

WESTERN SCIENCE SPEAKS PODCAST SEASON 3, EPISODE 3

EPISODE TITLE

Breaking the Code: The Adaptive Capabilities of DNA

PODCAST SUMMARY

DNA is our biological signature. If our DNA changes, naturally so do we. So what causes these changes? Listen to this episode of Western Science Speaks to have Kathleen Hill from the [Department of Biology](#) break down how DNA is the thread that joins us to our ancestors, plus a conversation about the biological impacts of modern life.

INTERVIEW

You're listening to the Western science speaks podcast. Presented by Henry Standage.

Henry Standage 0:16

What's the weirdest thing you do? Something that lacks explanation, but in the larger picture, helps makes you uniquely you. It's strange to consider that behind every subtle quirk, slight idiosyncrasy, and peculiar characteristic, is a code. Our DNA defines us individually and what we are collectively. Molecular biologists attempt to study DNA and a multitude of organisms with the hopes of finding the concrete similarities and differences between the creatures that inhabit Earth. Dr. Kathleen Hill from the Department of Biology at Western University studies the signatures of DNA with the hope of obtaining a greater understanding of how DNA is affected over the course of a lifetime. On this episode of the podcast, her and I examine how our DNA can change, what effects that has, and the important role genetic variation plays in society.

Henry Standage 1:18

How does DNA actively change over the course of a lifetime? Because I mean, from an evolutionary standpoint, it's easy to see and I'm sure the patterns change drastically as we go away from our original ancestor. But over the course of my lifetime, can I expect my DNA to change in any way?

Kathleen Hill 1:35

Yes, you could. So, in my classes last year in human genetics, and in the mutagenesis course, we looked at embryo development as one place where the genome was changing dramatically. Duplications, deletions, cells where it's the same organism that's developing. It's increasing from the single cell zygote to the multi celled organism and during that process very early on in pre implantation, so many changes that they're finding, in fact, they use it to sort of study cancer mechanisms because there's such rapid division during embryo growth, rapid division during cancer. So, we're learning that all of those cells can have a different genome. So, what we might call a blueprint, and then people would think it's static, it doesn't change. But no, we need to think of it as very dynamic. I'm working on a paper right now about the brain. And the brain is probably one of the places where if we took cells from different areas, sequence their individual genomes, we would find that they're different. This can add to the complexity of how our brain works, but it also in cases of schizophrenia or autism, this could be a contributor to too much variation in the brain. So, it might be essential for brain function, but there might be a threshold or there might be a change in the there that is just too much in terms of differences between the cells. Technology right now, though, is that you can take single cells in the brain and they're publishing it, in the last six months you'll see, they look at single cells of the brain populations of them individually, they find that they have differences in their genome, in their transcriptome and in their proteome. So, they are from the same zygote. But they're different.

Henry Standage 3:29

So, it sounds like you actually want stable DNA throughout your lifetime. All the examples you had there sounds like negative things like schizophrenia, cancer mutation.

Kathleen Hill 3:38

Except for brain function, we could think of the complexity of neural connections that are there and the partitioning of function within the brain and creating a higher order. Even if we had a mathematician look at the complexity of function. If you had many component parts with differences, that would be the positive, so that might be normal for brain function and how the brain uses diversity for complex function and adaptability and change ability over a lifespan.

Henry Standage 4:12

So, what does genetic variation offspring do for an organism?

Kathleen Hill 4:17

So, if we look at genetic variation in the context of a single individual, it might be bad, I could carry a variant that leads to disease, I could have lower fitness because I'm not able to reproduce and have offspring. So that would be the negative of having a particular variant that is actually affecting a function in the cell, and that would be measured in terms of how fit an individual was to reproduce. It could be neutral, could have no effect on that fitness, or it could be positive. It could be that in a particular environment, one variant is great. For cold adaptation, or it's great for a very arid environment. So, variation as a whole in a population can be a very healthy way of having adaptability there. So that if environments change, there will be some individuals who would be able to express the variant they have that is good and fit in that particular environment. You might think of it like in a crop science, if you had a monoculture, and everyone in that population was susceptible to a parasite and the parasite came in, then you would have the whole culture responding in the same way. Whereas if you had some variation, there might be individuals in that culture that then could survive.

Henry Standage 5:45

Hmm. I want to transition to synthetic biology. Can you take us through the process of deciding to design something for function and then that process all the way to its eventual application?

Kathleen Hill 5:59

So, synthetic biology has many, many meanings, and the one we might start with is taking component parts of new genomes and assembling them into a new mosaic genome. So, we've been making transgenic animals or transgenic plants for some time and we would say that we were putting some new function in, and we might say that we have synthesized something in that way.

Henry Standage 6:27

By transgenic, do you mean a crossbreed or?

Kathleen Hill 6:30

By taking a gene from one organism and putting it into a non-native or brand-new organisms, so we often have transgenic mice, they have human genes, or they have fruit fly genes, and we see what it does within a mouse as an organism. It's often done in precariat cultures, or we might think of many bacterial cultures, if we want them to express some new enzyme. You might find this used in different industries, if you wanted to have a different enzyme that gives a different flavour to a food or a different consistency, you could see that being engineered. Engineered was a really popular word, even in the 70s to bioengineer something and have bio-engineering degrees. Now synthesis has moved to a stage of creating from scratch, from very component parts. So, there are individuals who have research programmes to make a genome letter by letter, not take parts that are already assembled and put them together but nucleotide by nucleotide, single letter by single letter create a genome. There's a great study to try to make the minimal genome, what's the minimum you need in terms of function, maybe it'll be no redundancy. You just want, what's the basics to get a cell to live, to divide or have a basic function. So, there are people that synthesise from scratch. And then there's people that assemble from component parts. And they desire to have a function like making fuel or making products taste in a particular way and have a unique flavour.

Henry Standage 8:19

And you're looking at, you said fruit flies with mice, but the end game for this sort of thing always seems to be humans.

Kathleen Hill 8:26

So, there might be a particular sequence that has a function that you value for humans. And you could start with a simple one, there's an individual with vision loss and you want to restore vision. So, there might be for particular cells, a function you want to restore. So, you may synthesise a sequence that will deliver that particular function. So, we might be interested in DNA that could, if there was a mutation in one gene, restore a proper function to that gene. So, you can think of it as a component part that then gives that function.

Henry Standage 9:07

This really is Jurassic Park. They should have done this.

Kathleen Hill 9:10

I haven't seen the newest Jurassic Park, so I don't know what new things they have. It's really exciting because there are students in universities, as undergraduates that are doing that component part assembly. So, if they want to design things that fluoresce or that have electrical current in some way or have some building block of function, they can make a proposal and order in the component parts. And then they can create that particular organism that has that feature they want.

Henry Standage 9:47

And once they do create it, are they able to duplicate it, which is also I something want to talk about. Deletions and duplications, what happens with chromosomes there?

Kathleen Hill 9:57

So, one part we study with analysing mutations, is deletions and duplications within the genome. These are structural variants. So, we would be thinking that we know the number of chromosomes and the amount of DNA that an individual would inherit from mom and dad. But then sometimes in looking at the DNA of the offspring, we would notice that there are large deletions, so 1000 nucleotides, or more mega bases of DNA that are deleted, or they're duplicated. And then scientists are trying to figure out what happens when you have less or more of a gene function, because that can sort of act to regulate how much product or how much function you're actually getting. And it's actually many researchers here in Canada, who study these copy number variants. So, you're supposed to have two copies, one for mom, one from dad, and the individual has 3, 4, 5 or they have 1 or they have none. Then these copy number variants start to be some of that missing information for diseases like autism, he's a specialist in autism research. So, there's a lot of genetics behind some diseases and some behaviours that can't be described by a single nucleotide switch or change. But there are large chunks of DNA that are missing, or they're duplicated.

Henry Standage 11:25

I want to end on this, what changes has modern life brought to our DNA?

Kathleen Hill 11:31

That's a super question. We can think of some great examples because there are people that track the introduction and the popularity of cigarette smoking. They do it for men then they do it for women. And then they look at cancer incidences and they can see this being mirrored later on because there's sort of a lag as to when women were smoking versus men. And they see that trajectory of the increases in lung cancers and they can see the effect of a particular environmental agent. That became popularised. And then they can see the end result. And in between all of that, we now know a mutation signature associated with cigarette smoke. In our modern world, we have drugs that cure cancer, but they also do that by damaging DNA. So we can see a signature for some of the chemo therapeutic agents. When people discovered radiation and what it could do, we saw the effects of individuals having leukemias or other cancers, and then we have a signature for that. And we know about ultraviolet light and how our modern world and our decaying ozone and how quickly we become sunburn and we look at the incidence of different skin cancers and we see a rise in the mutation signatures. There are people that

actually study the eyelid of individuals that are middle aged and they can already see the damage in that skin. And they can see it at the single cell level all across the eyelid. And it has all of the mutations that can lead to a skin cancer. So, some of its environmental, its industrial. Some of it we'll notice with things eat what we drink, you might remember a bisphenol. And then there are just some areas of the environment. If we think of the Smaug that exists in certain countries like China, and then you start to track what that can be doing to epithelial cells and in lung and nasal passages.

Henry Standage 13:39

Just as an absurd example, I was joking with my buddies the other day that in 100 years, the average human might walk around with a lump coming out of the right pocket or left pocket from all the cell phone radiation.

Kathleen Hill 13:53

Well, you know, there are people that study those things about cell phones and the proximity that the phone is and I haven't seen the outcome of the research, I saw it sort of proposed and being started. It will be interesting. What habits do we have today that were fads, dietary or products that we became, you know, in intimate contact with or eating and applying, and then we'll see what that is later. Now that is why we have Health Canada, and we have the National Institute of Health, the National Institute of Environmental Health, and they're constantly looking at the chemical compositions of agents and they're constantly doing studies to figure out is this mutagenic? Is this DNA damaging in any way?

Henry Standage 14:39

We rely on them so much that it's actually only been eight years or so since it feels like everyone had a cell phone, maybe around 2010.

Kathleen Hill 14:52

With the iPad and with iPhone and I was probably late to coming to all of it, but then you realise it. Like how do you run life without it, like the amount of correspondence, the amount of networking and the amount that you learn, I use it as a data resource. It's kind of tiny print, but you know, even a student's thesis can come there, and assignments can be seen there. And all classes can be run from the whole thing.

Henry Standage 15:20

I think people are less oblivious than they used to be because it took 30 years for people to figure out that cigarettes were really toxic for us, and I think maybe were a bit more suspecting with that sort of thing. But yeah, definitely interesting to see as time passes.

Henry Standage 15:39

By looking at a picture, Kathleen can tell you more about an organism than your eyes ever could. As species get further and further away from their original ancestors. It's important that we have reference to where everything came from, allowing us to see what developments have taken place in order to be a fit in the modern world. As humans, we're still waiting to see what effects our prominent modern technologies may have on us, which is a scary thing to consider. In the meantime, put your phone away and enjoy the unique people you have around you. I'm Henry Standage, signing out. Thanks for listening.