URS Thesis Proposal Example – STEM

Download a blank URS Application Planning Template to draft your proposal here:
http://tx.ag/2526URSPlanningTemplate

Refer to the **Application Instructions & Examples Guide** for content requirements expectations.

Section 1: Contact Information

Student Applicant

Aggie First	Click or tap here to enter text.	Aggie Last	123456789
First Name	*Middle Name*	*Last Name*	*9-digit UIN*

Check Thesis Type

☐ Team Thesis (Up to 5 Members) ☒ Individual Thesis

Faculty Advisor(s)

PRIMARY ADVISOR:

Advisor First	Advisor Last	DEPT	advisor@tamu.edu
First Name (and Middle Initial)	*Last Name*	*Department*	*Email Address*

SECONDARY ADVISOR (IF APPLICABLE):

Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.
First Name (and Middle Initial)	*Last Name*	*Department*	*Email Address*

TERTIARY ADVISOR (IF APPLICABLE):

Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.	Click or tap here to enter text.
First Name (and Middle Initial)	*Last Name*	*Department*	*Email Address*

Section 2: Proposal

Section 2.1: Project Summary

PROPOSAL TITLE:

Angiogenesis on a Chip

PROJECT SUMMARY:

Angiogenesis is a complex process involving the formation of new blood vessels from existing ones. This process is particularly elevated in cancer within the tumor microenvironment. The goal of this project is to advance an existing organ-on-chip model that can recreate angiogenesis in an ovarian tumor microenvironment and capture the dynamic events that lead to a parent vessel near cancer cells to initiate angiogenesis and form new angiogenic sprouts. A second goal is to make a measurement of the extent to which antiangiogenic drug bevacizumab, approved clinically, may arrest the process of angiogenesis and starve the tumor. Finally, the dynamics of angiogenesis will be measured after the drug is withdrawn to test if cancer cells recuperate and reinitiate the angiogenic signaling as has been observed clinically in some patients who develop resistance against this therapy. This device will find potential application in testing effect of standalone drug and/or drugs in combination to control cancer.

Section 2.2: Introduction

Angiogenesis is the process of forming new blood vessels from the existing ones. This process is normally latent in adults except for ovulation, pregnancy, and would healing. The angiogenic process is regulated by microenvironmental factors that can lead to proliferation or arrest of endothelial cell growth [1]. In cancer physiologies, angiogenesis is upregulated due to the hypoxic environment created from metabolic demand of the tumor. The resultant oxygen-poor microenvironment leads to the release of vascular endothelial growth factor (VEGF), promoting angiogenesis. In turn, the increase in VEGF promotes tumor blood vessel density to increase distribution of resources [1], leading to tumor proliferation and growth. As a result, arresting tumor angiogenesis has become a target of numerous cancer therapies.

Organ-on-chips are devices fabricated using soft lithography to combine cell culture and microfluidics. These microfluidic devices can be engineered to model physiological processes and recreate cellular microenvironments [2]. They have been heavily developed in the past decade to fill the gap between static testing methods using cell culture studies and confounding animal models [3]. Organ-chips have the advantage of being targeted engineered microenvironments that can be used for the development of drugs and other therapies [2, 3]. This study focuses on recapitulating an angiogenic microfluidic organ-on-chip model by introducing ovarian tumor spheroids to better understand the effect of anti-angiogenic therapy in cancer management.

The purpose of this study is to advance an existing model to evaluate the anti-angiogenic effect of an anti-VEGF drug in ovarian tumor microenvironments using in house fabricated organ-on-chip devices (aTME-Chip). The angiogenesis modulator that will be added to the aTME-Chip to observe the effect of anti-angiogenesis in the microenvironment is bevacizumab. Bevacizumab is an anti-VEGF monoclonal antibody that is used to treat multiple types of cancer and has been shown to have promising anti-angiogenic effects clinically [4]. However, after drug withdrawal, a resurgence of tumor angiogenesis is expected to be seen, showing disease relapse [5]. Previously, bevacizumab has been used in a tumor scaffold microenvironment to demonstrate a detrimental effect of existing angiogenic vessels at a concentration of 1 mg/mL [6]. Thus, a dose dependent study will be performed to test the dynamics of blood vessel sprouting, and the effect when a drug is administered for the entire duration of study or removed after some time. Using the determined dose, experiments will be conducted in the aTME-Chip to observe the effects of this angiogenesis modulator.

Section 2.3: Objective(s)/Goal(s)

The objective of this project is to engineer a microfluidic device (aTME-Chip) to model an angiogenic tumor microenvironment. There are 3 major aims in this project to achieve the objectives:

Aim 1: Modify the existing angiogenesis-enabled ovarian tumor microenvironment-chip (aTME-Chip) and measure the dynamics of new vessel formation in the presence or absence of human ovarian cancer cells.

Aim 2: Characterize the influence of antiangiogenic drug in arresting angiogenesis within the aTME-Chip.

Aim 3: Characterize the recovery of angiogenesis after drug withdrawal within the aTME-Chip.

Impact: Upon execution, this project will result in the development of an engineered platform to investigate the influence of antiangiogenic drugs within the tumor microenvironment, and a model to test drug resistance upon withdrawal, that is an unmet clinical need. Postdocs and graduate students of the lab will collaboratively use this system to screen different cancers, drugs and expand on gaining mechanistic insights in cancer biology.

Section 2.4: Methodology/Theoretical Framework

The aTME-Chip will be fabricated using polydimethylsiloxane (PDMS) poured on a silicon wafer with embedded print and cured overnight [7]. After curing, the PDMS with the imprint will be punched with 1 mm hole punch to create inlet and outlet flow holes. Next, the PDMS devices will be treated with oxygen plasma and bonded to the glass slides to form the microdevices.

A2780 ovarian cancer cell line will be used in the study. A2780 cells will be made into compact spheroids. These spheroids will then be suspended in a fibrin hydrogel and introduced in the center channel of aTME-Chip.

Human umbilical vein endothelial cells (HUVECs) will be seeded in a lateral channel of aTME-Chip to form parent endothelial lumen and cultured for 5 days to model angiogenesis on chip. Growth factor gradient will be introduced to promote faster angiogenesis in the device. Next, bevacizumab will be administered in the chip through the endothelial lumen to arrest angiogenesis. The drug exposure will be withdrawn from the system after 2 days and the aTME-chip will be maintained and observed for the event of angiogenic relapse post drug withdrawal till day 12. The experiment will be repeated without withdrawing bevacizumab to understand the effects of constant administration. Temporal live cell imaging will be done every 48 hours throughout the study duration using fluorescence microscopy and data will be analyzed using ImageJ.

Section 2.5: Bibliography/References/Works Cited

ACS (AMERICAN CHEMICAL SOCIETY) EXAMPLE

Mathis, C.; Ramos, H.; Gonzalez, E; and Datta, S. What Prevents Business Faculty and Students from Participating in Undergraduate Research? *Cou. Undergrad. Res. Qtrly*. **2015**, *35* (4), 35-41.

AMA (AMERICAN MEDICAL ASSOCIATION) EXAMPLE

Mathis C, Ramos H, Gonzalez E, Datta S. What prevents business faculty and students from participating in undergraduate research? *Cou. Undergrad. Res. Qtrly*. 2015; 35(4), 35-41.

IEEE (INSTITUTE OF ELECTRICAL AND ELECTRONICS ENGINEERS) EXAMPLE

[1] C. Mathis, H. Ramos, E. Gonzalez, and S. Datta, "What prevents business faculty and students from participating in undergraduate research?," *Council on Undergraduate Research Quarterly*, vol. 35, no. 4, pp. 35-41, 2015. Accessed: June 15, 2023.

Section 5: Contingency Plan

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If the experimental timeline becomes lengthened due to unforeseen circumstances, such as the non-availability of the A2780 ovarian cancer cell line, I will switch to using the SKOV3 cell line, which is widely used and compatible with the study objectives. I have already reviewed the literature to ensure this substitution would still yield meaningful and comparable results. If neither A2780 nor SKOV3 is accessible, I will consult with my mentor to identify another validated ovarian cancer cell line to avoid delays in the experimental workflow.

In the case of limited lab access due to emergencies like a public health crisis or institutional closures, I would check with my mentor and supervisor to request access to the lab to complete my experiment. If in-person lab access is not possible, I will seek support from my mentor for the completion of my experiments so that I can process the data remotely working from home.

Additionally, I plan to prioritize the completion of in-lab experiments early in the project period. This will allow me to shift my focus to data analysis and writing if lab access becomes restricted. If I experience any difficulties planning out the experiment or acquiring materials for research, I can discuss with my mentor and faculty advisor to figure out options that will help keep my project on track. To keep the project on schedule, I have built flexibility into the experimental timeline, allowing time for repeat experiments or adjustments if necessary. If lab-based experimentation is significantly delayed or halted, I will pivot to a data-driven backup project by analyzing publicly available datasets (e.g., TCGA or GEO) to investigate VEGF expression patterns and anti-angiogenic response in ovarian cancer. Overall, planning well in advance and constant communication are my main tools to account for any unforeseen circumstances that could cause delays in the project.

Section 6: Timeline

Section 6.1: September and October Goals

September

Week 1: Finalize and submit URS Application. Complete compliance and lab training.

Week 2: Wait to receive application comments/revise application. Continue preliminary literature review work.

Week 3: Wait to receive application comments/revise application. Continue preliminary literature review work.

Week 4: Make aTME-Chip devices.

October

Week 1: Culture and maintain A2780 cells. Review URS Canvas Community and mark requirements/deadlines in calendar.

Week 2: Culture and maintain HUVEC cells. Download thesis template and start writing.

Week 3: Attend URS group meeting. Bond the aTME-Chip devices to glass slides. Generate A2780 spheroids. Continue literature review and methods documentation.

Week 4: Seed HUVEC and A2780 spheroids in the aTME-Chip. Continue literature review and methods documentation. Plan to complete methods documentation.

Section 6.2: November and December Goals

November

Week 1: Submit URS Orientation Module Quiz on Canvas. Revisit literature review.

Week 2: Attend URS group meeting. Continue culture of aTME-Chip, add Bevacizumab, and live cell fluorescence microscopy imaging every 48 h.

Week 3: Complete the Thesis Formatting Module on Canvas. Process images and data. Prepare Fall progress report.

Week 4: Thanksgiving Break.

December

Week 1: Process images and data from experiment set 1. Start drafting Results section, revising Methods as necessary. Attend Writing Productivity Workshop.

Week 2: Continue analysis and draft of Results section. Send draft to advisor before Winter Break. Submit Fall Progress Report on Canvas

Week 3: Continue writing and prepare figure captions from experiment set 1. Check on feedback from advisor. Work to finalize plans to make a public presentation.

Week 4: Winter Break.

Section 6.3: January and February Goals

January

Week 1: Winter Break.

Week 2: Begin experiment set 2. Make set 2 aTME-Chip devices. Confirm plans to present with advisor. Revisit thesis draft and prepare for first installment deadline. Attend Writing Abstracts Workshop.

Week 3: Culture set 2 A2780 cells to confluency. Finalize draft abstract and register for the URS Symposium. Continue drafting Methods section with set 2 information. Attend URS group meeting.

Week 4: Culture set 2 HUVEC cells to confluency. Create set 2 A2780 spheroids. Continue drafting Methods section with set 2 information. Send current draft to advisor before installment deadline. Begin presentation preparation.

February

Week 1: Bond set 2 aTME-Chip devices. Submit first installment and revise as requested. Submit spring Progress Report 1. Send presentation draft to advisor for feedback.

Week 2: Seed set 2 HUVEC and A2780 cells into the aTME-Chip. Finalize and print poster.

Week 3: Continue culture of aTME-Chip, add Bevacizumab without withdrawal, and live cell fluorescence microscopy imaging every 48 h. Present at the URS Symposium.

Week 4: Process images and data. Continue drafting Results based on set 2 experiment. Start to prepare thesis draft for the second installment submission. Send current draft to advisor for review.

Section 6.4: March and April Goals

March

Week 1: Experiment buffer time, if needed. Meet advisor for thesis proofing and feedback session. Submit second installment and revise as requested. Begin drafting conclusion and discussion sections. Submit spring Progress Report 2.

Week 2: Spring Break

Week 3: Attend URS group meeting. Review thesis draft and fill in missing components, including Introduction. Prepare new figures and captions. Finalize all citations and check formatting. Send final thesis draft to faculty advisor by March 18 and incorporate suggested edits.

Week 4: Finalize thesis and incorporate new edits. Review draft one last time and re-check formatting.

April

Week 1: Attend Drop-in Sessions for thesis help. Submit final thesis.

Week 2: Final thesis document formatting check, fix document as requested.

Week 3: Make sure Presentation Report is submitted. Complete program.