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Science AMA Series: Hi Reddit! I'm Eric Green, Director of the National Human Genome Research Institute (NHGRI) at the National Institutes of Health (NIH). I'm excited to talk about the Human Genome Project, and Genomic Medicine. Ask Me Anything!

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[1]Affiliation not available

April 17, 2023

Abstract

Hi Reddit - I'm Eric Green, Director of the National Human Genome Research Institute (NHGRI) since 2009. NHGRI is the largest organization in the world solely dedicated to genomics research, and a part of the National Institutes of Health. I started my career in genomics research in the lab of Dr. Maynard Olson at Washington University, and was then appointed Assistant Professor of Pathology and Genetics and Co-Investigator in the Human Genome Center at Washington University. Two years later, I joined the brand new "Intramural Research Program of the National Center for Human Genome Research", which was later renamed the National Human Genome Research Institute (NHGRI). Prior to becoming Director of NHGRI, I served as Scientific Director of the NHGRI Intramural Research Program, Chief of the NHGRI Genome Technology Branch, and Director of the NIH Intramural Sequencing Center. During that time, and for almost two decades, my lab was at the forefront of efforts to map, sequence, and understand eukaryotic genomes. I was significantly involved in the Human Genome Project from start to finish. As Director of NHGRI, I am responsible for providing overall leadership of the Institute's research portfolio and other initiatives. In 2011, we developed a new vision for the future of genomics research, entitled Charting a course for genomic medicine from base pairs to bedside (Nature 470:204-213, 2011). Since that time, I have led the Institute in broadening our research mission, including designing and launching a number of major programs to accelerate the application of genomics to medical care. I'll be back at 1 pm EST (10 am PST, 6 pm UTC) to answer your questions, ask me anything!

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REDDIT

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ERIC_GREEN R/SCIENCE

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I am a layman, but boy do I enjoy a dramatic science headline. What is the most amazing, holy grail sort of discovery in genome research that we might expect to see within 10 years?

Edit: Obviously, the most amazing discoveries are.. yet to be discovered. I guess a better thing to ask is are there are any theories you find particularly interesting that might be proven or disproven soon?

sufjams

I could readily imagine a headline within the next decade that reads "All cancers now diagnosed using genome sequencing." I give this example because, in my opinion, cancer care will be one of the first clinical areas in which genomics will become mainstream. This is already becoming the case for some types of cancer, but within a decade, I could imagine that genome sequencing will be used as part of the diagnosis process for all types of cancer.

If you do not mind, I am going to ask you a question my father always asks me. I try to explain that science takes time, and results need to be tested and verified, to no avail, to answer his question. I work in IT and I do the best I can to answer, but it never seems to satisfy his mind.

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So in laymen terms: "If we have already mapped the human genome, why can't we cure cancer, Lupus, and MS, and other ailments?"

If you could give me a easy simple explanation that my father could understand, that would be greatly appreciated. Then next time he asks the same question I can have a print out of your answer, and all I will do is say "listen to the scientist who is a master in this field".

HaroldPlease

I really like the responses that you received to this simple but important question. Great analogies, folks!

Let me add a 'practical' answer to the mix, one that emphasizes the need to manage expectations in the face of amazing progress. If you look back on the history of biomedical discoveries and the eventual changes to medical practice that came about from them, there is typically a sizable time lag--often measured in multiple decades! Classic examples of this include the discovery of antibiotics and then their eventual use clinically to treat infections AND the fundamental biochemistry discovery that eventually led to the use of medications to lower cholesterol levels.

So landmark scientific discoveries do not lead to changes in medical practice overnight or even within a decade. Most often, it takes several or more decades before changes in medical practice are seen. The Human Genome Project ended a short 13 years ago. We have already seen a few genomic medicine examples emerge. BUT the best is yet to come! Be patient and recognize that inevitable time lag associated with making true medical progress. Many more awesome examples of genomic medicine in action will arrive in the coming years and decades.

How can someone identified with a genetic abnormality find research opportunities for their abnormality and offer to participate?
My family was recently screened for genetic disorders. The screening turned up a 'significant' gene mutation in both sufferers. However, there is very little our doctors, or myself, can find about this gene or impact of it's malfunction.

Thank you for this AMA!!

TheOnlyTxLiberal

Thanks for this important question. A great place to start would be the Genetic and Rare Diseases Information Center, which is a resource at the National Institutes of Health that provides information about rare diseases and aims to help families like yours. I urge you to contact them at https://rarediseases.info.nih.gov/gard.

How big a deal is CRISPR from your standpoint?

cary_granite

As a research tool to ‘edit’ DNA and help us answer difficult questions about how the genome functions-- a HUGE deal. CRISPR is a very powerful experimental tool!

As a tool for possible use in possible treatments, it is not clear what role CRISPR will play. While it has great potential, there are many challenges associated with using CRISPR outside of a research laboratory. However, perhaps some day, CRISPR or another similar technology might be important for treating human disease.

Do you think Direct to Consumer testing services like 23andMe are helping in bringing genetic testing to clinical relevance? Or do you see it as potentially dangerous for the many people who receive results without proper genetic counselling?

ritz37

Direct-to-consumer DNA testing services have increased the ability of the average person to gain access to information about their own genome and, through this, to begin to learn about how their genomic information can be useful for managing health. Many people are thrilled with the possibility of finding out the underlying causes of specific traits that they have -- whether it is a “fun” trait such as ear wax texture (which also happens to be linked to armpit smells!), information about ancestry, or a more medically informative trait or risk to develop a disease. There are diseases with serious implications for which some people are not sure they want to know their predisposition. In addition, genomic information is only part of the story. There are environmental influences that affect a person’s susceptibility to disease, so it is important to think about genomic information related to health in the context of a person as a whole. This is where a genetic counselor or another health provider can be important to consult. But, making genomics interesting and fun to learn about for the public is a good thing and I appreciate what direct-to-consumer DNA testing companies have done in stimulating interest in genomics.

Hi Dr. Green, thanks for doing this AMA. Chromatin conformation capture techniques have revealed that the genome is not randomly packed into the nucleus, but is intricately folded into origami-like loops and domains that help regulate gene expression. This technology will likely provide mechanistic insight into the characteristic translocations observed in some cancers (non-Hodgkin's lymphoma) and the mutation hotspots in promoter regions described in the latest issue of Nature.

So my question is: How much resources are you investing into understanding the 3-dimensional genome?

EDIT: Non-Hodgkin's lymphoma

PombeResearcher

Wow-- a very sophisticated and important question! You nicely point out that DNA is not an innocent linear molecule in our cells, with all the information contained in the one-dimensional series of letters. Rather the DNA in our genome adopts very complicated three-dimensional conformations, creating interactions among different genomic regions. Those interactions are important for the functioning of DNA in ways that we could not have imagined a decade ago. To study these, interactions, genomics researchers are developing new technologies for detecting these three-dimensional structures and determining how they influence genome function.

If you want to read more about some of the projects NHGRI has funded for better understanding the 3-dimensional structure of the genome, here are some relevant links: --Functional Genomics Program https://www.genome.gov/10000612/functional-analysis-program/ --ENCODE Project https://www.genome.gov/10005107/encode-project/ --The recently initiated NIH Common Fund's 4D Nucleome program aims to understand the principles behind the three-dimensional organization of the nucleus in space and time https://commonfund.nih.gov/4Dnucleome/index

What are the biggest challenges you have faced on your line of work, and how did you overcome them?

Clemen11

The word ‘genomics’ was not coined until around 1987-- and the field of genomics did not exist until then. Meanwhile, I graduated medical school and graduate school in 1987, which means that I never once heard the word ‘genomics’ at any time during my formal education. Yet here I am leading the largest organization in the world dedicated to genomics research! This means that I had to learn everything I know today about genomics AFTER all my formal education was over. While a challenge at times, this illustrates the importance of being a ‘lifelong learner’ in your pursuits. You should regard your formal education as the floor for your knowledge, not the ceiling.

Hello Dr Green!

If I may ask, what are the biggest challenges/limitations in genomic medicine that scientists will have to tackle in near future? Are there anything hindering the technique from being utilised on the bedside now, or it simply needs some more time?

Thanks!

Motherofcurry

To be clear, some applications of genomic medicine are ‘here and now’! One example-- we can now perform prenatal testing of unborn babies for genetic disorders by analyzing the very small amounts of fetal DNA floating around in maternal blood. Previously, more invasive methods were needed to get fetal DNA, but now a simple blood draw of a pregnant woman will suffice. Such ‘non-invasive genomic testing’ was performed over a million times worldwide last year!

For most other areas of genomic medicine, the biggest challenges relate to having established sufficient evidence to show how best to use genomic information to improve clinical care. While we have good hints about many such applications, we need proof about them before allowing them to be used in healthcare. Many such studies are ongoing, for example by our Clinical Sequencing Exploratory Research program (https://www.genome.gov/27546194/clinical-sequencing-exploratory-research/).

What is your/your team's aim? I don't mean the organization or anything like that. I mean either your personal aim or goal or your team's if you are all aligned on this project. What do you personally hope to achieve? Is this your dream coming true? How does it apply to your average Joe on the street?

Best of luck and keep on rockin' and sciencin'!

ThatGamerDude

The organization that I direct-- the National Human Genome Research Institute-- was originally established to lead the U.S.’s effort in the Human Genome Project. When that Project was completed in 2003, we expanded our mission to include the application of genomics to understand human disease and to improve human health. In short, we aim to establish how best to use information about each person’s ‘blueprint’ (that is, their genome) to tailor their medical care.

Hello Eric! My question is:

- What is the number 1 piece of advice you could give to a student wishing to move into the field of genomics?.

Thanks.

BrumBiologist

The obvious advice is to get a strong, broad-based education, eventually taking more in-depth classes in genetics and genomics. However, being involved in 'genomics' could come from many different careers-- ranging from becoming a physician, a researcher, a nurse, a pharmacist, a lawyer, a policy expert, etc. (For more information on potential careers or course of study, you can visit the NHGRI Genomic Careers Resource which has a listing of more than 50 careers, including careers in genomic medicine: https://www.genome.gov/genomiccareers/). My less obvious advice is to make sure you become proficient at writing well and at speaking well-- the field needs people who are good at communicating, and being skilled at written and spoken communication would be valuable. Good luck!

NIH patient here, part of an NHGRI protocol. Thank you for all the amazing work that you do.

What challenges does NHGRI face when it comes to genomic sequencing? Specifically, scouring that data and finding generic bases for established and rare disorders? How can we make the process go faster?

AlbinoAlex

First of all, thank you for your participation!
That is a great question-- and one that we are working hard to answer. It is becoming obvious that there won't be a single 'thing' makes this process go faster. Rather, we will need a 'toolbox' of options from which we can grab for use in figuring out the genomic causes of disease. Some of these tools will be purely computational, others will require laboratory work. In some cases, we will need the help of studies involving experimental organisms-- like fruit flies, worms, yeast, mice, etc. This is absolutely an area that we need to improve in over the coming decade, and so we have many researchers developing new strategies and new technologies for this exact purpose.

Good morning Dr. Green,

My questions are, do you think we'll be able to break through the 1 genome for a $1000, if we haven't done so already?

Follow up, if it does become possible to sequence genomes for under $1000, what do you think will be the challenges in being able to utilize personalized sequencing data in bringing that data to the bed-side in regards to healthcare?

LostinWV

Yes, I am very confident that we will be able to sequence a human for less than $1000 within a year or two (or possibly three). There are a number of very cool new technologies that are becoming available that will help us cross that threshold. One of the 'coolest' ones just being implemented is a small device that plugs into the USB port of a laptop computer and, hopefully, will be able to sequence a human genome in about a day for less than $1000. We are watching developments of that technology very carefully! I am told that the device works equally well in a PC or Mac laptop, which makes it particularly amazing...

Regarding bringing the data bedside: You raise a really terrific and insightful question! Just because we can read out all the letters in a human genome at a technical level, it does not mean that we are (yet) able to understand what those letters mean for a person with respect to their healthcare. So, we find ourselves in a challenging situation right now where we can generate the sequence, but can't fully interpret it yet. Genomics researchers are working very hard to 'close this gap' and develop better, quicker, more accurate ways to analyze a patient's genome sequence for use in their clinical care. This really represents a 'cutting-edge' area of genomics research today (and probably for the next decade).

I'm an undergrad about to graduate with a B.S. in biology. One thing I've heard often in my classes is that the Human Genome Project, like most major research initiatives, has left us with more questions than answers. I'm wondering what you think are the biggest questions in genetics that the results of the Human Genome Project has left us with? Going further, are there any major questions you think we are close to answering, maybe within the next decade or two? Thanks for doing this AMA!

milky-star

The big questions following the Human Genome Project: How does the human genome actually function? How do differences in people's genome result in disease? How can we use information about a patient's genome to better provide them medical care?

"Going further, are there any major questions you think we are close to answering, maybe within the next decade or two? "

All of the above-- especially if you give us two decades!