

We are Richard Gibbs, Director of the Human Genome Sequencing Center at Baylor College of Medicine, and Stacey Gabriel, Senior Director of the Broad Institute’s Genomics Platform. We study genetic variation using DNA sequencing, AUA!

Dr *RichardGibbs*¹ and *r/ScienceAMAs*¹

¹Affiliation not available

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Abstract

Hi Reddit! I am Richard Gibbs, a human geneticist, who researches genetic variation using DNA sequencing at the Human Genome Sequencing Center at Baylor College of Medicine. Human genetic diseases are usually dichotomized – contrasting disorders caused by rare, single gene defects that are mainly found in children (such as Mendelian diseases) versus adult, common complex diseases that have can have subtle genetic contributions from multiple changes (such as cardiovascular disease, neurodegenerative diseases, and immunological diseases). My team works to build better ways to sequence and interpret genomes, to translate that technology into the clinic and to better understand the link between rare and common disease. I believe that we are experiencing a social revolution by the propagation of the knowledge and awareness of genetics and genomics in society. I will be back at 1 pm ET (10 am PT, 6 pm UTC) to answer your questions, ask me anything! I am Stacey Gabriel, I have worked at the Broad Institute (formerly the Whitehead Genome Center) for the last 17 years. I joined the Broad after completing my Ph.D. in Human Genetics at Case Western Reserve University where I discovered genes for a congenital disorder, Hirschsprung Disease. This work drove my interest in disease gene discovery via human genetics and with an ultimate desire to drive discovery in more common diseases like cancer, diabetes, heart disease, and others. During my time I have led the Broad’s contribution to several important international efforts to build genomic resources to enable disease gene research. These include the Human Hap Map project, The Cancer Genome Atlas, the 1000 Genomes Project and the NHLBI Exome Sequence Project. I also serve as a Co-Principle Investigator (along with Eric Lander) on a very large grant from the National Genome Research Institute which has established us over the past 25 years or so as a Large-scale Sequencing Center. We operate one of the world’s largest fleets of MPS (massively parallel sequencing) DNA sequencers, generating data for ~ one new human genome every 15 minutes! This data is used by researchers at the Broad and all over the world to make discoveries about human disease, the human genome, and hopefully will fuel initiatives like the President’s Precision Medicine Initiative. I will be here answering your questions for about an hour starting at 2:30 pm ET (11:30 am PT, 7:30 pm UTC). Richard Gibbs here (1,30 pm ET): thanks for some terrific questions! Back to work but I hope to drop in later for a short while. I know Stacey Gabriel is joining in a few minutes. Thanks again. Thanks everyone...was a lot of fun to read and think about all these questions and heartening to see the interest in modern genetics and genomics! Bye RG

[REDDIT](#)

Science AMA Series: We are Richard Gibbs, Director of the Human Genome Sequencing Center at Baylor College of Medicine, and Stacey Gabriel, Senior Director of the Broad Institute's Genomics Platform. W

DR_RICHARD_GIBBS [R/SCIENCE](#)

ABSTRACT

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CORRESPONDENCE:

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In your opinion, how long until this information is a part of the average individual's electronic health record? How will current infrastructure need to change to accommodate this?

One more question: do physicians want this information in health records?

Thank you!

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[RedditPatron](#)

Its hard to define the 'average individual' – but the answer has to be 'very soon'. We already are doing this in pediatrics, in pharmacogenomics and in some cancers – although the adaptation is, from the perspective of some, agonizingly slow. Right now the obstacles are not technical – they are mostly to do with the utility of the information for acute care. If we had a health care approach that was heavily oriented towards prediction, then there would be more enthusiasm to reduce the barriers to getting these data into the health records. Of course some of the hesitation is that the data do not yet provide strong enough predictors for common disease. But even if that changed dramatically (and we are doing our best to change it) then the structure of the health care system will not make it easy. As far as infrastructure goes – we need better informatic tools and systems. Most physicians are open minded and pleased to take on new information and tools – but they need to be able to access the data in a clear and direct way so they can rapidly integrate that into their thinking.

Genetic research centers across the world generate large amounts of data faster than we can analyze and appreciate. The current boiler-plate method of gene discovery involves filtering down the massive number of variants to most likely contributors to disease (using some risk estimation algorithm based on effect on gene product). Then projects follow-up these variants with replication studies and functional analyses.

With advances in methods, do you expect this process to change and in what ways might you improve it? Are we doing ourselves a disservice as scientists to only pursue the most obvious results instead of reaching (even if it means coming up short) for a comprehensive understanding of datasets? Is that what postdoc positions are for?

[MacBelieve](#)

Wow! A lot of territory in these questions: First – yes! We are skimming the surface right now. But our 'genetic architecture' is a bit like a jigsaw puzzle – as we get more information the next part comes easier. So more data, more complete stories, will bring us closer to the finish line. Postdoc positions are primarily for training – you have all those hard-earned skill sets after graduate school – now is the time to hone them and to learn about the larger world! Your postdoc is also without doubt – one of your best chances to have the best time in your life!

Thank you for taking the time to do this AMA. Regarding the future applications of your work, is it mainly diagnosis, or is it to edit the genes to not include the ones that cause disease? If editing do you believe it be possible to change an adults genes or would it only work in vitro or before?

[Switchbak](#)

Thanks for this question! It is 'all of the above' – but in a step wise fashion. As wise person said once – 'first you have to describe, then you can understand, then you change!'. Right now we are in the process of improving diagnostic procedures for genes that are known to cause disease. Meanwhile we are researching and finding more examples – more genes that are medically relevant. As we do that we also gain the power to understand gene contributions to features that are not considered medically important. We want to understand all of these. As for 'changing adult genes' for therapy – that should be possible in some instances. Indeed there is already success in examples in treating forms of retinal disease and in blood – for restoration of immune function. On the other hand it is unfortunately true that there are examples of genetic disorders that influence very early processes – so they are intrinsically likely to be difficult to alter.

Hi Drs Gabriel and Gibbs! Many thanks for taking the time to do this AMA.

Looking backward, do you have any good stories from the original sequencing of the first human genome? Was there anything about the process that surprised you?

Looking forward, what new technology do you think is going to replace next generation sequencing as the hot new tool for understanding human disease? Or said another way, what do you wish we could accomplish with a massively parallelized, big data approach, that is currently not automated/parallelizable?

[p1percub](#)

Looking back – lots of stories! (Some need a ‘throwaway’ or else they will never be told). But lots of wonderful moments of an enormously talented and dedicated community pulling together to do the impossible in a time of hope and uncertainty. Pretty much right from the beginning. A big surprise – at least to me – was the vast and far reaching impact of the early decision to openly and freely release all the raw data. This was all consolidated at an international meeting at Bermuda in 1996 (https://en.wikipedia.org/wiki/Bermuda_Principles). At that time it was so hard to work on the data that the early access did not provide any obvious change in the landscape. But history soon proved that the tools would evolve and major discoveries could be catalyzed quickly from the data access. Now there is pressure on all scientists to release all large scale biological data early and freely – a major product of the HGP.

Looking forward: right now we are intently focused on DNA sequencing to detect gene changes. But in the future we may rely at least as much on other methods for diagnostics – very high resolution imaging, antibody detection and metabolite detection. Better handling of large data sets will improve integration of these different diagnostic leaders together with prior information. The pendulum swings!

How do you feel ethically about the possible future usage of genetic manipulation to change the human genome? Would you use this technology just to cure diseases or would you support the creation of a superior human?

[asiangangster007](#)

Anything in this arena gives great pause! Let's leave the notion of a ‘superior human’ off the table until EVERYONE agrees what that is! We need wide engagement of thoughtful individuals to address these issues head on – for the benefit and protection of all. For better or worse, we have faced difficult questions like this already in the area of reproductive choice and policy. We do need to engage these questions fully so we can be able, where appropriate, save individuals with devastating disease. As usual, we must be rational, fearless and compassionate.

Some of my favorite translational genetics stories involve sequencing populations of humans who 'just don't get sick' (for one ailment or another). For example, the [story of PCSK9 is quite fascinating](#) -- people with mutations in the gene have astoundingly low levels of cholesterol. Using this information, Amgen and Regeneron have designed drugs which can similarly inactivate the protein product of this gene, providing an entirely new way to help patients with dangerously high levels of cholesterol. Do you have any favorite sequencing stories that come from looking at populations of people who have won the genetic lottery in one way or another?

[SirT6](#)

Yes -CCR5 although that is not really a sequencing discovery! A great paper: Harper, Nayee and Topf 2015 'Protective alleles and modifier variants in human health and disease.' Nat Rev Genet 16:689-

701

Are you incorporating Hi-C chromatin conformation technology into your studies and interpretation of the genome?

Cute video for anyone interested in Hi-C: <https://www.youtube.com/watch?v=dES-ozV65u4>

[PombeResearcher](#)

Yes – very useful for long range assembly and worth the extra overhead in many situations. Nice video! This is an exciting new area for understanding genome organization.

What do you think of the quality of 23andme results?

[bitcoins](#)

I love 23andme! (No COI). The reason is that they have promoted genetic literacy – particularly through ancestry and other 'recreational' utilities. I believe their data are technically accurate (with some qualifications) but of course the real issue is medical applicability. Others have a lot more to say about that than I!

Dear Dr. Gibbs and Gabriel,

I'm currently an undergraduate researcher at BCM with Dr. Erez Aiden, who did his PhD at the Broad (under Dr. Lander). One of my goals is to do my Ph.D. at the Broad Institute in 4 years--it's been a dream of mine for years. What steps would you recommend to an undergraduate researcher (I have 5+ years of research experience prior to this) to become a leader in the field of human molecular or computational genetics. What have you noticed about previous individuals, such as Dr. Feng Zhang, or others that made them extraordinary contributors and scientific leaders?

On the scientific side, how do you think NGS pricing reductions (lowering faster than Moore's Law) will allow sequencing to integrate with clinical workflows and what clinical (as opposed to research) role do you see sequencing playing?

Thanks so much for doing this AMA!

[airfreedom22](#)

Good for you! Focus on excellence. Work hard. Keep an open mind. I am sure Dr Zhang and others would say the same. Good luck. RG

What do you believe are the advantages and risks of having over the counter genetic testing kits?

[Fullthrottle200](#)

Big question! At least three relevant considerations: (i) are the tests technically accurate (ii) is the interpretation of the data sound (iii) are individuals being properly supported and guided if they get 'difficult' results. (i) is under a lot of discussion and scrutiny – that's a good thing. (ii) needs some work to divide 'clear actionable results' from 'uncertain results'. But this is not new to medicine and physicians should be empowered to work in that space. (iii) we need more genetic counselling and literacy. This is a huge discussion in the community. My own opinion – these are a good thing and

noone should have barriers between themselves and access to genetic data, if that's what they want.

Hi! How plausible do you think it is to use [DNA as a storage device](#) in future?

Thank you :)

[unspeakableact](#)

The problem is the I/O of course. If you want data to be very stable it is already looking good. But we need some dramatic improvement in the bussing to and fro. Super fast cheap DNA sequencing will help a lot. But we are a long way away. I love this paper by Goldman et al (PMID: 23354052) and take a look at my friend George Church's video <http://www.extremetech.com/extreme/134672-harvard-cracks-dna-storage-crams-700-terabytes-of-data-into-a-single-gram>. He has been thinking about this a long time.

How long does it take to prepare DNA from sample before it is sequenced? What kind of robots do you use?

[coyotebody](#)

It really depends! Some samples and methods are very fast and easy.....hours even with library preparation etc. See papers by Stephen Kingsmore for some elegant examples of fast turn around clinical sequencing!

Has any work been done to monitor a persons genome as they age on a large scale? For example taking DNA samples from a person since birth, then every year there after?

[norml329](#)

Another exciting area to study – aging and other effects on somatic variation. Humans age slowly (relative to scientific careers) so there is more focus on tissue specific somatic variation and comparison with near relatives, instead of sampling the person as they age. Search 'somatic variation mosaicism' in pubmed reviews for some excellent recent papers!

IYO, What aspect of genomics will have the highest demand for skilled labor over the next few years? Bioinformatics?

[coyotebody](#)

Yes – bioinformatics – but don't underestimate translation! Individuals who can take the digital results of genomics and genetics and translate then into research into functional biology and to clinical relevance are key.

Thanks for taking the time to do this AMA.

I see lots of resources about genetic engineering and what we can do with it. I have read about how data from genome sequencing can be used to better understand genetic disorders, and more importantly be useful to the medical community.

How long do you think it will be before we can overcome the ethical barrier of widespread genetic

engineering in humans or at least research with embryonic cells, and observe the effectiveness before proceeding.

PS: I'm no where related to the Biology field. Just interesting in how genetic research can *really* benefit the next generation.

[keepthethreadalive](#)

Your question is appreciated – and I don't want to seem nuanced - but we should be wary of trying to 'overcome the ethical barrier'! We need to embrace the ethical challenges and do what is right. I expect that is what you meant! There is a thread above about engineering for specific disease cures discussing this –we need precision in the technology before we can tackle that.

Hi Richard and Stacey. I was recently diagnosed with Sertoli Cell Only syndrome, i.e. my body does not have the ability to produce sperm. My urologist said this is most likely caused by a variation in the genome, but they aren't sure where or why. Are variations like this being studied, and how long before affects like this are understood? I'm aware that we have mapped the genome, but how are researchers determining random variation effects like SCO?

Edit: punctuation

[infertihelp2](#)

Sorry to hear. This (and other contributors to infertility) is a very active area of research. OMIM and other online resources are informative. Due to technical developments, the study of gene defects has dramatically shifted from a dependency on family history to study of single individuals or trios (parents plus offspring). This is very helpful to studies of infertility that arise in a person as a new genetic change.

There has been a lot of talk lately on further incorporation of other -omics (metabolomics, proteomics, microbiomics, etc.) into our genomic studies of disease. What are your thoughts on this? Are these areas of interest at the HGSC or the Broad? If so, how has this impacted your work?

[foodisfood](#)

Fast moving area! Some papers from here using metabolomic screens to improve/supplement clinical diagnoses (e.g. PMID: 26283345) and also now to deeply phenotype cohorts for discovery of gene effects. Watch this space! Proteomics and microbiomics are longer established and important tools and research areas as well.

Hi, thanks for taking the time to do this! What is one book that you would recommend to give the reader a good introductory foundation on genetics?

[teamcocopuffs](#)

I don't think there is a one-book-suits all – but you should target the Molecular Biology of the Gene (now in 7th edition). This may be too general or too advanced, depending on you.

With illumina essentially cornering the NGS market do you foresee the pace of innovation, particularly cost, slowing? Absent Oxford nanopore or some other disruptive new technology, are we essentially stuck with a monopoly in the medium-term future?

[ranting_swede](#)

Probably (upside-down smiley-face....)

Hello! (This starts personal, but my question really isn't.) My son has Smith-Magenis Syndrome, which in his case, is a deletion on his 17th chromosome at the 17.11.2 locus. Some with SMS have a mutation there. In short, SMS sucks.

Through the foundation I work with, the SMS Research Foundation, we've been able to fund a lab at... the Baylor College of Medicine! (Dr. Sarah Elsea and Dr. Potocki head the lab and I love them very much.)

The RAI1 gene my son is missing is a rather important gene. The proteins within it play a part in coding for lots and lots of things - melatonin cycle, fat cell retention, and most importantly, impulse control and general behavior components. SMS has been termed "the eternal toddler syndrome" because those with SMS have tantrums like toddlers through life. Furthermore, SMS almost always includes lots of self-injury; my son punches himself in the head and face every day... many, many times a day. Others with SMS pull out their hair, rip off fingernails, and all sorts of creative things like that.

Like I said, SMS sucks. We follow - and try to emulate - the work on Angelmans and Fragile X, both of which have made strides with genetic research and protein replacement. Amazing stuff.

So my question: What is the future of genetic research as it pertains to this? Of course we can't "replace a gene" in an individual, but the idea that flooding those missing a gene with the protein(s) they are missing that would most help them. I know I'm dumbing this done (because I'm no geneticist), but I hope you know what I mean.

TL;DR - my son is missing the RAI1 gene and it results in global delays, self injury, and a host of behavioral difficulties. Will genetic research, being done mostly at BCM(!) get to the point of "replacing" his missing gene somehow?

Thanks!

[CTMQ](#)

First – thank you for your parenting – you have and deserve enormous respect for that. Thanks for the kind words for my amazing colleagues. For cures, especially for early onset disorders, we have to better understand neurological development and what is needed to be fixed. The good news is that research in this area is exploding! So many new genetic discoveries. Talented groups are exploring therapeutics. Gene replacement in an individual with a disorder that arises in early development is a very tough challenge, but there are other possibilities. I wish you all the best with your family.

Hi Drs. Gibbs and Gabriel, and thank you for doing this AMA!

GWASs have certainly played an important role in driving insight into the biology of complex traits and diseases in the past decade.

An emerging view, however, suggests that rare variants which are not well-interrogated by GWASs may be responsible for a substantial portion of complex human diseases. If true, this would put a lot of pressure on current genomics groups to revise their sequencing strategies -- for example, instead of focusing on cohorts of 'controls' versus 'diseased patients' it would make much more sense to focus on families via trio sequencing/linkage analysis.

I would love to hear your thoughts on what portion of disease you think is caused by these types of

rare-variants, and what the best ways to detect them are. Thanks!

[SirT6](#)

You are 'singing to the choir' to me, most of my colleagues at Baylor College of Medicine and many, many others. We have a long history of studying rare variants in the context of rare disease (Mendelian disease). So the new question is 'what about rare variants in common disease'?. Data are clearly showing that rare variants can be important in cases of common diseases – and our task now is to see how generalizable this is and how much of the overall genetic risk burden is made up of these variants. We – and others - are tackling this on several fronts including adding family data into larger case-control studies, deeper phenotyping and expanding studies of aggregate genetic in syndromic conditions with some fraction already resolved by mendelian studies. I think we can all agree about one very healthy trend – genetics research is now proceeding on 'all fronts'.

How many more years would you say until we have truly personalized sequencing (at a realistic price point) for personalized diagnostics/treatment? For example, I go to the doctor, then they sequence my DNA quickly to check for SNPs/mutations/epigenetic changes, etc, then apply targeted treatment.

[slickguy](#)

We are on the edge of that. If you have paid for an MRI lately then by comparison genome sequencing looks pretty accessible! Most in the field are lamenting that the trend for rapid drop in cost is slowing. But there are possible disruptive technologies on the way. Also, even with current methods the streamlining of the sequencing is inching us in the direction you describe. So it is an 'if', not a 'when'.

What are the most common gene defects in children, and what's the known cause of them, if any?
Thanks for doing this AMA!

[deathstar3548](#)

Thank you I love this question because there are both easy and non-obvious answers/issues that are embedded! Cystic fibrosis, sickle cell anemia etc are the usual answers – along with chromosomal disorders (e.g. Downs). But the reality is that we really do not know! So far we have focused studies mostly on acute, identifiable disorders- children who are really ill. What about the vast numbers that have mild conditions, perhaps not even getting them to medical care for the specific cause? Or for whom a genetic underpinning is not suspected? Learning ability, dietary reactions, sun sensitivity, frequent injury while growing due to a connective tissue 'anomaly' etc? One day we will have a long list reflecting our understanding of these things.

With the commoditization of the wet lab and sequencing portions of the NGS workflow, how do you feel about the "build vs buy" decision in bioinformatics analysis?

Both Baylor and Broad have two of the best bioinformatics teams (and in-house pipelines) in the world. For smaller institutions, however, do you feel the "build" option is realistic?

How do you see the field of bioinformatics support evolving in the next five years?

[r4nd0m_us3rn4m3](#)

Build vs Buy: No tools are perfect and few approach that. Ideally some of both. If your institution has the people and infrastructure then build what you can when the options out there to buy are not quite right. As a large scale center, our tensions and needs are a little different than many groups. Part of

our mission is to stay ahead of the curve and innovate. By the time something is feasible as a commercial product, we are usually working on the next problem. Example: people trying to sell us SNV solutions, we are working on SVs, and no one has that.

For the next five years? Bioinformatic tool performance and access for basic data management is so terrible right now, it can only get better. Compare processing genomes to buying tires, pizza or books online! We need to get to the point of creative, thoughtful analyses being helped, not impeded, by processes that involve large data crunches. If building is not feasible buy is likely the way to go. In that case don't be hesitant to dig into specific problems and push back if the product isn't what you want. Science should drive business, not vice versa!

Hello! Thanks for this AMA! What do you think about the 1000 \$ genome sequencing? Since it's becoming cheaper and cheaper, more people are able to afford their DNA being sequenced. What are the chances /disadvantages of this?

[Herbivorix](#)

Big question: My own opinion is this a great thing – not just for research and medicine but for everyone. But there are tensions! Search 'should i have my genome sequenced' and you will get some other opinions!

Which effect did the development of bioinformatics algorithms have on your personal work in the last decade? What do you expect for the future?

[Herbivorix](#)

Where would we be without BLAST! Clearly all bioinformatic developments have been enabling. It is however interesting to contemplate the history of the impact of development of algorithms that do sophisticated data management versus the impact of the amount and quality of 'raw data'. I have to say that over time I am more and more amazed at how additional data gathering is so often transformative. The area of genome assembly is one good example – lots of accolades for new assembly algorithms but in general it is only when you get more data that you can improve the assemblies! This is also true for many other areas of genomics – and biology. I am not suggesting running out to measure and catalog all things. But it turns out that when you are ambitious in data gathering in a well defined area you can gain great insights and generate and test hypotheses as you go! Another way to approach your question is to rephrase it as 'where are the abstractions and mathematical models in biology – are they in the algorithms we use?' The answer is 'not really'. Almost everything we call a bioinformatic algorithm is a data management tool – not the core elements for prediction or hypothesis testing.

Thank you for doing this, Doctors. My daughter is special needs with an undiagnosed genetic disorder. We've had a WES done that showed a variant of unknown significance on the EBF3 gene. There's very little known about this variant to determine if this is the cause of her condition. It seems like our doctors have all but given up on finding a diagnosis. At what point would you recommend doing a whole genome sequence?

[jrcameraman](#)

Thanks for your query. (Reminder – I am not an MD). I am not sure if your current care givers have exhausted all the analytical paths they could. More details are needed but feel free to contact me privately and I can direct you to our genetics diagnostic group. Do not give up.

Did you purposefully change the prompt from AMA to AUA so it would be a codon?

More seriously, when do you think nanopore sequencing will become available and financially accessible to the general scientific community?

[LeftiesUnite](#)

Thanks I got quite a chuckle out of that. Nanopores come with a lot of challenges as you can see from the progress of the major player(s). However it is important not to underestimate the impact of even highly error containing long read data. Other methods have shown that if you have enough of it, and certainly if you have complementary data from other methods, this can highly impact the aggregate data quality and utility. So maybe sooner than we think.

Have you ever worked with microRNA before and do you have any tips for someone who is new to working with them? Any kits you suggest? I've come to learn that they're super sensitive and a pain in my rear, I can't seem to get amplification with qPCR. Thanks so much !

[samypooch25](#)

Hard but not super hard. But I am not the person to ask – my reply is really to remind everyone about the dangers of this: https://en.wikipedia.org/wiki/Peter_principle good luck!

Hi docs!

Do you have any insights into digital barcoding of libraries, and how feasible it would be to incorporate these techniques into an existing sequencing pipeline?

I've been trying to find literature on it, but there's not much out there in the way of publications--it seems a lot of dev is being done outside of academia!

[SexierThanMeiosis](#)

he vendor user groups are a good source – or contact me privately and I can direct you to the head of the HGSC Library group. I am sure Stacey Gabriel can do the same or any other large scale center. Good luck

Thank you for doing this AMA.

My question can lead to complexity really quickly.

As I have been studying in my biology course, I know that you can make as much human insulin as you want once the proper segment of DNA is spliced and placed in a vector/plasmid such as a bacteria. Recombinant DNA. The accepted DNA is then read by the bacteria and whatever read, the bacteria creates. In that case. Insulin.

My question is. How do you even start? Studying DNA and RNA. It's incredibly complex and the sequence of bases are in the trillions. My teacher basically told me it's a guessing game. You take a certain piece of DNA, and hopefully it does something. Since a lot of the DNA is unknown in what it does. Don't even get me started on oncogenes. Genes that specifically cause cancer but that's due to carcinogenic substances modifying the sequence of bases from an initially turned off proto-oncogene.

What would you look for first?

And my other question. After learning so much about the human body and how complex and amazing it is, trying to keep you alive, doing anything to help you stay healthy, I'm curious if it will ever be in the near future to create a cognitive enhancer of great magnitude. I say near future not "if it can be done" because I know it will be done. Eventually.

The brain is incredibly complex with many Neurons firing in many areas. For example. The movie (also now a series) Limitless where the character ingests a drug called NZT-48. This drug causes massive cognitive increase where you can recall anything and learn much more quicker. Having the pupils slightly dilated which could explain why colours look more brighter.

Sequencing massive amounts of DNA, have you found anything regarding a segment of DNA that is linked to neurological pathways in the brain? Can it be modified? Well. I know it can be, but it's the correct sequence that makes it tricky.

I take Adderall to treat my ADD. I'm not on it right now so this large text isn't due to it, you tend to pick up habits the drug gives you and it lets you act out on them. I guess being on Adderall and experiencing these NZT like boosts made me curious to expand on it more. Thoughts?

Thank you for reading this massive comment. Writing on mobile early in the morning so there might be typos.

[Unknown_Citizen](#)

To start – you need a hypothesis! What are you trying to find out? The brain – we know a lot of the DNA that is needed to make it function 'normally'. But no enhancements yet. Stay tuned!

Not the most interesting question but how often do you replace your sequencing equipment and how do you balance this with the costs of doing so? It seems that every couple of years, the latest Next-Gen sequencing machines become very obsolete.

[El-Lid](#)

We build a 3 year amortization cost into the machine activities. Comes out about right.

What's the cheapest and broadest DNA test any layman can have done? (For checking humans)

[NUMBerONEisFIRST](#)

23andme and ancestry.com are two I know about. I think they have periodic special rates - and there are others but I am not familiar. Check their web sites!

How often do you meet negative reactions from the public, caused by people's belief that genetics is not an area where we should be "meddling"? Additionally, do you consider this to be the result of scientific illiteracy or just plain stubbornness?

[BlueSkyBG](#)

Negative reactions are rare – but indifference is abundant. Usually it is the onset of a 'genetic problem' in a friend or relative that gets interest. But not too much anti-meddling sentiment. I think the GMO folks might give a different answer.

Hi, and thanks for this AMA! I am a Molecular Genetics major at Ohio State, where we are looking to start a genome sequencing project of our own - but for ash trees, not humans. Do you have any advice for how to get started setting up a genome project? For instance, are there software suites you would suggest, or annotation tutorials that you have found useful?

[RedDragonJ](#)

Visit a lab – or reach out to experienced colleagues. Your time is precious so please don't learn all the hard lessons that others have!

How long until your work can be used to fix diseases like this by editing genes?

[ReasonablyBadass](#)

Complicated question: Some dramatic moves in this direction (e.g. check out <http://crisprtx.com/>). Nothing is certain in this area, but there is enormous promise.

Hey there, what are your thoughts on the ethical implications of personalized medicine? i.e. It's great to be able to steer a therapy based on the patient's genome, but what about the possible discrimination?

[sofakiller](#)

Health disparities are an important issue. Genetics research is trying to make a positive contribution in this area by tackling a wide portfolio of disorders.

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Mosaicism yes. Not based upon my experience – but on published data. There are also publications on MTOR pathway mutations and possible ASD (search autism mtor).

Have you found any genome sequences that determine one's personality type? If so, are certain types more prone to certain psychological diseases/mental disorders?

[WhiteLodgeVaporLab](#)

Strictly speaking you can say that certain rare genetic conditions display clear behavioral patterns. But this is really not the same as a 'genetic personality type'. That concept, and the general understanding of all personality types, is one of the big questions in genetics and all of biology.

what does this help or do ? use to saves lives ? develop super human ?

[mgic92](#)

Save lives: Yes. Super human: No.

This is kind of abstract, but, do you believe there is any mechanism built into living organisms that purposefully creates mutations to create adaptations to experienced stress over time, or are all mutations random?

[Passing Thru Forest](#)

Ha! Old, intense debate. Check out: Galhardo RS, Hastings PJ, Rosenberg SM 2007 Mutation as a stress response and the regulation of evolvability. Crit Rev Biochem Mol Biol. 42:399-435.

Do you guys have any good study tips/resources? Sorry off topic.

[TruGabu](#)

Just do it. Seriously.

Can you recommend software for a molecular biologist, with minimal computer programming skills, to analyze whole genome or exome sequence data for variants, on the cloud (probably through google genomics, or amazon)?

I am currently planning to learn to use the GATK software package from Broad, but I am wondering if there is a more user friendly option for the non-coder.

[26point2Beast](#)

You may wish to look at the Mercury Pipeline available via DNAnexus (<http://blog.dnanexus.com/2013-10-22-run-mercury-variant-calling-pipeline/>) and check out resources from X et al 2015 WGS: an annotation pipeline for human genome sequencing studies J Med Genet. 103423. [Epub ahead of print]

This is so exciting! Dr. Gibbs, my dad worked with your department at Baylor some years ago, and I was friends with your son for a while. I had a couple of opportunities to meet you but I was too nervous at the time! I've been hearing about your work since I was very young, and it's only affirmed my love for genetics. I'm passionate about this field and am trying my best to get into a program to study it in-depth. You guys are kind of my heroes! I have kind of a lot of questions and I understand y'all may not have time to answer all of them or any at all, but even if y'all just skim over them I'll be thrilled!

What would y'all consider the most underappreciated part of your work?

Is a background in medicine necessary for genetics research? To what extent? (Just a few pre-med undergraduate classes, or a full MD?)

I'm looking into genetic counseling as a career path. Do you think it will remain a somewhat niche profession or become more widespread as genome sequencing becomes faster and less expensive?

What's the most difficult project you've ever worked on and what was the outcome?

Does gene therapy look as promising to professionals as it does to the general public? Why or why not (cost, efficiency, reliability)?

Do you think the role of genetics is over- or understated? Specifically in early education and media. Does that help or harm your research?

The interaction between environment and genetics is pretty complex, but (I'm sorry if this is incorrect) I understand that certain environmental stimuli can actually physically change people's genome. Is there

any way we could use this to modify living people's genes so that, for example, an adult with Huntington's could have children without the risk of the child inheriting the disease?

And finally, what are your strongest arguments for and against modifying egg and sperm cells to create "designer babies"?

I'm sorry if any of these are repeated elsewhere in the thread, and as always, thank you so much for taking the time to do this!

[bundlesofjoy](#)

Great! It sounds like you love science! Underappreciated? I think almost all scientists actually work really hard. Even though it is usually a 'labor of love' it does not leave much room for other things. Background: No, I don't think a background in medicine is necessary for genetics research...but increasingly a background in genetics is needed for medical practice! Genetic counseling is a wonderful career choice! Don't hesitate! Role of genetics – understated in most cases. But we are getting the data to show exactly what the contributions of genetics really are. The most difficult project? The current one! And your great questions about gene editing? Some other threads here but you ask about the toughest one – human germ line editing! We might need a whole forum for that. Great to hear from you!

What has been the most personally fulfilling part of the human genome project for you? Have you learned something that helps you understand yourself better?

[sjgw137](#)

It is a real privilege to have a career centered on helping humanity. That is a great feeling - and it is felt every day. Working on the HGP was a wonderful experience. Since then, the field of personal genomics has been incredible and making the methods for translating genomics into routine clinical use is very rewarding. I sequenced my genome and found a couple of carrier mutations in neurosensory pathways....so perhaps I understand myself a little better!

Hi,

I've been running BOINC for about 10 years, and have done folding@home for some time also. I'd like to contribute more. I have a degree in computer science and currently work as a software developer. Do you have any recommendations for projects where I could donate my time? I don't have any experience in bioinformatics.

[_Foxtrot_](#)

Exciting! I think it would be great to have you interface with some of the local bioinformatics mavens....and take it from there! Please feel free to contact me privately. RG

Hi! I have a question but first I just want to say thank you for the work you do! I am currently being evaluated for a condition that previously required a liver biopsy for dx but now just requires a simple blood test to look for the gene. Way easier for me so i'm very grateful!

My question is, how do you determine which gene mutations are significant for a disease, and whether there are multiple mutations that may come together to cause an issue?

[yochana8](#)

Thank you! This is the main thrust of human molecular genetics. Bottom line – we need a lot of genetic data (i.e. genome sequences) and a lot of clinical data. Then we perform correlative analyses and follow-up biological studies. There is a much longer answer but this is the basic approach.

What areas of study does your team hail from? Asking for a friend who is interested in this sort of research and doesn't know what major to pursue. Im guessing bioinformatics/biotech as well as genetics and other areas of biology? Thanks for doing this Ama!

[Tittytickler](#)

All kinds. My own background is in radiation biology. In general it is harder for biologists to learn quantitative methods and approaches than the reverse. So some mathematics, physics and computer science is a great start.

Is it true that our DNA is changing currently? Is there a big difference from the way DNA looked 20 years ago to now?

[UnLikeableSource](#)

There are a couple of hundred new changes (de novo mutations) per generation so...yes! However the genome is vast (6 billion per diploid) and many other factors are at work (particularly negative selection where the mutation is lost) so 1-2 generations is not enough to make a real difference.

I started studying genetics at university in 2004 after being inspired by the human genome project. I cannot believe that just 10 years later I have been able to sequence a patients genome in just a few hours and look at it on my laptop anywhere I go. Your software has been invaluable to my research. A very big thank you from Melbourne, Australia.

[schoome](#)

Terrific! Melbourne is my home town!

Hi, how do you like the administration at BCM? Have you had any problems with them? I have heard some terrible things, like people getting canned through PIs making up accusations about creating hostile work environments through political speech, I have known two different people from two different labs at BCM who had this happen to them.

[magnora7](#)

I have to close out and also normally would avoid a question like this - that seemed to have slipped through filters. But I have to say that BCM is enjoying an amazing period of terrific leadership! If interested, search the news services for BCM pre 2010....versus now. Our President and Senior VP of Research (aka Dean) each run labs with active NIH grants! I think that is unique.

Hi Richard and Stacey. What would you consider to be the single most important technological development in terms of genome sequencing during your careers?

[erberger](#)

Have to chime in on this one as I am older than Stacey.....PCR and the microprocessor!!