Nonthesis proposal preparation

2010

Wen Chang
## Statistics about passing the test

<table>
<thead>
<tr>
<th>Year</th>
<th>Failed - 1st time</th>
<th>Failed - 2nd time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NDMC</td>
<td>TIGP-MCB</td>
</tr>
<tr>
<td>2001</td>
<td>12/38 (32%)</td>
<td></td>
</tr>
<tr>
<td>2002</td>
<td>10/33 (30%)</td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>14/34 (41%)</td>
<td></td>
</tr>
<tr>
<td>2004</td>
<td>16/39 (41%)</td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>12/31 (39%)</td>
<td>2/5</td>
</tr>
<tr>
<td>2006</td>
<td>17/32 (53%)</td>
<td>0/1</td>
</tr>
<tr>
<td>2007</td>
<td>16/36 (44%)</td>
<td>0/6</td>
</tr>
<tr>
<td>2008</td>
<td>35/69 (51%)</td>
<td>2/6</td>
</tr>
<tr>
<td>2009</td>
<td>25/51 (50%)</td>
<td>3/4</td>
</tr>
</tbody>
</table>
### Time table

<table>
<thead>
<tr>
<th>Event</th>
<th>YMU-IMB</th>
<th>TIGP-MCB</th>
<th>NDMC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application time</td>
<td>First 2 wks (Before Sep 25)</td>
<td>April 15-30</td>
<td>Before April 30</td>
</tr>
<tr>
<td>Abstract submission</td>
<td>+2wks (Before Oct 9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decision</td>
<td>+2wks (Before Oct 23)</td>
<td>May 10</td>
<td>May 31</td>
</tr>
<tr>
<td>Oral presentation</td>
<td>within 6wks (Before Dec 4)</td>
<td>June 1 - August 31</td>
<td>July 12-Sep 3</td>
</tr>
<tr>
<td>Second test</td>
<td>Before the end of the 3rd year</td>
<td>Within 3-6 months</td>
<td></td>
</tr>
</tbody>
</table>
Nonthesis vs. thesis proposal

improve “your” research ability to
define a question,
establish rationale,
design experimental approaches,
present the idea in a logical way,
justify its significance
Nonthesis vs. thesis proposal

improve your research ability to
define a question,
establish rationale,
design experimental approaches,
present the idea in a logical way,
justify its significance

..................Whose idea???
Attitude in nonthesis preparation

• Be positive- Think about it as a training or a course that prepares you for the future research ability.

• Start early, try not to juggle with heavy lab work at the same time.

• The process itself is as important as the end.

=>You learn to recognize each important ingredients in a proposal writing.

• There is no shortcut of doing it.

⇒You will be benefited from the experience. An important skill to get you ready for the real world
1. Pick a subject that is not related with your (Undergraduate), MS and Ph.D. studies.

2. Writing in English (new rule For NDMC).

3. Follow scientific ethics. - if violated, your 1st exam will be forfeited.
A serious problems in writing

- **Ethical issues**

- **Plagiarism** (Webster’s dictionary)
  - A. “the act of stealing and passing off (the ideas or words of another) as one’s own”
  - B. “Use without crediting the source”
  - C. “Presenting as new and original an idea or product derived from an existing source”

- Acts of Plagiarism in scientific proposal writing
  - Verbatim (=word for word) copying of text written by another person
  - Deliberate modification of text with the intent of disguising its origin
  - Duplicate/repeat experiments of the previous (or essentially the same) published works without properly disclosing/citing earlier publications
  - Propose other’s on-going (unpublished) experimental designs/thesis

Modified from Teaching the responsible conduct of Research, AAMC
Nonthesis proposal writing

Proposal writing: similar to **NSC** grant proposal format

- **Title:** the goals of the proposed research.
- **Abstract:** Concentrate the proposal content
- **Background:** provide up-to-date knowledge in a relevant field, the unanswered questions, the rationale and significance of the proposal, and evidence supporting the working hypothesis. **Why**
- **Specific aims:** list stepwise goals and biological questions/issues that are to be investigated. **What**
- **The research plan:** describe the experimental design and discuss anticipated results. **How**
- **References:** citations in full format

- Project title:
- Abstract: single space. (1 page)
- Research plan:
  -- • Specific Aims.
  List the broad, long-term objectives and what the specific research proposed in the application is intended to accomplish. State the hypothesis to be tested. (Do not exceed two pages)

• Background, Innovation, and Significance.
  Briefly sketch the background leading to the present project, critically evaluate existing knowledge, and specifically identify the gaps that the project is intended to fill. State concisely the importance and biological/medical/health relevance of the research described in this application by relating the specific aims to the broad, long-term objectives, as well as the overall goals of the project.
● **Preliminary Studies.**
preliminary studies pertinent to the project and/or any other information.

● **Research Design and Methods.**
Describe the research design and the procedures to be used to accomplish the specific aims of the project. Include how the data will be collected, analyzed, and interpreted. Describe any new methodology and its advantage over existing methodologies. Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims. Point out any procedures, situations, or materials that may be hazardous to personnel and the precautions to be exercised. If human subjects and vertebrate animals are involved, please identify the sources of these research materials and how these specimens will be safeguarded. This section should be written in such a way that original ideas, concepts, and hypotheses, innovative scientific strategies, the deployment of novel technologies, and any unusual aspects of your laboratory or work environment could be readily delineated.
● Anticipated Achievements
Briefly mention the significant results that might be anticipated or are likely to emerge from the research outlined in this Project. Limit the discussion to potential discovery of new knowledge; advances in basic understanding, including paradigm shifts; opportunities for scientific breakthroughs; and possible inventions and new technologies.

● Project Time Table
Provide a reasonable timetable for the execution of the work outlined in the project. Highlight appropriate milestones that you might use to target the studies. Indicate technical hurdles that might slow down the execution of the work and discuss any contingencies that you have or might have built in the research plan in anticipation of these difficulties.

● References
Elements of a good proposal

- **Title:** reflect the central theme, concise and informative.
- **Abstract:** Concentrate the proposal content, 1 page
- **Background:** thorough and focused with updated citations to establish a “working hypothesis” - supported by sufficient evidence
- **Specific aims:** 2-4 are most common. Each aim uses one sentence. Be brief and specific.
  - All the aims are related (but *not dependent on each other*), and focused (but not narrow).
  - Address original and important questions (*Not me-too*)
Elements of a good proposal

• The research design: Better to firmly establish one point by several approaches than present several weak points. Think about feasibility and justification. The anticipated results are logical on the scientific basis. Alternative approach is always favorable.
• Reasonable workload: within 3 years.
• Clear writing and no misspelling.
• References: complete and updated
Read to learn, Learn to read

• Read the grant proposals of your advisor so that you get some feeling about how to define each component of a proposal
• Read previous nonthesis proposals of other students so that you know how “different” these proposals are from their thesis proposals
• When preparing your proposal, read broadly and read the manuscripts of the cited references in your nonthesis proposal, not just the abstracts ===> It is relatively easy to write when you have an extensive knowledge base for what you write about.
Time factor

- It takes time to find a subject.
- It takes time to identify a question.
- It takes time to compose the idea.
- It takes time to write the proposal.
- It takes time to prepare for the presentation.

- Remember to take time to discuss and debate
Timeline of proposal Preparation

**Phase I:** Anytime fits, the earlier the better
- A good reading habit,
  read new papers, subscribe e-J. contents, keyword updates,
- Attend seminars and journal club,
- Collect ideas,
  look for interesting and important questions,
  write down all the ideas,
  discuss with your colleagues
Timeline of proposal Preparation

**Phase II**: 1-3 months before handing in the abstract(s)
- Decide 2-3 subjects of your interest first
  (Not just easy, hot or familiar subjects)
- Read (but not limited to) reviews and the primary publications thoroughly
  - read the whole papers, not just abstracts
  - pay attention to discussion section which may raise
    - interesting questions and unsolved issues in the field.
- Come up with ideas - based on facts, not just speculation
- Checking literatures again for similar ideas done in other systems
- Evolving idea into a working hypothesis.
- Define your specific questions. *what/why/how*
  - debate and modify repeatedly
Timeline of proposal Preparation

Phase II (cont’d):
- Know your approaches
  - up-to-date techniques
  - consult with experts
- Alternative or back-up approach is important
- Have a clear outline of your proposal before handing in the abstract
- Have an experienced colleague or PI edit your text (not the science) before abstract submission
**Phase III:** Writing the proposal and prepare for the oral exam

1. Writing takes time and repeated rewriting is necessary- so do not wait around.
   - Digest what you read and write down everything in mind (not too worry about your grammar yet).
   - Incorporate the “relevant” knowledge to provide strong arguments for why your proposal is worth doing and the significance is.....
   - Clearly state the working hypothesis; building your hypothesis with literature evidence (based on single paper is dangerous...); emphasize the novelty; use diagrams or figures to help explaining your thinking.

2. Be specific about the aims. Not ambiguous, Be realistic and achievable. Aims are logically connected and correspond to orders of experimental designs.
Phase III (cont’d):

3. Describe and Justify your methodology of choice, the advantage of this method is...
   - Design experiments with proper controls,
   - Include alternative approaches when possible.
   - Not “Materials and methods” section

4. Discuss the anticipated results
   - be careful and objective on data interpretations.
   - potential problems may encountered?

5. Allow enough time to modify the aims and re-write

6. Update your background knowledge till the last minute.

7. Spell and format checking
Keys to Oral Presentation

• 1. Be prepared.
  - (Make presentations in the lab meeting)
  - Practise your talk and cross-examination with your classmates; don’t just murmur to yourself.

• 2. Max 40-45 slides in a consistent format for illustrations. Each illustration has a point. Add citations to the figures when needed.

• 3. No more than 60 min.
  - Try to make a presentation between 45-60 min.

• 4. Relaxed. Pay attention to your audience.

• 5. Be concise in speaking = short and accurate

• 6. Be objective and flexible in idea debating

• 7. Be straight with your mistakes or ignorance

• 8. Understand the questions before answering
Common problems with proposal writing

- **Scientific level**
  - Proposal subjects or goals are not carefully thought out (why bother doing it?)
  - Weak rationale or justification (*Me-too*)
  - Not hypothesis driven- like fishing expedition
  - Trying to cover too many aims = out of focus
  - Experimental approaches are too rough, tedious or simply routines or fashion- lack of understanding
  - Proposal relies on single experiment to work- lottery
  - Lack of comprehension of the overall picture- impact?
Common problems with proposal writing

- **Writing skill**
  - Title too broad with not enough specificity
  - Background too long with little relevance
  - Specific aims are not connected with experimental design
  - Experimental design becomes materials and methods
  - Grammar and typing errors
  - Incomplete or inaccurate references
A serious problems in writing

- **Ethical issues**

- **Plagiarism** (Webster’s dictionary)
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Modified from Teaching the responsible conduct of Research, AAMC
Common problems with proposal presentation

• Slides arrangement
  - too many slides or contain slides with no focus
  - refer to previous works without literature citations
  - data mimicking with copy-and-paste
• Presentation style
  - Over-interpretation of the data
  - Lack of confidence or overconfidence
  - Lack of basic knowledge
  - Lack of an objective view
  - Inability to understand or to discuss a question
  - Inability to admit the above problems
Abstract selection

- **Example 1**
  - Ms thesis: Development of the carrier for the preparation of potent carbohydrate immunogen
  - Ph.D. thesis: A novel approach to generate anti-glycotope antibody for cancer diagnosis

- **Nonthesis Abr:** To study how chromosomal passenger complex (CPC) disrupts the interaction between Survivin and CRM1 as a result to inhibit Survivin export from nucleus to cytosol.

- **Example 2**
  - Ms thesis: Identification and Evaluation of BIGH3, CD109, and Prosaposin as Potential Nasopharyngeal Carcinoma Biomarkers
  - Nonthesis Abr: Discover Extra-Genomic Information in Arabidopsis

- **Example 3**
  - Ms thesis: Prevalence of class 1 integron among clinical isolates of *Acinetobacter baumannii* and molecular characterization of its horizontal mobile unit.
  - Ph.D. thesis: Study of tracheal extension during *Drosophila* eye development
  - Nonthesis: To elucidate the putative mechanism of the copper effect on APP processing and cholesterol synthesis of Wilson disease
Abstract selection

- **Example 4**
- Ms thesis: EB病毒感染鼻咽癌促进癌细胞增生的分子机转
- Nonthesis Abst: To investigate arginine methylation regulates KSRP function on pre-RNA splicing mechanism.
- **Example 5**
- Ms thesis: Investigation of HSV strains varied in their virulence
- Ph.D. thesis: Molecular regulation of polarized secretion in *Saccharomyces cerevisiae*
- Nonthesis abst: A potential role of Drp1 in mitochondrial dysfunction, an important feature of Parkinson’s disease
- **Example 6**
- Ms thesis: The role of plasminogen fragment K4_{418} in apoptosis of endothelial cells
- Ph.D. thesis: Functions of Ubx6 protein in yeast cell cycle
- Nonthesis: Integrin-regulated Arf6- and adhesion-dependent trafficking of lipid rafts
Other examples—Title too broad

1. Novel proteins in protein trafficking in the plant vacuole system
2. The function of the polyglutamine proteins in nucleus
3. The biological role of the TT virus in virus-mediated liver diseases
Proposals - Lack of novelty or significance

1. Novel proteins in protein trafficking in the plant vacuole system
2. To distinguish the role of small TIM complexes: Tim8-Tim13 and Tim9-Tim10 in Saccharomyces cerevisiae
   • ----Done in a different species before
General comments from committees

There are too many "copy and paste". They should only cite and use those references that they have read and understood.

The proposals are usually too techniques oriented. The students like to apply one fancy techniques they find in one subject and then apply it to another subject. They should ask "What biological problems I want to ask and understand?", not "What techniques I can use to make this subject look novel and big?".
General comments from committees

Some students propose an approach that is not feasible, but do not provide alternative approaches. You need to give alternatives.

Some people propose something that is too big. On the other hand, some people propose something that is too small and can be done in a few months.

Tip: The proposal has to be logical. When you do not know the answer during the examination, please say so honestly. This is much better than pretending that you know.
Why students failed in the first time in 2008-9 (NDMC)

- Lack of background understanding 14-9 wordy 2-0
- Weak rationale or bias in logics 18-18
- Weak experimental designs 18-19
- No novelty 10-8 or lack of depth/focus 10-12
- Experiments lack of control 6-4, or low in feasibility 3-2
- Lack of alternative approaches 12-5
- Insufficient citations 2-3
- Poor writing 14-10
- **Plagiarism; Copy-and-paste 6-3 copy other's work 2-0**

- Presentation time control and skill 7-1
- Lack of flexibility in data interpretation and discussion 8-4
- English problem
- Attitude problem, passive 1
- Overall, ==> It is rare that you failed for only one reason.
Why some (3) failed in the first time in 2008 (TIGP-MCB)

- Lack of background understanding 1
- Weak rationale 3
- Weak experimental designs 2; not specific 2
- No novelty 1
- Experiments details are missing 2
- Lack of alternative approaches 1
- Citation problems 1
- Poor writing 1, typo1

- Presentation time control and skill 1

- Overall, => It is rare that you failed for only one reason.
Top 5 Suggestions for improving the second test

- Rationale/logics and Experimental design
- Background understanding and Proposal writing
- Alternative approaches
- Novelty/depth/focus
- Flexibility in data interpretation and discussion
- (Change the proposal 6/34 in 2008)
Why some failed twice

• Committee comments for 1st case:
  - Literature reading is not sufficient
  - Question is not well defined
  - Lack of rationale in experimental design
  - Lack of understanding of the questions
  - No improvement in the 2nd exam

• Committee comments for the 2nd case:
  - Lack of basic knowledge in background information
  - Lack of originality in proposal
  - Problems in experimental designs
  - Lack of understanding of the questions and expected results
  - No improvement in the 2nd exam
Why some failed twice

- Committee comments for the 3rd case:
  - Problems in logical thinking
  - Lack of rationale in experimental design
  - Lack of understanding of the questions
  - Not suited for Ph.D. study
What if you fail the first time?

1. Write down the committee comments
2. Discuss with your committee chair/members to
   - understand the reasons why you failed
   - understand their criticisms and suggestions
3. Take a short break to rest
4. Discuss with your advisor about time management.
5. Focus on the weakness and improve these points-
   think about it like mileage accumulation

Relax!!! You are OK!
What if you fail the second time?

1. Take some time off.
2. Get consultations, if necessary.
3. Think about your alternative options.
4. Discuss with your advisors/ mentors/ family.
5. Maybe this is not a right career track for you.
6. Remember, all roads lead to Rome.
Identification of the Rickettsia gene involved in actin-based motility

Specific aims:
- Isolate mutants of Rickettsia rickettsii that do not form actin tail and identify Rickettsia genes that initiate actin-based motility
- Use complementation analyses in order to identify how the Rickettsia gene(s) are involved in actin motility in order to understand their biological, biochemical and cellular functions in actin-based motility
- Use two-hybrid, immunoprecipitation and cross-linking analyses to identify host protein that are involved in actin-based motility

Experimental designs
- Isolation of actin-motility mutants of Rickettsia rickettsii using transposon mutagenesis
- Analysis of the gene product identified by above insertions
- Identification of host proteins binding to the putative motility protein
Example 1 (Original, cont’d)

- Virulence of the mutant analyses
- Establishment of actin-based motility model system for Rickettsia

• Anticipated results
  - Successful isolation of Rickettsia genes that are involved in actin-based motility and understand how they are distributed in Rickettsia
  - Understand the mechanism of actin-based motility of Rickettsia
  - Successful identification of host proteins that are involve in Rickettsia motility in cells
  - Establishment of actin-based motility for Rickettsia in order to compare with other systems such as Listeria and Shigella
Example 1 (Modified)

- Title:
  - Identification of the Rickettsia gene involved in actin-based motility

  => Investigate the role of a Rickettsia surface protein rOmpA in actin tail formation
Specific aims:
- Isolate mutants of Richettsia rickettsii that do not form actin tail and identify Richettsia genes that initiate actin-based motility
- Use complementation analyses in order to identify how the Richettsia gene(s) are involved in actin motility in order to understand their biological, biochemical and cellular functions in actin-based motility
- Use two-hybrid, immunoprecipitation and cross-linking analyses to identify host protein that are involved in actin-based motility

⇒ 1. Involvement of Rickettsiae rOmpA protein in actin-based motility \textit{in vitro}
2. Study of Rickettsiae rOmpA protein in actin-based motility \textit{in vivo}
3. Isolation of rOmpA-deficient Rickettsiae mutant in order to understand the role of rOmpA protein in actin-based motility
Experimental designs
Isolation of actin-motility mutants of Rickettsia rickettsii using transposon mutagenesis
- Analysis of the gene product identified by above insertions
- Identification of host proteins binding to the putative motility protein
- Virulence of the mutant analyses
- Establishment of actin-based motility model system for Rickettsia

⇒ 1. Establish a role of rOmpA in actin polymerization in vitro
   1-1. generate blocking Abs for functional analyses in vitro
   1-2. Purification of rOmpA protein for actin polymerization in vitro

2. Study the role of rOmpA protein in Rickettsia & host interaction
   2-1. Expression of rOmpA gene into host cells to determine whether actin recruitment is induced by OmpA protein
   2-2. rOmpA-associated molecules identification

3. Isolation of rOmpA deficient Rickettsia mutant in order to determine its role in actin-based motility

Passed the 2nd exam in 2000
- Experimental designs
  - Isolation of actin-motility mutants of Rickettsia rickettsii using transposon mutagenesis
    - Analysis of the gene product identified by above insertions
    - Identification of host proteins binding to the putative motility protein
    - Virulence of the mutant analyses
    - Establishment of actin-based motility model system for Rickettsia

⇒ 1. Establish a role of rOmpA in actin polymerization *in vitro*
   1-1. generate blocking Abs for functional analyses *in vitro*
   1-2. Purification of rOmpA protein for actin polymerization *in vitro*

2. Study the role of rOmpA protein in Rickettsia & host interaction
   2-1. Expression of rOmpA gene into host cells to determine whether actin recruitment is induced by OmpA protein
   2-2. rOmpA-associated molecules identification

3. Isolation of rOmpA deficient Rickettsia mutant in order to determine its role in actin-based motility

Always consider alternative approaches
Anticipated results

- Successful isolation of Richettsia genes that are involved in actin-based motility and understand how they are distributed in Richettsia
- Understand the mechanism of actin-based motility of Richettsia
- Successful identification of host proteins that are involve in Richettsia motility in cells
- Establishement of actin-based motility for Richettsia in order to compare with other systems such as Listeria and Shigella

⇒ Understand the role of rOmpA protein involved in Rickettsiae actin-based motility in vitro and in vivo
One student’s comment

“I've learned very much in the process of the qualify exam, especially in the second time. The suggestion and questions from the committee induce my deep thinking about the proposal. This experience is very important and helpful for my thesis.”