Keck School of Medicine of USC

# Syllabus: INTD 531 — Cell Biology (Fall 2019)

**Credit: 4 units**
**Course Sessions: Tuesdays and Thursdays**
**Time: 9:00 am – 10:50 am**
**Location of Lectures: McKibben Hall (MCH) 256**
**Location of Exams: McKibben Annex (MCA) 149 and 249**
**First Day of Class: August 27, 2019**


**Course Director:** **Dr. Axel H. Schönthal (schontha@usc.edu)**
**Teaching Assistant:** **Angela (Yun Kyung) Park (yunkyunp@usc.edu)**


## Course Background

INTD 531 is a graduate-level course in cell biology that is offered on the Health Sciences Campus. Three major areas of cell biology and related biomedical research will be emphasized:

- Module I: Cellular Growth Control and Regulation, with Relation to Cancer Biology
- Module II: The Dynamic Architecture and Composition of Cells
- Module III: Cells In Their Social Context, with Relation to Cancer Metastasis

Each of these areas is covered in a separate module of the course. The course will use the material in the recommended textbook as a starting point, and original recent work and advances in the individual areas (published and unpublished primary research) will be added.

## Course Goals

Students who successfully complete this course will acquire in-depth understanding and advanced knowledge of a range of general and specialized areas in cell biology. They will develop insight into the complexities of cell structure and function, the molecular controls that govern the cells' dynamic properties, and cellular interactions with the organism as a whole. They will also appreciate how some cellular functions can change to create a tumor cell phenotype.

A further goal of this course is to educate and train the students in skills required for the assembly of a fellowship or grant application. Therefore, an important component of this course will be a homework assignment consisting of developing a research proposal based on selected course topics. This assignment will receive written feedback from faculty who will comment on strengths and weaknesses of each student's proposal.

## Message from the Course Director

My vision for this course is this: To provide a challenging and interesting learning environment, where every student not only learns a lot, but also completes the course with a good grade. To achieve this, I

have implemented a strategy that combines different types of incentives to encourage students to study: multiple-choice-type exams (which emphasize fact learning and memorization), a research proposal (which challenges creativity and practical application of the learned material), and extra credit tasks (which develop critical thinking and stimulate interest in biomedical research). These three types of challenges require the application of different cognitive styles and abilities, and therefore aim to support success by all students, irrespective of their highly variable individual learning styles. In the end, when I have to decide on grades, I seek to honor and reward not only performance, but also effort.

## Course Correspondence

All correspondence between instructors and students will be made using email. All information regarding lectures, reading assignments, and homework will be posted on the Blackboard web site for INTD 531. The Blackboard web site may be entered at https://blackboard.usc.edu/webapps/login/ Only students who are registered for the course will have access to the Blackboard web site. If you cannot access the web site, inform TA Angela Park at yunkyunp@usc.edu

➔ Much of the correspondence regarding this course will be distributed via email to each student. It is expected that you regularly check your USC email account.

## Course Textbook

The recommended text is the Sixth Edition (2015) of *MOLECULAR BIOLOGY OF THE CELL*, by Alberts, Johnson, Lewis, Morgan, Raff, Roberts and Walter. (Garland Science publisher). A copy of this text is on hold in the Norris Medical Library.

## Class Format

The course will consist of 2 two-hour class sessions per week. The lecture schedule and assigned lecturers are listed in the "Course Schedule" (see below). Lecture dates may vary with advance notice. Pre-class assignments (homework) will be required for most classes and will be posted on Blackboard. It is advisable that students login to the course on Blackboard and check for updates regularly.

Each class meeting will consist of no more than one hour of lecturing by the instructor. Some instructors may post introductory reading assignment on Blackboard, which students need to review in order to be sufficiently prepared for that class.

About half of the time in each class will be used for interactive exercises that will emphasize data analysis, experimental design, research proposal preparation, or discussion of primary research reports and relevant research methods.

## Exams

There will be a total of four (4) exams:

- Three (3) exams will take place after the three course modules and will consist of multiple-choice questions, based on topics presented during the course section immediately preceding the exam. This exam will take place during the regular course schedule, but in a different location: instead of lecture hall MCH-256, exams will be either in MCA-149 or in MCA-249.

- One (1) exam will be a take-home homework assignments, consisting of writing a research proposal. Topics for this research proposal will be given to students about ten days before the deadline. This typed research proposal must be uploaded (in PDF format) to the course website on Blackboard at the latest by the deadline listed in the course schedule. It is advised that each student becomes familiar with Blackboard well in advance of upload deadlines. The students will receive written feedback regarding strengths and weaknesses of their research proposals.

## Exam Dates

See section: Schedule of Lectures and Exams (below).

## Extra Credit

Details for extra credit will be distributed sometime mid-course. The format is flexible and these tasks are optional (i.e., the students are not obligated to perform extra credit work). In the past, extra credit tasks consisted of critically analyzing published literature or attending one or two seminars by invited speakers here on campus. In both cases, a 2-page written summary was requested. Students can choose to do 1 extra credit task, or 2 extra credit tasks, or none at all; they are voluntary.

## Grading

The final grade for each student will be assigned based on the student's performance on the research proposal and the three sit-in exams. Each of these 4 components is worth up to 100 points (i.e., each part is weighted equally). The projected final grades can be improved in those cases where students have submitted satisfactory extra credit assignments.

## Composition of Final Grades

[Points from Exam 1] + [points from Exam 2] + [points from Exam 3] + [points from Homework Assignment] divided by 4, will yield a number between 0 (worst) and 100 (best). This number is component A.

Extra credit Assignment 1 receives between 0 (worst) and 5 (best) points. This number is component B.

Extra credit Assignment 2 receives between 0 (worst) and 5 (best) points. This number is component C.

Final point calculation: Component A + Component B + Component C. Maximum is 110 points.

Conversion of points to grades:

≥95 points: A (USC has no A+)
≥90 to <95: A–
≥85 to <90: B+
≥80 to <85: B
≥75 to <80: B–
≥70 to <75: C+
≥65 to <70: C
≥60 to <65: C–
≥60: D

## Course Policies

As per USC policies, recordings of lecture material requires the express permission of the instructor and announcement to the class, and can only be used for individual or group study.

## Special Needs

Any student requesting academic accommodations based on a disability is required to register with Disability Services and Programs (DSP) each semester. A letter of verification for approved accommodations can be obtained from DSP. Please be sure the letter is delivered to the Course Director as early in the semester as possible. DSP is located in GFS-120 (University Park Campus) and is open 8:30 a.m. – 4:30 p.m., Monday through Friday. The phone number for DSP is (213) 740-0776. Their website is http://dsp.usc.edu.

## Stress Management

Students are under a lot of pressure. If you start to feel overwhelmed, it is important that you reach out for help. A good place to start is the Eric Cohen Student Health Center on this campus (the Health Sciences Campus, HSC). The phone number is (323) 442-5631 and the website is http://ecohenshc.usc.edu. The service is confidential, and there is no charge.

## Student Counseling Services

Tel: (213) 740-7711 – 24/7 on call
Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.
https://engemannshc.usc.edu/counseling/

## National Suicide Prevention Lifeline

Tel: 1-800-273-8255
Provides free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week. http://www.suicidepreventionlifeline.org/

## Beyond Academic Challenges

Balancing course work, midterms, finals, and laboratory research presents a challenge and at times can feel overwhelming. On top of that, many students are far away from home and family, perhaps even their country and their native language, which can feel quite depressing. Sometimes, relationship problems come up and make life miserable. But no matter the problem, USC offers resources to help students deal with depression, anxiety, and other types of distress. USC's services are not only geared toward helping students with academic challenges, but also with personal problems. Students in need should not hesitate to take advantage of the services that are listed above (and on the next page); there is no need to feel embarrassed or ashamed. USC is offering these services and resources so that students are in the best position to meet their academic and personal goals.

## Content of the Following Pages

- **Statement on Academic Conduct and Support Systems**
- **Schedule for Lectures and Assignments**
- **Email Contacts of Lecturers**
- **Details on Homework Assignment (incl. Example of Research Proposal)**

## ACADEMIC INTEGRITY STANDARDS

The University prides itself in maintaining high academic integrity standards. The entire academic community benefits from the adherence to such standards. An academic integrity overview, including descriptions of dishonest acts and consequences for students found responsible, is available online at: https://sjacs.usc.edu/students/academic-integrity/.

Further information, including a number of tutorials for students, can be found online at: https://libraries.usc.edu/research/reference-tutorials. This website has tutorials such as: how to avoid plagiarism, how to prevent academic dishonesty, how to manage your research, and other useful how-to tools and tutorials.

## ACADEMIC CONDUCT

Plagiarism – presenting someone else's ideas as your own, either verbatim or recast in your own words – is a serious academic offense with serious consequences. Please familiarize yourself with the discussion of plagiarism in Section 11 of the *SCampus* publication (online at: https://policy.usc.edu/student/scampus).

Other forms of academic dishonesty are equally unacceptable. See additional information in *SCampus* and university policies on scientific misconduct, http://policy.usc.edu/scientific-misconduct/.

## DISCRIMINATION, HARASSMENT, ASSAULT

Discrimination, sexual assault, and harassment are not tolerated by the university. You are encouraged to report any incidents to the *Office of Equity and Diversity* http://equity.usc.edu/ or to the *Department of Public Safety* http://dps.usc.edu/. This is important for the safety of the whole USC community. Another member of the university community – such as a friend, classmate, advisor, or faculty member – can help initiate the report, or can initiate the report on behalf of another person. The Relationship and Sexual Violence Prevention (RSVP) Services at https://engemannshc.usc.edu/rsvp/ provide 24/7 confidential support, and the Sexual Assault Resource Center webpage https://sarc.usc.edu/ describes reporting options and other resources.

## OTHER SUPPORT SYSTEMS

A number of USC schools provide support for students who need help with scholarly writing. Check with your advisor or program staff to find out more. Students whose primary language is not English should check with the *American Language Institute* http://dornsife.usc.edu/ali, which sponsors courses and workshops specifically for international graduate students. *The Office of Disability Services and Programs* http://sait.usc.edu/academicsupport/centerprograms/dsp/home_index.html provides certification for students with disabilities and helps arrange the relevant accommodations. If an officially declared emergency makes travel to campus infeasible, *USC Emergency Information* http://emergency.usc.edu/ will provide safety and other updates, including ways in which instruction will be continued by means of blackboard, teleconferencing, and other technology.

**INTD-531 SCHEDULE OF LECTURES AND EXAMS — Fall Semester 2019**

**All dates are Tuesdays or Thursdays 9:00 a.m. — 10:50 a.m.**

## Module I: Mechanisms of Cell Growth, Survival, and Death

| *Date* | *Topic* | *Lecturer* |
|---|---|---|
| Aug. 27 | Introduction to Cellular Growth Control and Cell Cycle | Dr. A. Schönthal |
| Aug. 29 | Autophagy | Dr. C. Liang |
| Sept. 3 | Cell Death | Dr. C. Liang |
| Sept. 5 | Cell Culture Models to Study Disease | Dr. A. Firth |
| Sept. 10 | Principles of Intracellular Signaling | Dr. E. Zandi |
| Sept. 12 | Regulation of Stem Cell Self-Renewal and Growth | Dr. Q. Ying |
| Sept. 17 | Introduction to Cancer Cell Biology | Dr. A. Schönthal |
| Sept. 19 | Metabolism of Normal and Cancer Cells | Dr. N. Graham |
| Sept. 24 | Cancer Stem Cells | Dr. F. Hofman |
| Sept. 26 | Systems Biology Approaches to Study Cell Metabolism | Dr. N. Graham |
| Oct. 1 | No class – Rosh Hashanah | |
| Oct. 3 | Exam for Module I (Location: MCA-249) | TA: A. Park |

## Module II: The Dynamic Architecture and Composition of Cells

| *Date* | *Topic* | *Lecturer* |
|---|---|---|
| Oct. 8 | TBD | |
| Oct. 10 | Mitochondrial Function in Health and Liver Disease | Dr. S. Win |
| Oct. 15 | Membranes and Organelles | Dr. C. Okamoto |
| Oct. 17 | Fall Recess | |
| Oct. 22 | Cytoskeleton and Motors | Dr. S. Hamm-Alvarez |
| Oct. 24 | Motors and Trafficking: Literature and Discussion | Dr. S. Hamm-Alvarez |
| Oct. 29 | Endocytosis and Exocytosis | Dr. C. Okamoto |
| Oct. 31 | TBD | |
| Nov. 5 | Exam for Module II (Location: MCA-149) | TA: A. Park |

**Module III: Cells In Their Social Context**

| *Date* | *Topic* | *Lecturer* |
|---|---|---|
| Nov. 7 | Overview of the Microenvironment of the Cell | Dr. Y. DeClerck |
| Nov. 12 | The Extracellular Matrix: Structure, Function, and Applications in Tissue Engineering | Dr. M. McCain |
| Nov. 14 | Cell-Matrix Interactions: Integrins and Other ECM Adhesion Molecules | Dr. S. Swenson |
| Nov. 19 | Cell-Cell and Epithelial-Mesenchymal Interactions | Dr. R. Widelitz |
| Nov. 21 | The Tumor Microenvironment: Social Environment of the Cancer Cell | Dr. Y. DeClerck |
| Nov. 22 | Distribution of Topics for Research Proposal | |
| Nov. 26 | Extracellular Vesicles as Communicators between Cells | Dr. L. Sarte |
| Nov. 28 | No Class – Thanksgiving | |
| Dec. 3 | The Brain Microenvironment | Dr. J. Neman |
| Dec. 5 | Inflammation: A Disease of the Social Environment<br>Paper review and discussion session | Dr. Y. DeClerck |
| Dec. 6 | Deadline for upload of Research Proposal (11:00 a.m.) | |
| Dec. 17 | Exam for Module III (Location: MCA-149) | TA: A. Park |

End of course

## E-MAIL CONTACTS FOR LECTURERS

**Module I: Mechanisms of Cell Growth, Survival, and Death**

| *Lecturer* | *Email Address* |
|---|---|
| Dr. Axel Schönthal | schontha@usc.edu |
| Dr. Chengyu Liang | liang2@usc.edu |
| Dr. Qilong Ying | qying@usc.edu |
| Dr. Florence Hofman | hofman@usc.edu |
| Dr. Amy Firth | Amy.Firth@med.usc.edu |
| Dr. Nicholas Graham | nagraham@usc.edu |
| Dr. Ebrahim Zandi | zandi@usc.edu |

**Module II: The Dynamic Architecture and Composition of Cells**

| *Lecturer* | *Email Address* |
|---|---|
| Dr. Sanda Win | swin@usc.edu |
| Dr. Sarah Hamm-Alvarez | shalvar@pharmacy.usc.edu |
| Dr. Curtis Okamoto | cokamoto@usc.edu |

**Module III: Cells In Their Social Context**

| *Lecturer* | *Email Address* |
|---|---|
| Dr. Yves DeClerck | ydeclerck@chla.usc.edu |
| Dr. Megan McCain | mlmccain@usc.edu |
| Dr. Steve Swenson | sswenson@usc.edu |
| Dr. Randall Widelitz | widelitz@usc.edu |
| Dr. Laurence Sarte | LSarte@chla.usc.edu |
| Dr. Josh Neman | yebrahim@usc.edu |

## INTD-531: Instructions and Formatting Guidelines for Research Proposal

1. Format and Sections of Research Proposal

(A) The length of the research proposal is limited to 1 page text + 1 page for diagrams and figures (inclusive of legends) + 1 page references, for an overall length of 3 pages. On all pages, keep the margins (top, bottom, left, right) to at least 0.5 inches. Use single-spaced text with 12-point Times New Roman font (shown here: this is 12-point Times New Roman font) or 11-point Arial font (shown here: this is 11-point Arial font). Alignment of the text on the right side (flush/not flush) is optional.

(B) The first page of your proposal should contain the following components (in this order):

- **Your name and ID**: LAST NAME IN CAPITAL LETTERS, followed by first name in small letters, followed by your USC student ID.
- **Name of Professor** (whose topic you are presenting)
- Optional: **Project title** (not required)
- **Project summary** (1-2 sentences) – in no more than 2 sentences provide an overview of the topic being studied; mention its overall goal.
- **Background** (quarter page) – briefly present the relevant background of your project.
- **Relevance** (1-2 sentences) – in no more than 2 sentences, describe why your project is important and how it advances scientific knowledge.
- **Specific aims** (less than a quarter page) – list 2-4 specific aims.
- **Methods** (quarter page) – briefly outline your experimental approach to achieve the specific aims.
- **Pitfalls** (2-3 sentences) – present one potential pitfall (a problem that you might encounter in pursuing your specific aims; an experiment that might not yield the expected result), and mention an alternative (how you would deal with the problem; how you would change your experimental approach).

(C) The second page of your research proposal must contain at least 1 diagram or figure. The figure (if any) provided by the professor does not count (you can include that figure, but you must present at least 1 other figure or diagram). For example, you can present a graphical outline of the problem or your experimental approach or your hypothesis. You could also show a figure from the literature in support of your approach or as an example of expected results. Add a figure legend that provides some background of the figure. Make sure you refer to all figure(s) within the text on the first page (e.g., see Fig. 1).

(D) The third page should list all references used. For each reference, provide the names of all authors, the full title of the paper, the journal name, as well as volume, page numbers, and year published. Number the references in the order they appear in the text of pages 1 and 2 of your research proposal. On page 1 and 2, cite the references by referring to their numbers. It is highly recommended that you use a software tool (citation manager) for the insertion and formatting of references, such as Zotero (zotero.org; free for Mac and Windows), EndNote, RefWorks, or other. Ask the Norris Medical Library for support and instructions, if needed. Some of these programs have tutorials on YouTube.

— over —

2. Content of your Research Proposal

An example of a research proposal is shown on the following pages.

3. Submission of Your Research Proposal

To submit your research proposal, follow these steps:

- ✓ Convert your document to PDF format and submit as a 3-page PDF.
- ✓ Upload your document to Blackboard (3-step process):
  - locate Assignments folder for this course,
  - inside this folder, click on the assignment; a new window opens,
  - upload your PDF (you can add comments, if you wish) in the new window.

There is a video tutorial demonstrating the upload of assignments to Blackboard:

- ✓ inside Blackboard, click on Student Help (top row)
- ✓ new window: under Getting Started with Blackboard, click on Coursework
- ✓ new window: under Coursework, click on Submitting Assignments

➔ as of this writing, Blackboard was undergoing construction. The above details might have changed as a result of it.

4. Deadlines for Submission of Your Research Proposal

You must submit the electronic copy of your research proposal by the time and date outlined further above in this syllabus. There will be a 1-hour grace period, but Blackboard will not accept any more proposals after 12:00 noon on that day.

If you have problems uploading to Blackboard, you can hand-deliver a printed copy of your proposal to Dr. Schönthal, or you can email a digital copy. However, any submissions outside of Blackboard will incur automatic deductions of points.

5. Example of Research Proposal

The following pages show an example of a research proposal that is formatted according to the above guidelines.

**Name:** SCHONTHAL, Axel (USC ID: 123456789)

**Name of Professor:** This is the topic from Dr. Schönthal.

**Project title**: Novel Therapeutic Approach for Tuberous Sclerosis

**Project summary**: I propose to determine whether pharmacologic approaches targeting the endoplasmic reticulum (ER) stress response can trigger apoptosis in tuberous sclerosis cells. The overall goal is to develop a novel therapy for tuberous sclerosis.

**Background**: In general terms, ER stress can be viewed as a cellular "yin-yang" mechanism, where low-level or chronic activation provides profound protection against certain types of stress ("yin"), but were more severe activation will switch to the pro-apoptotic mode of this system and will lead to cell death ("yang") [1]. Most tumor cells (including tuberous sclerosis cells [2]) exhibit low-level, chronic ER stress in a defensive ("yin") mode that ensures their survival under adverse microenvironmental conditions (e.g., hypoxia, low glucose levels, acidity, etc.), and also increases their chemoresistance. The novel therapeutic strategy of my study consists of the controlled pharmacologic aggravation of ER stress to the point where this system overloads and selectively triggers apoptosis in tuberous sclerosis cells (which harbor chronic ER stress), but spares normal cells (which do not have chronic ER stress and therefore are able to adapt and survive treatment with CXB) (see Fig. 1).

**Relevance**: There is currently no effective treatment for tuberous sclerosis. If my study is successful, it has the potential to create a new therapeutic approach for the treatment of this disease.

**Specific Aims**: I intend to establish that celecoxib (CXB; Celebrex), a cyclooxygenase-2 (COX-2) inhibitor with known potential to trigger ER stress [3], is able to cause aggravation of ER stress and will result in apoptosis of tuberous sclerosis cells in vitro and in vivo.

Specific Aim 1: Determine whether treatment of tuberous sclerosis cells with CXB in vitro leads to ER stress.

Specific Aim 2: Investigate whether treatment of tuberous sclerosis cells with CXB in vitro leads to apoptosis.

Specific Aim 2: Characterize the effects of CXB on tuberous sclerosis tumors in an animal tumor model.

**Methods**: For SA1, I will treat tuberous sclerosis cells with increasing concentrations of CXB for 24, 48, and 96 hours, and then harvest total cellular lysate to perform Western blot analysis. I will use antibodies against GRP78 (glucose regulated protein of molecular mass 78 [4]) and CHOP (CCAAT/enhancer binding protein homologous transcription factor [5]). Both of these targets are markers for ER stress; their increased expression is indicative of ER stress. As a control, I will use an antibody against actin; actin is the loading control and will confirm that equal amounts of protein lysate have been used in each lane.

For SA2, I will perform two experiments. Both will be set up similar to the above (with different CXB concentration and different time points). In one part, I will measure cellular survival by using an MTT assay, which determines the viability of cells after treatment with CXB. The other will be a Western blot with antibodies against different caspases, which will reveal whether drug treatment results in the proteolytic cleavage (=activation) of caspases as markers for cells undergoing apoptosis.

For SA3, I will implant tuberous sclerosis cells under the skin of 10 nude mice. After palpable tumors have formed, I will treat 5 mice with CXB (5 mg once daily per gavage). The other 5 mice will form the control group and will receive only salt solution (vehicle) on the same schedule. I will measure tumor growth in both groups of animals over the course of 6 weeks of treatment. Tumor size will be plotted over time in a graph. At the end of the experiment, all animals will be euthanized and the tumors collected. I will perform Western blot analysis of tumor tissue to investigate markers of ER stress and apoptosis (as in SA1 and 2), in order to investigate whether CXB causes ER stress and apoptosis in tuberous sclerosis tumor cells in vivo.

**Pitfalls**: It is possible that, contrary to my expectation, CXB may not cause ER stress in tuberous sclerosis cells in vitro (or in vivo). If I obtain this outcome, I would then investigate the Akt survival pathway, because CXB is known to down-regulate Akt, and, if I can demonstrate this effect in tuberous sclerosis cells, it would explain how CXB triggers apoptosis without ER stress.

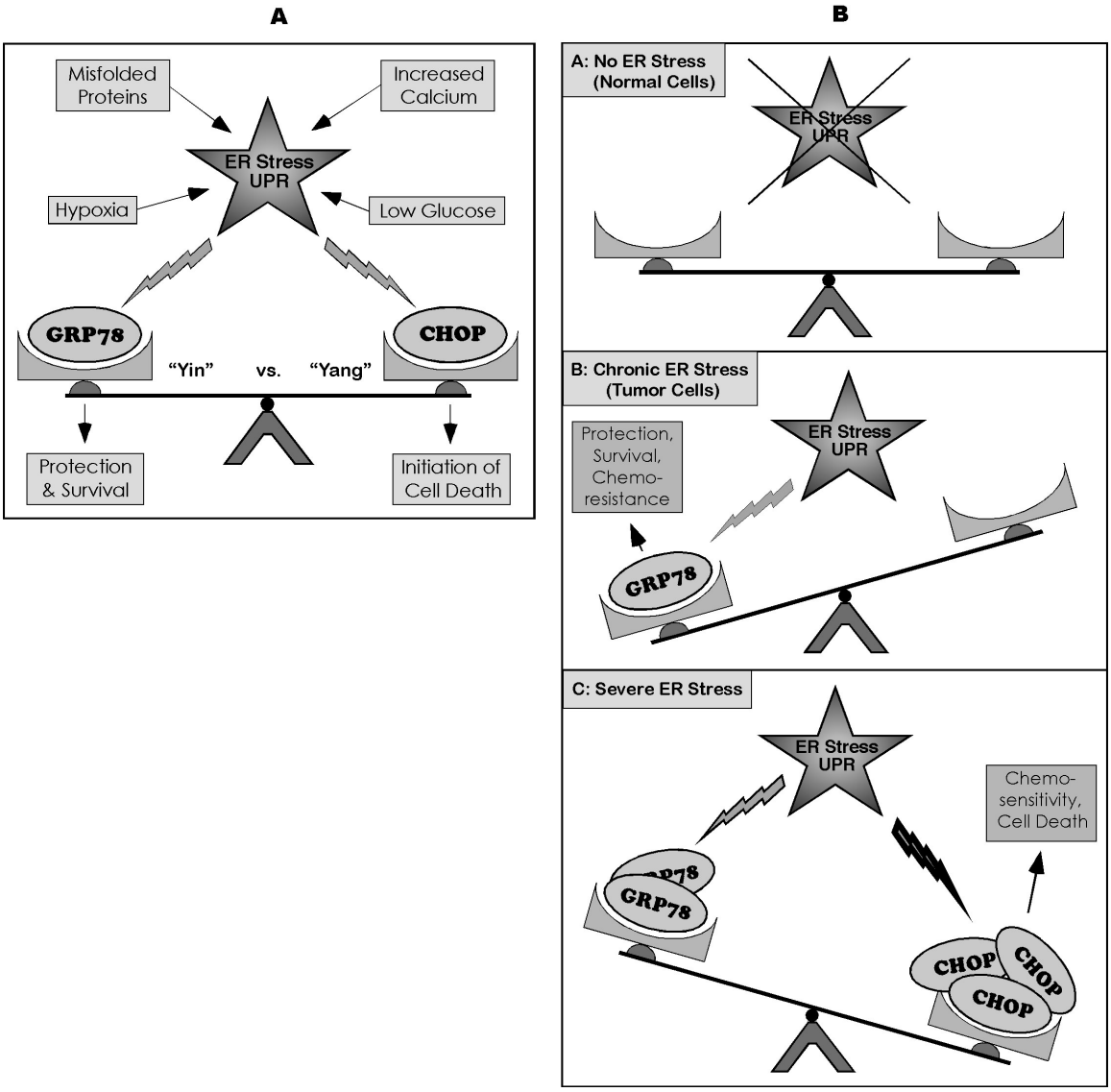


**Figure 1:** Simplified diagram of the "Yin-Yang" balance of ER stress and how it relates to the project

(**A**) ER stress can be triggered by various unfavorable conditions, such as the accumulation of misfolded proteins, changes in the calcium balance between the ER and the cytosol, low levels of glucose, hypoxia, and others [6; 7]. The ERS response is also called the unfolded protein response (UPR), as some of the above stressors can impinge on proper protein folding [8]. The mechanism of ERS/UPR involves the increased expression of anti-apoptotic GRP78 and pro-apoptotic CHOP, and—depending on the severity of the initial insult—one of these two master executors will gain dominance and decisively determine the resulting consequences, i.e., protection from stress or initiation of cell death.

(**B**) There are three activity levels of the ER stress response system. (A) The "No ER Stress" condition is the default situation in normal cells. (B) In cancer cells, continuous, low-intensity stress generates the "Chronic ER Stress" condition, indicated by elevated levels of GRP78, which, among its various functions, suppresses pro-apoptotic components and thereby supports cellular survival and chemo-resistance. (C) Persistent, high-level stress generates the "Severe ER Stress" situation, where pro-apoptotic components (such as CHOP) dominate and trigger cell death. The protective effort of GRP78 is overwhelmed, which contributes to the chemo-sensitization of tumor cells. Note that thickness of bolts corresponds to the intensity of stimulated expression of GRP78 and CHOP.

➔ My hypothesis is that CXB is able to convert condition B to condition C (in diagram to the right) and thereby leads to the killing of tuberous sclerosis cells. My research study is designed to investigate this hypothesis.

## References


[1] A.H. Schönthal. Targeting endoplasmic reticulum stress for cancer therapy. Front Biosci S4 (2012) 412-431.

[2] U. Ozcan, L. Ozcan, E. Yilmaz, K. Duvel, M. Sahin, B.D. Manning, G.S. Hotamisligil. Loss of the tuberous sclerosis complex tumor suppressors triggers the unfolded protein response to regulate insulin signaling and apoptosis. Mol Cell 29 (2008) 541-551.

[3] H.-C. Chuang, A. Kardosh, K.J. Gaffney, N.A. Petasis, A.H. Schönthal. COX-2 inhibition is neither necessary nor sufficient for celecoxib to suppress tumor cell proliferation and focus formation in vitro. Mol Cancer (2008) 38.

[4] J. Li, A.S. Lee. Stress induction of GRP78/BiP and its role in cancer. Curr Mol Med 6 (2006) 45-54.

[5] S. Oyadomari, M. Mori. Roles of CHOP/GADD153 in endoplasmic reticulum stress. Cell Death Differ 11 (2004) 381-389.

[6] A.S. Lee, L.M. Hendershot. ER stress and cancer. Cancer Biol Ther 5 (2006) 721-722.

[7] A.H. Schönthal. Pharmacological targeting of endoplasmic reticulum stress signaling in cancer. Biochem Pharmacol 85 (2013) 653-666.

[8] J.D. Atkin, M.A. Farg, A.K. Walker, C. McLean, D. Tomas, M.K. Horne. Endoplasmic reticulum stress and induction of the unfolded protein response in human sporadic amyotrophic lateral sclerosis. Neurobiol Dis 30 (2008) 400-407.