Science AMA Series: I'm Carl Zimmer, and I'm here to talk about my Game of Genomes.

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Abstract

Greetings–My name is Carl Zimmer. I'm a contributing national correspondent for Stat, a new online publication about medicine and life sciences. (You can find out more at http://carlzimmer.com) I'm also a columnist at the New York Times. Also, I write books about biology (and one about science tattoos). I'm in the midst of publishing a three-part series at Stat about my genome, called "Game of Genomes." When I got the opportunity to get my genome sequenced, I found a way to get my hands on the raw data (a 70 GB hard disk, to be specific). I then enlisted two dozen scientists to guide me through its depths. Along the way, I got to see how my unique DNA alters the shape of the molecules that make up my body. I found out that 613 of my genes come from Neanderthals, and discovered how they are influencing my health. I learned my genome is littered with broken genes and overrun by ancient viruses. I even discovered my health is protected by mutations that are the basis for new blockbuster drugs. In the process, I learned how much our genomes can reveal to us, but also how many mysteries they hold back. Here is part one of the series:https://www.statnews.com/feature/game-of-genomes/season-one/ And here is part two:https://www.statnews.com/feature/game-of-genomes/season-two/ Part three will come out next Monday And here is a site where you can find all the data and analysis (including my genome): https://zimmerome.gersteinlab.org/ I'll be back at 3 pm ET (12 noon PT) to answer your questions, ask me anything! EDIT, 4 pm: Thanks for all the great questions so far! I'll zip back in an hour to answer any new ones that arrive.

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CARL_ZIMMER R/SCIENCE

Greetings--My name is Carl Zimmer. I'm a contributing national correspondent for Stat, a new online publication about medicine and life sciences. (You can find out more at http://carlzimmer.com)
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I'm trying super hard not to fan nerd out here, because your books have been very influential over my interest in science since Parasite Rex, so, eeeeeeeeeeeeeeeeeee thank you for being awesome and writing on awesome things and I think you're great and hope you keep being awesome!

What I mean to say is - with the promise of CRISPR and the lowering costs of sequencing, do you foresee a future wherein preventative genetic therapy is part of healthcare?

And perhaps a little more esoterically - you've written before about the intellectual/cultural tools available to us that allow us to deal with biological/physiological/environmental challenges in a far more potent manner than what is found in the rest of the natural world, and I'm wondering if you could weigh in on how understanding our genome more thoroughly will further empower that toolkit.

lzawwlgood

Thanks—it always means a lot to hear from people who get something out of my writing.

I can definitely envision CRISPR and genome sequencing combining to lead to more effective gene therapy—that is, changing faulty genes to treat genetic disorders in people. But that's not "preventative." I'm guessing you're wondering about germ-line engineering. This will only become common once people decide they're okay with tinkering with heredity. I suspect that time will come, judging from controversies in the past such as over IVF. But it will still require a lot of slow, expensive

fertility procedures, which I think will severely limit it.

Understanding our own genome will certainly give us more power to control our own health and well-being, although it will take a long time to really live up to its full potential, and even then it won't be a panacea.

Hi Carl, I love reading your writing!

I have a question I know you get a lot, but how do you recommend aspiring science writers get started? What strategies worked best for you? Thanks!

superhelical

I actually get asked this fairly often, and so I've written down some of my advice (such as it is): http://carlzimmer.com/writers.html

Do you have a sense of how much more useful information you got by having your entire genome sequenced, as compared to services such as 23andMe, which just sequence a few hundred thousand SNPs? If it was much more informative, do you think there will be a time in the future when it is standard for everyone to have their entire genome sequenced?

godsenfrik

Please be sure to check out cariaso's reply--and check out snpedia and promethease, which he runs. They are remarkable sites that have been very useful to me in getting to know my genome.

There are a lot of things you can discover by looking at the full data from your genome that you can't by looking at SNPs you can get from places like 23andMe. SNPs are variants at particular points in the genome. A few hundred thousand SNPs make up less than a thousandth of all your DNA. In this week's installment of Game of Genomes, for example, I looked at how many copies of particular genes I had and also looked for giant chunks of missing DNA. SNPs alone can't help you find them. It's kind of ironic that it's easier to spot a single altered base in DNA than to find a place where you're missing half a million missing bases!

Hello Carl. I really like the series. So far, the focus has been on the hard wiring. Will part III cover any nature/environmental impacts on our genetics or will that be a potential follow up piece?

Second: It seems like most genetic human health research looks into what's wrong - diseases and how to cure them and/or treat symptoms. Is there a push being made to find out how to enhance or capitalize on beneficial aspects? (Or maybe I'm looking at it the wrong way - unlocking obesity or diabetes factors will make humans stronger versus making the immune system more efficient or making skeletal muscle stronger.)

1900grs

I agree that there's way too much emphasis on genome sequencing as revealing tales of woe. In this week's installment of "Game of Genomes," I write about discovering that I have a protective variant that lowers my risk of auto-immune disorders. And understanding this good side of the genome could help scientists develop new drugs (like the one based on my own variant, it turns out!)

I'm mostly focused in this series on what I can discover in my genome, so I don't have that much to say about the environment. But that's important, obviously. I have a mutation in the region of a gene called

FTO that makes me more likely to gain a few pounds. What's interesting is that this was not a risk factor for people born in the early 1900s. The mutation didn't change. The environment did. I wrote about this more here: http://www.nytimes.com/2015/01/01/science/gene-linked-to-obesity-hasnt-always-been-a-problem-study-finds.html

You mentioned you have Neanderthal DNA and it is influencing your health. Since most Europeans and Asians have said DNA while some indigenous peoples don't, what difference (beyond the cosmetic) do you think that admixture has produced in these populations? Anything frightfully interesting? Thanks!

BaronVonButternickle

I will write in more detail about my Neanderthal DNA in the third installment of "Game of Genomes," which will be published on Stat on Monday 7/25. Neanderthal DNA is found in all non-Africans, because of interbreeding between the Neanderthals of Eurasia with modern humans who expanded from Africa ~100,000-50,000 years ago. The big question I wanted to know was not just my percentage of Neanderthal DNA, but to look at a list of my Neanderthal genes. Like many other non-Africans, I have Neanderthal genes that affect my health in subtle ways for good and for bad. Some results are just weird--like, I have a slightly elevated risk of nosebleeds thanks to one of my Neanderthal genes. But others speak to big lessons about our admixture--such as the abundance of immunity genes I inherited from Neanderthals. I'm working on a book about heredity, and this experience has given me a new way of thinking about it!

Carl, Thanks for doing this AMA!

I listened to a TED talk by Sam Sternberg on the groundbreaking CRISPR technology and its uses now and possibilities in the future. What are your thoughts on this, genetic editing and manipulation, and the ethics/consequences that go along with this in the near future?

-PM_ME_YOUR_SMILE-

CRISPR is already changing the scientific playing field, making biomedical research a lot faster and reliable than in the past. (Ask anybody who needed to make a mouse model with traditional methods!) I expect that we'll see a lot of edited animals and plants in the near future, producing new sources of food and compounds. As for the ethics of CRISPR, the big issue is whether we should alter the germline. I think people are still getting their heads around this issue. Is it wrong because we shouldn't alter heredity ever? Is it wrong because it might be unhealthy? Is it wrong because it might work well--and give some people advantages that others don't have? I predict that it will slowly enter into use, starting with extreme cases where people carry dangerous mutations. George Church of Harvard has sketched out a scenario where CRISPR could fix those mutations in sperm and eggs, which could then be fertilized in vitro to produce healthy embryos. Once we cross that line, the question will be whether enhancement is ok. You could make a similar argument about vaccination--which makes me think that germline CRISPR may become more common.

Any concern that making your genomic information public could have consequences (negative or positive) down the line for your offspring (if you have any?) and/or your other family members?

e_swartz

I thought a lot about that and talked a lot about that with geneticists and with my family. I think that everyone should have the right to control how much of their genome becomes public (including people

who get involved in research). But I don't feel uncomfortable about sharing my genome in public. Part of the reason for that is because I'm 50 years old and my kids are healthy. Part of the reason is that I know already that I don't have any flashing alarms in terms of known, huge disease risks. Then again, I have a lot of "variants of unknown significance" which may someday get deciphered. But at this point, I would actually *prefer* for someone to let me know if one of them gets solved and has some bearing on my health.

What's your favorite bit of ancient virus DNA in your genome, or the human genome in general?

jtotheizzoe

It's hard to beat the viral DNA that encodes proteins in the human placenta. We literally would not alive if not for the virus DNA that our mammal ancestors domesticated millions of years ago. I wrote about this a few years ago on my blog: http://phenomena.nationalgeographic.com/2012/02/14/mammals-made-by-viruses/

What is required for myself, an average Joe, to get their genomes sequenced? Is there a list? How much does it cost? How long does it take? Thanks for doing an AMA on such an interesting topic!

kom0do

cariaso linked to a good guide below. I should point out that what I did is not something that is available readily to consumers. I managed to get my BAM file, and then persuaded a bunch of scientists to analyze it for a lot of different things. Perhaps that will change. More than one scientist I worked with said they had never done something like this before and they could see the value of showing the public how their research works. I think a lot of people would be curious to dig into their genome below the "do I have a mutation for disease X?" layer.

How long will it take until DNA samples become an everyday means of identification?

Lintheru

Do you mean for forensics? Or like a fingerprint for buying stuff on your iPhone?

Hello and thank you for taking the time to answer our questions.

It is to my understanding that is just not which genes that we inherit that define our unique characteristics but also the constant turning on and off of the genes. Has there been any time series analysis of tracking the active genes of an individual and how it varied over this person's lifetime?

seungryul93

That's a huge issue, which sometimes gets labeled as "epigenetics." Yes indeed, it's not just what genes you inherit, but how you use them through life, switching them on or off in particular tissues. Scientists are just beginning to get detailed data on epigenetics over time. I wrote about some of the controversy over this data for the Times a couple weeks ago: http://www.nytimes.com/2016/07/02/science/epigenetic-marks-dna-genes.html

Can you please discuss in more detail (or maybe even give an example) of the relationship between

identifying gene mutations and how they are used to synthesize new drugs?

OhwhatupCarlandJonny

A mutation that raises or lowers the risk for a disease can potentially reveal to scientists a new dimension to the biology of that disease. For example, the mutation may alter a receptor that sits on cells. That receptor may receive certain signals, and then relay signals into the cell. That whole communication relay can become a target for drugs. In my own case, a drug against auto-immune disorders was invented based on a protective variant I discovered I have in my genome. There is a woman in Texas who has very low cholesterol, and the discovery of the gene that gave her that protection is now leading to cholesterol lowering drugs. See this story for some details: http://www.nytimes.com/2013/07/10/health/rare-mutation-prompts-race-for-cholesterol-drug.html

Great series! really really exciting :) Thank you. I wonder if current technology allows to know which percentage of SNPs is variation between our own cells and specially taking into account the SNPs of the germ line cells. Also, if I read correctly, 9% of unique SNPs compared to the 1000 genomes is still a lot of unique SNPs , (more than 300,000!), are these SNPs in the whole genome or only the gene coding parts of it?. Finally, I wonder which were the genes that you have lost both copies and if you have extra copies of them that are complete.

zoviyer

About the 1000 Genomes project (http://www.1000genomes.org/): I discovered that 91 percent of my variants [SNPs] are shared by at least one person in that database. But that's just 1000 people! I would bet that a 100,000 Genome Project would drop my "unique" variants even lower. That's not to say I have no unique variants. We each get ~100 new mutations that are not found in our parents. But that's a tiny portion of the genome compared to the variants that slosh around the human gene pool.

If I understand the other part of your question correctly, you were asking about mutations that arise in some of our cells as we develop. Scientists do study this (it's called mosaicism), but it's not something that you can regularly buy as a consumer (yet). I'd love to find out about my own mosaicism. Here's a story I wrote about that: http://www.nytimes.com/2014/07/31/science/having-more-than-one-set-of-dna-carries-legacy-of-risk.html

Hey Carl, I initially found out about your work through listening to Radiolab and I've enjoyed your writing since.

I can't help but wonder is there anything you found out during this process that you wish you wouldn't have?

first_name_steve

Honestly, I haven't! I'm sure that if I discovered I had a mutation that put me at serious risk of a sudden, fatal heart attack, I wouldn't be thrilled. But if I could do something about it, I would want to know. That's not to say that everything has been kittens and rainbows--I have my own burden of mutations that raise my risk of all sorts of diseases. But the risks are small and may disappear with further research on bigger groups of people.

Dear Carl, I notice you are an admirer of the elk (Cervus canadensis I assume). How many (protein coding) genes do you share (estimated via homology) with this magnificent beast?

mutationalMeltdown

I'll need to get back to you on that one. I'd love it if someone could dig up some Irish elk DNA and bring them back to life!

Hello Carl! I've read and loved many of your books. Keep up the great work!

My question: Are you looking into epigenetics as well, and what do you think about the importance of the study of epigenetics in terms of evolution, therapeutic targets in medicine, etc?

Sapientharmony

As I mentioned earlier, yes epigenetics are a big deal. And I'm hoping to delve into my epigenome soon!

Thanks for the great reporting, analysis, and data/methods availability--at a high level of documentation for a scientific paper, let alone a general interest article! I'm curious about the hurdles you had to jump through just to get your own data, that you paid to sequence! I'm a strong believer in the idea that I should own my own medical data, and don't understand the paternalistic attitude of doctors, sequencing companies, and researchers to release the information. Of course, it is difficult to interpret, and the algorithms are still being worked out, but it seems to me that signing some sort of informed consent form should be an option, as well as 23andMe style options, where you have to click through individual opt-in to see variants like BRCA1 or ApoE.

So, an actual question--in going through your data in detail, was there any moment where you thought that the guidelines that generally don't let consumers get their raw data were warranted?

pettyPeas

I think this issue is a tough one. I agree that we should have our own data about our own bodies. But genome sequencing--while very accurate--is far from error-free. So people who act on their genome sequencing may be relying on a false positive or negative result. Also, as I'll explain in more detail in next week's installment, there's a lot of fuzziness in the scientific literature on disease risks in our genes. If you read the literature, you may find links that scientists now realize don't exist.

If I had found something really worrisome in my own genome, I would have followed up with a clinical geneticist and a targeted gene test to make sure it was accurate and see if I should do anything about it.

What do you think is the greatest existential risk that we face with future technologies?

computerpoop

Who needs future technologies? All our old-fashioned carbon-emitting power plants and cars are already wreaking global havoc that we are not dealing with fast enough.

Been a fan since hearing your work on RadioLab. My question is: with all the services like 23 and me, which have sequences millions of people, and have collected tons of data, what findings you expect to see once they start comparing all the sequenced sets?

miniaturetitan

The real avalanche of data is going to be the millions of people who get whole-genome sequencing (as

opposed to just SNPs). Here, for example, is a new paper on 10,000 people: http://biorxiv.org/content/early/2016/07/01/061663 Rare mutations will start to emerge that tell us new things about disease risk and other traits. Genealogy will also be transformed by these big studies, because these rare mutations will link us to small groups of people (as opposed to discovering your ancestors are from one continent or another).

Hi interesting read. One, fairly big, question. Most, if not all common variants have very small effect sizes and are quite often not linked to a specific gene through any direct experiments. Don't you think it's a bit premature, and also potentially detrimental especially on a person basis to start talking about using personal genome data today? This of course excluding the clinically validated variants in for example BRCA1/2 for example?

pettervikman

That's an important issue. But there are literally thousands of genetic disorders with strong ties to particular variants. Most of them may be rare, but they do add up. Would that make it worthwhile to each of us to get our own genome sequenced for a thousand dollars? In the majority of cases, no. But if you turn around and look at this as a public health issue, widespread genome sequence might be able to lead to early diagnosis and treatment of a lot of disorders. This may seem far-fetched right now, but if genome sequencing keeps crashing (especially exome sequencing), then one can imagine the familiar heel-prick screen at birth for diseases like PKU turning into a standard search for all validated pathogenic variants.