Chad Cowan

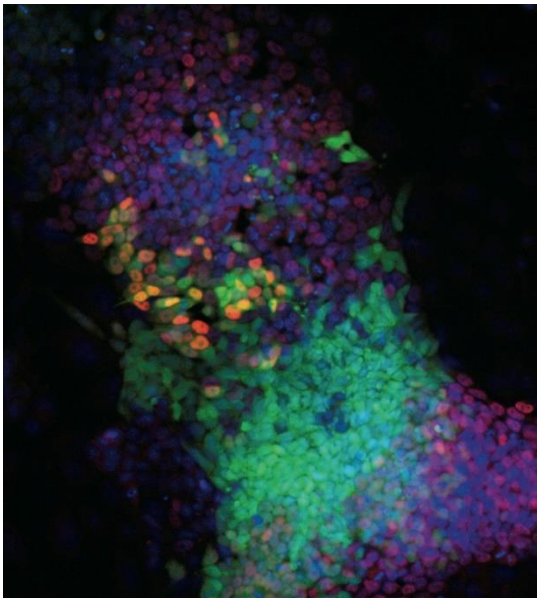
8. September 2022

My name is Chad Cowan.

This is what I do: I am the Chief Executive Officer and Co-Founder of a biotechnology company Clade Therapeutics. At Clade, we discover and deliver the next generation of cell medicines to improve the lives of patients.

This is what I could teach you, that you cannot learn from a book: How to translate discoveries in the lab to create new medicines. Why some discoveries you read about in a textbook, or a scientific paper become new medicines and why others do not.

This is what culture means to me: Culture is often referred to as the way of life for an entire society. I spend a considerable amount of time thinking about certain aspects of culture. In particular, our scientific knowledge and its depth and breadth in certain areas of biology. I also think about the norms and habits that help build effective teams, as this is an important part of building a company.



This is how my work reflects my culture/s: Western culture has become a very science driven culture, and as a result, my
forming a company that leverages recent discoveries to create new medicines is the culmination of one story line in modern culture.

This is my utopia: In my utopia, we would all work together in the service of the world and/or humankind.

Quick bits

My favorite book genre: Sci-Fi/Fantasy

My favorite book: Grapes of Wrath

My favorite place to read: Our sunroom

Where I buy my books: I don't buy books, I check them out from the library.

My favorite museum: The Cape Ann Museum

My favorite artist (painter/sculptor/performance): This is too difficult a category to name just one.

My favorite source/s for news/information/further education: I read the New York Times and Wall Street Journal every day. I get a tremendous amount of information from scientific publications. I also read a lot of non-fiction books.

My favorite dish to eat: I love sea food

My favorite outside activity: Anything on, in or near the water

My favorite place in Annisquam: Wingaersheek Beach

A scientist’s weekend

23. November 2022

Fall is in full swing here in New England. It is always hard to let the last days of summer go, but with their passing comes the routine of school and work. I am definitely a man of routine. I wake early (5:30am) and spend the first 30 minutes of the day feeding the dog, catching up on reading and the news and getting my kids out of bed. I exercise, a run or a walk or yoga, anything to get the blood moving. Then it is time for work.

I have just changed careers and am challenged every day at my job. For most of my professional life I was a professor at Harvard University, where I taught undergraduate and graduate students and ran a research lab. Eight years ago, I helped start and then led the research of a new company that sought to harness the newly discovered CRISPR/Cas gene editing system to make medicines. We did the early pre-clinical work to build medicines for CRISPR Therapeutics, which now has several medicines in patients. Today, many people with sickle cell disease no longer have any disease symptoms and lead largely normal lives as a result of our first medicine at CRISPR Therapeutics. This forever changed the course of my career and has put me on the path to working on the commercial side of drug discovery, or “biotech” as it is often referred to here in the Boston area. We have combined some of the key discoveries from my academic research lab with several additional advances in the field of stem cell differentiation to form a new company Clade Therapeutics.

CLADE THERAPEUTICS

At Clade, our goal is to make cell-based medicines accessible to everyone. The success of CAR-T cell therapies, wherein a patient’s own T cells are modified to express a chimeric-antigen receptor or CAR that targets cancer cells has proven the value of cellular medicines in fighting and in essence curing otherwise lethal cancers. The problem with these therapies is that they are only available at a few very highly specialized research hospitals, and they

cost millions of dollars to produce. We aim to change that by differentiating induced pluripotent stem cells into T cells that look and function the same as the T cells taken from patients. Arm these with a CAR, and you now have T cell therapies for everyone with a given cancer. We hope that by changing the scale and consistency with which these cell medicines can be produced we will also change their costs, so that in the long run these medicines become available globally for every patient in need. Day-to-day, I am excited by working with our research team to overcome some of the technical challenges that stand in the way of making our goal into a reality. I enjoy the process of solving hard problems together with some enormously talented scientists. This part of my job is not so different from running an academic research lab. The new challenges for me lie in learning to build and lead an organization that has all of the critical skills and know-how to make new medicines. In particular, I am not a gifted people manager, so learning to listen and understand everyone's perspective and knit those together into a tapestry of teamwork has been my biggest learning experience. I love learning and I am blessed that my new career has stretched both my academic knowledge and my people skills to their limits.

After work, I love spending time with my family. An important part of our day is dinner all together whenever possible. We sit at our dining room table, light the candles, eat on the fancy china, use the silver, and discuss our days. One of favorite things to do is to have one member of the family read a poem aloud. We keep several volumes of poetry next to the table for just this occasion. We have an eclectic mix of poems, some based on science, some from the acknowledged masters of the art and a few irreverent items such as poems from Cookie Monster and those told from the point of view of family pets. No matter who the author is we usually have a laugh or a thoughtful moment.

As my sons are both young and full of energy, we also have a new family rule that if you leave the table without asking to be excused you have to do a "chicken dance". We get one of these almost every night and it leaves all of us with a smile on our face.

This weekend we have the regular fall sports for our guys, soccer and tennis and the Annisquam Village Arts and Crafts Fair. The Arts and Crafts fair brings together artists and craftsmen from all over Cape Ann (this is the small island we live on that

has the larger cities of Gloucester and Rockport). I volunteered to work the “floor” on Saturday helping people with their purchases and keeping an eye on the merchandise. All of the proceeds will go to benefit the local church and the Annisquam Village Hall Association, which is a community center, library, community theater and gallery open to everyone. So, a packed weekend with fun for all ages.

Written by Chad Cowan

Language and Science

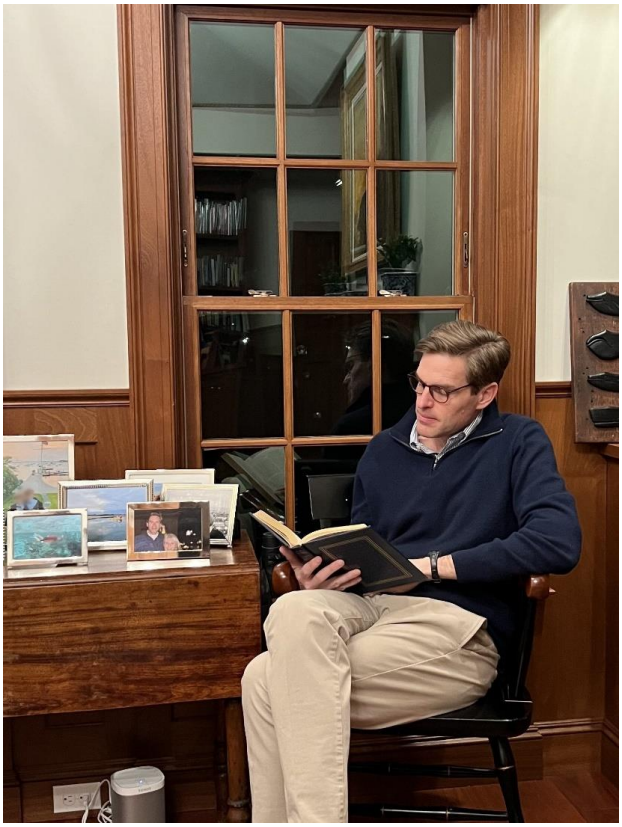
27. März 2023

T.S. Eliot begins the “Wasteland” with a line that has always stuck with me, “April is the cruelest month.” Now a resident of the cold northeast where he lived, I understand better than ever the sentiment. Although, I would argue it is March that has proven cruel this year by reminding us of winter’s doldrums. The last two months have been filled with work and colds and dark mornings and dark afternoons, but I see the beginnings of spring. At work, we are busy making plans for more social outings, including a company-wide event. At home, we are packing to go away for two weeks of glorious vacation in the Bahamas. Together these efforts combine what I seek in life, purpose, and joy. It has taken me years to realize that joy is not a private matter but found amongst those we love and those we live with and are together with. A hard truth to come by for a dedicated introvert. So, let’s hope some fun together will bring joy and make April seem less cruel.

As I have been reminded, this blog should speak about how my career path uses writing and language, so to business then. I am a scientist by training and now by mindset. In science, our greatest hope is to discover something worth communicating to others, be it a simple innovation or a deeper truth. As a native English speaker (if we as American’s can claim this), it has been my great fortune that the language of science is English, otherwise I may never have made progress in my chosen profession given my lack of facility in any other language. The reasons for English becoming the language of science are many and not worth re-hashing, but as of today, most if not practically all scientists communicate in a common language. We seek to share our insights and the problems we set ourselves against with the likeminded and learn from those who tilt against their own windmills but have inadvertently solved some of the riddles we seek to puzzle through.

As a result of our common language, I have travelled the world as an academic scientist and attended conferences on almost every continent (Antarctica is missing from my travels). It has been my pleasure to exchange information freely with scientists everywhere I’ve gone because we’ve agreed to communicate in a single language. Science and the community it fosters, transcends nations, cultures and

creeds. In a way I have never witnessed in any other endeavor, except sports, it unites us. In my lab at Harvard, we had people from all over the world working together on a common problem. The same was true in the lab next door and the one across the country in California. In the company I've founded, it is the same. People from all walks of life gathered around a common purpose and united in their ability to exchange information in a common language.



A final digression, I have taught many scientists over the years how to ask questions and design experiments that will help them understand the answers. The most important lesson I have imparted to those I have worked with the longest is that the best scientists are often also the best at telling stories. As humans, we have always been drawn to stories, whether around the campfire, in print, on the stage or on the screen. It is no different, in science. The scientists I admire take our limited understanding of the world around us, craft a story and tell it. In a way, they are like poets and playwrights for the natural world.

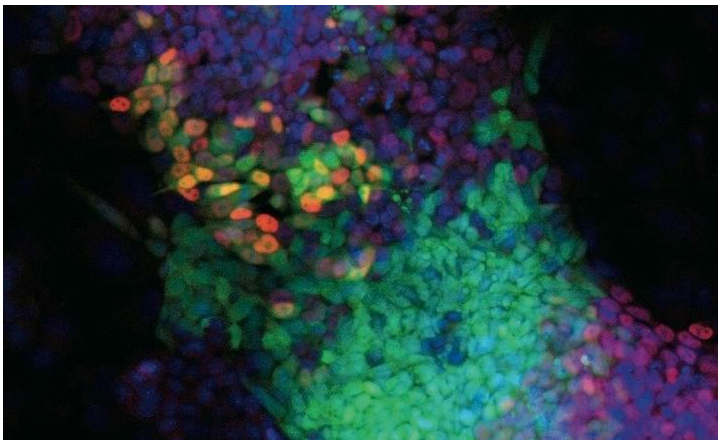
My last words of wisdom for my students, is that whether we tell others stories or not, we are always telling ourselves a story. To make sure the facts as we have collected them agree with the story, we tell ourselves before we tell others. In other words, be willing to rewrite your own story rather than fall in love with the first draft. Otherwise, you may do the world a disservice and communicate a fiction versus a description of the wonderful world around us.

Written by Chad Cowan

CLADE THERAPEUTICS

BIOTECHNOLOGY as more than just a JOB

23. August 2023



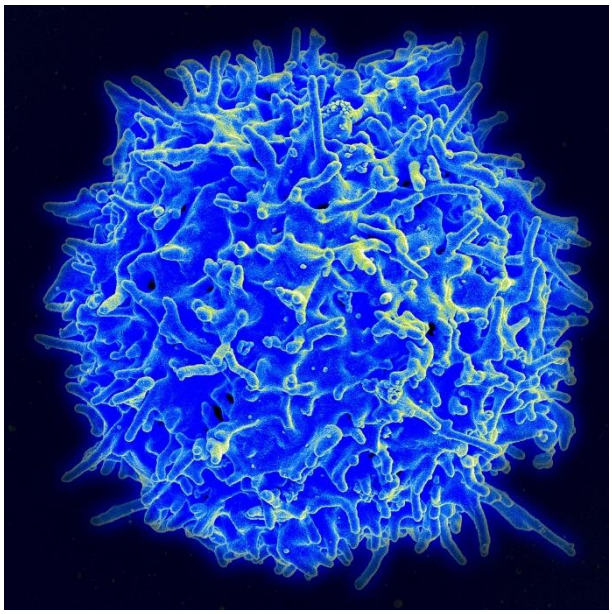
It has just started to feel like summer in **New England** and we are all getting ready to make the most of every sun-drenched, light-filled moment. For this installment of my blog, I thought I might try to answer a couple "**Big Questions**," notice the capital letters. The first question is **what do I do and why**? The second is **what are the differences between a job/work, a profession/occupation, and a calling/passion**?

In response to the first question, I have written before about the small biotech company, **Clade Therapeutics**, that I founded with two of my colleagues. What I may not have done is explain what we do. We are a cell therapy company, which means that we make drugs, but instead of a pill or an injection, **the medicine we are making and will deliver to patients is a cell**.

Many people may have already heard about some of the early breakthrough treatments with cell therapies. The most common of these are **CAR-T cell therapies**, wherein T cells are taken from a cancer patient "armed" with a CAR (**Chimeric Antigen Receptor**) and then reinfused. These CAR-T cells then specifically identify cancer cells and kill them. These treatments have been referred to as "miraculous" in that they have not only saved the lives of cancer patients, but have, in many cases, eliminated the disease. The problem with these therapies is that they are time consuming and difficult to make and bespoke (each patient's cells become the medicine). As a result, they are very expensive and difficult to manufacture, limiting the numbers of people who have access to these life-saving medicines.

At Clade Therapeutics, **we aim to democratize access to cell therapies, beginning with the CAR-T cell therapies that have proven so effective to date. We do this by combining a set of key innovations that are the culmination of the more than 20 years of academic research I performed while at Harvard University.** First, we start with a source of cells that are capable of making enough T

cells for everyone to receive cell-based therapies. These cells are called **induced pluripotent stem cells** (**iPSCs**) and their discovery by **Dr. Shinya Yamanaka** won the **Nobel prize in 2012**. What makes these cells special is that they have limitless self-renewal, meaning that they can divide and make more of themselves essentially forever. The other thing that makes them special is that they have the ability to differentiate into any cell in the adult human body. Put these two powers together, and you have a source of cells that can make a limitless number of human T cells from.



What we have worked on at Clade Therapeutics are the two key technologies necessary to fulfill the potential of iPSCS to produce new medicines. **First, we have focused on how to teach these cells to become T cells**, a process that in many ways mimics the natural development of these cells in your body, but we do it **in stirred tank bioreactors**. Our "secret sauce" is to differentiate iPSCs into cells that, for the most part, are indistinguishable from the T cells you would take out of a patient's arm. The difference is that we can make tens of thousands of patient doses out of these cells (instead of one patient at a time), and they are all the same quality (not sick or old or too few, like in some patients)! **Second, we have had to overcome one key barrier to using these cells for therapy in everyone, namely transplantation rejection**. The reason we currently use cells from a patient to treat a patient is that these cells are seen by the person's own immune system as "**self**" and are not rejected. If one tries to put cells from someone else into a patient, they are rapidly identified by the immune system as "**not self**" and are therefore rejected, or killed. We have taken a page from pregnancy to help solve this problem. Every pregnant mother should reject her developing fetus, as it is also "not self," with at least half being derived from the father. This so-called **"paradox" of pregnancy** has baffled and intrigued researchers since it was **first described by Sir Peter Medwar in 1953**. Recently, **we have identified "why" mothers don't reject their developing fetus**, and it is because the cells in the placenta have mastered the art of "**hiding**" from the mother's immune system. We have adopted a similar strategy wherein we genetically modify iPSCs so that they are immunologically hidden from the immune system, a technology we call "**immune cloaking**". By building these genetic changes into iPSCs, we can now make a limitless number of T cells that can be safely transplanted into anyone for the treatment of cancer. We are also exploring the ability to make other adult cell types from iPSCs, including other blood cell types and cell types that are often lost or damaged in disease, such as insulin producing

beta cells. **Our hope is that one day patients everywhere will have access to safe, affordable, lifesaving cellular medicines.**

And now for the second "Big Question", what is the difference between a job/work, a profession/occupation and a calling/passion? When I was younger, I had a more black-and-white view of these words and what they meant to me. I have always told people (especially my students) that **if you do what you love, it won't seem like work**. The problem with that advice is that for many it is difficult to find something they love doing that they can also make a living at. The other truth is that, even when you love what you do, sometimes it feels like work. I have been lucky in that I have always had a passion for science and especially experimental science. My career has been to be an experimental biologist, and I feel as though I have followed my passion, made it into a profession, which is now my job. **I no longer think that I have to make some great discovery, or win the regard and acclaim of my colleagues to be successful. Now, I measure my profession/work by the benefit it brings to my family and others.** If I am helping to make my family's life better and more comfortable, I feel as though I have been successful. If I am so lucky as to have my work improve someone else's life, then I have achieved something truly special, I have a made a difference. **I now give the advice that it is best to make sure that whatever you do, you are doing it with the goal of helping others (or the planet).** This at least helps me get out of bed every morning and feel excited to "go to work." I know this is an unsatisfactory answer to the question posed, but as I have gotten older, rather than black and whites and clear distinctions, I seem to see more grey between all choices and more similarities between, for instance, a job and a calling. I just count myself lucky to have a reason to get out of bed each day! If that reason is fun and interesting, so much the better!

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CLADE THERAPEUTICS