GOLD PAPERS

SPOTLIGHTING IMPACTFUL RESEARCH

FALL 2021

ISSUE 4

CSUGOLDPAPERS.BLOG

about the *Gold Papers*

From deep within the belly of the Food Science and Human Nutrition department at Colorado State University, came the idea for this project. A motley group of graduate students decided to clarify some of the confusion surrounding "health" while honing their scientific communication skills. This gave rise to the birth of the *Gold Papers* -- a CSU flavored spinoff to White Papers, which aims to summarize current research and perspectives in their fields of expertise.

The Easiest Way to Get an F: The Detriments of Pulling an All-Nighter

By Sophie Seward, M.S.

College students are put into a precarious situation. We are tasked with leaving home to become adults, balancing our social lives, and exceling in academia while simultaneously having nearly unlimited freedom for the first time in our lives. It is easy to see that the pressure we have as college students is pretty significant. However, the stressors that are unloaded on college students often lead to less-than-optimal stress and time management practices, including binge drinking, procrastinating for exams, not exercising, and forgoing the recommended 7-to-9 hours of sleep. One common, but detrimental, practice amongst college students is pulling an "all-nighter," or the practice of staying up all night to cram for an impending exam or project.

All-nighters run rampant across all colleges, and CSU is unfortunately not immune to this practice. Therefore, the aim of this article is twofold; to educate current college students on the consequences of pulling an all-nighter and to provide ways to avoid pulling an all-nighter as we approach finals week in a few months.

There is an irony that I am discussing this topic, being a doctoral student working in a sleep lab. Funny enough, I thought of writing this piece at the sleepless hour of 3 A.M. on one of my night shifts. I felt (maybe desperately) the repercussions of staying up all night and then being expected to assume productivity the next day. Unfortunately, I am not alone in the practice of the all-nighter.

Nearly 3/4 of college students report receiving less than 8 hours of sleep each night. Sleep is often the first pillar of health to be discarded when the stress of academics and social life are present for college students. In a study examining sleep habits in college students at a Midwestern university, 20% of college students between the ages of 17 and 24 years old reported that they stay awake all night at least once per month and 35% of college students acknowledge staying awake until 3 A.M. at least once per week. Even more striking, in a sample of students from an architectural college, students reported on average that they pulled 2.7 all-nighters per month.

Clearly, poor sleep habits and pulling all-nighters are common amongst college students to prepare for endeavors such as projects, tests, and presentations. Unfortunately, studies show that all-nighters do not help academic performance, as students who sleep less each night have on average worse GPAs. Additionally, even one night of sleep deprivation can hinder memory and time to complete tasks.

In a study, two groups were examined to understand the importance of sleep deprivation on learning capacity. One group included adults who slept 8-hours the night before and the second group consisted of adults who were completely sleep deprived for one night before. The adults who were completely sleep deprived had a 40 percent decrement in learning capacity compared to the adults who slept 8-hours.

Researchers have also proved the benefits of combating an all-nighter, showing that previously sleep-deprived students who were able to obtain the recommended 8 hours of sleep improved their academic performance.

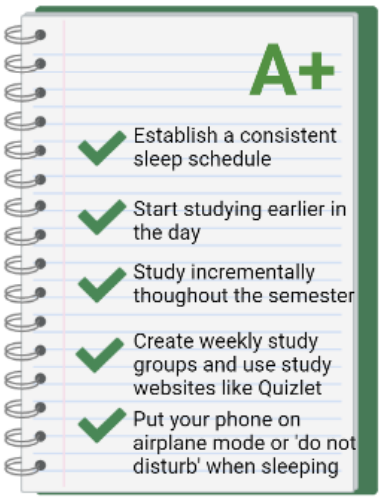
Getting insufficient sleep and pulling an all-nighter has a negative impact on academic performance. As we head into finals week, I want to equip students with ways to combat the inevitable temptation to neglect healthy sleeping habits. Therefore, here are a few helpful tips to consider:

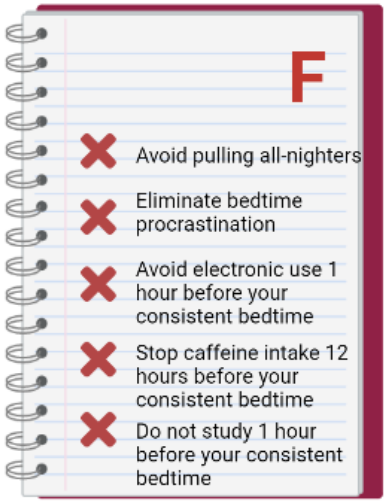
Research findings: Bedtime procrastination is a chronic problem amongst college students. Bedtime procrastination is linked to insufficient sleep and is one of the most common less-than-optimal stress and time management practices that attacks healthy sleep.

How-to for you: Start studying for your finals now to give yourself plenty of time before finals week. Studying incrementally throughout the semester has been shown to be more effective. Utilize study groups or study websites like Quizlet. Create small study sessions a few times a week to stay on top of the class material and assignments throughout the semester.

Research findings: Consistent sleep schedules decrease stress and improve well-being.

How-to for you: Utilize the "sleep schedule" function on your phone. You can also opt to use the airplane mode on your cell phone to limit distractions during the night. Also, avoid the intake of caffeine 12h before going to bed. This will help you feel sleepy when it is time to hit the hay.





How-to for you: Try to start studying earlier in the day than typical. Set an alarm on your phone an hour before bed to stop studying for the night. Additionally, avoid the use of electronics an hour before bed to minimize night-time light exposure, which can suppress melatonin, a hormone in your body that plays a role in sleep.

Research findings: Studying for an exam the night before does not maximize exam performance.

This might seem like a premature warning for finals week, but being proactive and prepared in advance is the whole point of this article! So, get some sleep, study incrementally, and crush finals!

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Playing with Worms: Why We Use Worms to Study Development and Disease

By Lindsay Winkenbach

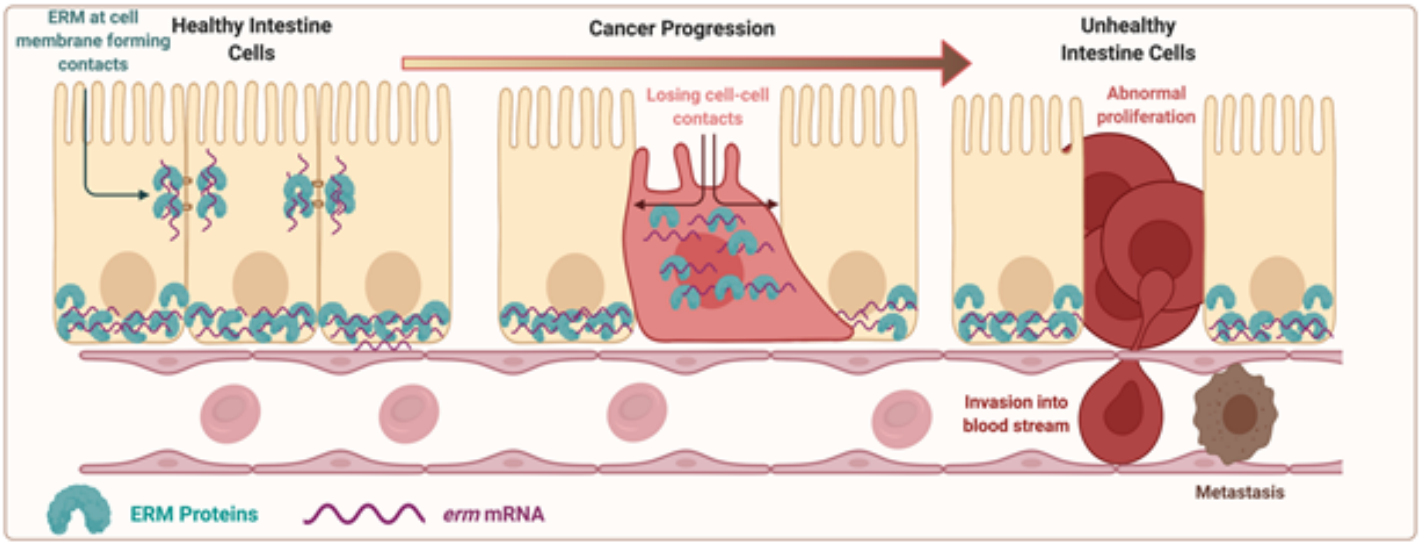
Here at CSU, in the Osborne Nishimura lab, we study how animals and humans change and grow over time. Specifically, our lab is fascinated by the marvel of how we all begin life as a single cell and amazingly develop into a complex organism.

During embryonic development, the building blocks of our body, our cells, must adopt specific fates to create functional organs. For example, when a single, fertilized egg cell, also known as a zygote, divides into two cells, how does one cell know it must become a brain cell and the other a muscle cell? It turns out that developing embryos inherit messages called messenger RNA (mRNA) from their mom that help cells differentiate and ultimately arrive at their cell identity. Due to our interest in animal and human development, our lab studies where these mRNAs go within cells, how they get there, and why they are essential for normal and healthy development.

The localization of mRNA to specific cellular locations is being recognized as a much more common and important occurrence than we initially thought, happening in organisms ranging in complexity from single-celled organisms, like bacteria, to humans. Some pathways are well defined for how mRNAs transit to different regions of the cell, like to the nucleus where our genetic blueprints are housed. However, less is known about how mRNAs are delivered to other cellular destinations, like the cell membrane, and how this can promote a variety of functions in the cell. Localization of mRNAs to cell membranes might help developing cells respond quickly to changes in their environment. Also, since mRNAs carry the instructions to make proteins, the ability to produce more protein on-site could help ensure the integrity of cell membranes and ultimately aid in creating a functional organ like the intestine.

In the Osborne Nishimura lab, we study the movement and purpose of localized mRNAs in a little worm called Caenorhabditis elegans (C. elegans). Why study mRNA localization in worms? Well, humans have trillions of cells, making it very difficult to track the fate of a single type of message from the start of development into adulthood. The humble C. elegans only has about one thousand cells, yet they possess similar cellular machinery to humans, making them a valuable model organism to study developmental questions. From a single-celled zygote to the adult worm with 959 cells, we can track the fate of each cell over time and observe potential developmental errors that take place early on during embryogenesis.

Similar to the lab's overarching theme of mRNA regulation and localization in embryonic development, I have been studying how a certain mRNA potentially functions in the process of C. elegans intestine development. My work has been focused on the erm-1 mRNA, which contains the instructions to make a specific protein in C. elegans called ERM-1. In a C. elegans embryo, the ERM-1 protein works at the edge of dividing and developing cells to help link it with neighboring cells through to adulthood. . Ultimately, ERM-1 is necessary for the C. elegans



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intestine, or gut, to develop. Specifically, when the ERM-1 protein doesn't get delivered to the edge of developing C. elegans cells, the intestine won't develop properly, and the worm won't be able to eat. Interestingly, the erm-1 mRNA that carries the instructions to make the ERM-1 protein is also found at the edge of the cell.

One question you still might have is how do the erm-1 mRNA and ERM-1 protein get delivered to the edge of the cells to promote gut development? Our lab has discovered that a part of the C. elegans ERM-1 protein brings the erm-1 mRNA and the ERM-1 protein to the edge of the cell. However, when we look at a mutant ERM-1 protein that has lost its ability to interact with the cell membrane, the erm-1 mRNA is not present and the developing worm dies immediately after hatching. This leads us to a tricky question to answer about proper gut development in C. elegans - Does the intestine not develop properly because of reduction in erm-1 mRNA delivery to the cell membrane or because of a mutation in the ERM-1 protein? Regardless, this is one of the first findings of what appears to be a novel pathway for mRNA localization to cell edges correlated with a devastating developmental defect.

We want to know more about the importance of the delivery of the erm-1 mRNA on the ultimate function of ERM-1 and health of the developing gut. Since ERM-1 is the only version of the entire ERM protein family found in humans, we want to continue unravelling the mysteries of erm-1 mRNA localization and ERM-1 function in C. elegans so we can one day relate our findings back to human health. Humans have multiple tissue types containing ERM family proteins, such as the lungs. Indeed, in humans, dysregulation of an ERM protein found in lungs has been linked to lung cancer. Furthermore, when ERM proteins aren't working and forming cell-cell linkages in tissues, cancer cells can proliferate in these previously healthy tissues. However, no studies have analyzed human erm mRNAs localization and its impact on tissue health. Thus, while we still don't completely understand the overall effects of mRNA localization and protein function in both C. elegans and humans, future studies must continue to unpack how localized mRNAs and their complement proteins regulate organ development and disease risk.

Up from the Desk: An Insider's Perspective to Medical School

By Raj Trikha, M.S.

Fall 2021

Dear Raj,

5:30 am alarm. 10 minutes of meditation. Turn on coffee pot. Turn on computer. Open Anki. Take a deep breath before seeing how many cards I need to review. Only 200? I can do that.

My medical school morning routine. Monotonous? Yes. Effective? I sure hope so.

Rewind six weeks.

"Sacrifices. Routine. Discipline. Self-care". These orientation mantras were a bit of a broken record. Nevertheless, worry and the exhaustion of orientation gave way to unrelenting excitement for the "Foundational Principles" block of medical school. I could handle routine. I could manage a lot of material. I could take care of myself. The past 18 months of my life have been filled with activities, positions, and achievements all in pursuit of an elusive goal that was finally within reach: medical school.

I was thrilled for class to begin. But just three days into the University of Colorado School of Medicine's Trek curriculum, I felt like I was drowning. My journal entry one-night reads, "Professor gave us a couple of practice questions and I think I got them all wrong. I eventually came to the correct answer—however, it was a bit eye-opening".

Woah. This is fast.

Every Friday we have a 30-question assessment over the previous week's lectures in preparation for the final exam. But, as I've heard from many, lectures go fast in medical school. Instructors set the bar low (we need only average 50% on these weekly check-in assessments) – yet, we're medical students! Who's going to fail?

Well, apparently, I was. I received a 60% on my first assessment. Technically passing, but it was a wakeup call. Is this what I signed up for? What was I doing wrong? I had been faithfully doing my Anki reviews each morning, asking my professors questions in class, and reviewing the next day's material the night before. I needed to figure out a new strategy. But there isn't much time for such experimentation in medical school. There's not much time for anything besides studying.

After a relatively restful first weekend, I still woke up with the fog of fatigue looming behind my eyes. My Monday morning lectures were a rude awakening: 8 hours of microbiology, immunology, pharmacology, and anatomy. This week however, I had a secret weapon: one massive white board adjacent to my computer with which to draw pathways, techniques, and mechanisms while reviewing my Anki cards—rad! This helped but did not ameliorate the familiar feeling of self-doubt that struck all over again the next morning, when many of my classmates seemed to handedly field questions on the previous day's material. So, after class Wednesday night I stuck around with a couple other students to review the "Learning Objectives" for that week. This proved both academically useful and internally distressing, as I had not reviewed a single objective. I was staring at a blank screen while my colleagues produced beautifully phrased answers to more than 100 broad, yet oddly specific objectives.

The session was awkward—what do you expect when you put a bunch of high-achieving individuals in a room together to study? We fretted the microscopic details while completely missing the important take home messages. There was the occasional humble brag about material that tied back into someone's past experience in a research lab or clinic. But luckily, I could only smell a hint of competition. Our cohort—only 12 students—was selected for our desire to work as a team. I was relieved to hear that my classmates felt just as burdened as I and thankful that many were willing to go out of their way to support one another. Apparently, this sense of impending doom was not unique to me. Despite some trustworthy mental preparations prior to beginning class, we were all unqualified for the challenges facing us in those first few weeks.

I grew tired, cranky, and irritable. I snapped at my girlfriend. I stopped calling my mom. My workouts suffered. I slept less than I had ever slept. One early journal entry reads, "Exhaustion infects all aspects of life". But again, my feelings were not unique. I recall one conversation with a classmate where, normally gregarious with his "Seinfeld-style humor", he reflected, with tears in his eyes that the weeks prior to orientation were filled with contemplations of which specialty would suit him best, yet all that was motivating him to continue was the shame he would feel upon informing his friends and family of dropping out.

Medical school is hard. It is hard in many ways that one does not expect.

But it does get better, and more importantly, it will be worth it.

I will always remember my first DOCS (Developing Our Clinical Skills) session. My journal entry that night reads, "Today was an exciting day—had our first DOCS session and got to call myself a 'student doctor'. Only to my classmates, but still!" This small revelation reminded me that all this hard work, all this effort, was going towards my dream of becoming a physician. Moments like these provide an opportunity for prospective reflection. Before I know it, this time of my life will become merely a memory. The mornings filled with coffee and Anki, the evenings where all I want to do is prolong conversations with my girlfriend at the dinner table. Medicine is a long and arduous journey, but the privilege of possibly helping someone in need will make it all worth it.

Sometime during my third or fourth week of classes, I felt I had traversed the initial hump of school and was on the downstroke. Like pendular motion, I experienced days where I understood every concept lectured at me. I also experienced days where every word out of my professor sounded garbled and unfamiliar. I experienced days where I didn't make it to bed until an hour later than normal. I experienced days where I took my girlfriend on a spontaneous dinner and movie date—on a Tuesday! Now, just as I am about to finish my first block of classes, I am settling into my routine. I know which days I need to spend all night studying and which days I won't skip my workout no matter how behind I feel. I know which days I need a little extra patience from my girlfriend and which days I carry out the cooking and cleaning. I also know that failure is going to come, that it's always looming. It might smack me in the face. Hard. But I'm anticipating that. I can only hope that all this prep will help me get up after I'm knocked down.

They say medical school is a marathon, but I disagree. It's more like a million sprints. Each day I am racing to get my reviews done in the morning, scrambling notes down as quickly as my professor is explaining one topic before moving on to the next. I rush from class to the gym, then home to cook dinner and hear about my girlfriend's day, then back to sitting in front of my computer to mentally solidify material from earlier. But I'm adapting. I don't always stick to my routine, but I always return to it. I know that this will all be worth it after that first patient encounter.

Sincerely,

Your MS1 Self

“Dear Human,” Let’s Talk About Your Relationship With Your Gut

By Jessica Hill, PhD, RN

Throughout one’s lifespan, the human gastrointestinal tract encounters a multitude of microorganisms. Some are only transient bystanders—imparting little to no effect. Others take up residence and participate in commensal and mutualistic interactions—contributing to our genetic diversity and our biology through critical functions like digestion, metabolism, and immune function. Alternatively, some interact in pathogenic or parasitic ways—disrupting the collective microbial community and our physiology. Those microbial communities which are stable and influence host fitness, for good or for worse, make up our gut microbiome.

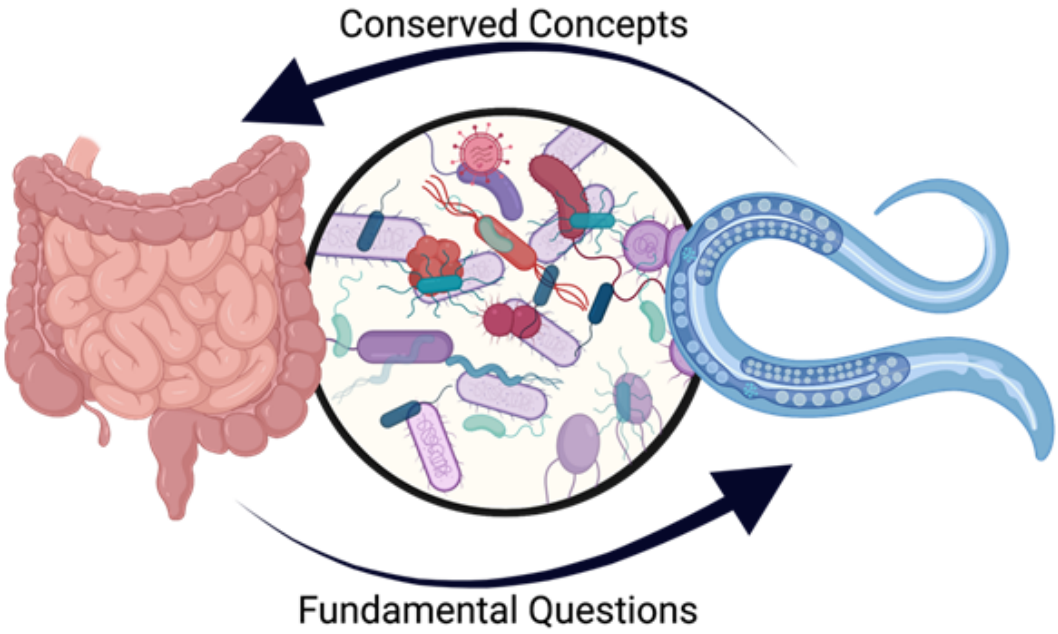
Given the far-reaching influence of gut microbes, it is unsurprising that they are considered critical determinants of health. Every so often, it seems that another disease has been linked in some way to gut dysbiosis—defined as a persistent imbalance of our gut microbial community. So how are these microbial relationships developed, controlled, and selected for?

Physical and chemical defenses implemented by our immune and non-immune cells are paramount to the division and maintenance of host (i.e., us) versus non-host (i.e., our gut microbes). While we typically think of these defensive measures as warding off potential invaders, they are also responsible for the positive selection of commensals and mutualists. Immunologic tolerance is one such example and is essential to the development of symbiotic relationships with our gut microflora.

Immune tolerance constitutes an active state of unresponsiveness to particular microbial signals. This delicate balance of offense and defense has been at the forefront of current microbiome research, as insights into its regulation are critical to our understanding of host-microbe crosstalk. Even though we have come far in our comprehension of gut immune function, there is still much that remains to be learned.

The primary barrier within our gut is a monolayer of polarized epithelial cells which forms the interface with our luminal environment. Here, intestinal epithelial cells act as distinct communication hubs, responsible for shaping and coordinating the activity of gut microbes and intestinal immune cells. Thus, they help regulate the development of inflammatory responses and immunologic tolerance within the gut. Intestinal epithelial cells come in a variety of flavors with some specializing in nutrient digestion and others in host defense. Although they are not considered bona fide immune cells, intestinal epithelial cells possess various innate immune receptors and defense mechanisms, allowing them to respond to and modulate gut microbes. Our understanding of host regulatory mechanisms however is very surface level, with this being a continuing area of intense research.

Currently, an intriguing area of study is how the mucus layer of the gut not only compartmentalizes gut microbes through the formation of a physical barrier but how it also regulates gut microbial composition.



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Goblet cells—a type of intestinal epithelial cell—produce and secrete mucus, which is made up largely of mucin glycoproteins. However, the mucus layer also acts as a reservoir for antimicrobial effector molecules and digestible sugars, allowing for the selection of beneficial symbionts and the repulsion of harmful pathogens. As we continue to learn more about the crosstalk that occurs between the intestinal epithelium and our gut microbes, we shall surely glean insight into how the gut microbial community assembles and influences our health.

An interesting model organism in which to study the basic principles governing gut microbial assembly and its regulation is Caenorhabditis elegans (C. elegans). This soil-dwelling nematode has recently been demonstrated to naturally harbor distinct and species-rich microbiomes.

C. elegans affords several benefits over traditional rodent models such as its simple and transparent body plan, stereotyped development, ease of maintenance, cost-effectiveness, and genetic tractability. Additionally, the C. elegans lifespan ranges from 2-3 weeks, allowing us to observe their full development and lifelong relationship with their gut microbiome. Most importantly, they maintain a high degree of conservation among core processes with other animals including rodents and humans. Although a bit unconventional, this 1 mm worm may just be what the scientific community needs to help address remaining questions concerning the fundamentals of gut microbial colonization, the dynamics which govern it, and how host-microbe relationships form and evolve.

Contributors

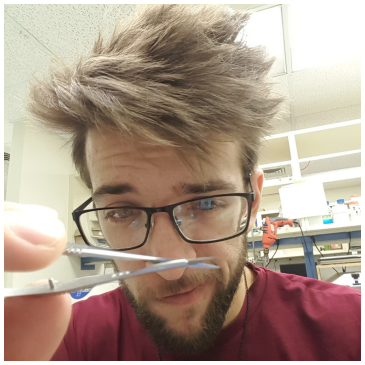
Elliot Graham is a graduate student pursuing his PhD in Food Science and Human Nutrition. His research focuses on how high fat and high sugar diets affect the abundance of microbes in the gut, contributing to cardiometabolic disease. In his free time, Elliot enjoys lifting weights, hiking, and, this should come as no surprise considering the department he is in, eating!

Jessica Hill is a postdoctoral researcher in the Nishimura lab with in the department of Biochemistry and Molecular Biology at Colorado State University. She works with the model organism Caenorhabditis elegans to study host-microbe interactions with in the intestine. At her leisure, Jessica likes to spend time outside with her family.

Sophie Seward is a doctoral student at Colorado State University. Her research is focused on the cardiovascular effects of sleep and circadian disruption. Sophie enjoys running and being outdoors and she is passionate about science communication.

Raj Trikha graduated with his Master's of Science in Human Nutrition in May of 2020. He began medical school this fall in hopes of working in academic medicine one day communicating the science of health to the general public. In his free time, Raj performs with a local improv team refining his craft of communication while trying, desperately, to make people laugh.

Lindsay Winkenbach is a graduate student pursuing her PhD in Biochemistry and Molecular Biology in the Nishimura lab. Her research is focused on understanding how the movement of molecular messages during embryonic development contributes to a healthy adult. Outside of the lab, she serves as the Co-President for the Graduate Student Council advocating on behalf of the graduate student body. Off-campus, she enjoys the Colorado classics of skiing, backpacking, and breweries.



Luke Whitcomb is working towards his Master's degree in Biomedical Science, researching metabolic dysfunction in heart and muscle cells. His interests lie in reducing the burden of chronic disease and combating health care inequity - as well as understanding how those two are linked. He plans to go on to medical school to pursue physician training, medical research and leadership in health care policy reform. In his free time, he enjoys black coffee, quirky podcasts and fast longboards.

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Photograph by Luke Treat

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