GCB Candidacy Exam Workshops

Workshop 1 - Principles of Clear Scientific Writing
Date/time/location: February 15, 2 – 3:30pm, 1412 BRB
Facilitators: Maja Bucan and Scott Poethig
Workshop topics:
-Address any questions arising from rewriting exercises
-Discuss revisions of "problematic" abstract and specific aims page
Assignments to be completed prior to the workshop:
-Read "Five Principles of Clear Scientific Writing" – Page 2
-Read "*The Science of Scientific Writing*" by Gopen and Swan
-Perform rewriting exercises from syllabus – Page 13 (suggested revisions are on page 23)
-Revise "problematic" abstract and specific aims page from syllabus using "Five Principles of Clear Scientific Writing" – Page 14

Workshop 2 – How to write Specific Aims
Date/time/location: March 1, 1 – 2:30pm, 1413 BRB
Facilitator: Kai Tan
Workshop topics:
-Address questions regarding "Parts of a Grant Proposal – Specific Aims, Research Design"
-Discuss Specific Aims of first 3 students
Assignments to be completed prior to the workshop:
-Read "Parts of a Grant Proposal – Specific Aims and Research Design" – Page 17
-Write a Specific Aims page describing your research

Workshop 3 - How to write Approach (grants), Discussion (papers)
Date/time/location: March 13, 3:30 – 5:00pm, 1412 BRB
Facilitators: Kate Nathanson and Kai Tan
Workshop topic:
-Discuss Specific Aims of remaining students
Assignments to be completed prior to the workshop:
-Read "How to write Approach (grants) and Discussion (papers) – Page 21

Workshop 4 – Reviewing proposals with classmates and giving/receiving feedback
Date/time/location: March 22, 2 – 3:30pm, 1412 BRB
Facilitators: Maja Bucan and Scott Poethig
Workshop topics:
-Work with classmates to review and give feedback of each other's proposals
Assignments to be completed prior to workshop:
None

Five Principles of Clear Scientific Writing

When scientists use dense language to describe their work, the story gets murky and no clear message emerges. In this course, we will show you how to assemble the parts of a research proposal into a comprehensible story that has a clear message.

1. **<u>Get to the subject quickly and follow the subject as soon as possible with its verb.</u>**
   Gopen and Swan pp 551-552 "Subject-Verb Separation"
   (Additional material: Williams *Style: The Basics* Chapter 8 "Shape" pp 94-97)

   - **Get to the subject quickly**
     - Avoid long, abstract subjects – noun clusters
       In English, one noun is commonly used to modify another noun, e.g. blood flow, lung function, ion concentration. But adding more nouns to an existing noun pair (a noun cluster) creates long, abstract subjects and is confusing. To untangle a noun cluster, start at the end of the cluster and add words to indicate how the nouns relate to each other.

       - <u>*Example*</u>: *Early childhood thought disorder misdiagnosis* often results from unfamiliarity with recent research describing such conditions.
         <u>*Problem:*</u> Confusing noun cluster, abstract subject
         <u>*Revision*</u>: Physicians *misdiagnose disordered thought in young children* because they are unfamiliar with recent research describing such conditions.

     - Avoid lots of introductory words - "throat clearing"
       Readers have a problem with sentences that open with long introductory phrases and clauses, because, as they read them, they have to keep in mind that the subject and verb of the main clause are still to come.

       - <u>*Exercise*</u>: In most cases, because of the efficacy of the recently available treatment regimens, physicians are able to diagnose and successfully treat PCP.
         <u>*Problem:*</u> Lots of introductory words
         <u>*Revision:*</u> Physicians are able to diagnose and successfully treat PCP because good treatments are now available.

   - **Get past the subject and to its verb quickly** – avoid subject-verb separation
     Readers expect the grammatical subject to be followed almost immediately by its verb. Anything of length that separates the subject and verb is read as an interruption. An interruption after the subject forces the reader to hold his mental breath until he reaches the verb. Without the verb, the reader does not know what the subject is doing, or what the sentence is about.

     - <u>*Example*</u>: The smallest of the URF's (URFA6L), a 207-nucleotide reading frame overlapping out of phase the NH_2-terminal portion of the adenosinetriphosphotase (ATPase) subunit 6 gene has been identified as the animal equivalent of the recently discovered yeast H^+-ATPase subunit 8 gene.
       <u>*Problem:*</u> 23 words separate the subject "the smallest" and the verb "has been identified."
       <u>*Revision A:*</u> The smallest of the URF's is URFA6L, a 207-nucleotide reading frame which overlaps, out of phase, the NH_2-terminal portion of the adenosinetriphosphotase (ATPase) subunit 6 gene. URFA6L is the animal equivalent of the recently discovered yeast H^+-ATPase subunit 8 gene.

This revision incorporates the interrupting material into the sentence structure.
Revision B: The smallest of the URF's (URFA6L) is the animal equivalent of the recently discovered yeast H^+-ATPase subunit 8 gene. This revision deletes the interrupting material and also eliminates the unnecessary phrase "has been identified."

- *Exercise*: Some scientists, because they write in a style that is impersonal and objective, do not communicate easily with laypeople.
  Problem: Subject-verb separation
  Revision: Some scientists do not communicate easily with laypeople because they write in a style that is impersonal and objective.

2. Put the action in the verb.

Gopen & Swan pp 557 "Locating the Action"
(Additional material: Williams *Style: The Basics* Chapter 3 "Actions" pp 27-38)

- Readers expect that the action of a sentence will be articulated by its verb. If the action of the sentence is expressed by the verb, the sentence is direct and easy to understand. If the action is not expressed as a verb, it is usually lodged in a noun made out of a verb. We call such a noun a *nominalization*.
  - *Examples*:

verb	*nominalization*
prolong	prolongation
inhibit	inhibition
measure	measurement
evaluate	evaluation
remove	removal
exist	existence

- Nominalizations are not bad in and of themselves, only in the way they are (mis)used. The thing is to know which nominalizations to keep and which to turn into verbs.

- Turn a nominalization into a verb when it expresses the action of the sentence.
  - *Example*: *Removal* of potassium perchlorate was achieved by centrifugation of the supernatant liquid at 1400xg for 10 min.
    Revision A: Potassium perchlorate *was removed* by centrifugation of the supernatant liquid at 1400xg for 10 min.
    Revision B: Centrifugation of the supernatant liquid at 1400xg for 10 min *removed* potassium perchlorate.
    Revision C: We *removed* potassium perchlorate by centrifuging the supernatant liquid at 1400xg for 10 min.

  - *Exercise*: Our lack of data prevented evaluation of the role of the D1 receptor in the locomotor stimulant effects of cocaine.
    Revision: We could not *evaluate* the role of the D1 receptor in the locomotor stimulant effects of cocaine because we lacked data.

- Keep a nominalization when it does the following:
  - Refers to the previous sentence

- *Example:* When added to the nuclear extract, the egg extract inhibited transcription generally. This *inhibition* could be alleviated in part by supplementing the mixture with RNA pol III.

- Replaces an awkward "The fact that"
  - *Example:* The fact that the Zip2 protein localized to discrete foci on meiotic chromosomes suggested that...
    vs
    Localization of the Zip2 protein to discrete foci on meiotic chromosomes suggested that...
    (However, an alternative would be "Zip2 protein localized to discrete foci on meiotic chromosomes, suggesting that …")
- Names what would be the object of the verb
  - *Example:* We accepted what they found.
    vs
    We accepted their *findings*.

3. Put information where the reader expects it.

- There are two moments in the reading process which occur over and over again and are very important to both writer and reader: They are the beginnings and the ends of sentences.
  - We'll label the ends of sentences the "**Stress Position**."
  - We'll label the beginnings of sentences the "**Topic Position**."

- **The Stress Position – save the best for last**
  Gopen and Swan pp 552-554 "The Stress Position"
  (Additional material: Williams *Style: The Basics* Chapter 6 "Emphasis" pp 66-71, 74-78)

  - Readers naturally assign emphasis to the words at the end of a sentence, the "Stress Position."

  - Use the stress position of a sentence to introduce long, complex, or otherwise difficult-to-process material, particularly unfamiliar technical terms and "NEW" information.
    - *Example:* The role of *calcium blocker drugs* in the control of *cardiac irregularity* can be seen through an understanding of the role of calcium in the activation of muscle groups.
      Problem: New, complex terms are at the beginning of the sentence.
      Revision: If we understand how calcium influences the contraction of muscles, we can see how *cardiac irregularity* is controlled by the family of *drugs called "calcium blockers."*

    - *Exercise*: A determination of involvement of lipid-linked saccarides in the assembly of the oligosaccharide chains of ovalbumin *in vivo* was the principal aim of this study. *In vitro* and *in vivo* studies utilizing oviduct membrane preparations and oviduct slices and the antibiotic tunicamycin were undertaken to accomplish this.
      Problem: New, complex terms are at the beginnings of the sentences.
      Revision: The principal aim of this study was to determine how lipid-linked saccarides are involved in the assembly of the oligosaccharide chains of ovalbumin *in vivo*. To accomplish this aim, we conducted studies on preparations of oviduct membrane and on oviduct slices *in vitro* and *in vivo*, utilizing the antibiotic tunicamycin.

- Use the stress position to place emphasis on words that you feel deserve it.
    - *Example*: compare (a) and (b)
        (a) Overall, although this proposal is scientifically sound, the preliminary results are not persuasive.
        (b) Although the preliminary results are not persuasive, overall this proposal is scientifically sound.

      While neither of those statements would be considered a rave review, version (a) will probably make the scientist less happy than version (b). In (a), the bad news occupies the stress position; in (b), the good news occupies the stress position.

    - *Exercise #1*: The data offered to prove ESP are too weak for the most part.
      Problem: The words at the end of the sentence are not emphasis-worthy.
      Revision: The data offered to prove ESP are generally too weak.

    - *Exercise #2*: Mucosal and vascular permeability altered by a toxin elaborated by the vibrio is a current hypothesis to explain this kind of severe condition.
      Problem: The words at the end of the sentence are not emphasis-worthy AND the long, complex material is at the beginning of the sentence.
      Revision: One explanation for this kind of severe condition is that a vibrio toxin alters mucosal and vascular permeability.

- **The Topic Position – first things first**

  Gopen and Swan pp 554-556 "The Topic Position"
  (Additional material: Williams *Style: The Basics* Chapter 4 "Characters" pp 39-45)

  - The topic position extends through the first few words of a sentence up to and including the grammatical subject. It stops short of the verb.

  - Use the topic position to introduce "whose story" a sentence is going to be. Readers expect a sentence to be a story about whoever shows up first.
      - *Example*: Compare (a) and (b) and (c)
          (a) In the 1970s a few scientists in the United States and Europe began to find a way through disorder. They were mathematicians, physicists, biologists, chemists, all seeking connections between different kinds of irregularity.
          (b) Finding a way through disorder was accomplished in the 1970s by American and European scientists. This goal was accomplished by a variety of scientists all seeking connections between different kinds of irregularity.
          (c) The United States and Europe made it a priority in the 1970s that their scientists should find a way through disorder. These two countries funded mathematicians, physicists, biologists, and chemists, to find connections between different kinds of irregularity.

        In each of these examples, by changing the occupant of the topic positions, we've changed the answer to "whose story is this?" In (a) the answer is "a few scientists," in (b) it is "finding a way through disorder," in (c) it is "the U.S. and Europe."

      - *Exercise*: Rewrite the following sentence. Make the story about "plants."
        Richly fertilized plains and river valley are places where plants grow most richly, but also at the edges of perpetual snow in high mountains.

Revision: Plants grow most richly in fertilized plains and river valleys, but plants also grow at the edges of perpetual snow in high mountains.

- Use the topic position to communicate "OLD" information that forges a logical backward link to the previous sentence. The term "old information" refers to any material that has already appeared in the particular piece of text. Often it will have appeared in the sentence immediately preceding; sometimes it will have appeared farther back within the paragraph. When a piece of old information appears at the beginning of a sentence it gives the reader context.
    - *Example*: In both (a) and (b), old information in the topic position of the second sentence provides a backward-link to the first sentence.
        (a) Meteorologists look cheerful and confident when they report normal weather, but tense and crisis-ridden when they warn us about *hurricanes*. *These storms* cannot be predicted with any sense of surety, despite the great leaps forward we have made in meteorology.
        (b) *Hurricanes* fascinate and haunt us, acting like irrational characters in a high-intensity, reality TV drama. *Hurricanes* cannot be predicted with any sense of surety, despite the great leaps forward we have made in meteorology.

    - *Exercise*: A is a B-class GTPase. C-type kinases phosphorylate some B-class GTPases.
      Problem: The old, backward-linking information in sentence 2 is at the end, not the beginning, of the sentence.
      Revision: A is a B-class GTPase. Some B-class GTPases are phosphorylated by the C-type kinases.

- **Two Ways to Depict Reader Expectations about Sentence Structure**

In terms of a diagrammed sentence

Topic Position		Stress Position
Old, simple, backward-linking information		New, complex, emphasis-worthy information
Subject	Verb	
Person, thing or concept whose story it is	Action, What is going on	

In terms of the progress readers expect as they travel through a sentence

Time	*Question a reader expects to have answered*
Right away	How does this link backward to what I've just read?
ASAP	Whose story is this? (=the grammatical subject)
Immediately thereafter	What's going on? (=the verb)
Then, at leisure	How will this thought develop?
At the end	What is the most important piece of information here?

4. Write cohesive sentences and coherent paragraphs.

Gopen and Swan pp 556-557 "Perceiving Logical Gaps"
(Additional material: Williams *Style: The Basics* Chapter 5 "Cohesion and Coherence" pp 59-60)

- **Cohesion: a sense of flow from sentence to sentence**
  - We judge sentences to be cohesive, or connected, when the first few words in a sentence lean backward (provide OLD information), and the last few words lean forward (provide NEW information).

  - This information flow in a sentence can be depicted as OLD→NEW.
    - Put old, familiar information in the topic position of a sentence.
    - Put new or complex information in the stress position. The information in the stress position often becomes the "whose story," or the old information in the topic position of the next sentence.

  - *Example*: Some astonishing questions about the nature of the universe have been raised by scientists studying black holes in space. The collapse of a dead star into a point perhaps no larger than a marble creates a black hole. So much matter compressed into so little volume changes the fabric of space around it in puzzling ways.
    Problem: The information flow from sentence to sentence is not old→new.
    Revision: Some astonishing questions about the nature of the universe have been raised by scientists studying black holes in space. A black hole is created by the collapse of a dead star into a point perhaps no larger than a marble. So much matter compressed into so little volume changes the fabric of space around it in puzzling ways.

- **Coherence: a sense of the whole point of a paragraph**
  - We judge a passage to be coherent when three features are present:
    - The opening sentence prepares us for the themes of the passage by emphasizing them in its stress position.
    - Individual sentences follow the old → new principle, connecting to the sentence before and after (see Cohesion, above)
    - The words beginning each sentence in the passage cumulatively constitute a limited and related set of words (a "topic string") that tell us what the passage is about.

  - *Example*: Compare (a) and (b).
    (a) Since the discovery that one factor of its development might be genetic, great strides in the early and accurate diagnosis of Alzheimer's disease have been made in recent years. Senility in an older patient who seemed to be losing touch with reality was often confused with Alzheimer's. Genetic clues have become the basis of newer and more reliable tests in the last few years. The risk of human tragedy of another kind, though, has resulted from the increasing accuracy of these tests: predictions about susceptibility to Alzheimer's have become possible, long before the appearance of any overt symptoms. An apparently healthy person could be devastated by such an early diagnosis.
    (b) In recent years, researchers have made great strides in the early and accurate diagnosis of Alzheimer's disease. However, these improved diagnoses have raised new concerns about how to inform those most at risk. Previously, when a physician examined an older patient who seemed out of touch with reality, she had to guess whether that person had Alzheimer's or was senile. Now, physicians can utilize new and more reliable tests focusing on genetic clues. Yet, in the accuracy of these new tests lies the risk of another kind of human tragedy: while physicians may be able to

predict Alzheimer's long before its overt appearance, such an early diagnosis could psychologically devastate an otherwise healthy person.

Version (a) feels unfocused and unorganized, while version (b) feels cohesive and coherent. Why?

In version (b) we revised the passage to make the topics more related – the topic string now focuses on researchers/physicians and testing.
Also, in (b) we revised the first sentence so that its end stressed those words expressing the themes that the rest of passage develops.

Exercise: 1. EGFR forms dimers and higher order oligomers with itself and other members of the ErbB family (ErbB2/HER2, Erbb3/HER3, and ErbB4) via a primary dimerization domain, as well as several secondary receptor–receptor contact points. 2. The 170 kD Epidermal Growth Factor Receptor (EGFR, also known as ErbB1), is one of four members of the ErbB/HER family of transmembrane tyrosine kinase growth factor receptors. 3. Binding of naturally ocurring extracellular ligands (e.g., amphiregulin, epiregulin, HB-EGF) to the extracellular ligand-binding domain (domain III) of EGFR induces conformational shifts that permit homo- and hetero-dimerization events between EGFR molecules and its family members. 4. EGFR autophosphorylation activates multiple key signal transduction cascades that are mitogenic, antiapoptotic, angiogenic and pro-invasive. 5. Multimer formation promotes tyrosine autophosphorylation of the EGFR intracellular domain; the resultant open configuration of the kinase domain enhances access by ATP and substrate and creates binding sites for signaling molecules. 6. The EGFR kinase is also active at a low level when the protein is in the unliganded state; the degree of activity varies by cell type, glycosylation state and environment.
Problem: The sequence of sentences does not develop coherently: there is not an old/new progression; no concluding "high note". Solution requires reordering of the sentences to be 2-1-3-5-6-4.
Revision: The 170 kD Epidermal Growth Factor Receptor (EGFR, also known as ErbB1), is one of four members of the ErbB/HER family of transmembrane tyrosine kinase growth factor receptors. EGFR forms dimers and higher order oligomers with itself and other members of the ErbB family (ErbB2/HER2, Erbb3/HER3, and ErbB4) via a primary dimerization domain, as well as several secondary receptor–receptor contact points. Binding of naturally ocurring extracellular ligands (e.g., amphiregulin, epiregulin, HB-EGF) to the extracellular ligand-binding domain (domain III) of EGFR induces conformational shifts that permit homo- and hetero-dimerization events between EGFR molecules and its family members. Multimer formation promotes tyrosine autophosphorylation of the EGFR intracellular domain; the resultant open configuration of the kinase domain enhances access by ATP and substrate and creates binding sites for signaling molecules. The EGFR kinase is also active at a low level when the protein is in the unliganded state; the degree of activity varies by cell type, glycosylation state and environment. EGFR autophosphorylation activates multiple key signal transduction cascades that are mitogenic, antiapoptotic, angiogenic and pro-invasive.

5. Make the words mean what you want them to say.

- Often, the words do not mean what you want them to say because they are not written in parallel form. If parallel ideas are not written in parallel form, the logical relation of the ideas (similarity, alternatives, contrast, comparison) is obscured.

- *Example #1*: DNase I nicking interference patterns correspond precisely to methylation interference patterns with both 10 bp sequences.
  Problem: Makes it sound like both patterns are 10 bp long.
  Revision: Interference patterns induced by DNase I nicking correspond precisely to interference patterns induced by methylation for both of the 10 bp sequences.

- *Example #2*: These results are similar to previous studies.
  Problem: Comparison of unlike things
  Revision A: These results are similar to the results of previous studies.
  Revision B: These results are similar to those of previous studies.

- *Example #3*: Like poliovirus, interaction of coxsackievirus with its receptor triggers release of its viral RNA.
  Problem: Interaction is not like poliovirus
  Revision A: Like the interaction of poliovirus with the poliovirus receptor, the interaction of coxsackievirus with its receptor triggers release of the viral RNA.
  Revision B: Like poliovirus, coxsackievirus interacts with its receptor to trigger release of its viral RNA.

- *Exercise #1*: Activation-controlled relaxation in these membrane-deprived cells resembled intact myocardium from frogs.
  Problem: Comparison of unlike things
  Revision: Activation-controlled relaxation in these membrane-deprived cells resembled relaxation in intact myocardium from frogs.

- *Exercise #2*: In the transgenic animals, expression of beta-galactosidase was limited to pharyngeal muscle, a pattern identical to that observed in wild-type animals.
  Problem: Makes it sound like pharyngeal muscle is the pattern.
  Revision: In the transgenic animals, expression of beta-galactosidase was limited to pharyngeal muscle; this pattern was identical to that observed in wild-type animals.

A few comments on ACTIVE versus PASSIVE voice:

Active is preferred …

For direct writing, we prefer "active" rather than "passive" verbs, especially if we can avoid nominalization. Here are three examples:

> Passive-nominalized:
> **An investigation** WAS CONDUCTED into why so few **interviews** of minority applicants WERE DONE.
>
> Active-nominalized:
> *We* CONDUCTED an **investigation** into why *the employment office* DID so few **interviews** of *minority applicants*.
>
> Active-verbal:
> *We* **INVESTIGATED** why *the employment office* **INTERVIEWED** so *few minority candidates*.

… but passive is OK

Passive can be useful!

Passive can help shift a long and complex bundle of information from the beginning to the end of a sentence. In the sciences, the passive contributes to an objective point of view.

> We must decide whether to focus on A or B. The weight given to two factors, X and Y, will influence this decision.

We must decide whether to focus on A or B. This decision will be influenced by two factors, X and Y.

GENERAL GUIDELINES ABOUT VERB TENSE USAGE

Use present tense to describe established findings that have passed peer review and are regarded as fact.

"Resting CD4+T cells are the best-defined reservoir of HIV-1 infection."

"Establishment of the intricate nervous system of vertebrate animals requires the specification of diverse neuronal cell types."

"Translation initiation of some viral and cellular mRNAs occurs by ribosome binding to an internal ribosome entry site."

Use present tense for the question.

"We hypothesized that cigarette smoking by young men causes abnormal metabolism of plasma cholesterol."

"We asked whether these fragments arise from the same point of cleavage as the naturally occurring fragments of B-100 and B-74."

"To determine whether four different asthma drugs inhibit the late asthmatic reaction, we…"

Use past tense for methods.

"We dehydrated the pellets and cleared them with propylene oxide."

"After 30 sec, we centrifuged the samples."

"To prepare surface layers for EM, we resuspended the pellets in…"

Use past tense to describe the experiments done.

"We assessed these variables in 24 sensitized subjects divided into 4 groups of 6 subjects each."

"We used kallikrein to digest LDL from human plasma and compared the resulting fragments with B-74."

"Subjects in each group received one drug for 7 days according to a double-blind, placebo-controlled study."

Use past tense to describe the results obtained.

"Slow-release theophylline partially inhibited the increase in FEV_1 but had no effect on airway responsiveness to methacholine."

"Sham nucleus tractus solitarius lesions and lesions lateral to the nucleus produced no changes."

"Pulmonary lymph flow doubled within 2 hr."

Use present tense for the answer.

"These results indicate that *ceh-22* and *nkx2.5* perform similar functions."

"These experiments demonstrate that lesions of the NTS alter PA pressures."

"Thus, only the high-dose inhaled steroid beclomethasone inhibits late asthmatic reactions."

Use hypothetical verbs for implications or speculations.

"These results suggest that the identified EGases may facilitate intracellular migration through plant roots by partially degrading the cell wall."

"We propose that Zip2 promotes the initiation of chromosome synapsis."

"Our findings could partly explain the high incidence of coronary artery disease in older male smokers."

Use future tense for future, planned, or proposed work.

"We will identify the steps involved in coxsackievirus B uncoating during entry into polarized epithelial cells."

"The temporal production of SarA will be assessed by Western blot of *S. aureus* whole cell extracts with an affinity-purified anti-SarA antibody."

"I will use heat shock-inducible transgenic zebrafish to determine when BMP signaling is required to specify *lim1*+ INs."

Homework/Reading for Workshop 1 – REWRITING EXERCISES AND "PROBLEMATIC" ABSTRACT AND SPECIFIC AIMS PAGE FOR REVISION AS PER THE 5 PRINCIPLES

REWRITING EXERCISES

For each of the five "blinded" re-writing exercises below do the following:
(1) Identify the writing principle that is ignored in the sentence(s)
(2) Re-write the sentence(s) so that it follows that principle

***Exercise #1*:** Prolongation of life for uremic patients has been made possible by improved conservative treatment and hemodialysis.

Put the action in the verb: Improved conservative treatment and hemodialysis has prolongated life for uremic patients.

***Exercise #2*:** A disease that progresses with few or no symptoms to indicate its gravity is an "insidious" disease, under this definition. Asbestosis, neoplasia, mesothelioma, and bronchogenic carcinoma are all examples of insidious diseases. Asbestos insulation installers who have inhaled asbestos fibers over a period of many years regularly contract these diseases. Cohesion fail: topic positions do not connect reader to previous sentence.

Insidious diseases are diseases that progresses with few or no symptoms to indicate its gravity. These diseases are regularly contracted by asbestos insulation installers who inhale asbestos fibers over a period of many years. Examples of insidious diseases include asbestosis, neoplasia, mesothelioma, and bronchogenic carcinoma.

***Exercise #3*:** Laboratory animals are not susceptible to these diseases, so research on them is hampered.

Confusing noun cluster, abstract subject: Research on laboratory animals is hampered because laboratory animals are not susceptible to disease

***Exercise #4*:** Propranolol had variable effects on the hypoxemia-induced changes in regional blood flow. In the cerebrum, the increase in blood flow caused by hypoxemia was not significantly altered by propranolol. However, in other organs and in the peripheral circulation, propranolol caused a more severe decrease in blood flow than did hypoxemia alone. Problem: The ideas are not parallel which makes these sentences really confusing. For example, I cannot tell whether Hypoxemia causes different changes in different regions of blood. I decided this was done in mice, but it is unclear.

Propranolol had variable effects on regional blood flow of hypoxemia-induced mice. For example, propanolol did not significantly alter blood flow in the cerebrum of hypoxemia-induced mice. However, propranolol caused a significant decrease in blood flow in peripheral blood circulation as well as in other organs of hypoxemia-induced mice.

Exercise #5: The molecular events determining the developmental lineage of the gonadotrope in the anterior pituitary, utilizing approaches in transgenic mice including ectopic expression of regulatory proteins, will be investigated.

Problem: 11 words separate the subject "The molecular events determining the developmental lineage of the gonadotrope in the anterior pituitary" and the verb "will"

The molecular events that determine the developmental lineage of the gonadotrope in the anterior pituitary will be investigated by utilizing approaches, such as ectopic expression of regulatory proteins, in transgenic mice.

"PROBLEMATIC" ABSTRACT AND SPECIFIC AIMS PAGE

For the "problematic" abstract and specific aims page below do the following:

(1) Identify the writing principles that are ignored
(2) Re-write each so that it follows the 5 principles
(3) Correct anything else that you consider problematic

"**PROBLEMATIC" ABSTRACT**

Third-stage larvae of parasitic nematodes, which, in most species are the infectious stages for the mammalian host, including humans, of whom more than 3.5 billion may be infected worldwide, share common behavioral, morphological and developmental characteristics with the developmentally arrested dauer larvae of the free-living nematode *Caenorhabditis elegans*. It is proposed that molecular regulation of the transition from free-living to parasitic forms of parasitic nematodes and *C. elegans* dauer larva development regulation are similar. Significantly for the present study, it has been shown that in *C. elegans,* one of the key factors regulating the dauer transition is the insulin-like receptor kinase DAF-2. The parasitic nematode *Haemonchus contortus* has an insulin-like receptor (*Hc-daf-2*), which displays significant homology to insulin receptors in both vertebrates and invertebrates and is predicted to contain conserved structural domains. Examination of the parasite by RT-PCR showed *Hc-daf-2* transcription in all life stages. An important proteolytic motif was identified in the predicted peptide sequence of *Hc*-DAF-2 and is consistent with the HIR (human insulin receptor), suggesting that it could be involved in the formation of the insulin receptor complex. To test this, comparison of the patterns of expression between *Hc-daf-2* and *Ce-daf-2* was performed with reporter constructs fusing the *Ce-daf-2* or *Hc-daf-2* promoter to the coding sequence of *gfp*. These were microinjected into the N2 strain of *C. elegans*, and establishment and examination of transgenic lines were performed. These showed similar patterns of expression in amphidial/head neurons for both genes, which may be related to sensation and signal transduction, which are important processes in host finding by infective parasitic nematode larvae. For further functional analyses of *Hc-daf-2*, heterologous genetic complementation studies were attempted in the CB1370 *daf-2* mutant strain of *C. elegans*. These studies revealed that this mutation can be partially rescued by *Hc-daf-2*. Taken together, these data support the hypothesis that *Hc*-DAF-2 plays a crucial role in the transition from the free-living state to parasitism.

"PROBLEMATIC" SPECIFIC AIMS

As part of the adult *Strongyloides stercoralis* (SS) life cycle (LC), female *SS* lay eggs in the intestinal mucosa that hatch into rhabditiform larvae, which are shed in the stool. Caused by the parasitic nematode (pn) *SS*, and being characterized by extreme hyperchronicity with infected individuals being diagnosed decades after leaving the endemic environment, human SS affects ~100 million people globally. It has been shown by Schad et al. (19) that maintenance of hyperchronic *SS* may be by a process unique to *SS* in which parasite larvae develop precociously to successive generations of parasitic females in the same host, which is called autoinfection (18). It has been shown that in most cases, senescent parasitic females are gradually replaced with new individuals through a continuous process of tightly regulated low-level autoinfection (9, 10). However, these chronic, clinically latent infections, in patients immunosuppressed by corticosteroid therapy (CT) or underlying HTLV-1 infection, become unregulated, resulting in a fulminant often-fatal hyperinfection (8). Clearly, a better understanding of mechanisms initiating and maintaining autoinfection by *SS* is critical for preventing disseminated strongyloidiasis in at-risk patients.

Hyperchronic strongyloidiasis can be modeled experimentally in infected dogs by administering low dose CT, and it is widely assumed that such autoinfection is driven primarily by steroid suppression of immune responses that would normally clear the parasite (10). However, our preliminary data are supportive of the fact that steroid-induced autoinfection results from direct action by the drug on a parasite-intrinsic steroid signaling pathway. First, we have shown that autoinfection by *SS* in immune-deficient NSG mice requires exogenous (hereafter 'medicinal') CT. Second, our multidisciplinary team, which includes the PI, a medicinal chemist, a statistician, and members of the PIs laboratory, including graduate students and post-docs, has amassed compelling evidence that endogenous steroid signaling regulates larval development in *SS*. Specifically, we have shown that DAF-12, a corticosteroid-class nuclear hormone receptor (NHR) signaling pathway that regulates larval development in *Caenorhabditis elegans* (CE), is conserved in *SS*. Moreover, dafachronic acids (DAs), natural ligands of the *CE* receptor DAF-12, regulate crucial developmental events when applied exogenously to *SS* (11).

Therefore, we will characterize the action of medicinal steroids or their host metabolites with the parasite homolog of DAF-12 during the process of autoinfection by *SS*. We will also evaluate how parasite-intrinsic NHR signaling relates to very low levels of autoinfection the relationship of this autoinfection to host immunity. We know that disseminated hyperinfection is observed in immunocompromised patients in the absence of CT. Therefore, in Aim 2, we will determine if the residual innate immune effectors of NSG mice prevents NHR-dependent autoinfection in the absence of medicinal steroids. Evidence that medicinal steroids or their metabolites function as ligands for endogenous NHR signaling in *SS* to promote autoinfection will constitute a milestone supporting translational studies where compounds identified as agonists or antagonists of *SS* NHR signaling in an existing high-throughput screen will be prioritized for in vivo testing. Prioritized compounds will be tested for efficacy in preventing autoinfection in gerbil and/or NSG mouse models of autoinfection. Milestones indicating success will be three or more lead compounds that clear hyperchronic *SS* infection. Our specific aims are to:

SPECIFIC AIM 1: Characterize the interaction of medicinal steroids or their host metabolites with *SS* during autoinfection. To this end, we will determine **a)** the effect of medicinal CT of young *SS* larvae on the frequency of autoinfection, **b)** whether medicinal steroids act as direct ligands for *SS* NHR signaling **c)** whether the DA-synthetic enzymes of *CE* are conserved in *SS,* and **d)** whether bile acid precursors in steroid-treated hosts are substrates for nematode DA-synthetic enzymes.

SPECIFIC AIM 2: Investigate the roles of remaining immune functions in the NSG mouse in regulating autoinfection. We will assess remaining components of immune functionality in the NSG mouse (neutrophils, basophils, and eosinophils) for their role in autoinfection in non-steroid treated mice.

SPECIFIC AIM 3: Identify hits from an existing high throughput screen (HTS) for compounds that agonize or antagonize the *Ss* NHR Ss-DAF-12. Using cell-based assays in a multi-well format we will screen small molecule libraries for hits that interfere with autoinfection.

SPECIFIC AIM 4: Advance HTS hits from Aim 3 as appropriate to testing in in vivo models of autoinfective strongyloidiasis. Hits from the HTS will be assayed for ability to prevent autoinfection in a well-characterized model of autoinfective strongyloidiasis in gerbils and in the NSG mouse model.

SPECIFIC AIM 5: Develop new in vivo models for testing. We will explore whether other animal models are also appropriate for testing hits from HTS.

Homework/Reading for Workshop 2 – HOW TO WRITE SPECIFIC AIMS

SPECIFIC AIMS

The Specific Aims page is the most important page of the grant. The Specific Aims should clearly lay out the problem you are addressing, the hypotheses you are testing, and the experimental steps you will take. The Research Design and Methods section of the proposal will expand on how you propose to accomplish the Aims. Reviewers will read the Specific Aims quite carefully; if they don't like what you propose, don't understand it, or think your goals are unrealistic, they may be prejudiced against you as they read on. The Specific Aims page also serves as a summary page of your grant for the reviewer; they'll return to that page often to remind them of the major goals of your proposal.

The first 1-2 paragraphs of the Specific Aims page should explain the scientific problem and its importance. The Aims follow and are usually listed as hypotheses that you will test or positive statements of what you intend to do. Preferably every Aim you propose will provide important information whether or not the experiments turn out the way you expect. That is not always possible. However, no Aim should depend on another Aim. The proposal should be structured so that a negative result in Aim I doesn't make it impossible to proceed to Aim II or III.

When writing the Specific Aims for your preliminary exam, keep in mind that the work should be able to be accomplished in 2 years. For people who are new to grant writing or are applying for their first R01, a common mistake is to outline a career rather than a piece of work that can reasonably be accomplished in 3-5 years. This is often criticized by reviewers as overly ambitious. If you have too many great ideas to fit in one grant, mention them as something you want to do in the future, once you've accomplished the Aims of the present proposal. Examples of successful Specific Aims pages are provided on the following pages (note 1 page limit!):

Sample Specific Aims Page #1 **(Arial 11 font, one of the NIH preferred fonts)**

*****The names have been changed to protect the innocent***

The esophageal lining is regularly exposed to irritants such as alcohol, cigarette smoke, hot beverages, dietary nitroso-compounds, and refluxate of gastro-duodenal contents, and the cells lining the esophagus respond to these stressors to maintain normal homeostasis. Nonetheless, disorders of the esophagus are significant health problems in the U.S. and throughout the world. For example, gastroesophageal reflux disease (GERD) leads to 8.9 million clinic visits in the U.S. annually, and esophageal cancer is the 6th most common cause of cancer death worldwide. In esophageal epithelia, the key transcriptional regulator Esophageal Factor 5 (EF5) promotes normal proliferation and migration, as we have shown, and we recently identified a novel relationship between EF5 and Factor X (FX) in esophageal epithelial cells, whereby FX acts as a "molecular switch" for EF5. FX mutation in primary human esophageal keratinocytes (HEK) converts EF5 from pro-proliferative to anti-proliferative, an effect mediated predominantly by *Factor X Target Gene1 (FXTG1)*, which is differentially bound and regulated by EF5 in the presence or absence of mutant FX. In HEK harboring mutant FX, EF5 loss alone is sufficient for transformation, epithelial-mesenchymal transition (EMT), and the development of invasive squamous cell cancer. As such, FX and EF5 coordinately regulate target genes, leading to biologically-relevant, functional responses. In *Preliminary Data*, we demonstrate that EF5 suppresses FX in HEK and provide evidence for genome-wide coordinate regulation by EF5 and FX. Our overarching hypothesis is that EF5 and FX orchestrate a broad transcriptional program in esophageal epithelial cells that controls proliferation, growth arrest, apoptosis, and transformation. To test this hypothesis, we will pursue the following interrelated **Specific Aims**:

Aim 1. To delineate the mechanisms through which EF5 regulates FX levels and function

When cells are stressed, FX protein increases rapidly, correlating with decreased activity of the factors that degrade FX protein and an increase in a variety of post-translational modifications that regulate FX levels and function. In unstressed normal cells, even with increased *FX* transcription, FX protein is rapidly degraded and levels remain low. Surprisingly, in unstressed HEK, *EF5* knockdown markedly increases FX mRNA and protein. Here, we will examine the mechanisms of FX regulation by EF5 in HEK and the effects on FX function.

Aim 2. To define the mechanism for EF5 functional switching on *FXTG1*

FX is a nodal point, directing cells towards arrest via FXTG1 or apoptosis via Pro-Apoptotic Protein X (PAPX). EF5 transcriptionally regulates *FXTG1* in HEK, and FX mutation converts EF5 from a transcriptional repressor of *FXTG1* to an activator. Here, we will explore how EF5 and FX coordinately regulate cell proliferation and growth arrest in esophageal keratinocytes through mechanistic studies of EF5 and FX on *FXTG1*.

Aim 3. To identify common and exclusive targets of EF5 in the context of wild-type and mutant FX

EF5 binding and function vary depending upon *FX* status, as we have shown for FXTG1. However, coordinate regulation by EF5 and FX has not been examined genome-wide. Here, we will employ ChIP-seq with validation of functional targets to identify the EF5 *cis*-acting targets (cistrome) on a genome-wide scale in HEK with wild-type FX and in HEK with FX mutation.

In sum, the work proposed in this application will define the functional interplay between EF5 and FX, two critical regulators of normal epithelial homeostasis, as well as delineate their downstream molecular targets. These studies will provide key insights into the transcriptional regulation of esophageal epithelial homeostasis and the molecular pathways that underlie esophageal diseases. Overall, through this work, we expect to identify new diagnostic and therapeutic targets for esophageal diseases, both benign and malignant.

Sample Specific Aims Page #2 **(Arial 11 font, one of the NIH preferred fonts)**

Parasitic nematodes infect over one billion people and cause morbidity, disfigurement and retarded physical and cognitive development in hundreds of millions (1-4). Lack of practical vaccines against these parasitisms, and a small armamentarium of drugs that is threatened by resistance make it imperative to discover new drug and vaccine targets in nematode parasites. Molecules regulating crucial steps in parasite development, such as developmental arrest of infective larvae in the extrinsic environment and resumption of development upon host invasion, are logical points of attack in such interventions. Because of their intractability to laboratory culture and the consequent difficulty in developing modern molecular methodologies for them, these processes have not yet been well characterized in parasitic nematodes. Notably, our laboratory has recently advanced this field by generating the first transgenic *Strongyloides stercoralis,* a medically important obligate parasitic nematode in humans and dogs that is also capable of undergoing one or more generations of free-living development. We have utilized this system to directly determine if mechanisms involved in the arrest of third-stage or "dauer" larvae under conditions of stress in the free-living nematode *Caenorhabditis elegans* (5) are functionally conserved in parasitic nematodes. Importantly, our data reveals that the insulin-like (6) signal (ILS) transduction pathway, regulated in part by a nuclear hormone receptor (NHR) and its steroid ligands(7, 8), that regulate dauer arrest in *C. elegans* are conserved in parasitic nematodes, leading us to hypothesize that these pathways are adapted to control larval development during the infective process. In support, in the previous funding period of this grant, we discovered orthologs of nine key insulin signaling molecules in *S. stercoralis*: seven insulin-like peptides (ILPs), the insulin-like receptor kinase Ss-DAF-2, the insulin-regulated PI3 kinase Ss-AGE-1 and the insulin-regulated fork head transcription factor Ss-DAF-16 (9). Moreover, using a novel strategy to generate transgenic *S. stercoralis* L3i (10, 11), we provided the first direct evidence that Ss-DAF-16 is essential for normal development of infective third-stage larvae (L3i) (12). Finally, we demonstrated that regulation of the Ss-DAF-12 NHR by its steroid ligands blocks formation of *S. stercoralis* L3i and promotes their development within the host. As the identification of novel endogenous small-molecule regulators of parasitic nematode development has strong implications for future drug development of clinically relevant chemotherapeutics, studies proposed in our competing renewal will continue to delineate ILS in *S. stercoralis* and identify new links to NHR signaling. Specifically, we will ask

1. How does ILS regulate formation and maintenance of infective *S. stercoralis* third-stage larvae (L3i)? We hypothesize that downregulated signaling through the insulin receptor Ss-DAF-2 and the PI3 kinase Ss-AGE-1 is required for normal development of *S. stercoralis* L3i and that its resumption is required for developmental reactivation upon host invasion. We will test this hypothesis in Aim 1A by evaluating phenotypes in transgenic *S. stercoralis* expressing Ss-DAF-2 and Ss-AGE-1 with putative dominant gain- and loss-of-function mutations. In Aim 1B, we will evaluate the function of two known ILPs in *S. stercoralis* by mis-expressing them in the parasite and assessing their effects on resumption of development by L3i in culture and their effects on developmental switching by post parasitic L1.

2. Does Ss-DAF-12 NHR signaling augment developmental regulatory effects of ILS in S*. stercoralis*? We will test the hypothesis that endogenous steroid-NHR signaling suppresses formation of L3i and autoinfective L3 (L3a) in *S. stercoralis* and promotes their developmental reactivation in the host. We will first identify the natural ligands of Ss-DAF-12 and assess their ability to suppress formation of L3i and L3a and accelerate clearance of adult worms from the host gut. We will also ascertain whether chemical inhibitors of steroidogenesis block resumption of L3i development in culture. Finally, we will ascertain links between Ss-DAF-12 signaling and ILS by assessing phenotypic effects of steroidogenic inhibitors in transgenic *S. stercoralis* expressing an activated mutant form of Ss-DAF-16.

Completing these aims will provide unequivocal evidence that ILS modulates formation of *S. stercoralis* L3i and, more importantly, promotes their development upon entering the host. Furthermore, new research on the interface between ILS and steroid/NHR signaling will identify the first endogenous small-molecule regulators of the infective process In doing so, it will open a much needed new approach to drug development for a large group of neglected tropical diseases that affect some 20% of the world's population.

Strong points of sample Specific Aims:

- Start with background for the informed non-expert, writing at about the level of *Scientific American.*
- Put less technical information first.

- Point out a gap in knowledge that will be addressed in the proposal.
- Scope of research is limited to no more than three specific aims listed in bold and followed by a brief description of how each aim will be accomplished.
- The aims are the steps designed to prove the hypothesis.
- Spaces and bold type add readability.
- Reiterate the importance of the proposed research near the page bottoms.

Specific Aims Checklist

- Introductory Paragraphs
  - Scientific problem
  - Its importance
  - Hypotheses you are testing
  - Steps by which you plan to go about testing your hypothesis
- Aims don't depend on each other
- Writing
  - Subject early
  - Verb nearby
  - Good use of topic and stress positions
  - Nominalizations --> verbs
  - Concise, cohesive sentences
  - Coherent paragraphs
- White space
- "Big finish"

Reading for Workshop 3 - HOW TO WRITE THE APPROACH (grants); HOW TO WRITE THE DISCUSSION (Papers)

HOW TO WRITE THE APPROACH for grants.

In this section, explain how you will accomplish your Specific Aims and convince the reviewers that you will be able to do what you propose. It is not enough just to describe the experiments-- you need to state why they are being performed, why you have chosen the specific approach, which methods will be employed, what results are possible, how the data will be interpreted, what problems you anticipate, and how you will deal with them.

Many people write the Approach section for each Aim in a standard format with the following subheadings:

> **Specific Aim #1.** Restate the Aim exactly as written on the Specific Aims page.
> **Rationale.** Explain why your proposed studies are important and how they will advance the field.
> **Research Design and Methods.** Describe the specific experiments, including methods, that you will perform in this Aim. Subdivide this section to clearly communicate the order of the experiments and how they relate to the Aim.
> **Possible Results and Interpretations.** Discuss the different results that are possible and how you would interpret their significance. For example: If we find X, then this supports our hypothesis that … If we find Y, then this does not support our hypothesis, but would be a very exciting result because…
> **Potential Problems and Alternative Approaches.** Are there potential pitfalls to the experiments you proposed? If a pitfall arises, what alternative method could you use? It is important to convince the reviewer that you have thought deeply about your experiments and have already considered and addressed alternatives for the obvious pitfalls.

If your proposed experiments involve techniques that are new to your lab, your proposal will be strengthened by letters from consultants or collaborators who will provide any help you need. If specific reagents are needed, be sure to document how you will obtain them.

HOW TO WRITE THE DISCUSSION (Papers)

A well-written Discussion puts the findings of the paper in the proper context, directing and guiding the reader through the implications of the study. The Discussion should not merely recapitulate or summarize the results but should extend the findings, making conclusions and examining the significance of these results to the field. Do not attempt to hide obvious limitations of the study but address these in the text; smart reviewers will have picked up on these already. The results and conclusions should also be compared and contrasted with previously published work; if these differ from published work, speculate on the reasons for these differences.

One should be bold in stating the importance of the conclusions but must also be careful not to overstate the significance or to misinterpret the meaning of the results. An example of this comes from the story of the biologist who trained a flea, from "How to Write and Publish a Scientific Paper" by Robert Day and Barbara Gastel:

> "After training the flea for many months, the biologist was able to get a response to certain commands. The most gratifying of the experiments was the one in which the professor would shout the command "Jump," and the flea would leap into the air each time the command was given. The professor was about to submit this remarkable feat to posterity via a scientific journal but he - in the manner of the true scientist - decided to take his experiments one step further. He sought to determine to location of the receptor organ involved. In one experiment, he removed the legs of the flea, one at a time. The flea obligingly continued to jump upon command, but as each successive leg was removed, its jumps became less spectacular. Finally, with the removal of its last leg, the flea remained motionless. Time after time

> the command failed to get the usual response. The professor decided that at last he could publish his findings. He set pen to paper and described in meticulous detail the experiments executed over the preceding months. His conclusion was one intended to startle the scientific world: *When the legs of a flea are removed, the flea can no longer hear*."

Day and Gastel also point out, "Much as the Methods and Results should correspond to each other, the Introduction and Discussion should function as a pair…Be sure the Discussion answers what the Introduction asked." Finally, the Discussion should end with a brief but strong summary of the overall significance of the paper. In other words, as Anderson and Thistle said in 1947, "good writing, like good music, has a fitting climax."

SUGGESTED REVISIONS FOR REWRITING EXERCISES FROM WEEK 1

***Note that some revisions may seem better than others, although all generally follow the 5 principles.**

***Exercise #1*:** Prolongation of life for uremic patients has been made possible by improved conservative treatment and hemodialysis.
Principle : Put the action in the verb.
Problem: The action of the sentence is expressed by a nominalization.
Revision A: The lives of uremic patients have been prolonged by improved conservative treatment and hemodialysis.
Revision B: Uremic patients live longer because of improved conservative treatment and hemodialysis.
Revision C: Improved conservative treatment and hemodialysis allow uremic patients to live longer.

***Exercise #2*:** A disease that progresses with few or no symptoms to indicate its gravity is an "insidious" disease, under this definition. Asbestosis, neoplasia, mesothelioma, and bronchogenic carcinoma are all examples of insidious diseases. Asbestos insulation installers who have inhaled asbestos fibers over a period of many years regularly contract these diseases.
Principle : Put information where the reader expects it.
Problem: The information flow is NEW→OLD, NEW→OLD, NEW→OLD.
Revision: Under this definition, a disease that progresses with few or no symptoms to indicate its gravity is an "insidious" disease. Examples of insidious diseases are asbestosis, neoplasia, mesothelioma, and bronchogenic carcinoma. These diseases are regularly contracted by asbestos insulation installers who have inhaled asbestos fibers over a period of many years.

***Exercise #3*:** Laboratory animals are not susceptible to these diseases, so research on them is hampered.
Principle: Make the words mean what you want them to say.
Problem: Unclear that "them" refers to "these diseases."
Revision A: Laboratory animals are not susceptible to these diseases, so research on these diseases is hampered.
Revision B: Research on these diseases is hampered because laboratory animals are not susceptible to them.

***Exercise #4*:** Propranolol had variable effects on the hypoxemia-induced changes in regional blood flow. In the cerebrum, the increase in blood flow caused by hypoxemia was not significantly altered by propranolol. However, in other organs and in the peripheral circulation, propranolol caused a more severe decrease in blood flow than did hypoxemia alone.
Principle : Write cohesive sentences and coherent paragraphs.
Problem: The information flow in sentence 2 is NEW→OLD. The subject of sentence 2 disrupts the topic string in the paragraph.
Revision: Propranolol had variable effects on the hypoxemia-induced changes in regional blood flow. In the cerebrum, propranolol did not significantly alter the increase in blood flow caused by hypoxemia. However, in other organs and in the peripheral circulation, propranolol caused a more severe decrease in blood flow than did hypoxemia alone.

Exercise #5: The molecular events determining the developmental lineage of the gonadotrope in the anterior pituitary, utilizing approaches in transgenic mice including ectopic expression of regulatory proteins, will be investigated.

Principle: Get to the subject quickly and follow the subject as soon as possible with its verb.
Problem: Subject-verb interruption.
Revision A: We will investigate the molecular events that determine the developmental lineage of the gonadotrope in the anterior pituitary by studying ectopic expression of regulatory proteins in transgenic mice.
Revision B: We will investigate the molecular events that determine the developmental lineage of the gonadotrope in the anterior pituitary. To do this, we will study ectopic expression of regulatory proteins in transgenic mice.