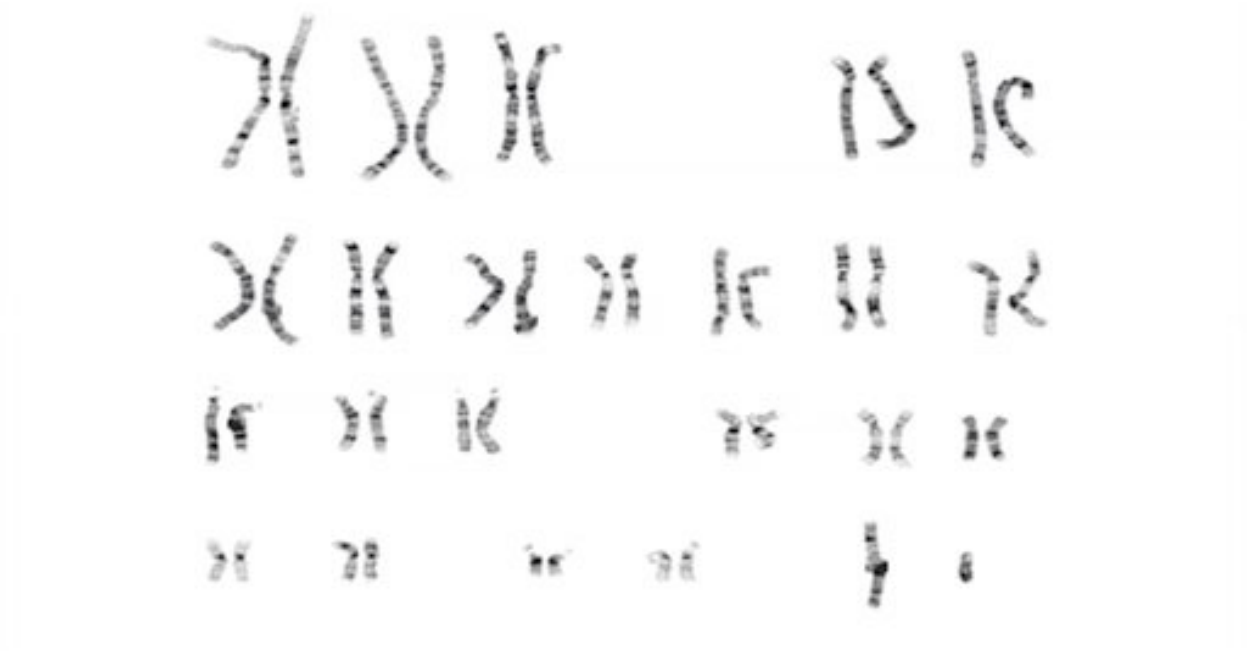
Richard Resnick @ TEDx Boston

Thank you.

Ladies and gentlemen, I present to you the human genome.



Chromosome one top left bottom right are the sex chromosomes. Women have two copies of that big X chromosome, men have the X and, of course, that small copy of the Y. Sorry boys but it's just a tiny little thing that makes you different.

If you zoom in on this genome, what you see of course is this double helix structure, the code of life spelled out with these four biochemical letters--we call them bases, ACGT.

How many are there in the human genome? 3 billion. Is that a big number? Well, everybody can throw around big numbers but, in fact, if I were to place one base on each pixel of this 1280 x 800 resolution screen, we would need 3,000 screens to take a look at the genome. So it's really quite big.

And perhaps because of its size a group of people--all by the way with Y chromosomes--decided they would want to sequence it. 15 years and $4 billion later the human genome was sequenced and published. In 2003, the final version was published and they keep working on it. That was all done on a machine that looks like this. It costs about a dollar for each base. Very slow way of doing it. Well folks, I'm here to tell you that the world has completely changed and none of you know about it.

So, now what we do is we take a genome. We make maybe 50 copies of it. We cut all those copies up into little 50 base reads and then we mass – we sequence them, massively parallel, and then we bring that into software and we reassemble it. Let me tell you what the story is.

Just to give you a picture of what this looks like, the human genome project, three gigabases, right? One run on one of these modern machines, 200 gigabases in a week and that 200 is going to change to 600 this summer and there's no sign of this pace slowing.

So, the price of a base, to sequence a base has fallen 100 million times. That's the equivalent of you filling up your car with gas in 1998, waiting until 2011 and now you can drive to Jupiter and back twice.

[Laughter]

Richard Resnick: World population, PC placements, the archive of all the medical literature, Moore's Law, the old way of sequencing and here's all the new stuff. Guys, this is a log scale. You don't typically see lines that go up like that, right? So the worldwide capacity to sequence human genomes is something like 50 to 100,000 human genomes this year and we know this based on the machines that are being placed. This is expected to double, triple or maybe quadruple year over year for the foreseeable future.

In fact, there's one lab in particular that represents 20 percent of all of that capacity. It's called the Beijing Genomics Institute. The Chinese are absolutely winning this race to the new moon, by the way. What does this mean for medicine? So a woman aged 37, she presents with stage two estrogen receptor positive breast cancer. She is treated with surgery, chemotherapy and radiation. She goes home. Two years later, she comes back with stage 3C ovarian cancer. Unfortunately, treated again with surgery and chemotherapy, comes back three years later at age 42 with more ovarian cancer, more chemotherapy. Six months later, she comes back with acute myeloid leukemia. She goes into respiratory failure and dies eight days later.

So first, the way in which this one was treated in as little as 10 years will look like blood-letting and it's because of people like my colleague Rick Wilson at The Genome Institute at Washington University who decided to take a look at this woman post-mortem and he sequenced. He took skin cells, healthy skin and cancerous bone marrow and he sequenced the whole genomes of both of them. Right? You know, a couple of weeks, no big deal, right?

And then he compared those two genomes in software and what he found among other things was a deletion. A 2000-base deletion across three billion bases, right? In a particular gene called TP53, if you have this deleterious mutation in this gene, you're 90 percent likely to get cancer in your life. So unfortunately, this doesn't help this woman but it does have severe--or profound, if you will--implications to her family. Right?

I mean if they have the same mutation and they get this genetic test and they understand it, then they can go and get regular screens and they can catch cancer early and potentially live a significantly longer life.

Let me introduce you now to the Beery twins. Diagnosed with cerebral palsy at the age of two. Their mom is a very brave woman who didn't believe it; the symptoms weren't

matching up--and through some heroic efforts and a lot of internet searching, she was able to convince the medical community that in fact, they had something else.

What they had was dopa-responsive dystonia and so they were given L-dopa and their symptoms **[0:05:00]** did improve but they weren't totally asymptomatic. Significant problems remained. Turns out the gentleman in this picture is a guy named Joe Beery who was lucky enough to be the CIO of a company called Life Technologies. They're one of the two companies that make these massive whole genome sequencing tools and so what he did was he got his kids sequenced and what they found was a series of mutations in a gene called SPR which is responsible for producing serotonin among other things. So, on top of L-dopa, they gave these kids a serotonin precursor drug and they're effectively normal now.

Guys, this would never have happened without whole genome sequencing and at the time, this was a few years ago. It cost 100,000. Today, it's 10,000. Next year, it's a thousand. A year after it's a hundred, give or take a year. That's how fast this is moving.

So here's little Nick. He likes Batman and squirt guns and turns out Nick shows up at the children's hospital with this distended belly like a famine victim and it's not that he's not eating. It's that when he eats, his intestine basically opens up and feces spill out into his gut. So a hundred surgeries later, right, he looks at his mom and says, "Mom, please pray for me. I'm in so much pain."

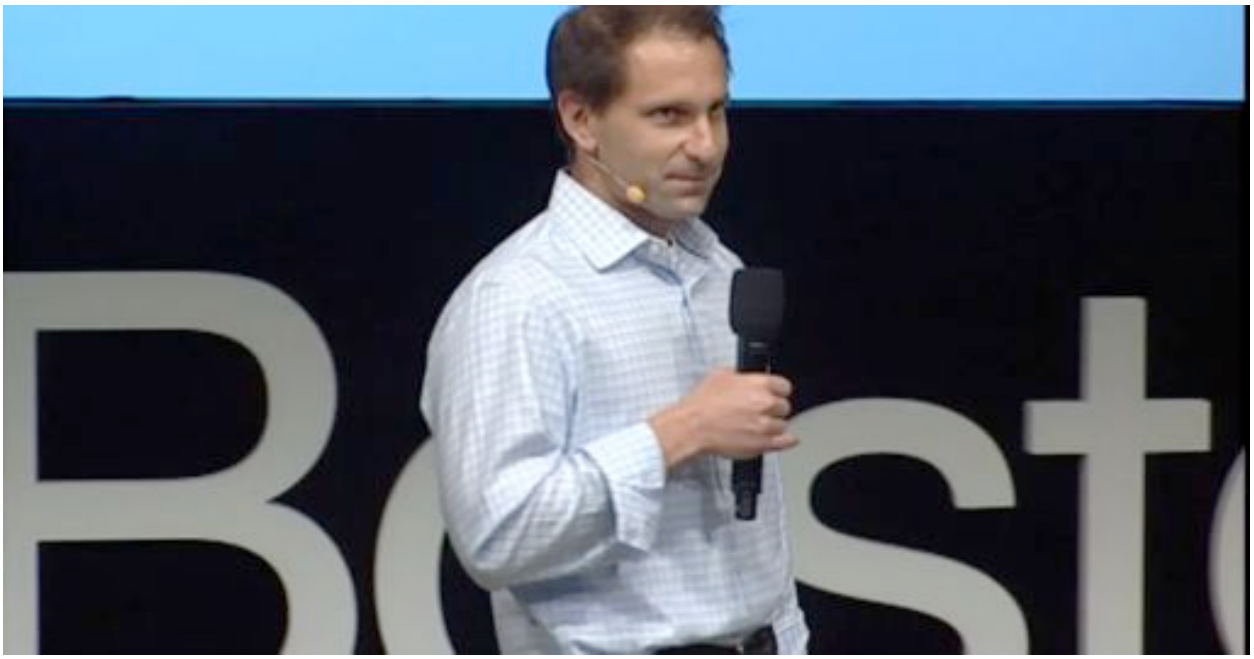
His pediatrician happens to have a background in clinical genetics and he has no idea what's going on but he says, "Let's get this kid's genome sequenced," and what they find is a single point mutation in a gene responsible for controlling programmed cell death. So the theory is that he's having some immunological reaction to what's going on to the food essentially. Right? And that's a natural reaction which causes some programmed cell death but the gene that regulates that down is broken and so this informs among other things of course a treatment for bone marrow transplant which he undertakes and after nine months of grueling recovery, he's now eating steak with A1 sauce.

The prospect of using the genome as a universal diagnostic is upon us today. Today. It's here. And what it means for all of us is that everybody in this room could live an extra 5, 10, 20 years just because of this one thing--which is a fantastic story, unless you think about humanity's footprint on the planet and our ability to keep up food production.

So it turns out that the very same technology is also being used to grow new lines of corn, wheat, soybean and other crops that are highly tolerant of drought, of flood, of pests and pesticides. Now look, as long as we continue to increase the population, we're going to have to continue to grow and eat genetically-modified food and that's the only position that I'll take today unless there's anybody in the audience that would like to volunteer to stop eating. None. Not one.

This is a typewriter, staple of every desktop for decades, right? And in fact, the typewriter was essentially deleted by this thing, and then more general versions of word processors came about but ultimately it was a disruption on top of a disruption. It was Bob Metcalfe inventing the Ethernet and the connection of all these computers that fundamentally changed everything. Right? And suddenly we had Netscape and we had Yahoo! and we had indeed the entire dotcom bubble. Not to worry though. That was quickly rescued by the iPod, Facebook and indeed angry birds.

[Laughter]



Richard Resnick: Look, this is where we are today. This is the genomic revolution today. This is where we are. Okay? So what I would like for you to consider is, “What does it mean when these dots don’t represent the individual basis of your genome but the connected genomes all across the planet?”

So I just recently had to buy life insurance and I was required to answer A, I have never had a genetic test, B I’ve had one, here you go and C, I’ve had one and I’m not telling. Thankfully, I was able to answer A and I say that honestly in case my life insurance agent is listening. But what would have happened if I had said C? Consumer applications for genomics, they will flourish. Want to see whether you’re genetically compatible with your girlfriend? Sure. DNA sequencing on your iPhone? There’s an app for that.

[Laughter]

Richard Resnick: Personalized genomic massage anyone? There’s already a lab today that tests for allele 334 of the AVPR1 gene, the so-called cheating gene. So anybody

who's here today with your significant other, just turn over to them and swab their mouths, send it to the lab and you'll know for sure.

[Laughter]

Richard Resnick: Do you really want to elect a president whose genome suggests cardiomyopathy? Now think of it. It's 2016 and the leading candidate releases not only her four years of back tax returns but also her personal genome and it looks really good and then she challenges all of her competitors to do the same. Do you think that's not going to happen? You think it would have helped John McCain?

[Laughter]

Richard Resnick: How many people in the audience have the last name Resnick like me? Raise your hand. Anybody? Nobody. Typically, there's one or two and so my father's father was one of 10 Resnick brothers. They all hated each other, right? And they all moved to different parts of the planet and so it's likely that I'm related to every Resnick that I ever meet but I don't know.

So imagine if my genome were de-identified, sitting in software, right? And a third cousin's genome was also sitting there and there was **[0:10:00]** software that could compare these two and make these associations. Not hard to imagine. My company has software that does this right now and so imagine one more thing that that software is able to ask both parties for mutual consents. Would you be willing to meet your third cousin? And if we both say yes, voila! Welcome to chromosomally LinkedIn, right?

[Laughter]

Richard Resnick: Now this is probably a good thing, right? Bigger clan gatherings and so on but maybe it's a bad thing as well. How many fathers in the room? Raise your hands. Okay. So it just turned – experts think that one to three percent of you are not actually the father of your child. Look …

[Laughter]

Richard Resnick: … these genomes, these 23 chromosomes, they don't in any way represent the quality of our relationships or the nature of our society, at least not yet, and like any new technology, it's really in humanity's hands to will it for the betterment of mankind or not. And so I urge you all to wake up and to tune in and to influence the genomic revolution that's happening all around you. Thank you.

[Applause]

[0:11:08]