QBQ 5749 – Scientific Writing

Deborah Schechtman and Fabio Forti 2023

Objectives of the course

Stimulate students to organize their data for their PhD thesis in the form of a manuscript for publication in na international jornal (QualisA)

At the end of the course the student must hand in a **scientific article**, of his ownership, related to their thesis, together with a **letter to the editor**.

The **manuscript** and the **letter** will be sent to the reviewers.

Peer Review Process

Fabio and Deborah will act as editors, selecting faculty members of the graduate program to review the manuscripts submitted by the students.

The reviewers will critically and anonymously evaluate the manuscripts, judging scientific content, presentation and may ask for changes.

Students will then submit a revised version of the comments and submit a revised version of the manuscript responding to the reviewer´s comments (date to be determined) with a letter to the editor.

Students excused from the peer review process

- Students that prove that they are **first authors of scientific papers related to their thesis, that are either published or undergoing revision will submit their manuscript which will not undergo an additional peer review process.**

- Obs.: Pre-prints are not valid since these have not undergone a peer review process, these will be submitted to review.

Program and Calendar

08/17	Introduction to the course (Deborah and Fabio)
08/31	Concepts of writing structure (Daniela Basseres)
09/14	The editor's point of view (Bianca Zingalis)
09/21	Follow up of the manuscripts Group 1(Students)
10/5	Follow up of the manuscripts Group 2 (Students)
11/09	Manuscripts are due
12/11	Response to reviewer is due

Why is it importante to write a *Paper?*

George Whitesides (Professor, Dept. of Chemistry, Harvard Univ, Top Highly Cited, >1200 papers):

“If your research does not generate papers, it might just as well not have been done.

Interesting and unpublished is equivalent to non-existing“

Advanced Materials, 2004, 16:1375-1377

https://gmwgroup.harvard.edu/news/george-whitesides-how-write-paper-communicate-your-research

Importance of the Scientific Article

Share and transmit knowledge obtained through research.

Essential for the Evolution of science.

Science is based on fundamentals of previous research.

Before you begin

- Organize your data.

- Read the literature (make notes).

- Remember you must always write in your own words or it my be considered plagiarism, journals do not accept even auto-plagiarism. Be careful!

A paper is not a report !!!

However:

Reports may help elaborating manuscripts

Have an organized Notebook!!

Data should be stored in an organized fashion so that anyone in the area is able to repeat your experiments/ results!

Articles to be accepted by referees and cited by coleagues must:

- Convene a precise and clear message.
- Have solid and reproducible data.
- Have conclusions supported by the data presented.
- Authors should convince readers their work is important.

How to write a *Scientific article ?*

When writing an article:

- Allways read articles related to your work.
- Organize your data.
- Include figures with complete legends.
- Reserve time to work on the manuscript.
- Choose the type of article to be written letter/short common
- Chose the journal for submission: see the format of the articles as well as references.
- Read the scope of the jornal as well as guidelines!

Parts of the paper

1. Title
2. Graphical Abstract/Highlights
3. Abstract
4. Introduction
5. Materials and Methods
6. Results and Discussion (may be seperate items)
7. Conclusions
8. Acknowledgements
9. Bibliography (References)
10. Figures with legends, Tabels
11. Supplementary material

Papers are not necessarily written in this order

How papers are usually read

- 1. Title
- 2. Graphical Abstract/Highlights
- 3. Abstract
- 4. Figures with legends/Tables
- 5. Conclusions
- 6. Results and Discussion
- 7. Introduction
- 8. Materials and Methods
- 9. Acknowledgements
- 10. References

How papers are usually written

1. Figures with legends/Tables
2. Results
3. Materials and Methods
4. Introduction
5. Discussion
6. Conclusion
7. Abstract
8. Acknowledgements
9. References
10. Graphical Abstract/Highlights
11. Title

Figures

Figures must be clear easily seen (avoid small fonts and be careful when choosing colors).

Maintain format and font consistent.

One should be able to understand the result just by looking at the figure.

Figure Legends

- Should be complete.

- Have a title: A highlight of the main result (some journals have diferent diferent styles).

- Inlude details so that the reader can understand how the experiment was performed. If necessary refer to Materials & Methods.

Materials & Methods

Objective: Give suficiente information so that the reader can repeat the experimente whenever necessary include references.

Description of materials used (name, brand, place and country)

Description of cells, animals and patients (patient samples).

Ethics committee

List all Methods then carefully describe them.

This section make take longer to write than expected.

Results and Discussion

-May be separate or together

-The order of the results is the order you want to tell the story, not necessarily the order the experiments were performed and may vary according to the message you want to convene.

-Take time to decide the best way to tell the story, this can be done even when you only have initial results.

-Include figures of expected results. These can guide your experiments.

Results and Discussion

Keep in mind your contribution to the literature.

Discussion of results relative to what is known in the literature.

Discrepancies with the literature should be discussed.

Limitations of the study may also be discussed

Conclusions

Based on the discussion write the conclusion.

Avoid repeating the results and discussion.

It is not a summary of the results.

Report what is really new and unique of your study.

Significance of your work.

Future perspectives.

Introduction

Contextualize / Give a **Background**

Motivation for the study.

Why are more studies necessary?

Are there different ideas to explain the same phenomenon , or gaps to specific hypothesis.

What are your objectives?

Introduction 3 paragraphs

I. Background – **Introduction to the theme** (Contextualization and need for the study.

Necessity for the study)

II. Gaps- Indicate the gaps in the area, **what is your main question?** Describe limitations, challenges and open questions. **Why is the study necessary?**

III. Describe the **objectives of the work. What are the strategies used to answer the main question?** Give a preview of what will be found in the article.

Introduction

Background

Gaps

Objectives
Preview of results

Context

However… Although….lacking

Strategies used, here we….

Find in the introduction

Background

Gaps

Objectives

nature chemical biology

ARTICLES

https://doi.org/10.1038/s41589-021-00751-4

Check for updates

A compendium of kinetic modulatory profiles identifies ferroptosis regulators

Megan Conlon[1,4], Carson D. Poltorack[1,4], Giovanni C. Forcina[1,4], David A. Armenta[1], Melodie Mallais[2], Marcos A. Perez[3], Alex Wells[1], Alexis Kahanu[1], Leslie Magtanong[1], Jennifer L. Watts[3], Derek A. Pratt[2] and Scott J. Dixon[1]✉

Cell death can be executed by regulated apoptotic and nonapoptotic pathways, including the iron-dependent process of ferroptosis. Small molecules are essential tools for studying the regulation of cell death. Using time-lapse imaging and a library of 1,833 bioactive compounds, we assembled a large compendium of kinetic cell death modulatory profiles for inducers of apoptosis and ferroptosis. From this dataset we identify dozens of ferroptosis suppressors, including numerous compounds that appear to act via cryptic off-target antioxidant or iron chelating activities. We show that the FDA-approved drug bazedoxifene acts as a potent radical trapping antioxidant inhibitor of ferroptosis both in vitro and in vivo. ATP-competitive mechanistic target of rapamycin (mTOR) inhibitors, by contrast, are on-target ferroptosis inhibitors. Further investigation revealed both mTOR-dependent and mTOR-independent mechanisms that link amino acid metabolism to ferroptosis sensitivity. These results highlight kinetic modulatory profiling as a useful tool to investigate cell death regulation.

Cell death can be executed by apoptosis or one of several nonapoptotic cell death mechanisms, including ferroptosis. Ferroptosis can be triggered by blocking the uptake of cystine by the system x_c^- cystine/glutamate antiporter[1]. Loss of cystine uptake leads to depletion of intracellular reduced glutathione (GSH), starving the phospholipid hydroperoxidase glutathione peroxidase 4 (GPX4) of its essential cofactor. Ultimately, GPX4 inactivation allows for iron-dependent accumulation of lipid hydroperoxides to lethal levels within the cell[2]. Many pathophysiological processes involve the induction of ferroptosis[3,4]. It is therefore of interest to better understand how ferroptosis is regulated and identify inhibitors of this process suitable for use in vivo.

Small molecules are useful mechanistic probes of cell death[5]. Apart from the intended target, small molecules can have off-target effects on other proteins or processes. Careful analysis of off-target effects can point to unexpected mechanisms of action and new drug repurposing opportunities[6,7]. Drug repurposing typically focuses on off-target modulation of protein function. However, compounds can also have direct chemical reactivities that may be of interest, especially in the context of ferroptosis[8,9]. Systematic analysis of chemical reactivities, especially for existing drugs, could lead to unanticipated drug repurposing opportunities.

One powerful means to gain insight into cell death mechanisms is to examine how the phenotype of one lethal molecule is enhanced or suppressed ('modulated') by a second compound[10]. Modulatory profiling also has the potential to uncover new activators or inhibitors of a given cell death mechanism[11]. Here, we use a direct time-lapse cell death imaging technique, scalable time-lapse analysis of cell death kinetics (STACK)[12], to generate a large compendium of kinetic modulatory profiles for apoptosis and ferroptosis-inducing compounds. Interrogation of this compendium identified numerous small molecules, including the drug bazedoxifene, that inhibit ferroptosis via unanticipated chemical reactivities. By contrast, inhibitors of the mechanistic target of rapamycin (mTOR) pathway can inhibit ferroptosis in an on-target manner. Investigation of the connection between mTOR signaling and ferroptosis also resulted in the discovery of an mTOR-independent mechanism linking amino acid levels to ferroptosis sensitivity.

Results

Kinetic modulatory profiling of cell death. We developed a kinetic modulatory profiling approach to identify new modulators of apoptosis and ferroptosis (Fig. 1a and Supplementary Fig. 1a,b). HT-1080^N fibrosarcoma cells were treated with one of eight different proapoptotic or proferroptotic lethal 'query' compounds and simultaneously exposed to one of 1,833 different bioactive 'modulator' compounds or vehicle (dimethylsulfoxide, DMSO), for a total of roughly 16,000 different conditions. Cell death in each condition was measured over time using STACK[12]. We computed the expected cell death for each query-modulator combination using the Bliss independence model[13], and then determined the deviation between the expected and the observed cell death for each compound combination (Supplementary Fig. 1c,d). To facilitate an initial exploration of this dataset, z-scored deviation values were hierarchically clustered in an unsupervised manner across both query and modulator compounds and plotted as a heat map (Fig. 1b).

Several features of this compendium were consistent with a high-quality dataset. First, the three ferroptosis-inducing query compounds and five apoptosis-inducing query compounds segregated into distinct clusters (Fig. 1c). Moreover, within the ferroptosis subcluster, the system x_c^- inhibitors erastin and sorafenib were more similar to each other than the GPX4 inhibitor ML162. This is consistent with ferroptosis induced by system x_c^- inhibition versus direct GPX4 inhibition having unique mechanisms of regulation[14]. Second, we observed functionally coherent clustering of modulator compounds. For example, eight known microtubule

Find in the introduction

Background

Gaps

Objectives

JBC ARTICLE

High affinity binding of SARS-CoV-2 spike protein enhances ACE2 carboxypeptidase activity

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Edited by Rurna Banerjee

The novel severe acute respiratory syndrome coronavirus (SARS-CoV-2) has emerged to a pandemic and caused global public health crisis. Human angiotensin-converting enzyme 2 (ACE2) was identified as the entry receptor for SARS-CoV-2. As a carboxypeptidase, ACE2 cleaves many biological substrates besides angiotensin II to control vasodilatation and vascular permeability. Given the nanomolar high affinity between ACE2 and SARS-CoV-2 spike protein, we investigated how this interaction would affect the enzymatic activity of ACE2. Surprisingly, SARS-CoV-2 trimeric spike protein increased ACE2 proteolytic activity ~3-10 fold against model peptide substrates, such as caspase-1 substrate and Bradykinin-analog. The enhancement in ACE2 enzymatic function was mediated by the binding of SARS-CoV-2 spike RBD domain. These results highlighted the potential for SARS-CoV-2 infection to enhance ACE2 activity, which may be relevant to the cardiovascular symptoms associated with COVID-19.

The novel coronavirus, SARS-CoV-2 (1, 2, 3), has emerged as an unprecedented global pandemic resulting in over 35 million confirmed cases and more than 1 million deaths as of October 11, 2020 (WHO). The infection of SARS-CoV-2 causes fever, dry cough, severe respiratory illness and pneumonia, a disease recently named COVID-19 (4). Pathological studies have revealed all features of diffuse alveolar damage (DAD) with excessive fluid in the lungs of infected individuals (5). In addition, abnormal blood clots were observed in many hospitalized patients (6). However, the mechanistic understanding of the pathogenicity of SARS-CoV-2 and its complications is still lacking.

ACE2 was identified as the entry receptor for both SARS-CoV-2 [2], and SARS-CoV (7–9). Structural studies revealed that both SARS-CoV-2 and SARS-CoV spike (S) glycoproteins bind ACE2 with higher affinity (10–13). The overall structure of SARS-CoV-2 S resembles that of SARS-CoV S with the spike RBD domain contacting the extracellular region of ACE2. Physiologically, ACE2 is a zinc metalloprotease (carboxypeptidase), a homolog to dipeptidase angiotensin-converting enzyme (ACE) but with different substrate specificity (14). ACE cleaves the C-terminal of angiotensin I (Ang I) to produce the potent vasopressor octapeptide angiotensin II (Ang II), which is further cleaved at its C terminus by ACE2 to deactivate Ang II and produce Ang 1-7. Together, ACE and ACE2 regulate vasoconstriction and vasodilatation in the rennin-angiotensin system (RAS). In addition, ACE and ACE2 regulate kinin-kallikrein system to control vascular permeability and vasodilatation (15). ACE deactivates Bradykinin (BK) nonapeptide, the ligand for constitutively expressed bradykinin receptor B2. Bradykinin can be further processed by carboxypeptidase N or M to form des-Arg9-bradykinin (desBK), a potent ligand for bradykinin receptor B1(16). Beyond renin-angiotensin and kinin-kallikrein systems, ACE2 also cleaves other biological peptides such as Apelin-13 that activates apelin receptor to cause vasodilatation (17). Despite the importance of ACE2 in RAS, there is limited understanding to the impact of coronavirus infection to the physiological function of ACE2.

ACE2 is predominantly expressed on type II pneumocytes in lung (18). Clinical observations showed that COVID-19 patients often had dyspnea and accumulation of fluid in lung resembling local angioedema (7, 16, 19), suggesting a pathology driven by changes in vascular permeability and vasodilatation during SARS-CoV-2 infection. However, there was no direct assessment of ACE2 enzymatic activity during the coronavirus infection. Here we examined the effect of the binding of SARS-CoV-2 spike protein to the intrinsic enzymatic activity of ACE2 using two fluorogenic substrates, the caspase-1 substrate (Mca-YVADAPK-Dnp) (14), and a bradykinin analog (Mca-RPPGFSAFK-Dnp) (20). To our surprise, SARS-CoV-2 spike enhanced ACE2 proteolytic activity on both caspase-1 substrate and bradykinin-analog, and the enzymatic enhancement was mediated by the spike RBD domain binding. The ability of SARS-CoV-2 spike protein to alter ACE2 enzymatic activity may result in dysregulation of RAS and contribute to the pathogenesis of COVID-19.

Results

SARS-CoV-2 spike protein enhances ACE2 activity

SARS-CoV-2 is highly homologous to SARS-CoV and both use ACE2 as their entry receptor (2, 9). Further structural studies demonstrated that both SARS-CoV-2 and SARS-CoV used their spike protein RBD domain to interact with ACE2 in similar binding modes (11). However, SARS-CoV-2 spike protein exhibited higher binding affinity to ACE2 than that of SARS-CoV. Given the nanomolar affinity between ACE2 and SARS-CoV-2 S spike protein, we wonder if the binding of SARS-CoV-2 spike protein to ACE2 affected its function as a carboxypeptidase regulating both the rennin-angiotensin and kinin-kallikrein systems (15, 21).

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References

- Use a reference manager fs (EndNote, Mendeley).
- Cite articles that gave origin to the concept you describe.
- Cite recent articles.
- Cite references that you read and that have helped you.
- Avoid too Much auto-citation
- Do not use too many references (some journals limit the number of references).

Acknowledgment

Funding agency (name and grant number)

Thank collaborators that helped with reagents or discussions (people that were helpfull but not enough to be considered co-authors).

Abstract

A concise paragraph that sumarizes

Motivation for the work

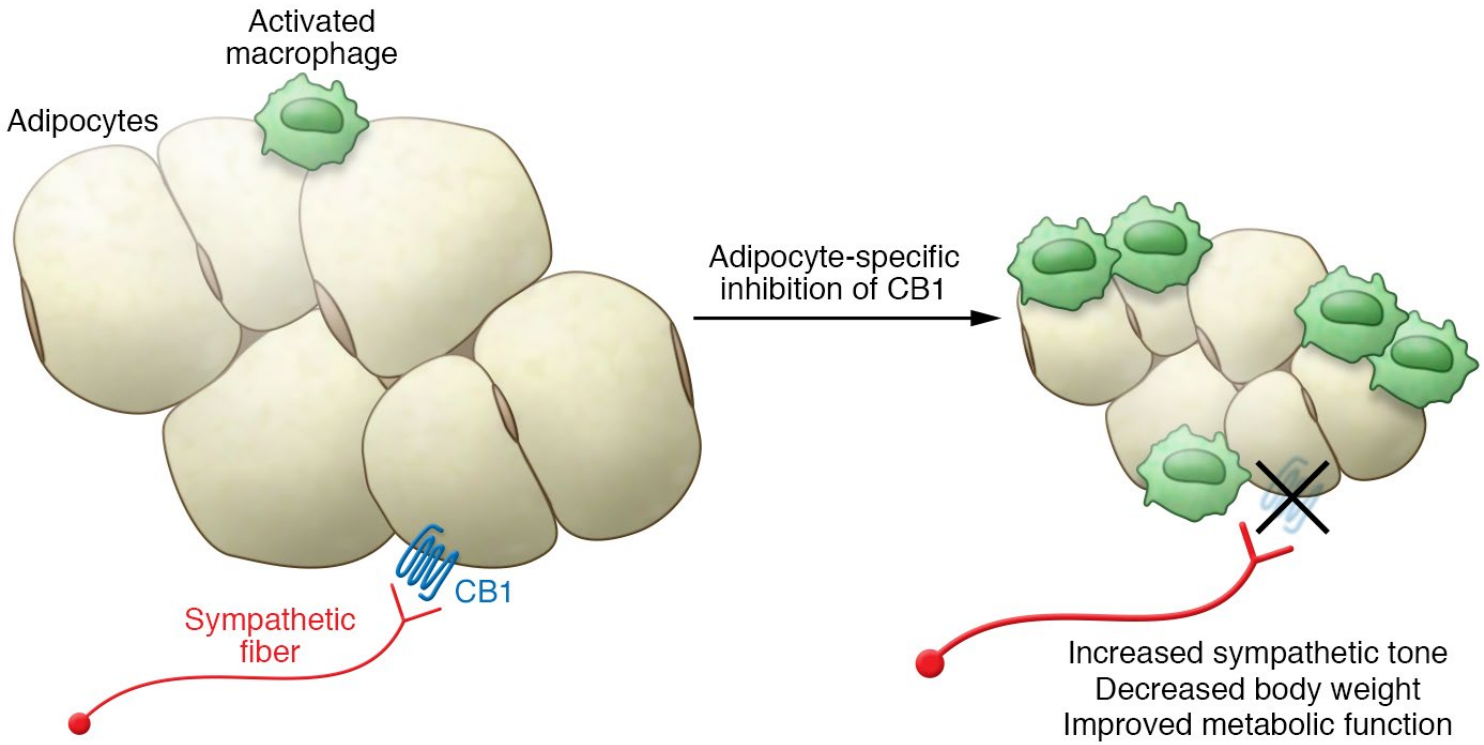
Experimental strategy

Main resultas

Conclusions and advances in the area

Graphical abstract

Capable of sumarizing the main message of the manuscript



https://www.jci.org/kiosks/publish/graphical

Title

- Short and specific (avoid long titles...)
- Should describe your work in a concise manner
- Include Keywords that will help find your work
- Be careful not to submit a manuscript with language errors in the title.

Finalizing

Consider professional editing services.

Prepare a submission letter.

Most manuscripts are rejected at least once don’t give up, don’t be discouraged.

Bibliography

WebSites

- George Whitesides - **How to Write a Paper to Communicate Your Research** (https://gmwgroup.harvard.edu/news/george-whitesides-how-write-paper-communicate-your-research)

- Scientific Writting - Videos

https://www.wetenschappelijkschrijven.nl/videos/