Episode 45—Donna Blackmond: Solving the origins of life and other mysteries in chemistry

Lauren (00:08):

Hello listeners and a warm welcome back to Science Changing Life. I'm your host, Lauren Fish. Today we're speaking with Scripps Research professor and chair in the Department of Chemistry, Donna Blackmond. In this episode airing during our centennial year, Donna will be taking us back billions of years to the prebiotic earth, showing how the earliest chemical reactions eventually gave rise to life as we know it today. But first, she tells us what sparked her passion for science in the first place.

Donna (00:37):

Mostly the decision to go into science was driven by my family. My father is an electrical engineer and he came up in the 1950s, went through college with the GI Bill. Never would've had money to go to college without that. He was very adamant. I have four sisters and one brother, so six kids in the family, pretty big family, and he was very ahead of his time from early sixties basically saying he didn't want any of his daughters to have to rely on a man for their wellbeing.

Lauren (01:05):

Good advice, right?

Donna (01:06):

Yes. And so he wanted all of us to be engineers. He felt you could always get a job as an engineer. Came from a generation where they went through the depression, and so this was a big deal. And so in high school I liked chemistry and I was good in math and they said, oh, chemical engineering, and that fit with what my father thought. So I had no idea, and I don't think anybody does when they start out studying what it really is. But it was a good choice for a lot of reasons. I mean, I'm not really doing what I would call chemical engineering now, or not what I started out doing as a chemical engineer, but a lot of the training that is very quantitative training really helped with what I do in chemistry now. It's actually more quantitative than a lot of the chemistry education is. So I can add something that's a little bit orthogonal to what organic chemistry are doing.

Lauren (01:56):

Having that background kind of gives you a different perspective as you're pursuing your research

Donna (02:00):

Now. And it really is, it's perfect for interdisciplinary studies, which are, science is becoming more and more this way with all this, the stuff coming up in chemistry now about data, rich data-driven chemistry, ai, machine learning, all the sort of buzzwords, but really it means that we have to draw from a lot of different backgrounds to solve big problems. I think having the quantitative engineering background gives me, you do have to learn to talk the language of the people in the other disciplines, and that is something that takes a while to do, but if you put the time in, then basically the sum can be greater than the parts when people collaborate from D Fields

Lauren (02:41):

Once you, yeah, I feel like that's so true. I've talked to biologists who've had to learn the language of computer scientists, and once you can narrow in on the objective, it's just a matter of mastering the vocabulary across all of those

Donna (02:54):

Disciplines. Just understanding what people say when they say certain words. You hear the words, but they may not have the meaning. You may not understand the meaning

Donna (03:04):

I used to joke that I went from academia as a sort of mainstream chemical engineer to Merck Pharma company, and then from there I moved to Germany and I used to joke that it took me longer to learn to talk to the organic chemist at Merck than it took me to learn German when I moved to Germany. But once I got so that we could communicate, then it just, that's when

Donna (03:25):

And it really changed my whole career, changed from the time that the work that I did when I went to Merck.

Lauren (03:31):

So is that when you started to transitioning more into that organic chemistry, physical organic chemistry focus?

Donna (03:37):

I mean, I was doing kinetics. I was looking at the rates of reactions from a chemical engineering perspective, really reactor design, and mainly not for pharma type products. But when I was asked to come and start this new group at Merck in the early nineties, it was essentially right around the time when the first clinical results were coming back about the anti-HIV protease inhibitors, and it was fantastic. It was basically going to turn what was a death sentence into a manageable disease. And so everybody that was exhilarating, but they were also terrified because this was, the volume of this drug was bigger than anything they were used to doing. Somebody told me they'd done a back of the envelope calculation at Merck that if they had taken every Merck plant in the world stop making whatever drugs they were making and tried to make caravan, which was their protease inhibitor, they wouldn't have been able to make enough. And so it was the first time really that pharma had to start thinking about efficiency and pharma process r and d. Basically, the driving force had always been get it online as fast as possible. As soon as it's approved, as soon as you get an NDA approved, the patent clock starts ticking.

Lauren (04:43):
Right? That's true.

Donna (04:43):
So if you don't start producing as fast as possible, you're going to lose

Lauren (04:47):
Your missing out on a lot. Yeah.

Donna (04:49):
A lot of the blockbuster drugs, they really didn't have the luxury of spending a lot of time on optimizing processes, which is the bread and butter of all the basic bulk chemical industry. I mean, tiny, tiny percentages improvement can make a huge difference. Where in pharma with smaller volume drugs, you don't really have that chance to make that big of a difference except in this case. And they realized it wasn't just that case. They realized that essentially the guy had hired me said, we thought if we understand our reactions better, we might run them better. That's really revelationary. And so they also knew at that time, in addition to the big push for the anti-HIV drugs, asymmetric catalysis was just starting to come in as a way of making very selectively and efficiently making a lot of drug molecules. And that's actually what my colleague Barry Sharpless won his first Nobel Prize.

Donna (05:46):
In 2001 was the area of asymmetric catalysis. So in the early nineties, there was one or two processes in the world that used asymmetric catalysis, but everybody knew that because it's basically, it allows you to do things in a selective way to make only the one molecule that you need that you

Lauren (06:06):
Actually need in that reaction. Okay.

Donna (06:07):
Yeah. So it, everybody knew it was going to become a big thing, but they didn't really know what to do with it. And so my group was tasked to sort of troubleshoot problems and understand reaction mechanisms and make things run more smoothly in the plant, and it really was what I know how to do, which is monitor reactions. We were one of the first groups that really started doing in studies to follow reactions while they happen and then model the results. We basically would take some data and do some modeling to predict what would happen and then show people that the prediction worked, and they kind of sometimes looked like we walked on water because they weren't used to this approach,

Lauren (06:55):
Especially if that hadn't been a priority for them in the past.

Donna (06:57):
It hadn't been, and they didn't really know how to go about doing this. And so with the work that we did, it actually spread throughout the whole industry. Even the FDA now has these, they call it quality by design, where you can approve drug processes using some of the tools that we use

rather than just say, in the old days it was if you could do three batches on Tuesday at the full moon and you get the same result, your drug is okay, but now it's a little bit more systematic controlled and controlled, and they understand why the impurity profile in a drug, you can show people that if I do it this way, I will get this result. Right.

Lauren (07:33):

It's very precise.

Donna (07:35):

And so a lot of other pharma companies, I mean Merck was always this sort of, they kind of consider themselves the Harvard of pharma,

Donna (07:44):

And so a lot of other companies would always follow what Merck was doing, and when Merck always had a much stronger engineering component to their R&D than other pharma companies did, mostly they had synthetic organic chemists who know how to work on a very small scale trying to make things big, which doesn't always work just by doubling or tripling or whatever. The sizes. After I left, I actually helped several companies set up similar labs to do the same work.

Donna (08:11):

Wow. Very cool. At Pfizer and at AstraZeneca in the UK. So it became a pretty big deal, and now it's really grown into a lot of the sort of, they call it HTE, high throughput experimentation, a lot of new analytical tools, and then combining these with computational tools to do predictive modeling and reactions.

Lauren (08:31):

So you've really just revolutionized the pharmaceutical development world. Then

Donna (08:35):

I think that the following reaction profiles and developing the equations that describe what the molecules are doing and getting the parameters from your experimental data that then you can go and run fake reactions on the computer and say, would it work better this way? Would it work better that way? But it's really the same tools that we use when we want to understand origin of life, for instance, are the same tools that will help us make a drug molecule faster, more efficiently, save the money, save us money on our prescriptions,

Lauren (09:11):

Right? Because you're actually laying that foundation to be able to have that predictive modeling or that optimization. You're laying the groundwork and you're being like, this is exactly why it's happening. So you're also giving that precursor to,

Donna (09:23):

And I would say the same thing happens here in my work here. One of the reasons I came to Scripps is we have the best synthetic organic chemist in the world. I mean basically two MacArthur geniuses in my apartment, and I worked with both of them, gin K Yu and Phil Baron, and it's just exhilarating to see that. So in the same sense, the way I can work with them is to show them, oh, this is why it happened. And they can go back and think, for instance, gin K Yu

will think of developing a new chiro ligand, or how do I change this chiro ligand now that I know what's going on and the reaction, my work isn't in making new catalysts or designing new reactions, but it's just helping people take the next step. They've discovered something, but they may not know enough about it to know where it's going to go. And so we try to be the step that helps them figure out the design of the next generation ligand for so much Kwan systems. For instance,

Lauren (10:21):

In the late 1990s, Donna pioneered a methodology called reaction progress, kinetic analysis, or RPKA for short, as she'll describe. RPKA enables chemists to better understand and monitor chemical reaction mechanisms when compared to traditional tactics truly transforming the field.

Donna (10:39):

What I took with me was the experience from Merck, and then I started having a lot more opportunities to collaborate with organic chemists, and it took a while because this was new at the time, this sort of reaction monitoring and quantitative approach to reactions and the kinetic methodology we developed, which we call RPKA reaction, progress, kinetic analysis, and it's really just making use. In the old days, the way people always did kinetics way back to McKayla menton equation published in 1913 was to do what are called initial rate experiments. So you set up a reaction with certain concentrations. Let's say it's two reactants A plus B is going to C, and you take a few data points at the very beginning of the reaction where you hold a constant and you watch what happens to B as it changes. And then you hold B constant and you see what happens to a as it changes and you have to do a lot of experiments, you have to keep starting over after the first few data points.

(11:37):

You start over under a new set of conditions and you throw away whatever happened in the rest of the reaction, you go to five or 10% conversion. That reaction, it's like the tree fell in the woods, and we weren't there to hear it make a sound. So we started to figure how could we extract more information out of data that we're throwing away? People are throwing away 90% of their data, and mostly it's because people don't like to think about more than one thing changing at once. They want to watch it rigorously, but a computer doesn't care. It really can tell. The analogy is algebra, where if you've got, do you remember simultaneous equations two x plus three Y equals seven, and you need two independent equations to solve fully and Y. Yeah, exactly. And so for our case, X and Y would be the concentration dependencies, which we call the reaction orders in our two substrates, A and B.

(12:28):

And so people would do 10 experiments changing A, keeping B constant, and then 10 more changing B, keeping a constant when all that information is available in two, basically all you need is two independent equations determine just like simultaneous equations in algebra, but you have to know how to define them to be independent. And that's where our methodology came in, was to show that if I picked the correct set of concentrations, then I would have two independent equations to, and then makes it much, we don't get straight lines. Everybody likes they do initial rate data because they plot a straight line through zero product for the first 5%. Straight lines are great, and they were great before we had computers because everybody can measure a slope and an intercept, and you can't necessarily look at a reaction that has a curved profile and extract immediately what's, what's happening, what's happening.

(13:24):

The first sort of the inspiration for what we did came from, I mentioned McKayla Menton equation that was published in 1913 in a German journal, a Leonor McKay, and Miss Ma Menon Menon was a woman in Germany in 1913 working as a chemist. She's actually a very impressive woman. She was a Canadian biophysicist, I think in, she went and worked with McKayla. So they published this equation, which basically described mathematically the rate of an enzyme reaction. It could be any catalyst actually that they did it for enzyme catalyst, but it was hard to make use of because you couldn't get a straight line rate, had a rate, equaled an equation which was not linear in the substrate concentration. So if you plotted data, it was going to be curved and it was hard to see what was there. But so 20 years after they published that, then the next big sort of revelation came with a paper, which became the most cited paper in the history of the Journal of the American Chemical Society.

(14:31):

And its first 125 years, they went back and looked, and this was called the line Weaver Burke paper line Weaver and Burke took the McKayla an equation, and you would call it linearized it. Okay. What they did was they turned it upside down. The denominator became the numerator rate became one over rate, and then you actually had a function that you could get a straight line one over rate and one over substrate concentration could give you a straight line. And so in 1934, there weren't computers, there weren't really good methods for taking data, but this was very empowering. All I have to do is get some data points and then

Donna (15:12):

Say one over that, rate one over that substrate, and then plot those data points to get, then you could extract the kinetic parameters from the equation. And so that became an enabling tool. It was the most cited paper in the first 125 years of Jax, the most, arguably the best chemistry journal, general chemistry journal in the world. And so we kind of were taking that as inspiration because that was so empowering to chemists because it allowed them to grasp what their data were telling them and so much more

Donna (15:45):

And so we basically were saying, and people had been using that tool and still throwing away 90% of the data we thought we really can get. We don't need to do the reaction for the first 10%, stop it, and then start over under new conditions. Those conditions were going to come later in that reaction

Donna (16:05):

Right? So anyway, so that was our inspiration, was to try to figure out how to develop this methodology. So with extremely accurate experimental measurements, nearly continuous measurements we can measure, get a data point every two seconds in a reaction with some of our tools. So you just see a virtual, you don't even see data points. You just see a line of how the concentrations are changing. And what we wanted to do was to develop a way that people could extract the kinetic parameters easily from fewer experiments. And in the beginning, it was very interesting because first of all, it was considered a heresy. A lot of this academic organic chemists thought, this can't be rigorous. We've been doing 10 times more experiments than we need to. No, that can't be true.

Lauren (16:55):

People are just automatically distrustful because they also don't want to know how much more time they can save in this, right?

Donna (17:01):
But pharma picked it up right away, and they're like,

Lauren (17:03):
The profit was

Donna (17:05):
More information, less time and money, and so they ran with it, and then people grudgingly got on board

Lauren (17:13):
Like, oh, this is real.

Donna (17:14):
I can tell you, I can quote some of the review comments that we got. But anyway, and so in the beginning, whenever, so when we first started this, we make plots, which we plot the kinetic data way. We call it a graphical rate equation. You write out an equation, and usually it's rate on the Y axis and something usually substrate or something on the X axis. And we basically developed a way to manipulate our data by changing what we put on the axes for these two, if you have two independent experiments and depending on what you plot, we actually found this out almost by accident, but if they on top of each other, there's some relationship between those two reaction conditions and the way you figure out what the relationship is, it's what you plotted. And so basically we have software now that can just figure this all out, but very quickly, but basically the data can tell you, we call it interrogating the data because it's like, what do you know? Tell us what you know. And so we call 'em RPKA plots, and in the beginning, if I saw a plot, RPKA plot in a paper, it was either my paper or somebody that had been trained in my group.

Lauren (18:23):
So I was also hoping we could talk about a lot of your work that's been done. We touched a little bit on it, like origins of life and how you've contributed to this field as well. Yeah,

Donna (18:32):
Yeah. That's also another sort of accident. I didn't start out thinking, I want to solve origin of life. Actually, this happens to quite a few scientists, chemists, as they get older and they've had a long career and they think, oh, I want to work on this. Very important, A number of scientists have gone that way. Maybe I'm getting old.

Lauren (18:52):
Or I feel like as you uncover more and more in your research, it just automatically brings up new questions, right? It does. So you're going to be brought down new

Donna (19:00):
Path. That's exactly what happens. And for me, it's always, I've gotten, like I said, I don't invent new catalysts and I don't invent new reactions, but I look at things, I see something in the literature like, well, that's interesting. Why did that happen? So I'm more like, why did it happen? How did it happen? And then how can we make it better? But I don't actually come up with it. So

the first thing was a reaction called the So I Reaction, which was published in 1995 by a Japanese scientist, and it was called in one of the top 50 papers of the last 50 years in nature when they do their 50 year thing. And it was a reaction where the product is the catalyst. So you make more of the catalyst. Normally the catalyst is a constant. It comes in, does its job, goes back, and you just shuttle around a cycle.

(19:47):

This time, every new product molecule is also a catalyst. Interesting. The rate just goes up and up and up until you run out of substrate and then it goes down. But the other thing that reaction did was that the product, it was an asymmetric, catalytic reaction, which we didn't probably define that, but many molecules have a property of asymmetry, like your hands, your left and right hands are identical, but you can't superimpose them on each other. So they're asymmetric. And that's, they're called mirror image molecules. And many drug molecules are mirror image molecules, and often only one of them will be the one that helps you like ibuprofen, both hands of ibuprofen. It's a chiro molecule. Both hands can cause stomach upset, but only the left hand helps your headache.

Lauren (20:32):

Interesting. I never knew

Donna (20:33):

That. Yeah, and there's, you can get some versions of ibuprofen where it's only the one hand, but it's more expensive to make it only one or the other. For many cases. And there are worse examples that are tragic, that's kind of trivial, but thalidomide, thalidomide was a drug that was given in the early sixties only as an experimental drug and more in Europe than in the US to women for morning sickness when they're pregnant. And it caused the one hand helped her stomach, but the other hand caused just the particular points during the fetus, the gestation, it caused capillaries to shut down. So the kids were born without limbs, with limbs that stopped at their arms. Oh my God. And that was the most tragic example that actually changed the way drugs are tested. They didn't used to test them on women or on the female of whatever species because there's lots of cycles and you got to take a lot more data.

(21:24):

And so they didn't know about this. And so it was tragic. But in terms of origin of life, that's awful. And the reason that drugs can have this kind of, it's kind of a question of molecular recognition. Basically, you're doing a handshake, drug molecule does a handshake, and if we both put out our right hands, that feels differently than if I put out my left hand in your right hand. And so that's what your body one handshake at new, okay, this is what I'm supposed to do. The other one, it's like, what is this? Did something else. And the reason that that happens is that the hands in your body that are shaking with the drug are also chiro. So they have that same property that when by themselves, they may not have that property, but when they meet another chiro molecule, it matters which hand they meet.

(22:14):

And the reason is, this goes back to the origin of life, is that the molecules in your body, the biological molecules that make up the proteins and enzymes and RNA and DNA are chiral, and they are single-handed. All the proteins are what we call left-handed. They come from left-handed amino acids. But how did that start? That's the question like Barry Sharpless won the Nobel Prize for showing how you could direct reactions very well, very selectively towards one hand or another. And that was what he won half of the 2001 Nobel Prize for oxidation reactions. But we have at our disposal now in the modern world, plants are also have chiro molecules. So

we have what's called a chiro pool of molecules that we can make molecules to direct reactions. Barry Sharpless is catalysts. If you don't have a way to direct the reaction, if you just try to run a reaction without any guide, one to left or right, you'll make half and half.

(23:14):

How did that happen in the very beginning of the world? What was the first guide? How did it even come about? We try to figure out how in what we call the prebiotic soup. In the beginning of the world, the first molecules that were being formed that could have this property of left or right handedness, probably there was an equal mixture, but somehow there are two parts. Somehow we broke symmetry so that we don't have an equal number, and then we amplified whichever one was the excess. And say, our work has basically been trying to look at both of those questions. How do we break symmetry and what kind of mechanisms could we use to amplify that broken symmetry?

Lauren (23:52):

Interesting. So what have you learned so far in terms of understanding that origin? There's

Donna (23:56):

A lot of different parts to it. I think it's a field that often people go in with blinders, but probably in the prebiotic world, it wouldn't matter if you were doing physical chemistry or organic chemistry or inorganic chemistry. I mean, I think the reactions would happen with whatever was there. And we tend to think they were

Lauren (24:14):

Limited

Donna (24:15):

Organic chemist, I'm only thinking about this, but we realized that the phase behavior of molecules, how they crystallize it gives us a couple of roots to amplify the nric excess of one hand over another for amino acids, for instance. Oh, interesting. And so we published that about eight years ago or so in nature about the crystallization behavior. We came up with two different models for how we could get this chiral amplification with phase behavior. So that's more towards the physical chemistry side. We also worked, and as I mentioned on the SOI reaction, that auto catalytic system, which was really only a model reaction because the particular chemistry of that reaction doesn't have any prebiotic plausibility. You wouldn't be able to do that in an aqueous prebiotic soup. But as a model for if we could find an auto catalytic reaction that did this, because not only did the product make itself, but it increased its imbalance. Oh, okay. So you could start out with a very small, less than, less than 1% difference between the two. And then over many rounds you amplify that it becomes even more extreme.

Lauren (25:19):

At the time of this recording, Donna had two papers upcoming in PNAS in Nature regarding her work into the origins of life. Those are now published and are linked in the show notes.

Donna (25:36):

Now, the stuff that we just are coming out just got accepted. They're going to be coming out soon, two papers on different chemical reactions that gives possibilities for how we could have amplified ee and also in antier excess, the difference between the two. And also break symmetry in mixers that are completely equal. And the first one's in a reaction called

transamination, which is the way many of the amino acids in our bodies are made. The amino acids that you don't have to eat that you could make are called non-essential. The ones you have to go out and eat are called essential. But basically the ones that your body makes, typically what it does is it takes one amino acid and it takes another compound called an alpha keto acid. And it takes the AM mean group from the amino acid and plunks it onto the alpha keto acid.

(26:27):

It makes a new amino acid. It takes an AM group, but it has enzymes to guide it. So if you had a left-hand amino acid, then the new one will be left-handed. And so we're thinking what could have been the first catalyst way before enzymes. So we looked at a series of just two amino acids stuck together called a dipeptide. If you make a long and long chain, thousands of amino acids in enzymes, but could we get any differentiation with a very small version, like a prebiotic version of an enzyme? And so that's the paper that's coming out in PNAS was looking at that. Both of the two papers that we have coming out now focus on a process called kinetic resolution, which is, and this is something Barry Sharpless worked on as well, is a equal mixture of molecules. We call it a racemic mixture.

(27:20):

If you have a catalyst that can guide so that you either make a new product or you destroy one of these faster than the other so that you have a race between these two, and one of them will win, you may want the one that got left behind. You may want the new product you're making. But basically kinetic resolution takes an equal mixture of molecules and gives you a way to increase the imbalance between the two. And so both of these two papers have that aspect. And in both cases, we thought we got the wrong answer. Really? Well, I mean, what does wrong answer mean in science? Yeah, that's true. The answer we thought we were looking for, we thought, so we were trying to make an amino acid from an alpha keto acid and the enzyme system, the modern enzyme system shuttles this am mean group in the transamination by something called paradoxical ox mean it pulls the amino off, one amino acid, sticks it on paradoxal makes mean, and then sticks it on the other molecule.

(28:18):

And so we tried to use that as a way to make amino acids from the alpha keto acid with alpha keto acid, with the ox amine. Do we make an amino acid? And we did. And we some, we could see that we had two products, so it wasn't equal numbers. We had two different amounts of two products. But then when we basically figured out which product was which, you have to do the analytical calibrations to see which one was left, which was right, we were making the wrong hand of the, it's like, oh, the biological hand is left-handed, and this reaction wants to make right-handed. How can that be periodically relevant? And then I remembered the concept that I've written about in a curmudgeonly essay about 10 years ago, more than that now, called microscopic reversibility. And you can think about it. You could think about it driving in traffic if it's faster.

(29:14):

Sometimes it isn't true. There may not be microscopic reversibility in many traffic routes, but if it's faster, if it's faster to go around the bottom of the mountain, then it's not faster to go up over it to come back. So the path forward has to match the path backwards. Otherwise, if there was a shortcut, you would do it both ways. Right, exactly. So microscopic reversibility, and so then I thought, okay, so we were trying to make an amino acid going this way, and we made D faster than L, the right hand faster than the left. If I start on the other side of the equation with L and D and I go backwards, then D will react if I made D faster than I would have to react D faster. And what would be left behind was the amino acid I need for making proteins.

(30:04):

Got it. So they're like, okay, let's just run it in reverse. And so maybe biology started out, and it makes actually some sense, this idea of the prebiotic soup may have been filled with equal racemic mixtures, molecules, 50 50 of every molecule in the beginning before any sophisticated ways to direct reactions. And so this might've been the first step to get some imbalance in these amino acids, which then could make peptides and then could make better catalysts. So it's like the first step towards the modern biology. It's fun in the sense that you often start out with an idea of what you think you're going to find, and you have to really resist the idea that I think it can make you look at evidence differently if you think, oh, that's not what I meant to find. I maybe there's something wrong. But actually if you just say, wow, if that's true, then, and then it leads you into things we wouldn't have thought of.

Lauren (31:03):

I was going to say, you're actually having to think about the core properties of what's going on and think creatively about why you're getting the result that you are. And just thinking about the implications of the work that you're doing, how much learning what happened in these original situations could impact our understanding even more broadly? Yeah,

Donna (31:24):

I mean, so this is an area, origin of Life is an area that had traditionally been very hard to get funding in NAH. They want to solve diseases. Pharma companies don't care about the origin of life. We were very lucky that we had a grant for 10 years from the Simons Foundation, Simon's collaboration on the origins of life, which was like everything from astrophysicists to geochemists to RNA world people, and fantastic meetings of incredibly interdisciplinary, really have to learn each other's languages there, I'm

Lauren (31:53):

Sure.

Donna (31:54):

So we were very lucky that we were able to pursue this work at a bigger scale than we normally had been. The grant was 10 years long. It just ended last year. But many of the things we found actually end up being quite important for pharma, for modern chemistry. One of the phase behavior models that we worked out about how molecules crystallize is now being used by places where DSM pharma has been bought by somebody, but companies that make chiro molecules have been using this crystallization

Lauren (32:26):

Methodology, right? Because it lays this much richer foundation, you have that much better of an understanding of what's going on.

Donna (32:32):

And if we're applying it to the amino acids for the origin life, we can also apply it to car molecules that are going to be drugs. And in fact, we did a lot of the model studies for this one crystallization method on the precursor to clopidogrel, which is the big blockbuster drug for, I think it's for cardiac disease. It's a BMS drug, I think. And so they can basically make the one hand of, because it's a chiro molecule, and this helps them make only the hand that they need.

Lauren (32:59):

See, I was hoping you could tell me more about how you've started the supporting growth for Women in science fund.

Donna (33:06):

So I got a humble award, which is from the Alexander Run Humble Society in Germany. And basically they give you this award. Typically it's for people if you're collaborating with German scientists and they want you to collaborate, but they give you the money as a personal thing. So I donated half of it.

Lauren (33:26):

Yeah, put it forward.

Donna (33:28):

And it seemed like a good, because I know that for me, when I was starting out, it had such an effect on me when I went to my first scientific meetings. And I remember the very first scientific meeting I ever went to was a plenary speaker at a local section of a catalysis society when I was an undergraduate doing undergraduate research. And this guy was just so dynamic. I had never been to a scientific conference I had been to, that's not true. I was president of the Society of Women Engineers. And so I'd gone to a couple of their annual conferences and I'd seen some really, I saw Anita Gale talk about the space shuttle before it was a thing, and I thought it was like science fiction. But in terms of my own research areas, this was the first meeting I'd been to. And this guy was a surface scientist from National Bureau of Standards at the time, NIST now.

(34:19):

And I was just blown away by how he was up there on stage, and he was just like, I didn't understand everything, but he really just gave off this enthusiasm. And there was a reception after it. And my research advisor took me up and introduced me to him. And I said, that was so impressive. And I still remember what he said back. He said, well, the work was fun. And I thought, well, that is really cool. And you could see that he was, thought it was fun, but you could do something and make this kind of impact and the work could be fun, and

Lauren (34:53):

You enjoyed the entire process.

Donna (34:55):

And I felt like, I don't know, I think I'm a closet introvert, but I also knew that I wanted to be up there. I wanted to be the one telling people, and that's been all through my career. As soon as I find something interesting and new, I want to teach it. As soon as you learn something, you want to teach it to somebody. So I thought that trying to give other young scientists a chance to go to these meetings, and especially for women to network to see they get fewer opportunities. We're doing better at it, but it just seemed like this would be one way that we could, at Scripps make sure that more of our students and postdocs get a chance to go out and show people what they can do.

Lauren (35:35):

Well, especially in being able, even having this fund, I feel like makes people more aware of these are opportunities that exist that I should go pursue. And Okay. Final roundup question. If you could give one piece of advice or wisdom to an up and coming scientist, what would it be and why?

Donna (35:51):

I think it's very easy today for young scientists to get discouraged for various reasons. I mean, maybe we had less information in my day, so we didn't know what we didn't know or something. It might've been harder to get discouraged when you can see everything online and what everybody else is doing. I mean, that may also help provide a community of people to talk to, which is part of what I would say to young scientists is try to stand your ground. I mean, if you are passionate about something and you want to do it, don't let people tell you. I mean, obviously you can take people's advice or you can listen to people, but you should stick with your guns if you think you've got something that, I mean, I mentioned earlier on about the RPKA methodology. I suffered a lot of abuse. People telling me it was ridiculous and crazy.

Lauren (36:40):

That's crazy.

Donna (36:41):

Yeah, it's the most important thing is to have faith in yourself. And that may mean asking for a lot of advice about whether your ideas are worthwhile, but you definitely need to not cave into other people if you know what you want to do.

Lauren (37:01):

Many thanks to Donna for joining us on this episode of Science Changing Life, where we explored everything from prebiotic chemistry to the mechanisms of catalytic reactions. To learn more about Donna's research, be sure to check out the show notes. Thanks for tuning in with us today, and until next time.