

Somatic Mutations in Vascular Malformations

by

Daniel Aaron Snellings

Department of Molecular Genetics and Microbiology
Duke University

Date: _____

Approved:

Douglas Marchuk, Supervisor

Beth Sullivan

Michael Hauser

Timothy Reddy

Craig Lowe

Dissertation submitted in partial fulfillment of the requirements for the degree of
Doctor of Philosophy in the Department of Molecular Genetics and Microbiology
in the Graduate School of Duke University

2021

ABSTRACT

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Abstract

Write your abstract here. You should not include references or mathematical notation.

If you want to dedicate your thesis to anyone do so here

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List of Abbreviations and Symbols

Symbols

Put general notes about symbol usage in text here. Notice this text is double-spaced, as required.

| | |
|----------------|----------------------------------|
| \mathbb{X} | A blackboard bold X . Neat. |
| \mathcal{X} | A caligraphic X . Neat. |
| \mathfrak{X} | A fraktur X . Neat. |
| X | A boldface X . |
| X | A sans-serif X . Bad notation. |
| X | A roman X . |

Abbreviations

Long lines in the `sympollist` environment are single spaced, like in the other front matter tables.

| | |
|---------------|--|
| AR | Aqua Regia, also known as hydrochloric acid plus a splash of nitric acid. |
| SHORT | Notice the change in alignment caused by the label width between this list and the one above. Also notice that this multiline description is properly spaced. |
| OMFGTXTMSG4ME | Abbreviations/Symbols in the item are limited to about a quarter of the textwidth, so don't pack too much in there. You'll bust the margins and it looks really bad. |

Acknowledgements

Thank anyone you like here. It's good practice to thank every granting agency that's given you money since you've been ABD, any other school you visited during your research, and any professional society that's funded your travel.

1

Introduction

1.1 Vascular Malformations

1.1.1 Common Genetic Mechanisms

1.2 Hereditary Hemorrhagic Telangiectasia

1.2.1 Genetics

1.2.2 Signaling of ACVRL1, ENG, and SMAD4

1.2.3 Relationship with Sporadic Arteriovenous Malformations

1.3 Sturge-Weber Syndrome

1.3.1 Mosaic Mutation of GNAQ p.R183Q

1.3.2 Function and Activity of GNAQ

1.3.3 Mutation of GNAQ in Other Diseases

1.4 Cerebral Cavernous Malformations

1.4.1 Genetics

1.4.2 Differences Between Familial and Sporadic Disease

1.4.3 Two-Hit Mechanism

1.4.4 Signaling of the CCM Complex and its Downstream Effectors

1.5 Infantile Hemangioma (??? Include Neg Data ???)

Two-Hit Mechanism of Hereditary Hemorrhagic Telangiectasia

`dukedisertation.cls` — a document class for dissertations and theses conforming to the 2011 Duke University guidelines. This class is by Michael Gratton and modified by Hugh Crumley. It is based on the 2004 L^AT_EX2_ε version of `report.cls` and code in the older `dukethesis.cls` dating back to 1987.

The `report.cls` is Copyright 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 The L^AT_EX3 Project.

The original `dukethesis.cls` contained work by Mark Holliday, Charlie Martin, Russ Tuck, Sean O’Connell, Michael Todd, Syam Gadde, and Rajiv Wickremesinghe. Some of this work has been folded into the new document class.

This file may be distributed and/or modified under the conditions of the L^AT_EX Project Public License, either version 1.3 of this license or (at your option) any later version. The latest version of this license is in <http://www.latex-project.org/lppl.txt> and version 1.3 or later is part of all distributions of L^AT_EX version 2003/12/01 or later.

This is the June 13,2011 version, 0.5,(updated by Hugh Crumley) by Michael Gratton.¹

2.1 Features

This class conforms to the 2011 style guidelines for dissertations, including:

1. Page numbers centered in the footer of each page
2. Margins: 1in top, 1in right, 1.5in left, 1in below footer
3. Title signature page, UMI abstract title signature page, and copyright page automatically generated at `\maketitle`
4. 'Double' spacing throughout body text (really about 10pt extra instead of 12pt extra.)
5. Double spacing between and single spacing within the Table of Contents, List of Tables, List of Figures, Bibliography, and in chapter, section titles, and figure/table captions.
6. Footnotes are numbered consecutively within a chapter and placed at the bottom of the page on which the reference number appears.
7. Page ordering and numbering: roman numeral page numbers appear in the frontmatter (prior to the introduction or Chapter 1). The first numbered page is the Abstract (iv). Arabic numbering from '1' starts in the Introduction or Chapter 1 if there's no Introduction.
8. Optional material supported:

- Dedication

¹ E-mail: mgratton@math.duke.edu

- Acknowledgements
- Introduction (different from 'Chapter 1: Introduction')
- Appendices

This class also provides some handy features:

1. Use the option 'economy' to get a single-spaced document appropriate for giving to colleagues.
2. Change your copyright from 'All rights reserved' if you're not actually reserving all your rights.
3. New Look: boldface mostly removed in headers for a lighter feel. The word 'Chapter' no longer appears on opener pages, only the number.

2.2 Limitations

In it's current form, this class does not support committees larger than six members, or titles longer than four lines. The figure-to-caption space has been abbreviated, as most plotting programs provide ample bottom margins. This default may not be acceptable in all cases.

2.3 Class options

The class supports the following options. Options appear in pairs with the default option in each pair listed first. The exception is the first listed option, which merely activates several other options for convenience.

economy Macro. Enables the options singlespace, nogradschool, and nobind. **Changed in version 0.3**

gradschool Default. Produces signature lines and a UMI abstract title page.

nogragschool Suppresses the above.

PhD Default. Format is suitable for a Ph.D dissertation.

MS Modifies the format for Masters Theses. Changes the text on the title page, omits the UMI page, and generates warnings when forbidden document parts are used (i.e., Biography).

openany Default. Allows a chapter to start on any page.

openright Chapters only start on right-hand pages. Only makes sense for twosided documents.

oneside Default. Wide margin (where the binding will be) always occurs on the left edge of a page.

twoside Wide margin occurs on the left of odd pages and the right of even pages. This is for binding duplex printed documents.

final Default. No extra marks, include all pictures.

draft Prints black bars on pages where the contents overflow the margins. Suppresses the inclusion of graphics for speed.

doublespace Default. Double-spaces body text and adds extra space between entries in the Table of Contents, List of Figures, List of Tables, List of Abbreviations, and Bibliography.

singlespace Normal distances between baselines in all cases. Normal spacing in all list-type environments.

newstyle Default. Lighter look for headings.

oldstyle Headings in the classic L^AT_EXstyle. **New in version 0.3**

bind Default. 1.5in margin for binding appears on spine-side of a page.

nobind Left and right margins are both 1.25in. **New in version 0.3**

The default options are chosen so that the document will pass the Ph.D format specifications of the graduate school.

Here are some handy examples. Format required by graduate school:

```
\documentclass{dukedissertation}
```

Easy-to-read format for printing, sending to collaborators, etc:

```
\documentclass[economy]{dukedissertation}
```

Suitable for spiral bound copies and the like

```
\documentclass[economy, twoside, bind]{dukedissertation}
```

Mutant *GNAQ* Alleles Produce Distinct Disease Phenotypes

MAP3K3 Mutations Seed Cerebral Cavernous Malformations

This chapter is an example of how to format normal material in the dissertation style. Most of this information is standard to L^AT_EX.

4.1 Intra-chapter divisions: Sections

Section headlines are \Large and in the standard font. Compare them to subsections below.

4.1.1 Subsections: Wow! Italics!

Yes, italics. You may now dance. Isn't it funny that upright letters are called "roman" while slanted letters are "italic". That's like Italian, and Romans are Italians too. What gives?

Subsubsections: Smaller and smaller

Subsubsections are allowed, but are not numbered and don't appear in the table of contents. Likewise, you can use the next level of sectioning.

Paragraphs These divisions are unnumbered and do not appear in the Table of Contents.

Subparagraphs This is the finest division possible. It's also unnumbered and omitted from the Table of Contents.

4.2 Let's do some math

Let's look at an equation:

$$\partial ft = f(t) \quad \text{subject to} \quad f(0) = c. \quad (4.1)$$

We've used the `\newcommand` defined in the preamble of `dissertation.tex` to produce the derivative. You can get a second derivative like $\partial^2 ft^2$ by adding some sneaky superscripts. Fancy.

More advanced equation formatting is available in the AMS environments. See the guide `amsmath user's guide`. Here are some nice examples of cases people usually have trouble with.

An equation that's too long for one line — use `multline`:

$$\begin{aligned} a + b + c + d + e + f + g + h + i + j + k + l + m + n + o \\ = p + q + r + s + t + u + v + w + x + y + z. \end{aligned} \quad (4.2)$$

An equation with multiple parts and one number per line — use `align`:

$$a_1 = b_1 + c_1 \quad (4.3)$$

$$a_2 = b_2 + c_2. \quad (4.4)$$

The same equation, set inside the `subequations` environment:

$$a_1 = b_1 + c_1 \quad (4.5a)$$

$$a_2 = b_2 + c_2. \quad (4.5b)$$

Notice that by clever placement of labels, I can reference the pair via (5), the first (4.5a), or the second (4.5b). One number for multiple equations can be accomplished using the `split` environment:

$$\begin{aligned} a &= b + c - d \\ &\quad + e - f \\ &= g + h \\ &= i. \end{aligned} \tag{4.6}$$

People often struggle under the complicated and ugly `'eqnarray'` environment. Don't do it! The AMS ones are easy. Other stumbling blocks are cases:

$$a = \begin{cases} b & \text{for } x > 0 \\ c & \text{otherwise,} \end{cases} \tag{4.7}$$

matrices:

$$A = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} = \begin{bmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{bmatrix}, \tag{4.8}$$

and evaluation bars:

$$a = \left. \frac{\partial u}{\partial x} \right|_{x=0}. \tag{4.9}$$

See the source file for details.

When we reference an equation with something like `\eqref (4.1)`. If you click on the above references in the PDF, your viewer should scroll up to the above equation. It's handy. Labels and references may be attached to all sorts of objects. There is a `\label` attached to this chapter (it appears at the top of this file), and we may reference it by `(Chapter~\ref{chap:example})`, producing “Chapter 4”. By default these ref's are hyperlinked as well. Later, we'll see labeled and referenced figures and tables. Particular pages may be labeled with standard `\label` commands in the text and referenced via `\pageref`.

You might also like the links from `\cite` commands to the corresponding bibliographic entry. Go look at this imaginary book by Stephen Colbert [?]. If you're not a bibtex expert, look in `mybib.bib` at the `@ARTICLE` that generated this entry. It shows an example of accents on author names and how to preserve upper-case for letters in the title. Other entries show the use of the `and` keyword between author names. You may order a particular author's name as either "first last" or as "last, first". The actual format of the bibliography is controlled by the `\bibliographystyle{}` command in `dissertation.tex`.

4.3 Table of Contents Behavior

Now is a good time to look back at the Table of Contents. Notice that you may click on entries here to warp to the corresponding document location. In Adobe Acrobat and many other viewers, you can open a 'bookmarks' pane. This should be populated with named and numbered sections and subsections identical to the Table of Contents.

4.4 Figures and footnotes

Figures are set with very little space between the caption and the bottom of the included graphic. This is because most graphics programs pad the edges of images. If you find the spacing unsatisfactory, you may always add a bit manually. The text of the caption is single-spaced, and the word 'Figure' is set in small caps. See Fig. 4.1. Notice the use of the nonbreakable space "`~`" between the "Fig." and the reference. Figures (and tables) are examples of 'floats' — objects that \LaTeX decides where to place for you. You may give \LaTeX some hints. Change the `\begin{figure}[tbp]` to a `\begin{figure}[b!]` to restrict the placement. Inside the `[]`, you can put the following



FIGURE 4.1: Longer caption for actual body of dissertation. Figure captions should be BELOW the figure.

- t Allow placement at the top of the page
- b Allow placement at the bottom of the page
- h Allow placement 'here', in the middle of the page close to the text that the figure environment appears next to.
- p Allow placement on a separate 'floats page' that has no body text.
- ! Tighten the screws on the placement algorithm. This doesn't force things to happen as you say, but it makes it much more likely. Be careful: the bang option can cause figures to appear above the chapter title and in other bad locations.

Notice that each entry just changes what is *allowed*, but no preference among the

entries can be registered. The default is `[tbp]`, which is a very good default for a document like this, since floats in the middle of a page trap too much whitespace for double-spaced text. There is also a prohibition against having a page with more than 75% float. Instead, long floats will get kicked over onto float pages. Float pages are often a bad idea, as the creation of one will often cause a domino effect, with all subsequent figures appearing on float pages themselves, and all these float pages appearing together at the end of the chapter. (This is more like sinking than floating.) Avoid this by physically moving where the figure environment appears in your source file to an earlier location. Don't be afraid to put the environment before the first spot you reference it! Many float problems can be solved by a combination of relocating the figure environment and a little fiddling with the `[]` options.

Also notice the order of the graphic, caption, and label. If you deviate from this, strange things can happen. The caption of this figure shows the use of short captions (inside `[]`). These caption appear in the List of Tables, while the `caption` captions appear in the body. If you omit the `[]` short caption, the long caption will be used in its place.

Another technical note: since this style sheet is designed for processing by `pdflatex`, `\includegraphics` looks for PDFs, PNGs, and JPGs instead of the usual PS, EPS, and TIFF formats. You can convert existing graphics with a vareity of tools. PDF graphics are preferred, as they scale nicely. The open-source software Inkscape runs on Mac OSX, Windows, Linux, and some UNIX variants. Versions 0.46 and beyond have great support for creating and editing PDFs. It can even be used to convert other docs.

4.4.1 List of Figures

If you've put even one measly figure in your document, grad school rules say you need a List of Figures. It's automatically generated for you if you do a `\listoffigures`

Table 4.1: Long table caption appears on in the body text. See the short caption in the List of Tables. Table captions need to be ABOVE the table.

| Numbers | Letters | Symbols |
|---------|---------|---------|
| 1 | a | † |
| 2 | b | ☺ |
| 3 | c | × |
| 4 | d | # |

in the master file (heck, it's there right now). Go look at the list of figures now. You should be able to click on the figure number to warp to the figure. You'll also see the result of the 'short caption' used above.

4.5 Table example

Just to make sure tables are formatted correctly, here's an example of a table float, see Table 4.1. You should note that [b] formatting (`\begin{table}[b]`) can cause floats to appear under the footnotes. Try changing it here and see the ugliness. Tables are identical to figures, except that the word 'Table' appears in the caption and its entry is in the List of Tables instead of the List of Figures.

4.5.1 Footnotes

Footnotes are allowed.¹ They are numbered with arabic numerals inside each chapter and appear at the bottom of the page.² The little footnote numbers are also hyperlinks. Try clicking them. You should place the footnote command immediately following the period of the sentence it is attached to. Any spaces or newlines will result in strange spacing between the number and the sentence.

¹ But, you should probably just work them into the text since it's annoying to jump around when reading.

² ...rather than the end of the chapter or the thesis. Those would properly be endnotes, I guess.

4.6 Corner cases in formatting, such as very very very long section titles. Man, this goes on forever.

Common corner-cases involve very long titles (like above). In these cases, the long titles are set single-spaced both here and in the Table of Contents.

4.6.1 Figure and Table caption cases are neat, and this is an absurdly long subsection heading

Consider the shield logo again with an absurd caption, as in Fig. 4.2. Also examine the new table, Table 4.2. Both of these have been forced onto a floats page so you can see what that looks like.

PIK3CA Mutations Fuel Cerebral Cavernous Malformation Growth

Enjoy some Lorem Ipsum text! This should create about two full pages of text so you can verify the margins are correct (especially if you're doing two-sided).

5.1 Lorem Ipsum

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Sed vitae leo. Pellentesque quis nisi id orci consectetur posuere. Quisque malesuada rhoncus dui. Vivamus mi. Mauris commodo. Phasellus lacus magna, feugiat ac, blandit ut, rutrum id, massa. In consectetur magna vel justo. Cras eu diam. Nullam tortor turpis, bibendum non, consequat ac, tincidunt non, nisi.

Curabitur sagittis dignissim arcu. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas. Vestibulum ullamcorper. Curabitur faucibus euismod nulla. Vivamus sagittis. Sed fermentum neque a risus vestibulum convallis. Morbi id massa ut arcu mollis commodo. Aliquam erat volutpat. Pellentesque fringilla pellentesque nisi. Morbi tristique ornare libero. Vestibulum turpis sapien, iaculis ut, cursus non, condimentum in, tortor. Aenean vehicula. Integer

egestas tincidunt erat. Aenean euismod ante vel lectus. Duis ac sapien vel erat euismod aliquet. Vivamus tempor placerat nibh. Curabitur pharetra, orci consequat pulvinar ultricies, orci enim tempor augue, non lacinia orci nisl et nibh. Nunc gravida dictum turpis. Duis sollicitudin commodo massa. Nam ac nunc. Fusce sodales posuere velit. Nunc ullamcorper sodales urna. Donec consectetur accumsan ante. Morbi feugiat rutrum mauris. Praesent malesuada auctor est. Pellentesque quis odio non nulla ornare imperdiet. Aliquam dapibus. Suspendisse posuere, magna in molestie varius, ipsum velit rhoncus nisi, nec bibendum pede mauris in urna. Morbi purus lectus, molestie quis, laoreet id, tincidunt at, ligula.

Praesent sit amet libero id arcu adipiscing tristique. Quisque libero erat, bibendum nec, malesuada in, gravida et, urna. Phasellus molestie vulputate nisi. Nullam massa magna, dignissim ac, accumsan a, scelerisque eu, erat. Nam tellus augue, tempus nec, molestie sit amet, rhoncus vel, libero. Vestibulum at neque. Aliquam laoreet tincidunt mi. Ut laoreet ligula ac urna. Nullam nisl pede, posuere id, dictum a, fermentum vitae, turpis. Nulla ante mauris, euismod et, mollis eu, tempor in, quam.

In pede augue, elementum varius, tincidunt in, condimentum ut, erat. Etiam vulputate faucibus velit. Aliquam porttitor. Nam fringilla adipiscing nisi. Sed in magna. Aenean non ante. Aenean facilisis, nunc sed aliquam porta, magna est aliquam nisi, vitae semper turpis orci ac dolor. Praesent nec tellus. Cras vulputate rhoncus sem. Curabitur eu mi. Mauris euismod lacinia nibh. Suspendisse eget sapien et nunc accumsan elementum. Nulla dapibus. Donec interdum elit mattis velit imperdiet aliquet. Mauris feugiat, ante vel faucibus rutrum, eros mauris sollicitudin neque, ut varius diam ipsum et massa. Nullam non nisi sit amet tortor rhoncus molestie. Cras consectetur condimentum ante. Phasellus fermentum risus fermentum turpis. Mauris dignissim iaculis sem. Fusce nisi lorem, viverra id, auctor et, scelerisque ut, massa. In hac habitasse platea dictumst. Vestibulum ante ipsum

primis in faucibus orci luctus et ultrices posuere cubilia Curae; Aliquam pulvinar neque ac dolor.

5.2 More nonsense

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Sed vitae leo. Pellentesque quis nisi id orci consectetur posuere. Quisque malesuada rhoncus dui. Vivamus mi. Mauris commodo. Phasellus lacus magna, feugiat ac, blandit ut, rutrum id, massa. In consectetur magna vel justo. Cras eu diam. Nullam tortor turpis, bibendum non, consequat ac, tincidunt non, nisi. Curabitur sagittis dignissim arcu. Pellentesque habitant morbi tristique senectus et netus et malesuada fames ac turpis egestas.

Vestibulum ullamcorper. Curabitur faucibus euismod nulla. Vivamus sagittis. Sed fermentum neque a risus vestibulum convallis. Morbi id massa ut arcu mollis commodo. Aliquam erat volutpat. Pellentesque fringilla pellentesque nisi. Morbi tristique ornare libero. Vestibulum turpis sapien, iaculis ut, cursus non, condimentum in, tortor. Aenean vehicula.

Integer egestas tincidunt erat. Aenean euismod ante vel lectus. Duis ac sapien vel erat euismod aliquet. Vivamus tempor placerat nibh. Curabitur pharetra, orci consequat pulvinar ultricies, orci enim tempor augue, non lacinia orci nisl et nibh. Nunc gravida dictum turpis. Duis sollicitudin commodo massa. Nam ac nunc. Fusce sodales posuere velit. Nunc ullamcorper sodales urna. Donec consectetur accumsan ante. Morbi feugiat rutrum mauris. Praesent malesuada auctor est.

Pellentesque quis odio non nulla ornare imperdiet. Aliquam dapibus. Suspendisse posuere, magna in molestie varius, ipsum velit rhoncus nisi, nec bibendum pede mauris in urna. Morbi purus lectus, molestie quis, laoreet id, tincidunt at, ligula. Praesent sit amet libero id arcu adipiscing tristique. Quisque libero erat, bibendum nec, malesuada in, gravida et, urna. Phasellus molestie vulputate nisi. Nullam massa magna, dignissim ac, accumsan a, scelerisque eu, erat. Nam tellus augue,

tempus nec, molestie sit amet, rhoncus vel, libero. Vestibulum at neque. Aliquam laoreet tincidunt mi. Ut laoreet ligula ac urna. Nullam nisl pede, posuere id, dictum a, fermentum vitae, turpis. Nulla ante mauris, euismod et, mollis eu, tempor in, quam. In pede augue, elementum varius, tincidunt in, condimentum ut, erat. Etiam vulputate faucibus velit. Aliquam porttitor.

Nam fringilla adipiscing nisi. Sed in magna. Aenean non ante. Aenean facilisis, nunc sed aliquam porta, magna est aliquam nisi, vitae semper turpis orci ac dolor. Praesent nec tellus. Cras vulputate rhoncus sem. Curabitur eu mi. Mauris euismod lacinia nibh. Suspendisse eget sapien et nunc accumsan elementum. Nulla dapibus. Donec interdum elit mattis velit imperdiet aliquet. Mauris feugiat, ante vel faucibus rutrum, eros mauris sollicitudin neque, ut varius diam ipsum et massa. Nullam non nisi sit amet tortor rhoncus molestie. Cras consectetur condimentum ante. Phasellus fermentum risus fermentum turpis. Mauris dignissim iaculis sem. Fusce nisi lorem, viverra id, auctor et, scelerisque ut, massa. In hac habitasse platea dictumst. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Aliquam pulvinar neque ac dolor.

6

Developmental Venous Anomalies Predispose to Malformation

Ea dico populo saperet nam, atqui mundi viris et vim. Te choro aperiri vim.

Duo ignota nonummy ei. Ex augue latine luptatum eum. Omnesque scaevola vis ne, erat perpetua convenire ius in. Duo cu movet sonet corrumpit. Ex eos reque prodesset.⁵

In sint veritus singulis pro, at audire regione luptatum eam. Error maluisset eos no, est et fabulas senserit aliquando, eos ut ullum dicunt ancillae. Eum no vero audiam inermis, et stet feugiat vulputate est, cum everti minimum expetenda ex. Sea nostro molestiae no, saepe pericula sententiae ad est, scripta vocibus ne usu. Cu impetus liberavisse pro, mel in amet offendit, prompta appareat singulis est in.

Te labitur petentium quaerendum sed, ut pro ipsum saepe splendide. Vel cu quidam facilisis, usu harum possit alienum ad. His id fuisset pertinax, ea diceret periculis principes mel. Cu vis aequae utamur deleniti, simul salutatus voluptaria vim cu. Stet natum decore ut eum, mel nulla tibi que et. Et sit commodo conceptam accommodare, per at altera impedit albucius.

6.1 Ea cum sanctus propriae forensibus, mea vidit iriure reprimique ut, ea nam agam kasd comprehensam Pro ei inani facilisi, labores detraxit ad cum

Congue consequat sed ne. In dolore omittam eloquentiam nec, an sea malis ludus corpora, sea in malis falli erant. Id veniam persequeris eam. Augue inani nemore usu at, sea an reque dicam, vis porro animal in. Alii dolorem prodesset quo eu.

Eu aequae definiebas voluptatibus pri. Vel ne meliore elaboraret, propriae scaevola omittantur an mei. His ei mucius ornatus delicata, diam etiam patrioque ea sed. Ut eos persius intellegam dissentiunt, causae impedit te mei. Torquatos signiferumque ut quo.

Vix nibh volutpat ad, an cum mutat facer possit. Pro possit causae facilis ex. Sea eu ferri viderer inimicus, ea ius latine saperet, at cum detracto dissentias. Mea ex epicurei atomorum mandamus, an his dicam molestiae. Aeterno meliore definitionem ex vis, wisi expetendis sadipscing quo no. Eos inermis accumsan ne.

Modo tritani ea duo, vis mazim affert argumentum no. Usu ne ferri utamur nominati. Mei ad modo oportere. Brute minim scribentur ex cum, te vel agam epicuri consetetur. Ea vel mundi ridens inimicus, ad eruditi interpretaris mea, eum eu ferri rebum lorem. Dolore populo quaeque sit ex.

In accusata urbanitas vituperata quo, consulatu torquatos eam ex, tota definitionem quo et. Atqui suscipit suavitate at sea, intellegam theophrastus qui no, te homero temporibus per. Id meis mucius petentium usu, cu nam sonet elaboraret. Sumo accommodare cu pro, ne ornatus delectus consulatu duo, exerci laboramus assentior duo et.

Ea eos dicat everti appetere. Tota lorem scribentur ius ad, an possim noluisse adversarium pro. Everti adipiscing voluptatibus ius an, in ullamcorper necessitatibus vis. Te pro nibh invenire, porro putant salutandi quo ad. Id exerci equidem

suavitate nec, cu sed erat veniam postea. In tale facilisi posidonium per, pri suscipit deterruisset an.

6.2 Ipsum

Lorem ipsum vis at liber dicit diceret. Id fierent omittam est, vis natum electram eu, prompta sensibus at vix. Ut mea modus novum reprimique, vel euismod referrentur an. Ne legimus placerat abhorreant nec, no deleniti interesset vis. Vel adhuc graeci cu, ea est graecis fabellas.

Vel ex facer suscipiantur definitiones, mea vituperatoribus sale porro no, ut aliquip disputando sit. Ad graece albucius oporteat nec, vim voluptatum interesset in. Autem mundi eos ei, omnesque voluptaria et pri, falli quaerendum quo cu. Dicit equidem ceteros ne duo, ad oratio nostrud fierent usu, ei aliquyam periculis intellegam vim. Audiam principes sententiae sed et, ex his dicant facilis. Posse primis melius an per, quod assueverit duo id, cu usu animal propriae.

An natum nemore est, et eum quidam semper voluptua, meliore euripidis ei sea. Mei mutat invidunt ex. Vix choro delicata te. Causae mediocrem an his, choro vidisse id est. Mundi dolor id mei, an duo tation omittam.

Ex magna facer torquatos vel. Te pro sumo legere consequat, duo ea luptatum phaedrum. Nec in laboramus interesset cotidieque, deleniti vivendum ex eam, at senserit hendrerit vel. Est rebum falli ad, cu latine viderer efficiendi nec. Vidisse delectus te mei. Eu sanctus patrioque philosophia usu.

At veniam malorum iuvaret his, eos soluta ullamcorper ut. Zzril integre sit ut, sed regione percipitur contentiones et, mea no aliquyam efficiendi. Vix et neglegentur definitiones, ne graeco dictas omittam est. Id mel eros soluta corrumpit, oportere torquatos vim an.

An est eligendi efficiendi intellegam, illud putent labitur eu duo. Id fabellas salutatus argumentum has. Qui malorum prompta ex, eu sea nostrud admodum

sensibus. Ex tamquam complectitur has, diceret volumus eam cu. Eam nusquam deleniti ponderum cu. No eam tale moderatius.

Est saepe dicam abhorreant ut, omnes soleat quo no. Duo ceteros pericula interesset ut. Nec eu iudico option, persius euismod no eum. Per ea luptatum oporteat qualisque.

Dico veri nec ei, est ne audiam graecis corrumpit. Dico possit an pri, illum feugiat cum ne, ne duo lorem corpora platonem. Cum no aequae feugait, in vis odio nihil. Iusto sadipscing scriptorem ne est. Ius ad salutandi intellegebat.

Nonummy mentitum his an, viris maiorum assentior pri cu, duo errem partiendo quaerendum ad. Cum aperiam sententiae ex. Dolor salutandi pro in, nec ei utinam causae, praesent concludaturque quo te. Id fuisset consequat eum, vide eirmod qui et. Cu tollit ubique concludaturque has, his id sale consectetur, eu mel discere scripserit. Mei diceret efficiantur eu, no sea doctus meliore reformidans.

Nihil accommodare sit ea, nec et mutat dolorum. Ut conceptam persequeris vis, ea luptatum consetetur nam. Vix ea deleniti evertitur. Has enim consequat id, falli clita duo an.

7

Conclusion

7.1 Model for HHT Pathogenesis

7.2 Model for CCM Pathogenesis

7.3 Contribution of Somatic Mutations to Non-Cancer Diseases

Biography

Your biography is limited to one page and must contain

1. Full name
2. Date and place of birth
3. Every degree you've earned, including this one, and where you earned it from.

Mostly, that information is to narrow down which John Smith wrote that dissertation on the mating habits of sea cucumbers. Sexy!

You may also include

1. Any awards you've won related to your discipline since your undergraduate degree.
2. Any fellowships you've held
3. Anything you've published (papers, books, book chapters). Don't be afraid to cite it here, so that the full bibliographic record of your article appears in the bibliography!
4. Where your next job will be, if you know