

INTD 531 — Cell Biology (Fall 2023)

Credit: 4 units

Course Sessions: Tuesdays and Thursdays

Time: 9:00 a.m. – 10:50 a.m.

Location of Lectures: MCH 156

→ a few sessions will be online-only

First Day of Class: August 22, 2023

Course Director: Axel H. Schönthal, PhD (schontha@usc.edu)

Teaching Assistant: Allison Brookshier (abrooksh@usc.edu)

Syllabus Version: 1.3 (current as of August 8, 2023)

Course Description

INTD 531 is a graduate-level course in cell biology that revolves around the concept that the cell is the fundamental unit of life. The cell represents the basic structural, functional, and biological unit of all known organisms. This course will focus on eukaryotic cells of animals, and will present, explore and discuss important aspects of their structure and function, both as individual units and within the context of an organism. Selected from many cell-based diseases, the course will illustrate certain pathological changes of cells within the background of cancer and metastasis as representative disease examples.

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recommended textbook as a starting point, and original recent work and advances in the individual areas (published and unpublished primary research) will be added, along with considerations of experimental procedures and techniques that are being applied to advance these research areas.

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 homework assignments consisting of developing research proposals based on selected course topics. These

assignments will receive feedback from faculty who will comment on strengths and weaknesses of each student's proposal.

Learning Objectives

Upon completion of this course, the students should be able to:

- Describe regulation and function of key cellular processes, such as cell division, autophagy, senescence, apoptosis, endo- and exocytosis, migration, as well as cellular communication and interactions with the microenvironment.
- Explain how certain cellular processes function differently in stem cells or cancer cells.
- Design experimental approaches to investigate the above cellular processes.
- Write a structured research proposal to propose an investigational approach to study a novel aspect of cell biology.

Pre-Requisites, Co-Requisites, Concurrent Enrollment, Recommended Preparation

There are no pre- or co-requisites, and no concurrent enrollment is required. While there is no specific recommended preparation, students should already be familiar with reading the scientific literature in the biomedical sciences and should have some basic knowledge of hands-on lab research and experimental design, all of which will make it easier for students to succeed in this course. As well, students should anticipate to allocate significant effort to several (graded) homework assignments outside of the regularly scheduled course meeting times, and should expect to spend 30-60 minutes in advance of each lecture to review required pre-lecture materials.

Course Correspondence and Communication

Much of the correspondence regarding this course will be distributed via email to each student. It is expected that students regularly (i.e., daily) check their USC email account.

Communications between instructors and students can be made using email, unless otherwise arranged. Students should expect to receive a response to an email inquiry within 48 hours, and are encouraged to re-send their email if a response was not received during this time frame. Email contacts for all lecturers are listed further below. The email address for the course TA is shown on p.1.

All information regarding lectures, reading assignments, and homework will be posted on the Blackboard web site. 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 the course TA.

Course Textbook

The recommended textbook is the Seventh Edition (2022) of *MOLECULAR BIOLOGY OF THE CELL*, by Alberts et al. (W. W. Norton & Company publisher). Second-best is the Sixth Edition (2015) of this text, which was published by Garland Science (note that the publisher has changed; but the format of the text has remained the same). The Course Director has requested that the Norris Medical Library

(NML) on the Health Sciences Campus (HSC) places this textbook on hold during the semester, so that students can loan the book for 3 hours at a time. But it is not currently known whether NML already has purchased the new (7th) Edition, or whether only the older version (6th Edition) is available.

For students interested in purchasing their own copy of this textbook (1552 pages), please note that different formats of this text are available (with different pricing). For example, the publisher (Norton) offers a Loose Leaf version with Ebook + Smartwork + Videos/Animations (\$174) in addition to a conventional Hardcover version (\$217.50 at Norton, \$200 on Amazon). Amazon also offers a 5091-page Kindle version (\$140) and a rental version for \$163. (Students are not required to acquire the textbook.)

Technological Proficiency and Hardware/Software Requirements

This course requires familiarity with use of the Zoom video-conferencing platform. Several discussion sessions will be held online-only via Zoom, without concurrent meeting in the lecture hall. It requires that enrolled students have secured individual access to the course on Blackboard and know how to navigate this educational technology. It is expected that students keep their cameras “on” during these online sessions; blurred backgrounds can be applied if additional privacy is desired.

Regular, in-person sessions that take place in the lecture hall will not be streamed online; for these in-person sessions, students need to be present in the lecture hall.

Attendance, Participation, and Expectations on Student Engagement

Students are expected to attend all class sessions, on time, for the entire course of the class. They are expected to come prepared (i.e., have reviewed and understood the pre-class assignments) and actively participate in each and every class.

Students are expected to act in a professional manner, meeting deadlines, solving problems, responding to questions from instructors voluntarily or when called upon, cooperating with classmates, and generally contributing in a positive way to the class. Working in the real world often means searching for solutions in a group context. Teamwork, listening, empathy, enthusiasm, emotional maturity, and consideration of other people’s concerns are all essential to success. Please bring these qualities and values with you to class. It is as important to ‘practice’ these interpersonal skills as it is to learn new intellectual content.

Class Format

The course will consist of two 2-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 review of introductory materials 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. Most class meetings 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 lecture time 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.

Zoom Etiquette

The course will consist of two 2-hour class sessions per week, and some of these sessions will be delivered via Zoom, i.e., entirely online, without physical presence in the lecture hall. This will allow the use of breakout rooms and facilitate small-group discussions. Students will find it more engaging if everyone is using “video on”, so that students and instructors can see each other. This is particularly true during small-group work in Zoom breakout rooms. It is therefore recommended that you prepare your environment in a manner so you feel comfortable showing yourself. Using “blurred background” can be helpful.

Exams

There will be a total of five (5) exams in three different formats. The different formats present challenges that 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.

- Two (2) exams will consist of multiple-choice questions, based on topics presented during the course section immediately preceding the exam. (*Didactic strategy: emphasizing fact learning and rote memorization.*)
- Two (2) exams will consist of writing and evaluating a research proposal. (*Didactic strategy: focus on critical thinking and creative application of the learned material.*)
- One (1) exam will consist of student presentations. (*Didactic strategy: independent collection, appraisal, consolidation, and communication of course-related topics.*)

Grading

The final grade for each student will be assigned based on the student’s performance on all five exams. Points will be given as follows. Distribution of obtainable points:

Max. Points	Exam Part	Exam Content
5	Exam 1, Part 1	Written 1-page Research Proposal
5	Exam 1, Part 2	Peer Critique of 1-page Research Proposal
5	Exam 1, Part 3	Review & Discussion
15	Exam 2	Multiple-Choice Test (in lecture hall)
20	Exam 3, Part 1	Written 2-page Research Proposal
5	Exam 3, Part 2	Peer Critique of 2-page Research Proposal
5	Exam 3, Part 3	Review & Discussion
20	Exam 4	Student Presentations
20	Exam 5	Multiple-Choice Test (take-home exam)

100	Total	Maximum Points Possible
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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–
	≥50 to <60: D
	>50: F

Please note: Any grade below C (i.e., C–, D, F) will be considered “fail” by the Graduate School, meaning that the student will not receive credit for this course, even though the grade still counts toward the GPA. A grade of C is considered “pass” by the Graduate School, meaning that the student receives full credit (4 units in this case).

Several (but not all) of the exam items are homework assignments that require upload to Blackboard by a specific deadline that will be clearly announced for each activity. Any late submissions will not be accepted. The upload feature in Blackboard will shut down by the deadline. If you miss the deadline for Blackboard upload for any of the exam items, you will not receive credit for this part of the exam.

Exam Dates and Deadlines for Upload of Homework Assignments to Blackboard

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

Late Policy

Some of the pre-class work and homework assignments require that students work in groups, and in-course discussion will be based on submitted responses. Therefore, late work will not be accepted. If you miss the deadline for Blackboard upload for any of the exam items, you will not receive credit for this part of the exam.

If you miss an upload deadline because of an unavoidable, documented, and serious reason, discuss the situation with the course director via email to discuss alternatives.

Course Recordings

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

Students and Disability Accommodations

USC welcomes students with disabilities into all of the University’s educational programs. The Office of Student Accessibility Services (OSAS) is responsible for the determination of appropriate accommodations for students who encounter disability-related barriers. Once a student has completed the OSAS process (registration, initial appointment, and submitted documentation) and accommodations are determined to be reasonable and appropriate, a Letter of Accommodation (LOA) will be available to generate for each course. The LOA must be given to each course instructor by the

student and followed up with a discussion. This should be done as early in the semester as possible as accommodations are not retroactive. DSP is located in GFS-120 (University Park Campus) and is open 8:30 a.m. – 4:30 p.m., Monday through Friday. More information can be found at osas.usc.edu. You may contact OSAS at (213) 740-0776 or via email at osasfrontdesk@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

- **Statements on Academic Conduct, Integrity Standards, Discrimination, Assault**
- **Support Systems Available to Students**
- **Schedule for Lectures and Assignments**
- **Email Contacts of Lecturers**
- **Details on Homework Assignment (incl. Example of Research Proposal)**

ACADEMIC CONDUCT AND ACADEMIC INTEGRITY STANDARDS

- Members of the USC community are expected to be honest and forthright in their academic endeavors.
- To falsify the results of one's research, to present the words, ideas, data, or work of another as one's own, or to cheat on an examination corrupts the essential process by which knowledge is advanced.
- When students accept their offer to USC they are also accepting to abide by the Student Conduct Code.
- This is a higher standard of conduct than expected in the general community because we are TROJANS.
- When USC confers a degree, it is acknowledging students' academic success and their ability to be a positive, honest, and outstanding citizen within society.
- In failing to uphold academic standards students cheat themselves and others out of learning, degrade the value of their education, and diminish the prestige of the USC education.
- Ignorance of these expectations is not an acceptable justification for violating the Student Conduct Code.

The University prides itself in maintaining high academic integrity standards. The entire academic community benefits from the adherence to such standards. Among the violations of integrity standards is plagiarism. Plagiarism has to be avoided. It is a serious academic offense with serious consequences. When it occurs, the consequences for the student can be severe. For example, credit for a course may be denied and a grade of F is given, permanent notation on transcript, suspension or expulsion from the University, or revocation of admission or degree.

What is Plagiarism?

- Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.
- For example, if you use a sentence from somebody else's paper and insert it into your own paper without clearly marking the source, you are plagiarizing.

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.

Understanding and Avoiding Plagiarism: Module 1 (What is plagiarism?)

<https://libraries.usc.edu/tutorial/understanding-and-avoiding-plagiarism-module-1-what-plagiarism-what-citation>

Understanding and Avoiding Plagiarism: Module 2 (Citing to avoid plagiarism)

<https://libraries.usc.edu/tutorial/understanding-and-avoiding-plagiarism-module-2-citing-avoid-plagiarism>

Students should expect that their work (such as term papers, research proposals, presentations, written theses, etc.) will be checked for plagiarism with the use of appropriate software (Turnitin; iThenticate; Copyscape; PaperRater; etc.).

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 Sexual Violence Prevention Services at <https://sites.google.com/usc.edu/rsvpclientservices/home> provide 24/7 confidential support, and further help in emergencies can be found here: <https://studenthealth.usc.edu/emergencies/>

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.

Counseling and Mental Health - (213) 740-9355 – 24/7 on call
sites.google.com/usc.edu/counseling-mental-health

Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.

988 Suicide and Crisis Lifeline - 988 for both calls and text messages – 24/7 on call
988lifeline.org

The 988 Suicide and Crisis Lifeline (formerly known as the National Suicide Prevention Lifeline) provides free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week, across the United States. The Lifeline is comprised of a national network of over 200 local crisis centers, combining custom local care and resources with national standards and best practices. The new, shorter phone number makes it easier for people to remember and access mental health crisis services (though the previous 1 (800) 273-8255 number will continue to function indefinitely) and represents a continued commitment to those in crisis.

Relationship and Sexual Violence Prevention Services (RSVP) - (213) 740-9355(WELL) – 24/7 on call
sites.google.com/usc.edu/rsvpclientservices/home

Free and confidential therapy services, workshops, and training for situations related to gender- and power-based harm (including sexual assault, intimate partner violence, and stalking).

Office for Equity, Equal Opportunity, and Title IX (EEO-TIX) - (213) 740-5086
eetix.usc.edu

Information about how to get help or help someone affected by harassment or discrimination, rights of protected classes, reporting options, and additional resources for students, faculty, staff, visitors, and applicants.

Reporting Incidents of Bias or Harassment - (213) 740-5086 or (213) 821-8298

usc-advocate.symplicity.com/care_report

Avenue to report incidents of bias, hate crimes, and microaggressions to the Office for Equity, Equal Opportunity, and Title for appropriate investigation, supportive measures, and response.

The Office of Student Accessibility Services (OSAS) - (213) 740-0776

osas.usc.edu

OSAS ensures equal access for students with disabilities through providing academic accommodations and auxiliary aids in accordance with federal laws and university policy.

USC Campus Support and Intervention - (213) 740-0411

campussupport.usc.edu

Assists students and families in resolving complex personal, financial, and academic issues adversely affecting their success as a student.

Diversity, Equity and Inclusion - (213) 740-2101

diversity.usc.edu

Information on events, programs and training, the Provost's Diversity and Inclusion Council, Diversity Liaisons for each academic school, chronology, participation, and various resources for students.

USC Emergency - UPC: (213) 740-4321, *HSC:* (323) 442-1000 – 24/7 on call

emergency.usc.edu

Emergency assistance and avenue to report a crime. Latest updates regarding safety, including ways in which instruction will be continued if an officially declared emergency makes travel to campus infeasible.

USC Department of Public Safety - UPC: (213) 740-6000, *HSC:* (323) 442-1200 – 24/7 on call

dps.usc.edu

Non-emergency assistance or information.

Office of the Ombuds - (213) 821-9556 (UPC) / (323-442-0382 (HSC)

ombuds.usc.edu

A safe and confidential place to share your USC-related issues with a University Ombuds who will work with you to explore options or paths to manage your concern.

Occupational Therapy Faculty Practice - (323) 442-2850 or otfp@med.usc.edu

chan.usc.edu/patient-care/faculty-practice

Confidential Lifestyle Redesign services for USC students to support health promoting habits and routines that enhance quality of life and academic performance.

INTD-531 SCHEDULE OF LECTURES AND EXAMS — Fall Semester 2023

Lecture dates are Tuesdays and Thursdays 9:00 a.m. — 10:50 a.m.

Location: MCH 156 (Health Sciences Campus)

Module I: Mechanisms of Cell Growth Control, Proliferation, Survival, and Death

<i>Date</i>	<i>Topic</i>	<i>Lecturer</i>
Aug. 22	Introduction — Review of Course Format — Assignments — Exams	Dr. A. Schönthal
Aug. 24	Cellular Growth Control and Cell Cycle	Dr. A. Schönthal
Aug. 29	Applied Methods: Autophagy – Senescence – Cell Death	Dr. A. Schönthal
Aug. 31	Principles of Intracellular Signaling	Dr. E. Zandi
Sept. 5	Mitochondrial Function in Health and Liver Disease	Dr. S. Win
Sept. 7	Applied Principles of Intracellular Signaling	Dr. E. Zandi
Sept. 12	Introduction to Cancer Cell Biology	Dr. A. Schönthal
Sept. 14	Regulation of Stem Cell Self-Renewal and Growth	Dr. Q. Ying
Sept. 19	Circulating Tumor Cells	Dr. A. Goldkorn
Sept. 21	tbd	
Sept. 26	Exam 1—ONLINE (Part 3: Discussion of 1-Page Research Proposal)	Dr. A. Schönthal

Module II: The Dynamic Architecture and Composition of Cells

<i>Date</i>	<i>Topic</i>	<i>Lecturer</i>
Sept. 28	Endoplasmic Reticulum Function and GRP78	Dr. R. Hill
Oct. 3	Manipulating Endoplasmic Reticulum Stress and GRP78	Dr. R. Hill
Oct. 5	Exam 2 (Multiple-Choice Test: in person, in lecture hall)	Dr. A. Schönthal
Oct. 10	Membranes and Organelles	Dr. C. Okamoto
Oct. 12	Fall Recess	
Oct. 17	Endocytosis and Exocytosis	Dr. C. Okamoto
Oct. 19	Cytoskeleton, Motors and Transport	Dr. R. Lansford
Oct. 24	Cell Motility and the Cytoskeleton	Dr. R. Lansford
Oct. 26	Exam 3—ONLINE (Part 3: Discussion of 2-Page Research Proposal)	Dr. A. Schönthal

Module III: Cells In Their Social Context

Date	Topic	Lecturer
Oct. 31	Overview of the Microenvironment of the Cell	Dr. Y. DeClerck
Nov. 2	The Tumor Microenvironment: Social Environment of the Cancer Cell	Dr. Y. DeClerck
Nov. 7	The Extracellular Matrix: Structure, Function, and Applications in Tissue Engineering	Dr. M. McCain
Nov. 9	From Hands-on Bench Work to Commercialization	Dr. S. Swenson
Nov. 14	Cell-Matrix Interactions: Integrins and Other ECM Adhesion Molecules	Dr. S. Swenson
Nov. 16	Extracellular Vesicles as Communicators between Cells	Dr. L. Sarte
Nov. 21	Extracellular Vesicles: Diagnostic and Therapeutic Potential	Dr. L. Sarte
Nov. 23	Thanksgiving Holiday	
Nov. 28	Inflammation: A Disease of the Social Environment	Dr. Y. DeClerck
Nov. 30	Exam 4 (throughout Module 3: Student Presentations & Discussion)	Dr. Y. DeClerck
Dec. 2-5	Study Days	
Dec. 12	Exam 5 (Multiple-Choice Test: take home + upload to Blackboard)	Dr. A. Schönthal

Dec. 14: Start of Winter Recess

INTD-531 SCHEDULE OF ASSIGNMENTS AND EXAMS — Fall Semester 2023

Date		Exam #1 (One-page research proposal)
Sept. 1	Dr. Schönthal's distribution of topic for 1-page research proposal (by 9:00 pm)	
Sept. 11	Students' upload of 1-page research proposal to Blackboard (by 12:00 noon)	
Sept. 12	Assignment of students to critique two 1-page research proposals (by 9:00 pm)	
Sept. 18	Students' upload of two critiques of 1-page research proposal to Blackboard (by 12:00 noon)	
Sept. 20	Dr. Schönthal's distribution of critiques of 1-page research proposal (by 9:00 pm)	
Sept. 26	Discussion of students' research proposals #1 + critiques #1 (Zoom online session)	

Date		Exam #2 (Multiple-choice test #1)
Oct. 5	Multiple-choice test #1 (in person in lecture hall)	

Date		Exam #3 (Two-page research proposal)
Oct. 5	Dr. Schönthal's distribution of topic for 2-page research proposal (by 9:00 pm)	
Oct. 17	Students' upload of 2-page research proposal to Blackboard (by 12:00 noon)	
Oct. 18	Assignment of students to critiques of two 2-page research proposals (by 9:00 pm)	
Oct. 23	Students' upload of two critiques of 2-page research proposal to Blackboard (by 12:00 noon)	
Oct. 24	Dr. Schönthal's distribution of critiques of 2-page research proposal (by 9:00 pm)	
Oct. 26	Discussion of students' research proposals #2 + critiques #2 (Zoom online session)	

Date		Exam #4 (Student Presentations + Participation)
Oct. 31 – Nov. 30	Details to be announced by Dr. DeClerck beforehand	

Date		Exam #5 (Multiple-choice test #2)
Dec. 8	Dr. Schönthal's distribution of multiple-choice test #2 (by 9:00 pm)	
Dec. 11	Students' upload of answers to multiple-choice test #2 (by 11:59 pm – before midnight)	

E-MAIL CONTACTS FOR LECTURERS

Module I: Mechanisms of Cell Growth Control, Proliferation, Survival, and Death

<i>Lecturer</i>	<i>Email Address</i>
Dr. Axel Schönthal	schontha@usc.edu
Dr. Amir Goldkorn	agoldkor@usc.edu
Dr. Qilong Ying	qying@usc.edu
Dr. Ebrahim Zandi	zandi@usc.edu
Dr. Sanda Win	swin@usc.edu

Module II: The Dynamic Architecture and Composition of Cells

<i>Lecturer</i>	<i>Email Address</i>
Dr. Reginald Hill	rhill@eitm.org
Dr. Rusty Lansford	lansford@usc.edu
Dr. Curtis Okamoto	cokamoto@usc.edu

Module III: Cells In Their Social Context

<i>Lecturer</i>	<i>Email Address</i>
Dr. Yves DeClerck	ydeclerck@chla.usc.edu
Dr. Megan McCain	mlmccain@usc.edu
Dr. Steve Swenson	sswenson@usc.edu
Dr. Laurence Sarte	LSarte@chla.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:** LAST NAME IN CAPITAL LETTERS, followed by first name in small letters (do not include your USC student ID)
 - **Project title** (feel free to pick a descriptive title)
 - **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 2-3 specific aims.
 - **Methods** (quarter page) – briefly outline your experimental approach to achieve the specific aims.
 - **Pitfalls** (2-4 sentences) – present 1-2 potential pitfalls (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. Blackboard will not accept any uploads after the deadline.

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

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.

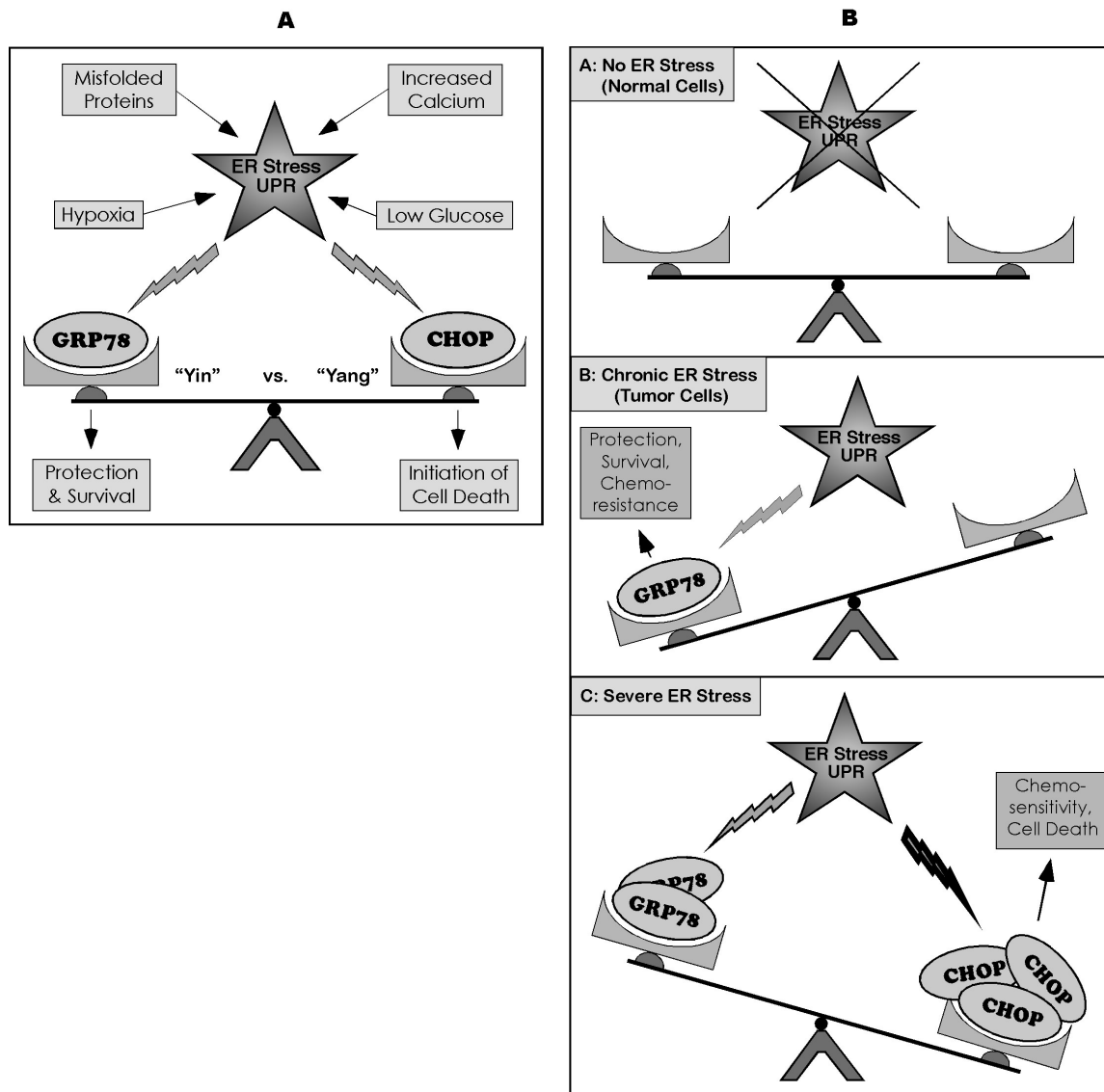


Figure 1: Simplified diagram of the “Yin-Yang” balance of ER stress and how it relates to the project

(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.

➔ I am proposing 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 will investigate this hypothesis.

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