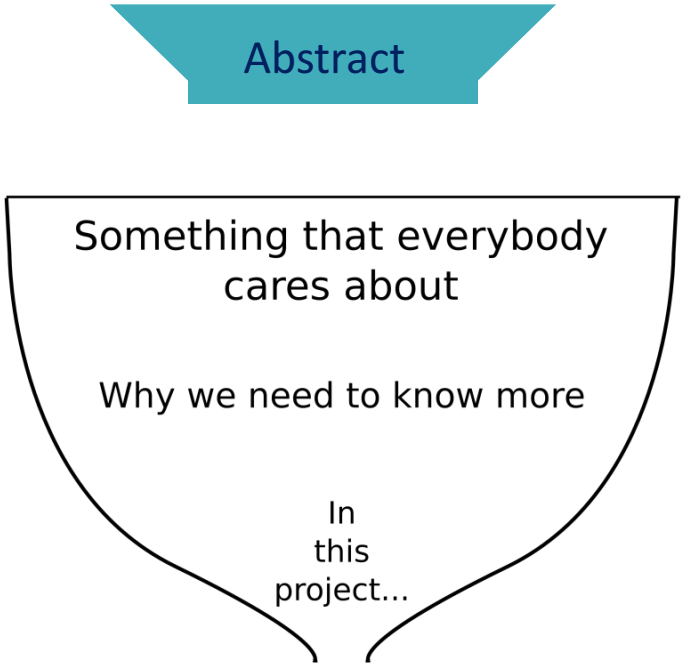
Currently, because of the large and dynamic binding surface of Hsp90-Cdc37 PPI, the biggest challenge to developing specific inhibitors is the uncertainty of accurate binding site for small molecules. Although DCZ3112 and many other natural products (such as celastrol) could inhibit Hsp90-Cdc37 PPI at the cellular level, the accurate binding site and regulation mechanism remained unclear. In summary, our work first revealed the binding determinants of the Hsp90-Cdc37 complex and identified them by a specific small molecule to provide further insights into the modulation of interactions between Hsp90 and Cdc37 or other cochaperones in cancer therapy.

Introduction

What do I need to know to understand your story?

Introduction = Why did you do this research?

- Your research taught you something, right?
- Introduction convinces the reader that this knowledge is worth having
- background + knowledge gap + here we show



Introduction: Clearly establish your central question and take-home message

- Clearly define the knowledge gap/central question of the study and follow with a clear hypothesis.
- Very briefly summarize the key results & conclusions of the paper.

General background
Specific background

Knowledge gap,
Unknown

HERE WE SHOW

Results
Implication, Significance

Introduction: Clearly establish your central question and take-home message

Until now, no small molecule has been reported to specifically bind to Hsp90 or Cdc37 with the potency to disrupt Hsp90-Cdc37 at the cellular level by blocking critical recognition residues, resulting in a lack of evidence for identifying the specific binding site and explicit inhibition mechanism, although several natural products were reported to exhibit anticancer activity via a mechanism of Hsp90-Cdc37 inhibition. Here, we are the first to describe a complete process from critical residue discovery on a protein-protein binding interface to the identification of a small-molecule binding site.

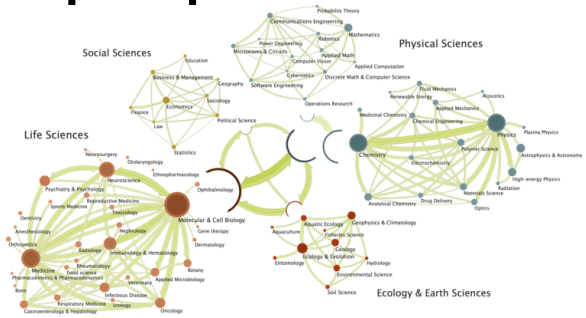
Introduction: Briefly summarize key results

Through molecular dynamics simulations, we focused on residues that contribute greatly to the Hsp90-Cdc37 binding interface and made further identifications by mutagenesis data; the results suggested an interaction between E47 and Q133 on Hsp90 and R167 on Cdc37 as a binding determinant for the Hsp90- Cdc37 PPI. To disrupt the most important interactions between Hsp90 and Cdc37, we designed a screening workflow that identified DDO-5936 as a cellularly active inhibitor that disrupted the Hsp90-Cdc37 interaction. Nuclear magnetic resonance (NMR) characterization and binding assays with different mutants confirmed that DDO-5636 selectively bound to a previously unknown site on the Hsp90 N terminus and exhibited almost no ATPase inhibition. As expected, DDO-5936 selectively down-regulated kinases without effects on other nonkinase clients of Hsp90, exhibited antiproliferative potency with a high correlation to the expression level of Hsp90-Cdc37, arrested the cell cycle via a cyclin-dependent kinase 4 (CDK4) decrease in HCT116 cells, and exhibited in vivo potency in a xenograft model.

Introduction: Identify the significance of your findings

Collectively, these results indicate that the discovery of DDO-5936 might have identified a previously unknown binding site on the Hsp90 N terminus that disrupts its interaction with Cdc37, which might lead to an advanced understanding of Hsp90-Cdc37 function as well as a promising lead compound for alternative drug discovery strategies through regulation of Hsp90 with its cochaperone cycles.

References connect your paper to the research ecosystem



- Build them over the course of writing
- All sections except the abstract have refs
- [Pro tips] Include papers that…
  - reach conflicting conclusions
  - are from competitors
  - were published during the course of your work

  (Reviewers will be looking)

Revising is ESSENTIAL!

- Do not try to write this paper in one day.
- **Outline**/draft the sections, then set aside the paper for several days.
- If you get stuck: outline, write topic sentences, work on the next section, look at examples
- Get feedback:

  peers, instructors, Comm Lab Fellows!

Assignment or paper questions?

20% of course grade (full rubric on wiki)

Title and Abstract		10%
Introduction	2-3 p.	10%
Methods	3-4 p.	20%
Results and Figures	4-5 p.	50%
Discussion	2-3 p.	10%

(12pt., double-space except abstract, max. 14 pages)