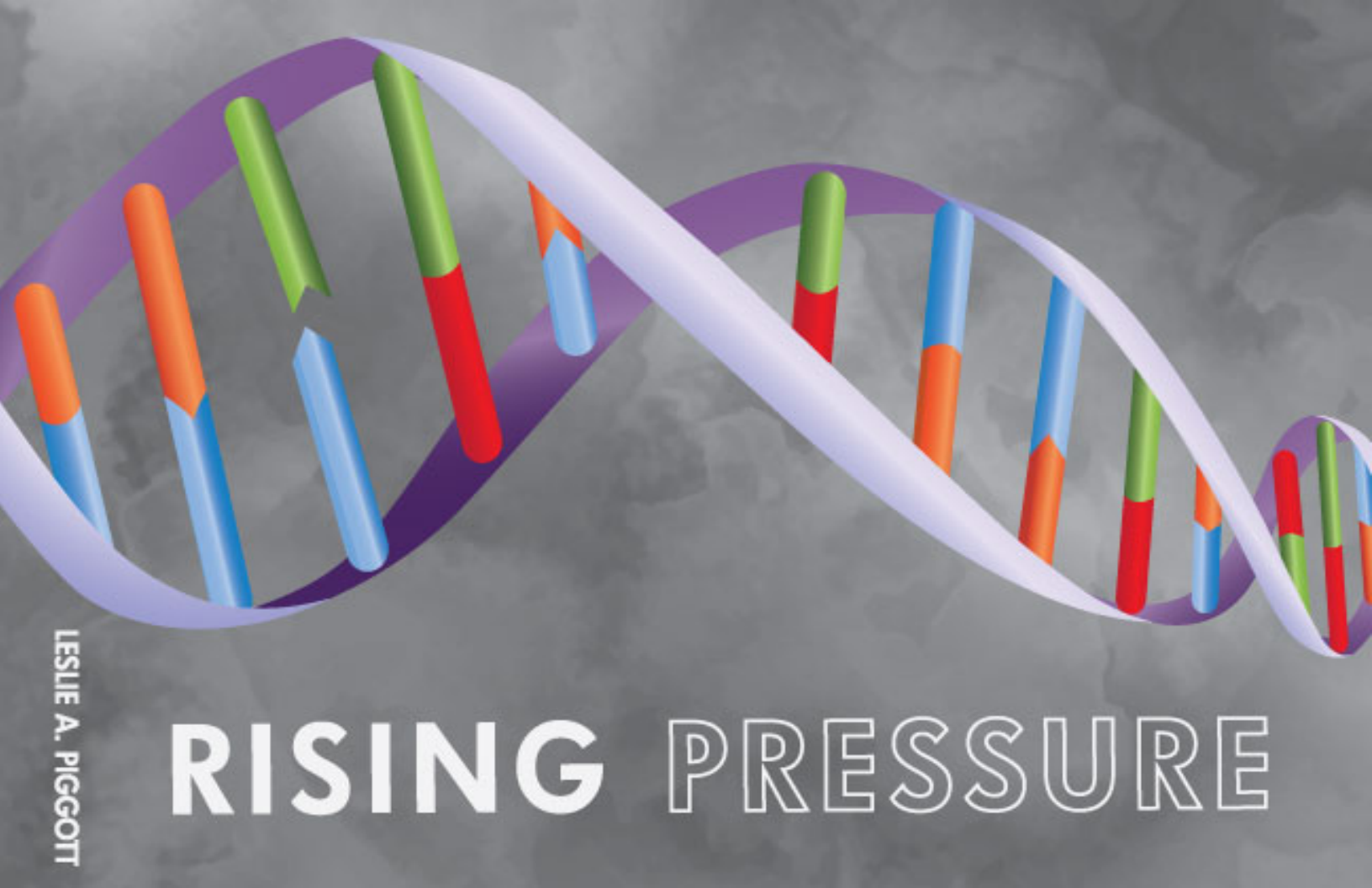

RISING PRESSURE

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Dedication

To Brad, Abby, and Simon: you are the joy of my life. Thank you for all of your support.

Acknowledgments

This is a work of fiction. None of the characters are real, nor are *Apothecom* or *Regulair*.

This book would not have been possible without the superb editing skills of Jennie Rosenblum. She helped me mold this story into something I think all of my readers will enjoy. Thank you, Jennie!

Danielle Johnston did a tremendous job on the cover art. I sent her a watercolor image of my idea and she made it shine. Thank you, Danielle!

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RISING PRESSURE

by Leslie A. Piggott

INDIES UNITED PUBLISHING HOUSE, LLC

Chapter 1

"Act natural, act natural," Dr. Emmitt Strydent coached himself as he stepped off the stage and approached the tall, copper-headed woman.

"Addison Feringer! Wow! What a small world. Who would have guessed that we'd end up at the same symposium? After all these years. I'm glad to see that the girl who challenged me for every local academic scholarship in high school is still putting her brain to good use. What are you up to these days?"

"Oh, hi, Emmitt. It's actually Dr. Fischer now. I'm married, 3 kids, have my own lab as a PI." Addison's blue-grey eyes flared as she tried to hide her offense at Emmitt's rather condescending comments. She had decided to attend the symposium after seeing his name as the keynote speaker. Emmitt Strydent had been the student she always tried to one-up in high school. Back then, he hadn't seemed so arrogant though.

"It seems like you have done well for yourself. I didn't realize you studied ion channels until I saw your name on a departmental flier. I enjoyed your talk."

"Well, thank you. It's an exciting world to be in right now. Dr. Fischer, you say? Of course. I know your work. I just never realized you were the same Addison from my younger years. A bit of a sodium channel expert, huh?"

Addison relaxed a bit when he complimented her. Maybe he was just another man that didn't realize how their vocabularies were outdated when it came to women in science.

She smiled. "I'm trying to carve a path, yes."

"We should grab lunch. Do you have time? I'd love to catch up."

She hesitated. She really needed to get back to the lab. One of her graduate students apparently needed constant supervision in order to finish his work and get to the point of writing his dissertation. She had a meeting set up with him for 1:30 that afternoon and wanted to review his scope before sitting down with him.

"C'mon. I won't keep you forever. It will be a quick lunch, I promise." Dr. Strydent extended his hand.

"Okay, I can squeeze in a quick lunch for an old friend. There's a café over by my building. Sandwiches and soup work for you?"

"Sounds perfect. I'm going to grab my rental car and pull it around. What's the restaurant's name?"

"'Santouits.' It's Greek for sandwich. I'm walking, so I'll see you there." She turned to grab her bag and headed for the exit.

"Clever. See you there." Dr. Strydent called after her, a smug grin on his face.

As Addison headed out the double doors of the auditorium, she thought back to her time in high school with Emmitt. He had been a hard worker and dependable as well as an athlete. He was the quarterback of their football team and a starting forward on the basketball team too. In their small town, everyone did a bit of everything, and he had excelled in multiple fields. She never expected to find him as a colleague of sorts in the academic world. Addison picked up her pace. Maybe she could get to the restaurant before him and look up some more background on the man. Rounding the corner, she saw the blue and white awning of the café up ahead. She'd grab a table and get to work.

As the hostess led Addison to a table for two near the salad bar, Addison pulled her phone from her bag, unlocking it. She was in the process of typing his name into the Google bar when she realized the hostess had asked her a question.

She looked up. "I'm sorry. I wasn't paying attention."

"Will your companion be here soon? Should I bring waters? Menus?" The hostess glanced around the dining area hinting at the busyness of the lunchtime rush.

"Oh yes. Any minute. Waters and menus would be great. Thank you." Addison said as she looked back to her phone screen.

Emmitt had done really well for himself. Numerous papers in high level journals, big lab at a big university; he was definitely a leader in the field. A recent news article hinted that he might be being considered for the Nobel Prize in medicine before too long.

He had discovered a protein involved with stabilizing ionic channels into cell membranes and displayed its role in regulating blood pressure. Not only that, he had taken his discovery a step further to identify an important mutation in this protein, which he named STABL. Fascinatingly, this mutation was found in the majority of otherwise seemingly healthy people that suffered from chronic high blood pressure.

Addison checked her watch and glanced around the café. Emmitt should be arriving soon, but she just wanted to read a little more about him. She went to the NCBI database and started to pull up some of his papers to see what methodology he typically used. In his talk earlier, he'd spoken in clinical terms regarding blood pressure control and less about the basic science he'd used to break down the puzzle of high blood pressure. She had just started to download his latest paper when she was startled back into reality. She quickly turned her phone's screen off as she looked up. Emmitt was standing next to the table.

"Doing some light reading before lunch?" He laughed.

Addison felt her cheeks start to flush. "Caught me red-handed. I was just reading about all your amazing discoveries. Fascinating work, Dr. Strydent."

"Sometimes I can't believe how far we've come. It's an exciting ride, for sure. But please, call me Emmitt." He beamed while taking a seat at the table. Addison realized that he still had his boyish good looks even though his hair had a few grays sprinkled in around the temples. If not for those, most people probably would have mistaken him for someone in their early 30s rather than a man pushing close to 50.

Just then, the waitress stepped over to take their order. The small café was filling up quickly and anyone could see that she was running from table to table to keep up. She had her pen and notepad up and ready.

"Oh wow! You got over here fast. I've never been here before. What would you recommend?" Emmitt said, looking at Addison.

"I always get the egg salad with tomatoes on honey wheat toast. It's delicious. Honestly, it's what I ordered the first time I

came here and I haven't tried anything else. Ryan, uh, my husband, usually orders the tuna." Addison said quickly as the waitress scribbled on her notepad.

"Egg salad it is. I'll get an iced tea too, if it's not too much trouble." Emmitt smiled.

"Sweet or unsweet?" The waitress responded.

"What? Oh right, the South and its sweet tea. That will be UN-sweet for me. Thank you."

The waitress gathered their menus and rushed off to the next table.

"Busy place. Is it always this crowded?" Emmitt asked.

"Ummm, I don't know. I usually order mine to go or Ryan picks it up. I haven't really paid attention, I guess." Addison stuttered a bit. Being around Emmitt again brought back memories of trying to match him in high school. Being female, she often wasn't taken as seriously as the boys in her classes. To be fair, most of the women in her small town were either stay at home moms or elementary school teachers. She was used to breaking stereotypes. She mentally chided herself for not having her usual self-confidence. "Anyway, tell me about your research. What questions are you trying to answer, Emmitt?"

"Still not one to mince words, huh?" He chuckled. "Well, my work started out on the fringe of ion channels. After college, I knew that I wanted to go into science research but wasn't sure what field or pathway. It seemed like everyone was heading to cancer research, and rather than be a small fish in a big pond… well you know the phrase, I'm sure. I decided to pick a relatively common disease that was poorly understood and stumbled onto blood pressure regulation. My advisor, Dr. Watt—"

"Wait, what? Dr. Watt?! As in Dr. Benjamin Watt?" Addison blinked.

"Ha ha. Yes, the one and only. He's your boss, your department chair, right? I'm surprised you hadn't found the common thread yet."

"It's a big department. He was only hired as the chair last spring." Addison explained.

"Oh, well that makes sense. It takes time to get to know the

help." Emmitt winked while Addison inwardly groaned. Emmitt still had the boyish charm that had helped him gain fame and popularity in their town. She respected Emmitt's intelligence, but only barely managed to paint on a grin in response to his joke. He cleared his throat and continued.

"Anyway, as you know, Dr. Watt studied membrane proteins and blood pressure, so I set up a meeting with him and knew I'd found my home. As you also know, he studies the proteins in the cell membrane by looking at their structures. The human genome had just been sequenced, so he was looking for anything that resembled a membrane protein within the endless genes in our DNA. He looked at things like a puzzle. You know, if this piece in the membrane has this shape, then there must be something else that fits in next to it, and so on. It was brilliant! He had a whole list of proteins that I could pick from to study for my dissertation. Sometimes it feels like I won the lottery. I picked STABL because it's small, one of the last five by size on the list. Of course, that list has just continued to grow in size over the years." Emmitt spread his hands as he finished speaking.

"That's incredible. But don't sell yourself short. You've really taken STABL to the big leagues, from what I've read. You made STABL. It sounds like it could be life changing for some people."

"I sure hope so. That's what got me into research. I wanted to make a positive impact on the health of others."

"So, what method do you use to study structure? Crystallography?"

"Yes, Dr. Watt has a great system for isolating membrane proteins and then figuring out their structure with crystallography. Side note, it is so nice to talk science with someone that understands it. Whenever I try to explain crystallography to my mom, she just glazes over. I try to simplify it, you know? It's so hard to get it down to her level, though. I remind her about growing salt or sugar crystals for science fair projects, but my crystals are just microscopic and require an electron microscope to view them. She waves her hands around and changes the subject. Ha ha."

Addison laughed. “It’s definitely a challenge to break things down into layman’s terms. I hate to eat and run, but I’ve got a grad student that I need to ride herd on. He cannot stay on task. Sometimes I wonder if his unspoken goal is to break the record of longest stint as a student before defending a dissertation.”

“I understand. There’s always that one student, huh? Let me give you my card, so we can stay in touch. Maybe there’s something we could collaborate on in the future.” Emmitt pulled a business card from his coat pocket.

“That sounds great, Emmitt. I’ll be in touch.” Addison took his card and tucked it into her bag, while signaling to the waitress for the check.

“Please, let me pay. I took you away from your schedule. I’ll take care of the bill while you get your student back on track.” Emmitt waved off her wallet.

“Don’t be ridiculous. We can just split it.” Addison pulled ten dollars from her wallet as the waitress laid down their ticket.

“As you wish. Thanks for joining me. It was great to see you again.” Emmitt said as they shook hands.

Chapter 2

Addison walked the short block back to her lab, excited at the possibility of collaborating with the Strydent lab. Her department chair would surely welcome the idea, as Emmitt was his former student, not to mention associating with someone as renowned as Emmitt could only be profitable for the lab as well as the department. Swiping her fob to enter the building, she pulled her phone out as she walked over to the elevator bay. Ryan wouldn't believe the opportunity that just fell into her lap.

"*You'll never guess who I ran into today. Tell you all about it at dinner tonight."*

"Sounds exciting. Hope he isn't hotter than me!"

"Where's that eyeroll emoji when you need it…love you!"

"You too."

Addison smiled as she stepped off the elevator. Ryan loved to joke around with her and always knew how to make her laugh. They kept a running banter going day in and day out. She checked her watch. She had twenty minutes before her meeting with Anthony. Time to find a way to get him on the straight and narrow.

She unlocked her office and logged into her computer. She had opted for an interior office that didn't have a window so that her lab could have windows. Most of the full professors in her department had office windows, but she figured that having a happy staff was more important. She had room for a fairly large desk, a cushioned office chair on wheels, two extra chairs as well as a filing cabinet that held most of her previous students and postdoctoral fellows' old notebooks. It was cozy, but it worked. She had several photos of her family on the walls, as well as her own diplomas.

Pulling up Anthony's file, she sighed. He was such an intelligent student, but he was SO lazy and messy. He was running through reagents and money without making any progress, but part of her role was to help him find his niche. What could she say to help motivate this kid?! He had started out promising and seemed fairly knowledgeable about the lab and the

techniques. All that fell away quickly after he finished his classwork within the degree program. Now that he was just completing experiments to round out his dissertation, he barely put forth any effort.

Although, she had to admit that his lab etiquette had been pretty rough from day one. He constantly "borrowed" solutions or reagents from other lab members, usually without asking. He rarely cleaned up after himself, frequently leaving full ice buckets out on the countertop for someone else to empty. Her lab assistant, Eleanor Ritkey, was very kind and forgiving, but Addison was fairly certain that she kept many of Anthony Wydrow's blunders to herself. The other lab members were much more forthcoming in regards to his messiness and *borrowing* habits. Addison had to continually remind him that not every lab would be so forgiving, and he needed to take care of his area and prepare his own reagents. Hearing the shuffle-step she recognized as Anthony's reluctant walk to her office, she pulled out a notebook and pen for their meeting.

Anthony was an attractive young man. Addison sometimes wondered if he had relied on his good looks and charm instead of his intelligence when he was in high school and college. He was a few inches north of six feet tall with dark brown hair that he kept a little longer than average, much like a California surfer. His eyes were dark blue to the point of almost seeming to be black when the lighting was right. The twenty-eight-year-old had come to her lab from the west coast and definitely had the *take it easy* air about him.

"Hi Dr. Fish. I brought my lab notebook. I got it all organized, just like you asked."

Addison looked up to see a binder with some pages hanging out unevenly from multiple sides and stifled a grimace. She couldn't bring herself to wonder what it looked like in an unorganized state.

"Wonderful! Let's see where you are with your project," Addison smiled as she reached for the binder, moving her own notebook to the side. She opened the binder carefully, hoping not to dislodge any free papers that hadn't been successfully locked

into place within the 3-ring binder. She gently flipped through the pages to where they had left off two weeks before and realized there was only one more page remaining.

"Anthony! Have you only done one experiment in the last two weeks?!" She asked, exasperated.

"Well, you see, Dr. Fish. I had planned to do more, of course. I set up an experiment for last week, but I think the power went out or something on my incubator. All of my cells were dead and floating when I went to harvest them on Thursday, so I had to scrap that idea. The page you're looking at is from my experiment this week." Anthony held his hands out, palms up, hoping for leniency.

"But, Anthony! You still need to keep a record of a planned experiment even if you don't get positive results from it—yes, even if you don't get to complete it. There is always something to learn from a failed experiment. I heard about your incubator problem. I don't think it was a power issue as no one else in the lab lost cells or experiments last week. Are you certain that you got the door completely closed when you put the cells back the day before? Small changes in temperature or humidity can result in cell death. You have to be very careful." Addison sighed. This meeting was not starting well.

"I mean, I thought I did. I'm sorry, Dr. Fish." Anthony said timidly. Addison sometimes felt like she was talking to her teenaged son about leaving dirty clothes around his room whenever she met with Anthony.

"Okay, well there's nothing we can do about that now, except try to be extra diligent from here on. You really do a great job with your experiments when you actually do them, Anthony. You aren't that far away from your next committee meeting, you know. If you really put in the work, you might have enough data to get permission from them to start writing your dissertation. You have great hands, Anthony, and you're really smart. You could make a great PI someday." She said encouragingly.

"Really? That's great to hear. I feel like I've been spinning my wheels on this for a long time and not really making any progress. PI. Wow! That acronym always makes me laugh. Like

we're undercover agents, not principal investigators—scientists! Ha, ahem." He cleared his throat when she wasn't laughing. "What are my next steps? What is my research missing?"

"As I said, you have really done a good job with your project, you just need to focus on completing it. Talk to me. Tell me what story you're trying to convey with your project. Getting your doctorate isn't just about doing experiments; it's about understanding why you did which experiments as well as what the results tell you." Addison knew that Anthony understood his project conceptually, but she wanted him to realize that too. Maybe that would help him see the big picture of getting it finished soon.

"Okay, right. Ummm, it just feels kind of funny explaining my project to you when it's really YOUR project from your grant and…" he coughed in response to her raised eyebrows. "And I would be happy to tell you all about it. My project tested the hypothesis that the sodium ion channel, $Na_V1.5$, is regulated by the small protein, alpha9. When alpha9 is activated by phosphorylation, it triggers $Na_V1.5$ to open, allowing the flow of sodium ions across the membrane. If you block phosphorylation with the drug mexipres, the flow of sodium ions is decreased. Furthermore—"

"Okay, I'm going to stop you for one second. We tossed around the idea of you writing an abstract in layman's terms. You know, something that your non-science friends or your parents or your great-aunt Bertha could understand. Have you thought about that anymore? Why don't you just try it for me, really quick? It's really an important exercise."

Anthony groaned and slumped his shoulders.

"Okay, Dr. Fish. Let's see. My project studies an ion channel —wait, can I say ion channel? Okay. My project studies an ion channel that is positioned within the outer membrane of heart cells in mammals. This channel opens to allow sodium ions into or out of the cell. A lot of things are responsible for getting this channel to open or close. My advisor identified a small, um molecule? Can I say protein? Okay, a small protein that plays a significant role in the opening and closing of the sodium channel

in the heart. This protein is called alpha9. My research shows that alpha9 gets turned on or activated by a process called phosphor __"

"You can't say phosphorylation. That is a ten-dollar word. It will be the beginning of eyes glazing over and your audience tuning you out." Addison interrupted.

"I was going to explain what phosphorylation is. I just hadn't gotten there yet."

"It's not necessary. While it is something *you* have to understand and explain as part of your dissertation for your degree, it is not necessary to explain to a lay audience. Continue, please."

"Fine. So, alpha9 gets activated, which results in a special signal—" Anthony paused to see if Addison was going to stop him again. "Signal to the ion channel. The activation of alpha9 causes it to, um, change shape, triggering the channel to open. The activation is not long-lasting and, much like flipping a light switch, alpha9 returns to its original shape and the ion channel closes. I hypothesized that the activation of alpha9 was a key step in the opening of the ion channel as well as one that could be regulated pharmaceutically." Anthony grinned as he finished, clearly pleased with his summary.

"That was actually very good, if you leave out the ums and the random pauses. It's important for us, as scientists, to be able to simplify our language into layman's terms. While the majority of funding for basic science labs comes from the government, from NIH, occasionally, you will come across grants from pharmaceutical companies that are not necessarily reviewed by scientists that have a firm grasp of your field of study. Also, NIH grant money is made possible because people pay taxes, but the budget for NIH can change at any time. If the people setting the budget don't see a need for your research, then the budget could decrease. Okay, okay, I'll get off my soapbox. Let's figure out which experiments you need to finish up your story." Addison said, grabbing her notebook and pen.

"Every experiment needs to be completed in the same way at least three times so that you can do statistical analysis on it. It

cannot be included unless you have shown that it is repeatable. Let's make a list. You have the first experiment showing the interaction between the channel and the protein. I know you did that one several times, right?" Anthony nodded. "Okay, good. Then the experiment showing the phosphorylation of alpha9 in response to the stimulus…" Addison flipped back through the binder to count the experiments.

"Okay, I found four. You definitely used all the same solutions and conditions, right?"

Anthony shrugged. "I mean, we only use certain ones, right? So, sure. I must have."

"You really need to do a better job of taking notes on your experiments. Okay, continuing on. The next experiment was to show that you can block alpha9 activation with mexipres, our pharmaceutical regulator. Thankfully, you repeated that one enough times so we don't have to go through the headache of working with the radioactive materials again. I don't think the rest of the lab could tolerate your care, or should I say, 'lack thereof' in handling radioactive isotopes again. So, what completes this story, Anthony?" Addison looked up, hoping her young student could connect the dots.

"I need to show that blocking phosphorylation also decreases channel activity. The best way to show that is the whole-cell patch experiment again, right? I run the experiment under normal conditions, then add the drug mexipres and show how it changes."

Addison beamed. "Perfect! That's exactly the experiment that you need to do."

"I was afraid you were going to agree. Those experiments are so tedious. And it's not just three times. I have to get multiple readings from multiple cells on multiple days. It's going to take FOR-EV-ER." Anthony slumped again.

"Oh Anthony. Chin up. You've already made it this far. Buckle down. You can do this. To help you stay on track, I'm going to need weekly updates from you."

"But—" Anthony started to protest.

"No. No complaining. You know what to do. There is no

reason this should take more than another few months of work. It could possibly take less. Go get to it. Eleanor can help you thaw out some new cells if you need them."

"Oh, I uh, just got some from Becky on Monday."

"Please tell me you asked first."

Anthony shrugged.

"You really need to be more responsible. Becky is a second-year student. You should not be taking reagents from her. You should be helping her, not pilfering from her supplies. You're better than this kind of behavior, Anthony. You have so much potential. In fact, there is a decent chance that I might have found a possible postdoctoral collaboration for you today. I ran into a former classmate…anyway. I can't recommend you to another lab if you continue to have such poor lab etiquette. It would reflect badly on me too." Addison admonished him.

Anthony looked at his feet. "I'm sorry, Dr. Fish. I know, I know. I'll try to do better."

"*You know what Yoda says…"* Addison thought as Anthony turned and walked out of her office.

About the Author

Leslie A. Piggott lives in the Austin, Texas area with her husband and their two children. She is a scientist-turned-mom who received her doctorate in Biomedical Sciences from the University of Texas Health Science Center at Houston. In addition to writing, she also enjoys running marathons, quilting, knitting, singing in the church choir, and watercolor painting. She has previously published two watercolor and poetry books, both in 2021: Poems in the Pandemic, and Art in Words. This is her first novel.