

The

ANATOMY & Physiology

of a **Specific Aims Page**

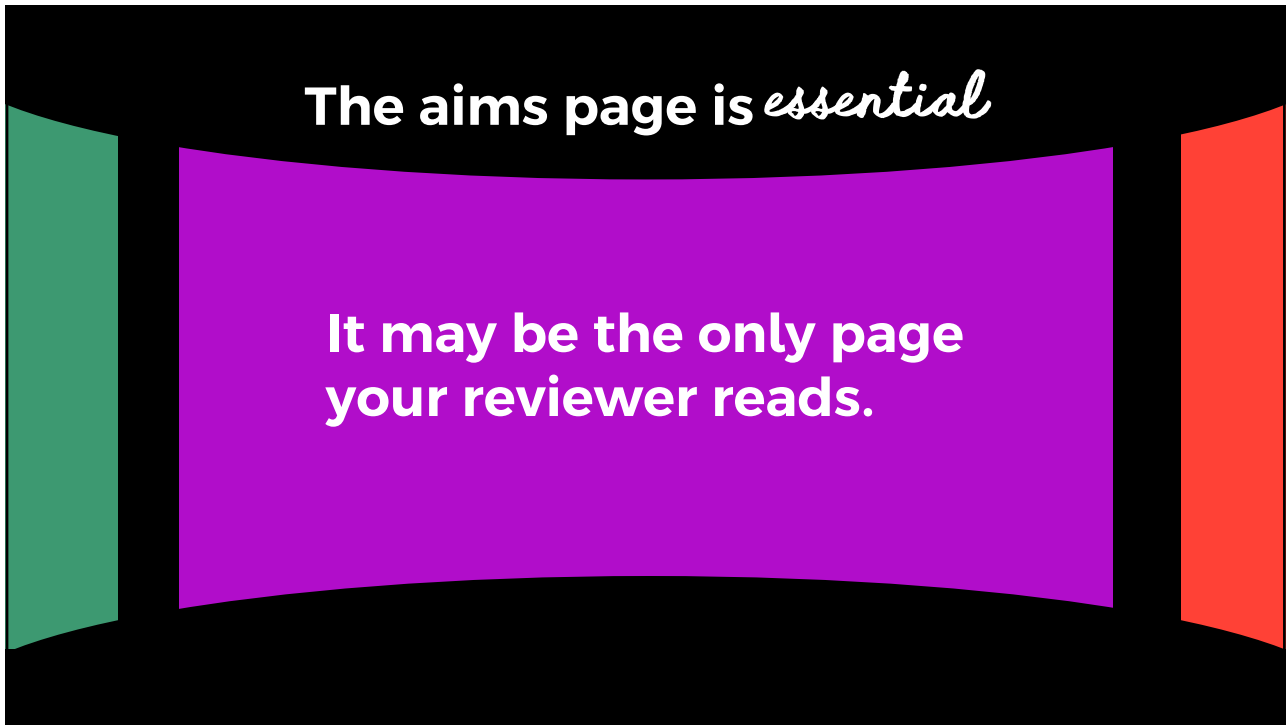
Justine M. Pinsky, PhD

1

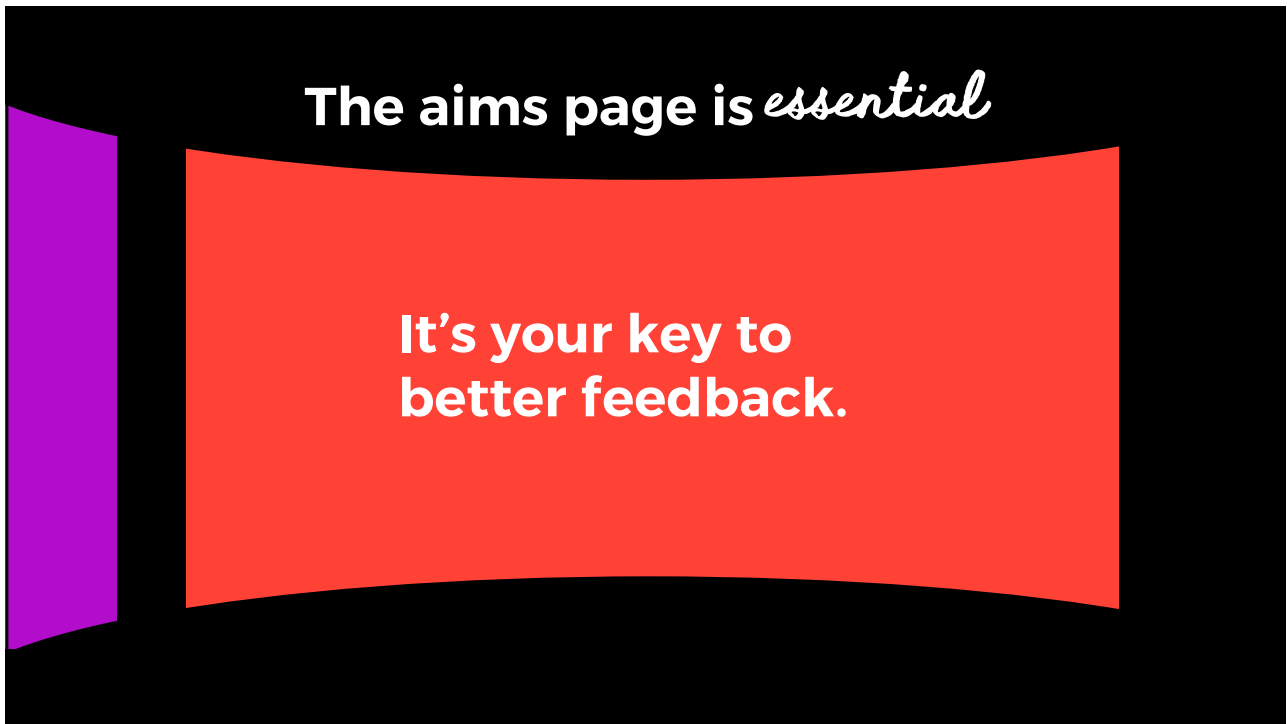
The aims page is *essential*

It's your application's first impression.

2



3



4

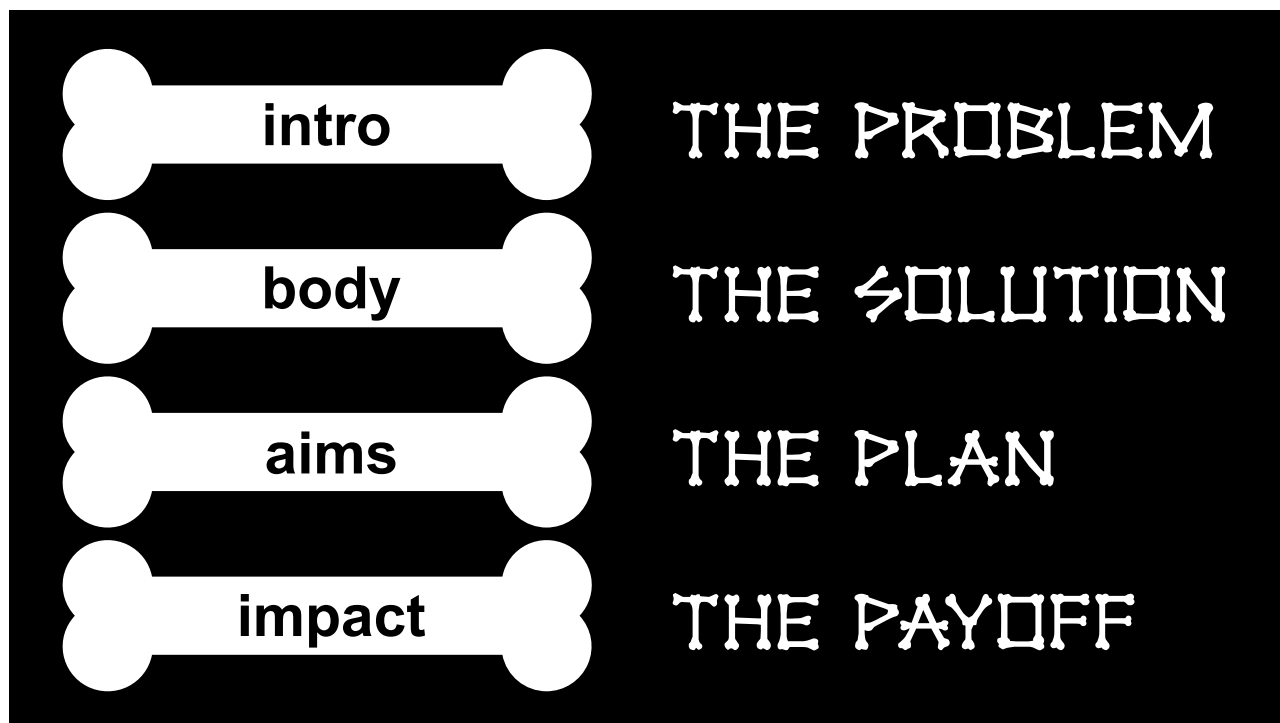
As the Sr. Scientific Writer for iCAP,

I help new, tenure-track faculty **improve their writing skills**



Photo by Loretta Opoku

5



6



intro

THE PROBLEM

hook

known information

gap

critical need

Examples modified from:


<https://www.biosciencewriters.com/NIH-Grant-Applications-The-Anatomy-of-a-Specific-Aims-Page.aspx>



NIH Grant Applications
The Anatomy of a Specific Aims Page

Release Date: April 09, 2015
Category: Scientific Grant Writing
Author: Michelle S., Ph.D., E.L.S.

7



intro

THE PROBLEM

hook

known information

gap

critical need

Viruses are involved in 15-20% of human cancers worldwide, highlighting their potential to reveal common oncogenic mechanisms. One such virus is human T cell leukemia virus type I (HTLV-1), the disease-causing agent of adult T cell leukemia/lymphoma (ATLL). HTLV-1 encodes a potent oncoprotein, Tax, which regulates important cellular processes, including gene expression, proliferation, apoptosis, and polarity. Although the Tax oncoprotein can transform cells in culture and induce tumors in various transgenic mouse models, the *mechanism by which Tax transforms cells is not well understood*. Though many Tax mutants have been generated and characterized, a *major obstacle in the field* is the variability between transgenic models due to random transgene integration sites, variable transgene copy number, and inconsistent transgene expression levels. These challenges make it difficult to link the biological activities of Tax mutants with their transforming potential.

8

intro

THE PROBLEM

hook

known information

gap

critical need

Viruses are involved in 15-20% of human cancers worldwide, highlighting their potential to reveal common oncogenic mechanisms. One such virus is human T cell leukemia virus type I (HTLV-1), the disease-causing agent of adult T cell leukemia/lymphoma (ATLL). HTLV-1 encodes a potent oncoprotein, Tax, which regulates important cellular processes, including gene expression, proliferation, apoptosis, and polarity. Although the Tax oncoprotein can transform cells in culture and induce tumors in various transgenic mouse models, the *mechanism by which Tax transforms cells is not well understood*. Though many Tax mutants have been generated and characterized, a *major obstacle in the field* is the variability between transgenic models due to random transgene integration sites, variable transgene copy number, and inconsistent transgene expression levels. These challenges make it difficult to link the biological activities of Tax mutants with their transforming potential.

9

intro

THE PROBLEM

hook


known information

gap

critical need

Viruses are involved in 15-20% of human cancers worldwide, highlighting their potential to reveal common oncogenic mechanisms. One such virus is human T cell leukemia virus type I (HTLV-1), the disease-causing agent of adult T cell leukemia/lymphoma (ATLL). HTLV-1 encodes a potent oncoprotein, Tax, which regulates important cellular processes, including gene expression, proliferation, apoptosis, and polarity. Although the Tax oncoprotein can transform cells in culture and induce tumors in various transgenic mouse models, the *mechanism by which Tax transforms cells is not well understood*. Though many Tax mutants have been generated and characterized, a *major obstacle in the field* is the variability between transgenic models due to random transgene integration sites, variable transgene copy number, and inconsistent transgene expression levels. These challenges make it difficult to link the biological activities of Tax mutants with their transforming potential.

10



intro

THE PROBLEM

hook

known information

gap

critical need

Viruses are involved in 15-20% of human cancers worldwide, highlighting their potential to reveal common oncogenic mechanisms. One such virus is human T cell leukemia virus type I (HTLV-1), the disease-causing agent of adult T cell leukemia/lymphoma (ATLL). HTLV-1 encodes a potent oncoprotein, Tax, which regulates important cellular processes, including gene expression, proliferation, apoptosis, and polarity. Although the Tax oncoprotein can transform cells in culture and induce tumors in various transgenic mouse models, the *mechanism by which Tax transforms cells is not well understood*. Though many Tax mutants have been generated and characterized, *a major obstacle in the field is the variability between transgenic models due to random transgene integration sites, variable transgene copy number, and inconsistent transgene expression levels*. These challenges make it difficult to link the biological activities of Tax mutants with their transforming potential.

11



body

THE SOLUTION

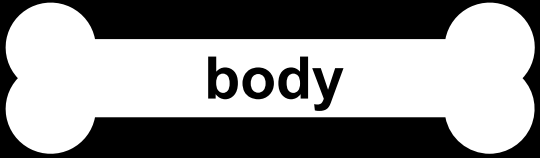
proposed solution

qualifications

objectives / rationale

hypothesis

12



THE SOLUTION

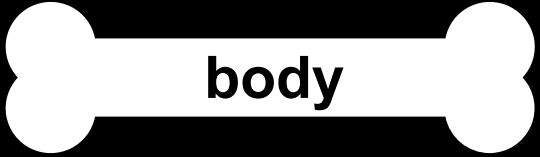
proposed solution *To solve this problem we will develop an innovative mouse model system to study Tax tumorigenesis. Recently, our group generated Lck-CRE mice, allowing conditional gene expression in T cells, the natural target of HTLV-1 infection. Here, we will generate targeting vectors containing wild-type or mutant Tax genes that are silenced by a preceding floxed stop cassette. By recombining these vectors into the Rosa26 locus, we will eliminate random integration sites and standardize gene copy number, resulting in consistent levels of wild-type and mutant Tax protein expression. Lck-Tax transgenic mice have already been developed and produce a leukemia that closely resembles ATLL, strongly supporting our proposed model's feasibility. Thus, we hypothesize that targeting Tax expression in cells with an active Lck promoter will produce a similar disease in our model, and that Tax mutants will ...*

qualifications

objectives / rationale

hypothesis

13



THE SOLUTION

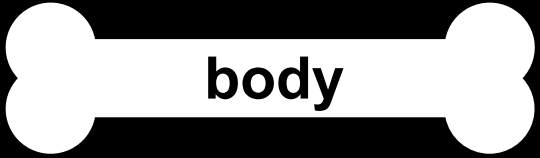
proposed solution *To solve this problem we will develop an innovative mouse model system to study Tax tumorigenesis. Recently, our group generated Lck-CRE mice, allowing conditional gene expression in T cells, the natural target of HTLV-1 infection. Here, we will generate targeting vectors containing wild-type or mutant Tax genes that are silenced by a preceding floxed stop cassette. By recombining these vectors into the Rosa26 locus, we will eliminate random integration sites and standardize gene copy number, resulting in consistent levels of wild-type and mutant Tax protein expression. Lck-Tax transgenic mice have already been developed and produce a leukemia that closely resembles ATLL, strongly supporting our proposed model's feasibility. Thus, we hypothesize that targeting Tax expression in cells with an active Lck promoter will produce a similar disease in our model, and that Tax mutants will ...*

qualifications

objectives / rationale

hypothesis

14



body THE SOLUTION

proposed solution

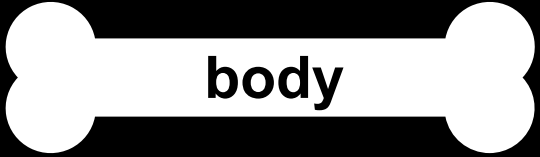
qualifications

objectives / rationale

hypothesis

*To solve this problem we will develop an innovative mouse model system to study Tax tumorigenesis. Recently, our group generated Lck-CRE mice, allowing conditional gene expression in T cells, the natural target of HTLV-1 infection. Here, we will generate targeting vectors containing wild-type or mutant Tax genes that are silenced by a preceding floxed stop cassette. By recombining these vectors into the *Rosa26* locus, we will eliminate random integration sites and standardize gene copy number, resulting in consistent levels of wild-type and mutant Tax protein expression. Lck-Tax transgenic mice have already been developed and produce a leukemia that closely resembles ATLL, strongly supporting our proposed model's feasibility. Thus, we hypothesize that targeting Tax expression in cells with an active Lck promoter will produce a similar disease in our model, and that Tax mutants will ...*

15



body THE SOLUTION

proposed solution

qualifications

objectives / rationale

hypothesis

*To solve this problem we will develop an innovative mouse model system to study Tax tumorigenesis. Recently, our group generated Lck-CRE mice, allowing conditional gene expression in T cells, the natural target of HTLV-1 infection. Here, we will generate targeting vectors containing wild-type or mutant Tax genes that are silenced by a preceding floxed stop cassette. By recombining these vectors into the *Rosa26* locus, we will eliminate random integration sites and standardize gene copy number, resulting in consistent levels of wild-type and mutant Tax protein expression. Lck-Tax transgenic mice have already been developed and produce a leukemia that closely resembles ATLL, strongly supporting our proposed model's feasibility. Thus, we hypothesize that targeting Tax expression in cells with an active Lck promoter will produce a similar disease in our model, and that Tax mutants will ...*

16

aims

THE PLAN

title

strategy

outcome/impact

17

aims

THE PLAN

title

strategy

outcome/impact

Aim 1: Establish an innovative mouse model for HTLV-1 Tax tumorigenesis. Targeting vectors containing silenced wild-type or mutant Tax genes will be knocked in to the Rosa26 locus of C57BL/6 mice. These mice will then be crossed with homozygous Lck-CRE mice, thereby removing the stop cassette and generating mice that express wild-type Tax proteins specifically in T cells. *By developing this model, we will enable unprecedented investigation into tax-mediated transformation mechanisms.*

18



THE PLAN

title

strategy

outcome/impact

Aim 1: Establish an innovative mouse model for HTLV-1 Tax tumorigenesis. Targeting vectors containing silenced wild-type or mutant Tax genes will be knocked in to the Rosa26 locus of C57BL/6 mice. These mice will then be crossed with homozygous Lck-CRE mice, thereby removing the stop cassette and generating mice that express wild-type Tax proteins specifically in T cells. *By developing this model, we will enable unprecedented investigation into tax-mediated transformation mechanisms.*

19



THE PLAN

title

strategy

outcome/impact

Aim 1: Establish an innovative mouse model for HTLV-1 Tax tumorigenesis. Targeting vectors containing silenced wild-type or mutant Tax genes will be knocked in to the Rosa26 locus of C57BL/6 mice. These mice will then be crossed with homozygous Lck-CRE mice, thereby removing the stop cassette and generating mice that express wild-type Tax proteins specifically in T cells. *By developing this model, we will enable unprecedented investigation into tax-mediated transformation mechanisms.*

20

impact **THE PAYOFF**

innovation

outcomes

overall impact

21

impact **THE PAYOFF**

innovation

outcomes

overall impact

Our proposed studies will establish a new mouse model that will overcome current limitations and provide greater insight into the mechanism of HTLV-1 Tax tumorigenesis. More broadly, this work will help us discover new facets of viral and cellular biology, identifying oncogenic mechanisms that might be used by other viruses. By developing this new and improved mouse model for Tax tumorigenesis, we will provide a valuable resource for the wider scientific community to pursue a multitude of studies that have not previously been possible due to limitations of existing mouse models of Tax, thus enabling development of improved ATLL therapeutics.

22

impact

THE PAYOFF

innovation

outcomes

overall impact

Our proposed studies will establish a new mouse model that will overcome current limitations and provide **greater insight into the mechanism of HTLV-1 Tax tumorigenesis**. More broadly, this work will help us discover **new facets of viral and cellular biology, identifying oncogenic mechanisms that might be used by other viruses**. By developing this new and improved mouse model for Tax tumorigenesis, we will provide a valuable resource for the wider scientific community to pursue a multitude of studies that have not previously been possible due to limitations of existing mouse models of Tax, thus enabling development of improved ATLL therapeutics.

23

impact

THE PAYOFF

innovation

outcomes

overall impact

Our proposed studies will establish a new mouse model that will overcome current limitations and provide greater insight into the mechanism of HTLV-1 Tax tumorigenesis. More broadly, this work will help us discover new facets of viral and cellular biology, identifying oncogenic mechanisms that might be used by other viruses. By developing this new and improved mouse model for Tax tumorigenesis, **we will provide a valuable resource for the wider scientific community to pursue a multitude of studies that have not previously been possible due to limitations of existing mouse models of Tax, thus enabling development of improved ATLL therapeutics**.

24

The Challenge

what & why

25

COMMON Pitfalls

26

Too much information



27



28

Too much information

Separate drafting from editing

Save your scraps

29

Too many hypotheses



30

Too many hypotheses

Choose **one** clear, overarching hypothesis*

Check that it is **tested** by each of the aims

Be **explicit**

**There are exceptions*

31

“Weak” words

“look around”
(no defined endpoint)

Analyze
Characterize
Explore
Investigate
Describe
Examine
Compare
Correlate
Survey

“find out”
(tangible progress)

Determine
Identify
Solve
Map
Establish
Visualize
Build
Delineate
Design
Implement

**There are exceptions*

32

“Weak” words

JAMA Network | **Open**



Original Investigation | Medical Journals and Publishing

Use of Promotional Language in Grant Applications and Grant Success

Huilian Sophie Qiu, PhD; Hao Peng, PhD; Henrik Barslund Fosse, PhD; Teresa K. Woodruff, PhD; Brian Uzzi, PhD

“...the percentage of **promotional language** used in medical science grants was **positively associated** with **receiving funding** ...”

*There are exceptions

33

Category	Promotional Words
Importance	compelling, critical, crucial, essential, foundational, fundamental, imperative, important, indispensable, invaluable, key, major, paramount, pivotal, significant, strategic, timely, ultimate, urgent, vital
Novelty	creative, emerging, first, groundbreaking, innovative, latest, novel, revolutionary, unique, unparalleled, unprecedented
Rigor	accurate, advanced, careful, cohesive, detailed, nuanced, powerful, quality, reproducible, rigorous, robust, scientific, sophisticated, strong, systematic
Utility	accessible, actionable, deployable, durable, easy, effective, efficacious, efficient, generalizable, ideal, impactful, intuitive, meaningful, productive, ready, relevant, rich, safer, scalable, seamless, sustainable, synergistic, tailored, tangible, transformative, user-friendly
Quality	ambitious, collegial, dedicated, exceptional, experienced, intellectual, longstanding, motivated, premier, prestigious, promising, qualified, renowned, senior, skilled, stellar, successful, talented, vibrant
Scale	ample, biggest, broad, comprehensive, considerable, deeper, diverse, enormous, expansive, extensive, fastest, greatest, huge, immediate, immense, interdisciplinary, international, interprofessional, largest, massive, multidisciplinary, myriad, overwhelming, substantial, top, transdisciplinary, tremendous, vast
Attitude	attractive, confident, exciting, incredible, interesting, intriguing, notable, outstanding, remarkable, surprising
Problem	alarming, daunting, desperate, devastating, dire, dismal, elusive, stark, unanswered, unmet
Examples sentences with Promotional Words	<p>“Further, a <i>unique</i> and <i>key</i> aspect of this program is the sharing of common mouse strains, reagents...”</p> <p>“There remains an <i>imperative</i> need for more <i>advanced</i> PACT breast imaging technologies.”</p> <p>“Addressing this severe knowledge gap in one of the most <i>fundamental</i> aspects of cytoskeletal biology is <i>paramount</i> to understanding how actin functions in cells.”</p> <p>“The proposed methods offer a <i>revolutionary</i> innovation and will be a game-changer in the...”</p> <p>“These <i>innovative</i> and <i>novel</i> studies will provide essential new information about the regulation of...”</p> <p>“We propose to go deep in analyzing a very <i>unique</i> and <i>unprecedented</i> large scale human genomic data set for ageing research.”</p>

34

Redundancy / lack of creativity

Example disease is bad.

Our approach will cure example disease.

This is important because we will cure example disease, and example disease is bad.

Example disease negatively impacts millions worldwide.

Our approach will provide new treatment options for example disease.

Not only will this research help cure example disease, but the knowledge/tools we gain will help cure other diseases too.

35

Redundancy / lack of creativity

Be specific

Example disease negatively impacts millions worldwide.

Our approach will provide new treatment options for example disease.

Think potential*

***without overstating**

Not only will this research help cure example disease, but the knowledge/tools we gain will help cure other diseases too.

36

Dependency



For each aim, ask yourself:
what if it completely fails?

37

“Academic” language

the writer



the reader



Also...



Additionally...



38

Short words

Subsequently, we investigated whether the compound would facilitate improvements in protein function.

Next, we studied whether the compound would improve protein function.

- Crystal Herron, PhD, ELS
Redwood Ink

39

Short words

Subsequently, we investigated whether the compound would facilitate improvements in protein function.

Next, we studied whether the compound would improve protein function.

- Crystal Herron, PhD, ELS
Redwood Ink

40

Short words

Subsequently, we **investigated** whether the compound would facilitate improvements in protein function.

Next, we **studied** whether the compound would improve protein function.

- Crystal Herron, PhD, ELS
Redwood Ink

41



Long vs. short



utilize

use

A large number of

many

important

key

predominant

main

optimal

best; ideal

components

parts

elucidate

clarify; resolve

42

Abstract Nouns vs. verbs

Subsequently, we investigated whether the compound would facilitate improvements in protein function.

Next, we studied whether the compound would improve protein function.

- Crystal Herron, PhD, ELS
Redwood Ink

43

Abstract Nouns vs. verbs

Subsequently, we investigated whether the compound would **facilitate improvements in** protein function.

Next, we studied whether the compound would **improve** protein function.

- Crystal Herron, PhD, ELS
Redwood Ink

44



Abstract Nouns vs. verbs



There is **an accumulation of** ATP in cells

ATP **accumulates** in cells

For purposes **of demonstration**

To **demonstrate**

To facilitate **improvement of** our protocol

To **improve** our protocol

This compound **influences the regulation of** ...

This compound **regulates** ...

With the **exception of**

Except

Over the **course of** the incubation

During the incubation

45

Prepositional Phrases

The reason **for** the failure **of** the big bad wolf **to** blow down the house **of** the third little pig was **that** the construction material was **of** a heavy type **of** brick that was resistant **to** all but the most significant **of** changes **in** wind pressure.

The big bad wolf could not blow the third little pig's house down because it was made **of** sturdy brick.

Because the third little pig had a sturdy brick house, the big bad wolf could not blow it down.

46

“Academic” language

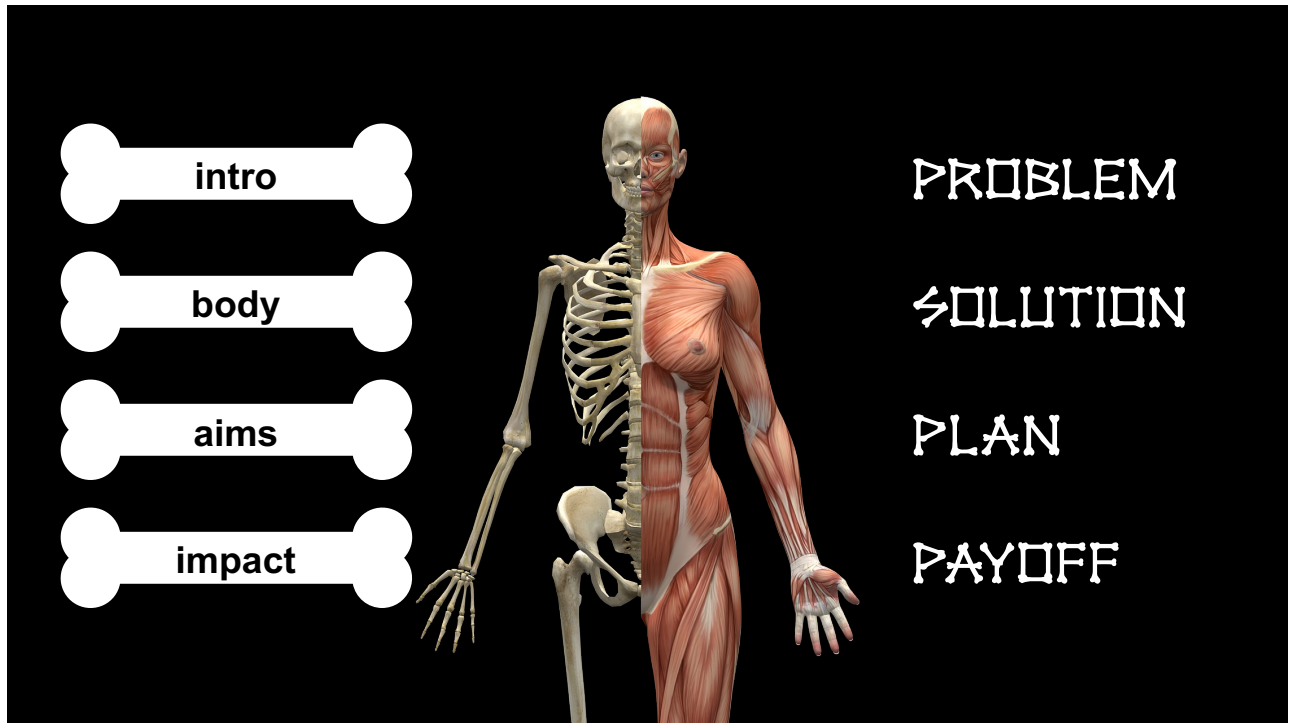
Search your document for:
“of, to, in, for, with, from,
through, at, over ...”

Ask for **feedback!**

47

KEY *Takeaways*

48



49

what & why

T

Too much information

Too many hypotheses

Weak words

Redundancy

Dependency

“Academic” language

Ask for feedback!

↑

Edit, save your scraps

Streamline

Strong words

Think potential

Stand alone aims

Search document

50

Resources



<https://www.umassmed.edu/scicomm/>



Contact



iCAP



UMass Chan
MEDICAL SCHOOL

justine.pinskey@umassmed.edu



@justinepinskey
.bksy.social

Linked in



<https://www.linkedin.com/in/justinempinskey/>

51

Acknowledgements







NIH Grant Applications
The Anatomy of a Specific Aims Page
Release Date: April 09, 2015
Category: Scientific Grant Writing
Author: Michelle S., Ph.D., E.L.S.











THE HARVARD CLINICAL AND TRANSLATIONAL SCIENCE CENTER | HARVARD CATALYST

Contact



iCAP



UMass Chan
MEDICAL SCHOOL

justine.pinskey@umassmed.edu



@justinepinskey
.bksy.social

Linked in



<https://www.linkedin.com/in/justinempinskey/>

52