

# One approach to teaching a writing intensive course

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# The course

- Biology 3191: Molecular mechanisms in development



# My goals for the course

- Goals
- Why?



# Why Writing Intensive?

- Active rather than passive
- Understanding instead of facts
- Ask questions and engage in dialog, not acquire information
- Bean 'Engaging Ideas' (2001), p. 29-31
  - “What.....students need to understand is that for expert writers, the actual act of writing causes further discovery, development, and modification of ideas.”

# Teaching writing and teaching in the discipline

Expert writer's process: unanswered questions and a dialog with the 'material'

1. Starting point: perception of a problem
2. Exploration
3. First draft
4. Reformulation and revision
5. Editing

# Bean, Engaging Ideas

This description of the writing process emphasizes the fact that expert academic writers are driven by their engagement with questions or problems and by their need to see their writing as a contribution to an ongoing conversation. ....[T]his problem-driven model of the writing process has a distinct advantage... It allows ...[the]... link[ing of] the teaching of writing to ... teaching the modes of inquiry and discovery in the.... discipline. ....[S]tudents [get] personally engaged with the kinds of questions that propel writers through the writing process. Thus, the writing process itself becomes a powerful means of active learning.

# Tools

- Primary literature
- SMARTBOARD
- Telesis
- Writing assignments
  - Journal
  - Analytical essays
  - ‘Thesis support’ outlines
  - Research paper
- Analysis of reading assignments in class
- Discussion not lecture
- Group work in class
- Analysis of writing examples in class
  - Writing issues
  - Content
    - Background information
    - Arguments/evidence



# Examples slide from ppts used in class

Amit et al. (2000)  
“Clonally derived  
Human Embryonic  
Stem Cell Lines  
Maintain Pluripotency  
and Proliferative  
Potential for  
Prolonged Periods in  
Culture.”

**Developmental  
Biology 227: 271-  
278.**

Reading assignment #1;  
posted on Telesis

Developmental Biology 227, 271-278 (2000)  
doi:10.1006/dbio.2000.9912, available online at <http://www.idealibrary.com> on IDEAL®



## Clonally Derived Human Embryonic Stem Cell Lines Maintain Pluripotency and Proliferative Potential for Prolonged Periods of Culture

Michal Amit,\* Melissa K. Carpenter,† Margaret S. Inokuma,†  
Choy-Pik Chiu,† Charles P. Harris,‡ Michelle A. Waknitz,§  
Joseph Itskovitz-Eldor,\* and James A. Thomson§,¹

\*Department of Obstetrics and Gynecology, The Rambam Medical Center, and Faculty of Medicine, Technion, Haifa 31096, Israel; †Geron Corporation, 230 Constitution Drive, Menlo Park, California 94025; ‡Texas Children's Hospital, Baylor College of Medicine, Houston, Texas 77030; and §The Wisconsin Regional Primate Research Center and ¹Department of Anatomy, School of Medicine, University of Wisconsin, Madison, Wisconsin 53715

Embryonic stem (ES) cell lines derived from human blastocysts have the developmental potential to form derivatives of all three embryonic germ layers even after prolonged culture. Here we describe the clonal derivation of two human ES cell lines, H9.1 and H9.2. At the time of the clonal derivation of the H9.1 and H9.2 ES cell lines, the parental ES cell line, H9, had already been continuously cultured for 6 months. After an additional 8 months of culture, H9.1 and H9.2 ES cell lines continued to: (1) actively proliferate, (2) express high levels of telomerase, and (3) retain normal karyotypes. Telomere lengths, while somewhat variable, were maintained between 8 and 12 kb in high-passage H9.1 and H9.2 cells. High-passage H9.1 and H9.2 cells both formed teratomas in SCID-beige mice that included differentiated derivatives of all three embryonic germ layers. These results demonstrate the pluripotency of single human ES cells, the maintenance of pluripotency during an extended period of culture, and the long-term self-renewing properties of cultured human ES cells. The remarkable developmental potential, proliferative capacity, and karyotypic stability of human ES cells distinguish them from adult cells. © 2000 Academic Press

*Key Words:* human embryonic stem cells; basic fibroblast growth factor; cloning; telomeres.

### INTRODUCTION

Human pluripotent cell lines have been derived from preimplantation embryos (embryonic stem cell lines, ES cells; Reubinoff *et al.*, 2000; Thomson *et al.*, 1998) and from fetal germ cells (embryonic germ cell lines, EG cells; Shambloft *et al.*, 1998) that for prolonged periods of culture maintain a stable developmental potential to form advanced derivatives of all three embryonic germ layers. Human ES cell lines have widespread implications for human developmental biology, drug discovery, drug testing, and transplantation medicine. For example, current knowledge of the postimplantation human embryo is largely based on a limited number of static histological sections, and because of ethical considerations, the underlying mechanisms that control the developmental decisions of the early human embryo remain essentially unexplored.

Although the mouse is the mainstay of experimental mammalian developmental biology, there are significant differences between early mouse and human development. These differences are especially prominent in the extraembryonic membranes, in the placenta, and in the arrangement of the germ layers at the time of gastrulation. The yolk sac, for example, is a robust, well-vascularized extraembryonic tissue that is important throughout mouse gestation, but in the human embryo, the yolk sac is essentially a vestigial structure during later gestation (Kaufman, 1992; O'Rahilly and Muller, 1987). Human ES cells should provide important new insights into the differentiation and function of tissues that differ significantly between mice and humans.

In addition to advancing basic developmental biology, human ES cells should have practical, applied uses. The differentiated derivatives of human ES cells could be used for: (1) identification of gene targets for new drugs, (2)



Examples slide from ppts used in class

# Pluripotency and germ layers

Examples slide from ppts used in class

# Reading a Research (data) paper

- Abstract
- Introduction
- Materials and methods
- Results
- Discussion

See help document 'read.primary.lit.pdf'



Examples slide from ppts used in class

# Abstract of Amit et al.

Work in groups (3-5)

Main question being addressed

Main conclusions

Why is this work important?

10 mins

# Abstract of Amit et al.

- Main question
- Sub-questions
- Main conclusion
- Sub-conclusion

Examples slide from ppts used in class

# FOR NEXT TIME

- Notes in journal on Amit et al. abstract, based on class discussion
- Read the rest of Amit et al. 2000
- Focus on Introduction and Results:
  - List relevant facts that relate to what was known prior to this work and what the authors want to ‘prove’
  - List experiments in paper
- On Tues, we will:
  - discuss context and background, why experimenters did the work: what question their work addresses, why they are asking this question
  - relate the data list to conclusions discussed in class today

## Examples slide from ppts used in class

# Analysis of Amit et al.

- Introduction
- Work in groups, 10 mins
- Describe context of work:
  - What was known prior to this work?
  - What do the authors state as their motivation for the study?
  - In what way is this study novel or does it differ from previous work?
  - What properties must human stem cells have to be useful?
- Re-state/revise question(s) addressed (use introduction and notes on Abstract)

## Discussion groups summary

- What was known prior to this work? (facts)
- What do the authors state as their motivation for the study?
- In what way is this study novel or does it differ from previous work?
- What properties must human stem cells have to be useful?



## Examples slide from ppts used in class

Can progeny of SINGLE human stem cells be cultured indefinitely and remain normal and pluripotent?

Sub-questions:	Experiment(s):	Result/Conclusion:	Interpretation:
SINGLE			
Cultured indefinitely			
Normal			
Pluripotent			

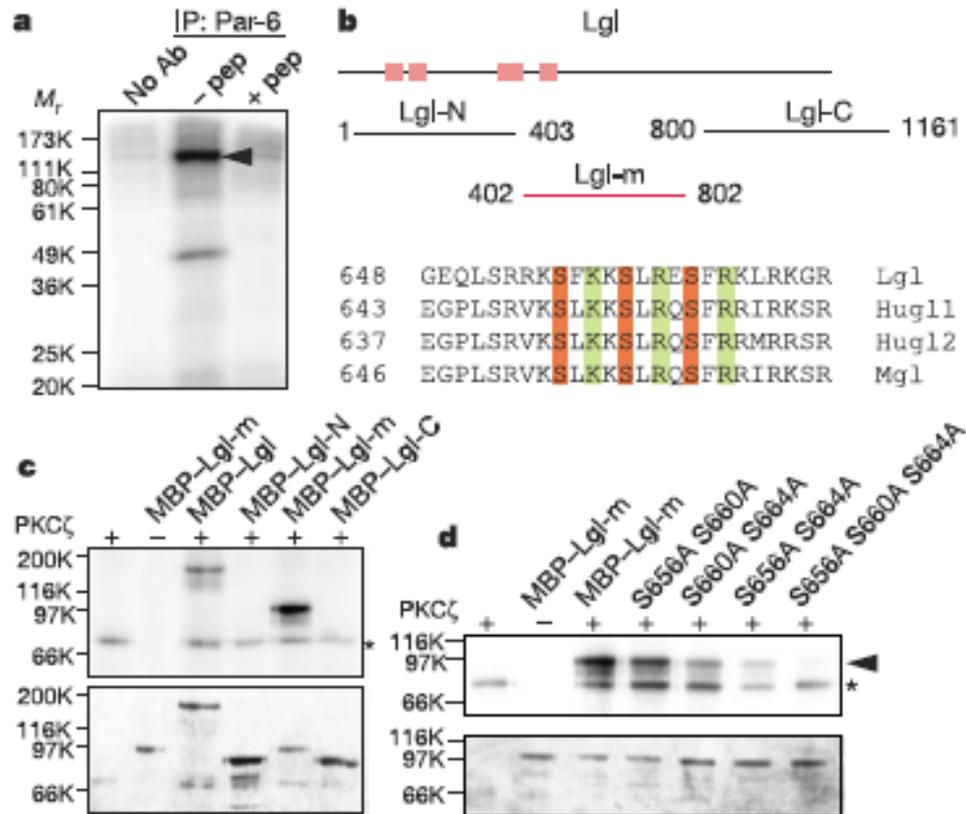
# Journal Writing

- Primary means of ‘studying’ for this course
- Entries are not graded on grammar, organization, sentence structure, spelling
- Write notes on data papers, to prepare for class sessions
- Other notes on reading, idea development and drafts to prepare for writing assignments
- Worth 100 pts out of 750 pts total

Refer to ‘Journal writing’ assignment and ‘Questions.data.pap

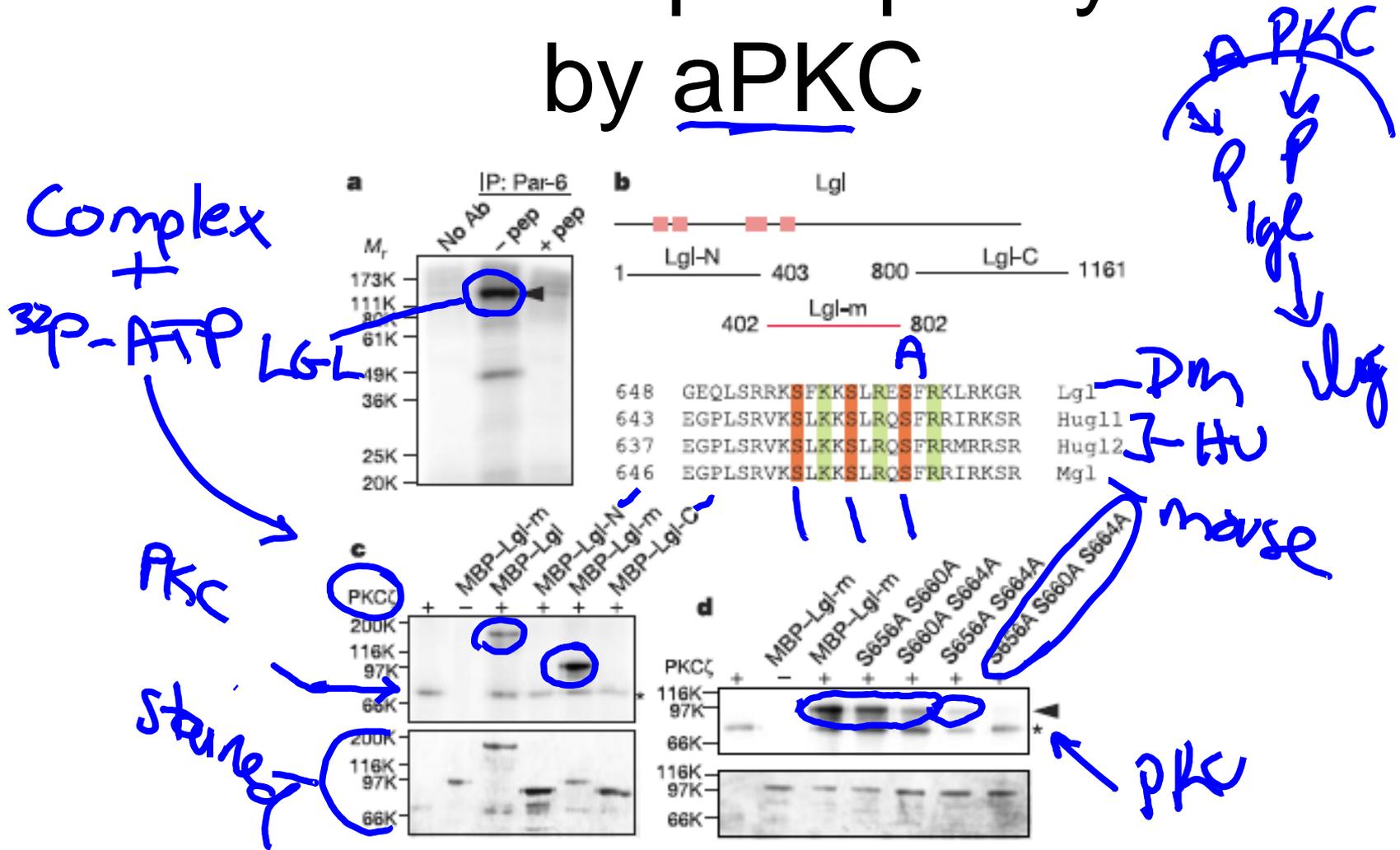
## Discussion of primary literature

# LGL can be phosphorylated by aPKC

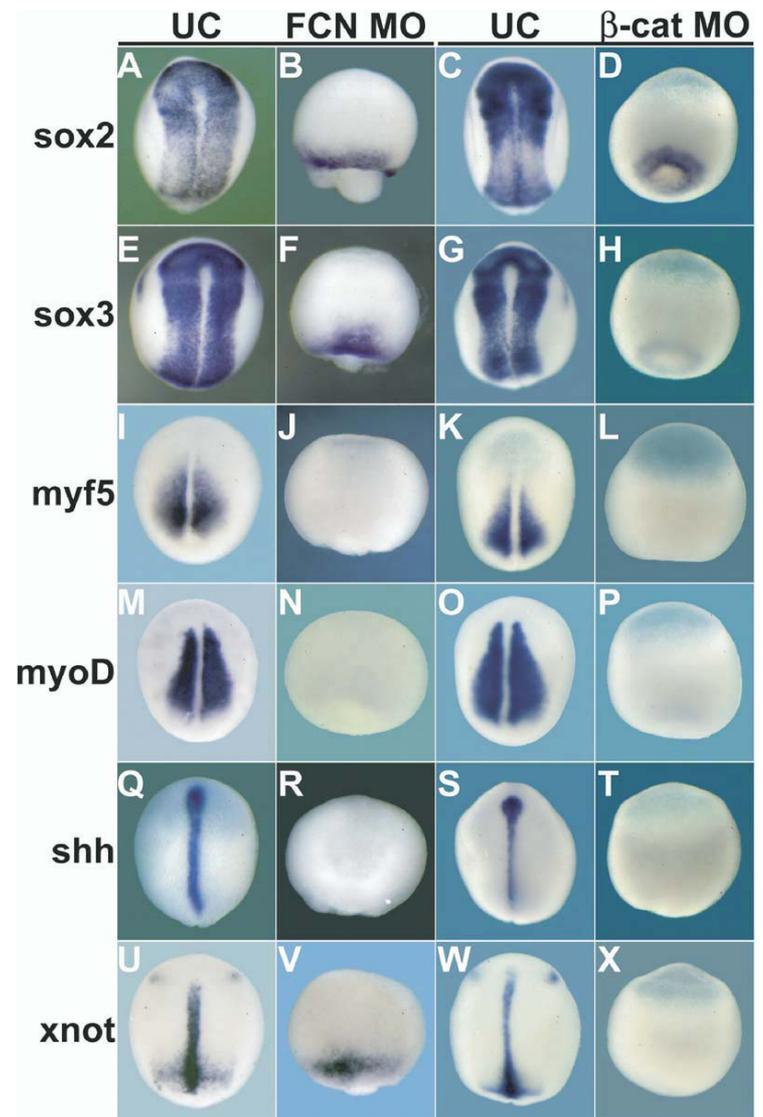


After class:

# LGL can be phosphorylated by aPKC



# Discussion of primary literature



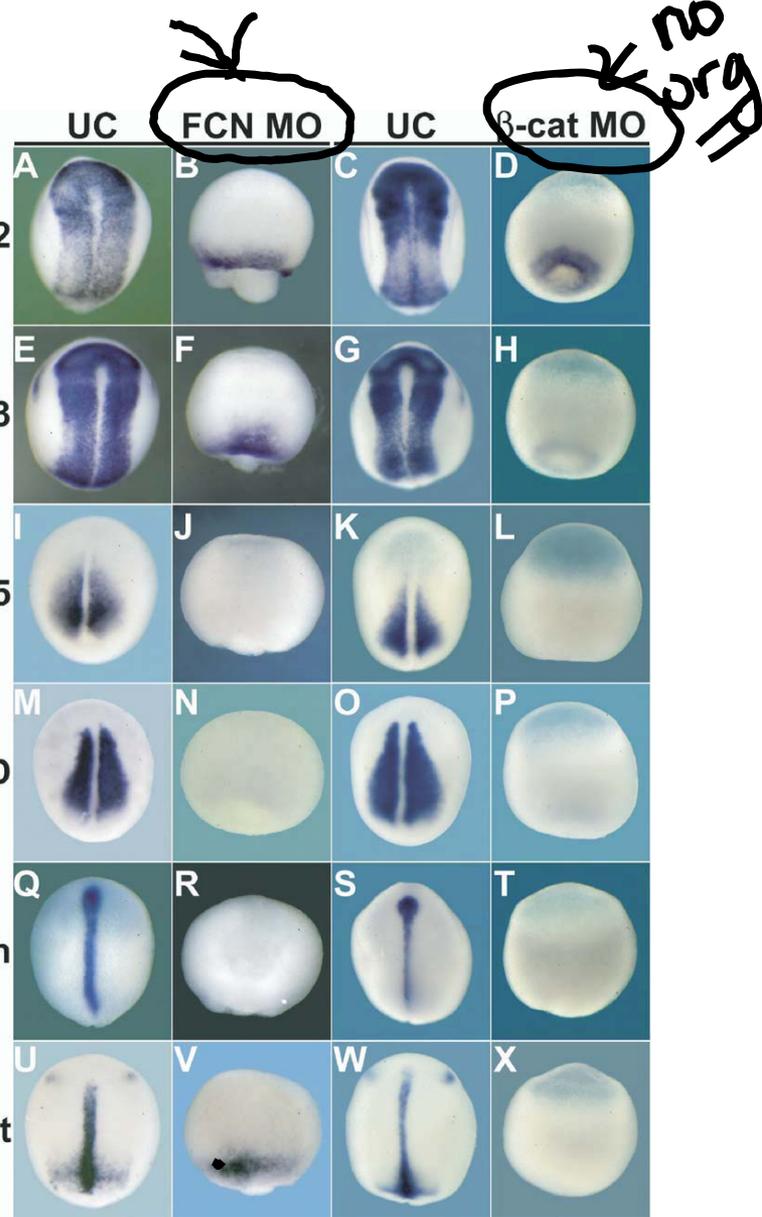
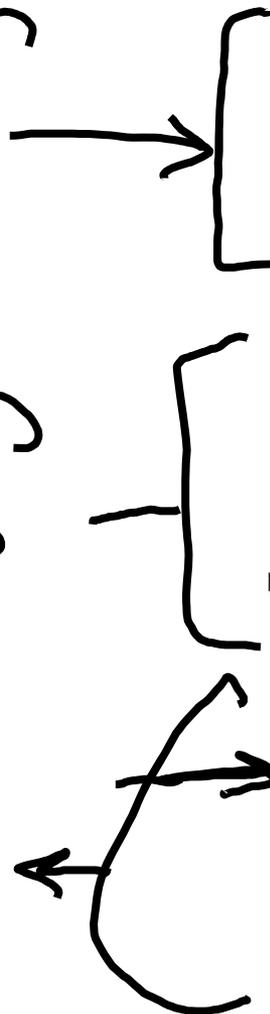


After class:

Ectoderm  
neural

mesoderm  
somites

Notochord



# COURSE WEB PAGE

- Telesis: <https://telesis.wustl.edu/>
- All assignments, including pdf files of readings
- additional materials: optional readings, movie clips, etc.
- Class session slides
- Course overview, syllabus, help documents, etc.
- Calendar - class session content information, assignments, etc

# Writing Assignments

- Journal
- Analytical essays
- Thesis support summaries
- Research paper
  - Prospectus
  - Thesis support
  - Introduction draft
  - Final paper
  - Optional: revision

# Essays

- Question or thesis
- Question designed to require synthesis of material from several sources
- Support answer with empirical data and arguments
- Organize around ideas

# Example

## Stem Cell Essay

Write an essay of 1-2 pages (double spaced typed) that answers the question:  
Are mouse ES cells a good model for understanding general mechanisms important for maintaining pluripotency? Why or why not?

**Audience:** a biology major with similar background to yours, who is not taking this course.

**Main point and purpose:** To learn skills in organizing information to support a thesis and practice writing an analytical essay.

**Due Date: Sept. 13, 2007**, at the beginning of class. A paper copy should be turned in plus **an electronic version of the final draft** should be deposited in the IN box on the Telesis Web page. I reserve the right to use essays (with your name removed) in future years as example papers.

**Format:** see posted help document, 'format guidelines.' These guidelines include instructions for type size, margins, title page, etc.

**Standards and Criteria:** Your essay will be graded according to the general criteria described in the posted document 'Criteria for grading formal writing.' In specific, your essay should

1. Introduces the question and its context: Why is it an interesting question? How does it relate to issues of importance in stem cell research and the existing knowledge?
2. Contain a clear statement of your thesis (answer to the question)
3. Present information and data from the papers we read and class discussions that provide support for your thesis statement.
4. State the points you want to make clearly and concisely in your own words.
5. Have good paragraph structure (topic sentence, one main idea, etc)
6. Be carefully proofread for spelling and grammar errors.
7. Avoid the first person

**Note:** Essays that have more than 3 grammatical, sentence structure (run-on or incomplete sentences) or spelling errors will be returned without a grade. Such assignments can be resubmitted after careful proofreading. In this case 5 points will be deducted from the final grade.

# Grading

Biology 3191

50 pts total

NAME \_\_\_\_\_

**Grading scale for Essay on stem cells:**

<b>1. Thesis</b>							
Poor or incorrect thesis		unclear or incomplete thesis		excellent, clearly -stated thesis			
1	2	3	4	5			
<b>2. Context and background</b>							
Major elements missing		some but elements missing/not clearly explained		great context/ very clear			
1	2	3	4	5			
<b>3. Experiments/Arguments logically connected to thesis</b>							
lack of appropriate logical connections		unclear or incomplete connections		complete, excellently stated connections			
1	2	3	4	5	6		
<b>4. Empirical/argument support/weaknesses (if appropriate) for thesis</b>							
important support/weakness not presented/irrelevant information included		support/weaknesses not clearly described/minor irrelevant details		all appropriate support/weaknesses described very clearly			
1	2	3	4	5	6	7	8
<b>5. Idea-based logical organization</b>							
'Book report' organization		idea-based but some organizational problems		idea-based logical organization			
1	2	3	4	5	6		
<b>6. Concluding paragraph</b>							
minimal or redundant summary				summary that highlights important ideas/ties to thesis			
1	2	3	4	5	6		
<b>7. Transitions and flow</b>							
Awkward, poorly stated or wordy sentences/lack of transitions				easy to read/understand good transitions			
1	2	3	4	5			
<b>8. Paragraph structure</b>							
no topic sentences/ paragraphs have too many ideas				each paragraph structured well			
1	2	3	4	5			
<b>9. Format as specified/citations</b>							
poor proofreading, format errors				no typos/grammar/spelling or format errors			
0	1	2	3	4			

Total points: 50

Score:

# Writing examples: 3 ways to write about the same thing

Biology 3191

**Does the binding assay reflect activation of the pathway?**

**Example summaries of first few experiments of Dyson and Gurdon in response to this question.**

**Chronological report of what the authors did (not good)**

The first thing the authors did was to make labeled activin. They did this by injecting activin RNA into *Xenopus* eggs and culturing the eggs with labeled amino acids. They saw that activin was the major protein secreted when its RNA was injected. It was in two forms, mature dimer and proform. The dimer is converted to monomer under reducing conditions. The specific activity was  $10^8$ , indicating that the authors can detect binding to cells in the picomolar range. This is the important range and means that they can do binding assays to detect activin binding to its receptor on cells.

Next, the authors used the labeled activin to bind to dissociated blastula cells. They did this to see which form bound to cells. What they found was that the dimer bound but the proform did not. This means that all the binding was due to dimer, which is important because the dimer is the active form and they did not want to measure inactive binding.

**Conclusion first (better, but not ideal)**

Using labeled activin, binding in the picomolar range to cells can be detected. This is the range of concentrations that is important for activin to activate cells. To conclude this, the authors made radioactively labeled activin. They injected 45 ng of activin mRNA into eggs, incubated with radioactively labeled amino acids, and then looked at what the eggs secreted. The secreted protein had a specific activity of  $10^8$  cpm/ $\mu$ g and was in two forms, biologically active dimer and proform. They conclude that this labeled activin can be used for their experiments.

Only the biologically active form, the dimer, binds to cells. To determine this, labeled activin was incubated with dissociated blastomeres, washed to remove unlabelled counts, and loaded the lysate onto protein gels. They saw that mostly dimer was present. This means that they are detecting only binding of active protein, making their results meaningful.

**Organized around ideas with motivation for the experiments stated first (best; still needs revision and editing)**

In order to understand the effects of different concentrations of activin on gene activation, activin binding to cells must be quantitatively and sensitively detected in the range of concentrations important for cellular responses. Radioactively labeled activin was made for this purpose by injecting mRNA encoding it into eggs incubated in radioactive amino acids. Labeled, secreted proteins were detected using SDS gel electrophoresis. Two forms of the protein were observed, the biologically active dimer and the precursor or proform. This shows that the protein is being properly processed to the active form in this expression system. The specific activity was  $10^8$  cpm/ $\mu$ m, which is high enough to permit detection of binding in the picomolar concentration range. Since cells respond to activin in this range of concentration, this specific activity will permit measurement of binding under conditions that activate activin responsive genes.

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dimer and proform, and proform binding would interfere with the quantitation, the form of activin bound to cells was analyzed. SDS gels show that only dimer binds. Thus, their assay measures biologically active activin binding.

**Revision of paragraph**

The main goal is to determine the number of activated receptors required to get different genes expressed. The binding of labeled activin will be used to determine the number of activated receptors. Therefore, the binding measured must reflect activated receptors. The labeled activin produced using this method consists of both dimer and proform. Dimer, but not proform, activates signaling of the receptor. However, if the proform binds to receptor, their measurements of binding would not reflect receptor activity. Therefore, the form of activin bound to cells was analyzed using SDS gels. Activin was incubated with the cells, the cells washed to remove unbound proteins, and labeled proteins associated with the cells analyzed. Only dimer was detected. Thus, their assay measures biologically active activin binding and quantitatively reflects receptor activation.

**Final Revised and Edited paragraph**

An important piece of information needed to understand how cells sense concentration is the number of activated receptors required to get different genes expressed. The binding of labeled activin is used to determine the number of activated receptors. Therefore, the binding measured must reflect activated receptors. The labeled activin preparation consists of both dimer and proform. Dimer, but not proform, activates signaling of the receptor. However, if the proform binds to receptor, measurements of binding would not reflect receptor activity. Therefore, to be sure that only dimer bound, activin was incubated with the cells, the cells washed to remove unbound proteins, and labeled proteins associated with the cells analyzed by SDS gel electrophoresis. Only dimer was detected. Thus, their assay measures only biologically active activin binding and quantitatively reflects receptor activation.

# Analysis of writing examples

Biology 3191

Name of Peer responder: \_\_\_\_\_

The main point of this peer review is to determine if your prospectus conveys an understandable view of your proposed mini-review. The audience for your mini-review is someone in this class who has not read the papers on which you plan to focus. This person is not familiar with the area of development you have chosen to research. Your partner's response to what you have written should be a good indication of how successfully you have explained what you plan to your target audience.

## Peer Response to Prospectus

Name of Prospectus Author: \_\_\_\_\_

1. The main question(s) the minireview will address is clear?

I had a hard time figuring out the main question      I think I understand the main question      I easily understood the question

**Underline the part that states the main question and write #1 next to it.**

**Write the main question addressed, as you understood it:**

2. The author's tentative thesis (answer to the question) was stated clearly?

I could not determine the presenter's thesis      I think I got it      The presenter's thesis was crystal clear

**Underline the part that states the thesis and write #2 next to it.**

**Write the presenters thesis, as you understood it:**

3. The background and context makes clear the state of knowledge that led to the work and why the work is interesting?

Disagree strongly      could have been better      agree entirely

**Underline the statement you think is most important and write #3 next to it.**

**Write the most important aspect of the background for making this question interesting, in your opinion:**

4. The main argument(s)/line(s) of evidence that supports the thesis was (were) described and the logic of how the evidence applied to the thesis was stated?

I am not sure if I really understand      I think I understand      It is very clear to me

**Underline the most important argument and write #4 next to it**

**Briefly summarize one main way the author plans to support his/her thesis:**

1. Circle one sentence that you found confusing or difficult to follow. Write what you think the author means by this sentence. (You must use your own words.)

2. Write one suggestion to make this prospectus better

After you have completed this form, wait until your partner completes his/her form. Take turns in reviewing what was written. Responders will read what they wrote in response to each question and show the author the sentences that they marked. Authors are only allowed to say, "That is correct" or "No, that is not what I meant." **THIS IS NOT THE TIME TO FIX A PROBLEM OR EXPLAIN WHAT YOU MEANT. FIXING WILL BE DONE LATER, after you have had time to think about what your partner has said.**

**AFTER YOU LEAVE THE SESSION:** Think about your partner's comments, even if your partner understood your prospectus. Do the comments suggest that there may be a better way of explaining? Or a different organization that would better convey your points? Remember, your response may be that you don't want to change anything. You are not required to use the responder's suggestions.

Thesis: Nanog is required for pluripotency of the epiblast

Background/context:

1. the mechanisms that are important for pluripotency are not well understood
2. the genes Oct 3/4 and Sox2, among others, are required for pluripotency, but not sufficient to maintain it.
3. The LIF>Jak/Stat pathway is required for pluripotency/maintenance of undifferentiated state in some mouse ES cells but not in mouse embryos or human ES cells
4. The first few events of cell differentiation should be described: trophectoderm, ICM, Extraembryonic endoderm and epiblast
5. These observations suggest that other factors are important
6. Nanog could be one important factor
  - a. Gene is highly expressed in ES cells compared to somatic cells
  - b. A transcription factor
  - c. forced expression can maintain mES cells in the undifferentiated and pluripotent state in the absence of LIF
7. If nanog is a key pluripotency factor it should be required for pluripotency in the early embryo

(NOTE: This part attempts to let the reader see why the thesis is interesting and the facts needed to understand the data and conclusions. These points would not need data support because they form the context for the thesis but do not directly address the thesis)

Points that need support:

1. Loss of function of nanog leads to loss of pluripotency in the embryo
2. This loss of pluripotency occurs at the epiblast stage

Experiment: Targeted disruption of nanog gene, generation of nanog null embryos

Results:

- a. No homozygous nanog mutant offspring; must be playing a role in embryonic development, but need to define when it acts and what it affects. This result is consistent with loss of pluripotency.
- b. Homozygous embryos are OK very early; they have ICM, so nanog does not act at this stage. This is consistent with nanog acting after the ICM stage.
- c. by late blastocyst/implantation, embryos had no epiblast, but had only differentiated extraembryonic tissues. Epiblast cells are the pluripotent cells in the embryo at this stage. Since none are present, those cells that would have become epiblast must have differentiated into another cell type, presumably extraembryonic endoderm
- d. Dissected ICM cells from early embryos could not be propagated in culture in an undifferentiated state – all cells differentiated in a short time into cells resembling extra embryonic endoderm. This suggests that ICM cell progeny cannot stay pluripotent - they differentiate into extraembryonic cells, instead becoming epiblast, the pluripotent cells of the embryo at this stage. They don't retain the ability to remain undifferentiated under appropriate culture conditions. Since ICM cells become either epiblast or extraembryonic cells, nanog must be required for the epiblast cells remaining pluripotent and undifferentiated.

Interpret and Conclude: loss of nanog function leads to loss of pluripotent cells of the embryo at the epiblast stage. Prior to this stage, the pluripotent cells (ICM) are present. Thus, nanog is required for epiblast pluripotency.

NOTE: this is a very limited thesis, consisting of only one main idea. The two things that need support are interconnected and the same experiments address both points. Thus, describing them together makes sense. Many times, and in the assignment in which you are being asked to assess the support for the idea that nanog is key pluripotency factor, a thesis that adequately incorporates relevant information that seems on the surface contradictory will require a number of different arguments with lines of support.

# Research paper

- Getting started
  - Pick area based on topic list
  - Literature review using Medline
  - Identify question addressed by recent work, 2-3 main data papers
- Prospectus and annotated bibliography
- Thesis support
- Introduction draft
- Final paper (10-12 pages double spaced)
- Optional: revision

# Active learning Tools

- Primary literature
- SMARTBOARD
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# Bean, Engaging Ideas

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# Thank you for listening

Additional questions/thoughts:

[miller@wustl.edu](mailto:miller@wustl.edu)