Science AMA Series: I'm Dr. Paul Knoepfler, back again to talk about CRISPR, human genetic modification & designer babies.AMA!

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Abstract

Hi, I'm Paul Knoepfler, stem cell and genetics researcher, author, & blogger. You may have heard about the new gene editing/genetic modification technology called CRISPR. It is totally changing how we scientists genetically modified cells and even organisms. What used to take years and potentially millions of dollars can be done in weeks or months for a few thousand bucks. In my lab we use CRISPR to do research on stem cells and cancer. Others are doing similar work for a variety of other conditions, while some are making new GMOs in record time such as plants, super-muscled cows or micro pigs CRISPR is transforming the way we do some of our science, but at the same time it is raising difficult questions that require public education and debate. For instance, are we ready to make genetically modified people (what I call GMO sapiens as a mashup of Homo sapiens and GMO)? Is it OK to do this for trying to prevent genetic diseases? What about for human enhancement via designer babies? Could we draw the line between the two? How does this technology even work and what are the risks? Are past works of art like Brave New World and GATTACA now appropriate to discuss as human genetic modification appears to be marching toward reality? Or is that just going to scare people? What about eugenics turbo-charged by new technology? How do we find the right balance in discussion of this revolutionary issue so that we do not freak people out, but at the same time we have a real discussion that doesn't sugar coat things or dodge real potential issues? There's a lot to talk about so let's dive in. You might want to check out my blog at http://www.ipscell.com and my new book on today's topic, [GMO Sapiens: The Life Changing Science of Designer Babies](http://www.worldscientific.com/worldscibooks/10.1142/9542 You can also view my TED talk on human genetic modification and the possibility of designer babies.) You can also want follow me on Twitter @pknoepfler if you like for all the latest, I will be answering questions starting at 1 PM EST (10 AM PST, 6 pm UTC) Ask Me Anything!

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PAULKNOEPFLER R/SCIENCE

ABSTRACT

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You may have heard about the new gene editing/genetic modification technology called CRISPR. It is totally changing how we scientists genetically modified cells and even organisms. What used to take years and potentially millions of dollars can be done in weeks or months for a few thousand bucks. In my lab we use CRISPR to do research on stem cells and cancer. Others are doing similar work for a variety of other conditions, while some are making new GMOs in record time such as plants, super-muscled cows or micro pigs CRISPR is transforming the way we do some of our science, but at the same time it is raising difficult questions that require public education and debate. For instance, are we ready to make genetically modified people (what I call GMO sapiens as a mashup of Homo sapiens and GMO)? Is it OK to do this for trying to prevent genetic diseases? What about for human enhancement via designer babies? Could we draw the line between the two? How does this technology even work and what are the risks? Are past works of art like Brave New World and GATTACA now appropriate to discuss as human genetic modification appears to be marching toward reality? Or is that just going to scare people? What about eugenics turbo-charged by new technology? How do we find the right balance in discussion of this revolutionary issue so that we do not freak people out, but at the same time we have a real discussion that doesn't sugar coat things or dodge real potential issues? There's a lot to talk about so let's dive in.
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What potential benefits does this CRISPR have for, I suppose for lack of a better way of saying, people already born? Would we be able to alter ourselves through some sort of gene therapy using CRISPR?

Would it be possible to alter/program bacteria to attack cancer cells exclusively? I know a method like this already exists, but would CRISPR make it cheaper/faster?

thesandman51

Hi SandMan51, Great question. There quite a lot of potential for gene editing via CRISPR in adults. The challenge is that unlike germline editing, genetic modification of adults can only reach some of our cells. Still it could be use for gene therapy in adults for certain genetic diseases, either alone or in combination with cell therapy. In the combo approach, you could take a patient's cells, CRISPR a desired change, and then return them via transplant. Cancer is trickier because it generally has many mutations. Making GM bacteria to attack cancer is a cool idea, but would come with risks too.

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CRISPR has become rapidly the future of genetic modification. Nevertheless, a couple questions rarely stated are: What are the limits of CRISPR? And what are the main difficulties when using this technique? Are there already any ideas to overcome these limits and difficulties?

Something I want to state is that I am interested about the technical aspects. Not ethical.

gerp92

Off-target effects are a major concern. Rapid advances in CRISPR have made these relatively less of a problem in research applications, but when you are talking about modifying the human germline then this remains a serious challenge. Because CRISPR can introduce as small as 1bp (one DNA unit) changes amongst billions, one would need to do whole genome sequencing and even though if you observe a small change how do you know if CRISPR did it or it is just a naturally occurring genetic variation?

Another concern is that even if you make only the desired DNA change, as Erik Lander pointed out at the DC meeting last week, we cannot be sure we will get the hoped for functional outcome and only that outcome. Gene's are mutlifunctional and there are many overlapping DNA elements.

Are US and Chinese scientific communities working together on these subjects or are they in competition?

Also, won't overzealous regulation or banning federal funds for some of these projects only force scientist to relocate and work elsewhere?

neuroeng

Hi Neuroeng, This is a great, even if touchy subject. There is both cooperation (e.g. the DC summit last week at which reps from many countries including the US and China were present), but in addition there is also a sense of competition amongst some for sure. There may be a race to be the first one to make a GM person, but there would be great risk to the scientists doing that racing depending on how things turn out. If things go badly they could find themselves in a lot of trouble.

As to possible regulations, you are right that there can be unintended consequences such as people going to do controversial work in a more permission environment. This is one argument for trying to have an international consensus, but perhaps we could never all agree. At the same time, I think we have to have the regulations we believe to be best even if others are more "anything goes". One person's "overzealous" can be another's "appropriate" or even "too weak". Lots of opinions on human modifications.

Hello Dr. Knoepfler, I am a student at UNC - Chapel Hill and I had a question about Marfan Syndrome. I recently found out I have Marfan (just this past Friday) and I know it is autosomal dominant. I understand there is a huge risk in having children and passing Marfan onto them. What are some methods I can look into that would allow me to have children of my own without Marfan 10 years in the future? Is Preimplantation Genetics Diagnosis (PGD) able to select out Marfan or are there better solutions? How could CRISPR help? Thank you for taking your time to answer questions!

Cha72

Hi Cha, Thanks for sharing your story. I'm not an expert on Marfan's, but in principle its transmission to future generations might be able to be stopped via heritable genetic modification. A quick Google search suggests PGD can work for Marfan, which to me would seem like a safer way to go than

genetic modification. It is possible that in 10 years we might have different views on this. CRISPR technology is evolving so fast that maybe it could provide an important alternative to genetic disease prevention in the future. Best wishes to you! Paul

Do you think people will be willing to modify their children in order for them to not have any type of problems or that they will more likely modify themselves?

Could this technology also be applied to livestock in order to produce meat?

More importantly, could we used technology that allows us to modify genes to bring back certain species from extinction?

Thanks for doing this AMA!

ariwake

I do believe that some people will be not just willing, but also enthusiastic to modify their children. Many people I've interacted with have a transhumanist vision whereby they want the human race to become better including their own children. Of course "better" is a tricky word when it comes to applying it to people...what is "better"? For some things such as health you might think it is clear, but even there some in the social justice community believe that we cannot assume that certain health-related conditions are "diseases". CRISPR is already being ramped up quickly in agriculture and for livestock such as to make cows without horns and to make animals with more meat on them such as super muscled pigs and cows. De-extinction does connect to CRISPR, but there's a lot more to it and I think in many cases it is unlikely to work. It is intriguing to watch the efforts at deextinction though.

Hi Dr. Knoepfler. Thank you very much for doing this AMA.

My question is about your comment on "Where do we draw the line?"

I have several cavernous malformations in my brain that have caused seizures in the past. I had brain surgery to have the largest one removed. Since then I've had genetic testing and discovered that I am positive for a heterozygous and dominant gene that caused the issue. All of my children will have a 50% chance of getting the gene and the condition has a 75% of being expressed for people with the gene.

My wife and I want to have a child very badly, but I don't want to put my child through what I've been through. We're currently exploring in vitro fertilization and testing the embryos for the gene before implantation. In our situation, this all seems like the right thing to do, but we've also talked about having a girl. Since we're going through this whole process anyway, it would be relatively easy and cheap (~$300 extra) to also select an embryo that is female. But I feel that this is somehow "cheating" nature, and it makes me very uncomfortable. In fact, the entire process seems to be "cheating" nature" a little, and is hard to get my mind around.

My question is when do you consider the work you are doing to be unethical or too much of "playing God"? Would you consider selecting for a gene to improve a baby's health ethically OK (like I am doing)? What about choosing a girl because we want one and it's easy? What if we could select for some other gene that would give our baby an edge in school? Where do we draw the line? In your experience, what is the opinion of the general scientific community? The general public?

swankpoppy

Hi swankpoppy, Thanks for sharing your story. I wish you and your family (now and future) all the best. At present, my feeling is we should draw the line on human modification between lab research (which

should continue) and clinical uses (where there should be a moratorium). I don't think that by doing embryo selection against the disease-causing gene that you would be cheating nature at all. There are much more widely varying views on embryo sex selection. It is outlawed in many countries in Europe, but as you know it can be done in the US. As a matter of parental choice, it's not for me to say whether this is right or wrong for you. I'm confident that you and your partner will make what is the "right" choice for you and your family. There are many considerations such as whether you want to have just one child or potentially more over the years. If the latter, then you could see what nature gives you this time and then make future decisions. More broadly issues have arisen with sex selection that are worth being educated about. For instance, sex selection by PGD has caused serious problems in some countries in Asia because of the selection against girls. There are literally hundreds of millions of "too many" men there. If we could select for specific genes by PGD, I'd start worrying more about societal problems. In theory some clinics may already be allowing couples to select for embryos with certain profiles of combinations of genes. It'll be harder and harder to say where we draw the line in coming years as this technology spreads.

Last I read, the technology to reliably and consistently edit the human genome using CRISPR technology was not up to snuff (at least, not up to GATTACA levels). Do you disagree?

I enjoyed your TED talk! Can you chime in on how you feel genetic engineering our children is an ethical issue that is different than all the other myriad choices parents make about their children?

lzawwlgood

Thanks for the feedback on the TED talk. It's hard to cram in everyone into just 15-18 minutes. CRISPR technology is outstanding compared to past versions of genetic modification technology. I've been doing genetic modification research in mice for a very long time and CRISPR is way better than what we used to do. It's not perfect though and to start making heritable modifications in people would require essentially perfection or near perfection. Even then there would be health risks that could span generations. You are right about the ethical issues and I believe that genetic modification of our children is not equivalent to things like picking schools for them, promoting their good nutrition, well-baby checkups, and such. We would be literally recoding them, which is unique and incredibly powerful (both potentially for good and bad). I don't think we've had time to have a broad discussion about the ethical side to this. Some ethicists and scientists also say that making designer babies would be similar to other choices that we make that may affect DNA (via mutations) such a smoking during pregnancy, but again to me that doesn't make common sense.

Hello! Thanks for doing this AMA. I'm really glad you mentioned the movie GATTACA, that was the first thing I thought of when I started reading this post. When watching that movie I honestly felt like I was looking at the future. What is your opinion? Do you think we're potentially headed to a future where genetic predisposition can dictate the paths of our lives?

Jayrobinson92

Hi Jay, I do think GATTACA is relevant here. Many scientists get upset with the movie is mentioned in this context because they think it scares people, but at the same time this kind of technology is now here today so what's the point in pretending it isn't? My sense is that the makers of GATTACA were very good at predicting the future in some ways. It remains unclear if human genetic selection and modification will permanently change our species and our world, but today it seems far more possible at least relatively speaking than just 3 years ago. At the same time I agree with one of the commenters below that an important message of the movie is that genetics is not destiny. I make that point in my book too. There's a catchy notion floating around out there --genetic determinism --that argues the opposite. It says genetics is more powerful than anything else. I don't think it's everything, but it is

powerful. One of my concerns about human genetic modification that was a focus of my TED talk is that it could become driven by pop culture and even by governments with bad consequences. Eugenics is a real possibility. To those who say, "don't mention GATTACA or Brave New World" in the discussion of human gene editing, I say go watch the movie and read the book again, and then ask yourself if they really don't belong in the discussion.

In regards to designer babies, would the alteration of the unborn child's DNA completely eliminate hereditary diseases, such as Huntington's or sickle cell? Or would it be recessive, Making the altered child safe but their offspring still at risk?

Braxent

It depends on how the genetic modification was done and the starting states of the parents involved. In theory it might be possible to completely eliminate a hereditary disease in a designer baby. Once gone, their future offspring would not be at risk to that disease. If both parents carried genetic mutations then it becomes harder to create GM embryos completely lacking those mutations, but still might be possible. A concern is that the gene editing may create new changes elsewhere, which also can be hard to track, and those new mutations might be harmful. So it would be a gamble. Right now for many families genetic screening of embryos, an already proven technology, is an effective way to avoid genetic diseases, but it isn't perfect and that raises ethical issues too.

As you imply, the science is coming like a freight train that cannot be stopped so it's not a question of "if" but "when and how". The big questions seem to be ethical and moral and boil down to control and regulation. So who should make decisions about other people's lives and how do we regulate it? I mean, yeah it would be cool to have a glowing kid expressing jellyfish green florescent protein so you could find him in the dark, but is that fair to the kid?

Jobediah

Hi Jobedish, Excellent questions. It feels to me that we need more of what some call democratic deliberation on human genetic modification, but we don't have much time as the technology takes on a life of its own. Even at the DC meeting on this topic last week there was no consensus on a moratorium. I think we are going to see it become harder to control human genetic modification in the next few years. As to your last question, I don't think that (or even other changes to attempt to make them say taller) would be fair.

It seems that "GMO" has become a bad word in a lot of circles, I think mainly as a result of an abundance of misinformation and misunderstanding out there on social media. How do you combat that as a scientist? Unfortunately, the average Joe won't look to the literature to accept/reject a sensationalized article he/she sees on their news feed.

chaddybox

It can be tricky discussing GMOs because of the powerful associations. My own view is that GMO can be an important and accurate term. It doesn't have to be a "bad word". More education and public outreach are needed without being driven by commercial agendas one way or another. As you know the GMO plant/food area is one of intense discussion/debate right now. It can be hard to find unbiased sources of information for the public on that outside of science and you right that the average person won't look to science articles. In my book I mainly focus on GM people and have tried to take a common sense, logical approach to discussing these issues.

Dr Knoepfler, I'm a person with hemophilia deeply involved in education and activism within the bleeding disorders community. The entire community has been watching the field of genetic engineering very carefully, and lots of people are very excited about the incredible innovations that CRISPR makes possible. At the same time, however, the hemophilia community has an incredibly troubled history when it comes to medical innovation and securing access to safe and affordable treatments. During the 70s and 80s thousands of hemophiliacs died of HIV and Hep C contracted from tainted blood products while the factor companies and FDA failed to warn us, and today those very same companies who create our meds in the 80s have used every trick in the book to ensure that factor prices remain exorbitantly high. In view of this history, my question for you is a personal one and not necessarily a professional one. What are your biggest concerns about CRISPR's application, and do you think that the world economy is structured in such a way that it's ready for CRISPR? If not, why and what needs to be done?

wiibiiz

Hi, Thanks for sharing your story and that of your community. I really admire those who work on education and are patient activists. Commercial interests is a big issue with CRISPR that wasn't discussed much at all at last week's National Academy Summit that I attended. Some have patent applications and companies focused on CRISPR. Clearly investors view CRISPR as a potential big source of profit. How will the money side of things influence the evolution of this technology? I don't know for sure, but there is likely to be a strong influence. How will the FDA handle CRISPR? I'm not sure, but it is unlikely to be able to do much in advance. We need to view this very cautiously and avoid hyping the potential clinical applications. I was disappointed that the Summit failed to recommend a moratorium on clinical use because I think there are quite some risks here both to individuals and to society. There's real potential too. We need a balanced, democratic discussion on all of this that includes the public. So far that hasn't happened. The main driving force for me to write my new book was to educate people and spark discussion because there are huge issues here.

If China agrees to the moratorium on human genome editing, will you believe them?

Epistaxis

It's not so much a question of belief, but rather what happens in the actual labs around the world. One could ask the same question of the US. Governments or scientific bodies can say, "Hey, we have a moratorium", but some may not respect that. Still I believe a temporary moratorium on heritable clinical use of CRISPR and other gene editing in humans is wise. The meeting last week in DC did not propose a moratorium though. So I'm not sure what comes next.

Hi Dr Knoepfler, thank you so much for doing an AMA! I've been writing a short paper on CRISPR for my undergrad so I can't believe the timing.

My questions:

1. How many years do you think it'll take for CRISPR to be used in the clinic?
2. I know that scientists in China recently modified tripronuclear zygotes with CRISPR and it was quite a disappointing result if you ask me, but I guess it's to be expected. I read a comment within an article stating that they think it is just a publicity stunt (since they were modifying the HBB gene for beta-thalassemia, which can already be done by PGD). Do you think this is true?

daft_strawberry

Good luck on your paper! I think CRISPR could be "in the clinic" for humans in a heritable manner in

only a few years in the sense of risk takers plunging in with reckless attempts that could cause great harm. Legit, gene therapy (non-heritable) efforts via CRISPR could be in the clinic soon too, and there's real hope there. As to responsible, heritable attempts to make GM babies (aka CRISPR babies), I don't think we'd be ready for at least a decade and possibly never if it turns out to be dangerous. The field is moving so fast though that it is hard to make predictions, especially about timing. I have mixed feelings on the human embryo editing paper from China. It's not clear to me that the researchers did anything wrong per se (e.g. it seems to have been done in an ethical manner as defined by their institutional committee), but I'm not sure it was necessary to do this work in human embryos and they didn't use up-to-date CRISPR technology. What did we learn that was unique? I wouldn't call it a PR stunt, but there can be pressures to be "first" to do something new.

As this technology matures and become more accessible, how do you think it will effect natural ecosystems?

Meaning: When folks can get their hands on this tech, we can assume *someone* will apply it liberally (i.e. on the organisms in their backyard). Certainly this will have an impact on local biological systems, but if a reproductive advantage is gained, it will spread much further than the local system. How long can these systems handle such drastic changes?

Also, existential angst is a problem I have. As this tech becomes more available, nothing is stopping the nefarious from making biological weapons with it (i.e. parasites, etc). Thoughts?

Moth4Moth

The use of this technology in nature has already been proposed such as targeting mosquitoes or other disease-associated or destructive pests. There would be risks to ecosystems as well as possible benefits such as increased crop yields or reduced exposure of humans to diseases such as malaria. One particularly powerful and frankly unsettling approach is called "gene drive", where the introduced GM organisms are special and take over natural populations. Essentially gene drive organisms are designed to be self-propagating. The risks would be that by introducing gene drive GM organisms into the natural world we could accidentally create negative outcomes and there might be no way to undo it. Weapons based on this kind of technology are certainly possible as well and that was discussed at recent meetings as well as in my book. Genetic weapons could be devastating and certain kinds could even attack us in a very personal way by changing our DNA and in a sense making us not be the same person any more. I believe the US government is investigating such concerns.

Hi Dr. Knoepfler, my question is about the ethics of successful gene therapy. If we are able to "patch" a genomic defect, let's say Spinal Muscular Atrophy for example, should we follow up with restrictions on that individual's ability to reproduce? Is it ethical to ask an individual who survives a disorder that would remove their genetic information from the gene pool before puberty to abstain from procreation?

DiscursiveMind

Hi DiscursiveMind, Great question. I don't know some kind of universal answer, but interfering with people's reproduction sounds like Eugenics to me. In my book I talk about the idea of "reproductive quarantine" that might be enforced by governments on genetically modified people should things go wrong. It seems undemocratic to me, but not without precedent such as in US Eugenics of the last century, the Nazis, etc. Some say that kind of stuff could never happen again, but I'm less confident that we can be sure about that.

I've just started learning about this area for a project! How does CRISPR compare to zinc-finger

nucleases? It is a different technique? What are the merits of CRISPR versus other potential or actual techniques?

Most of what I'm doing right now involves people talking about ZFNs, but a few of them have mentioned CRISPR, so I'm very curious about it. Also, the Wikipedia article says CRISPR is more advanced than ZFNs, so I'm curious why I'm still hearing so much about the ZFNs. Is it just because of the slow rollout of technology to labs?

EDIT: And what does the CRISPR technology actually look like? Is it just something in a petri dish, is there a machine? Is it a system of techniques to create the genetic modification effect?

emiteal

CRISPR seems to be far more efficient, cheaper, and simpler than other gene editing methods like ZFNs. In short, it works better and is easier to get going. It consists of plasmids that you get for a small fee from the repository Addgene. You need to modify them in certain ways to make a specific genetic modification targeting system. It is targeted to specific genome locations (e.g. a mutation in a gene) by something called "guide RNAs" that can be very specific. If you go to the Addgene website and search for Cas9 or CRISPR you can find not only the plasmid listings, but also helpful tutorials on how it all works.

Which applications are you most excited to see this technology applied to?

enemysfrenemy

I'm excited about almost all of it, but much of it also worries me given the unprecedented power. Right now I'm most excited about the potential of CRISPR technology to teach us new, important things at the basic research level about cell and developmental biology of humans. It's a surprisingly understudied area...perhaps not so surprising I guess given the controversial nature of working with human germ cells and embryos over the years. CRISPR is going to help us know ourselves as a species far better and to understand how many diseases arise. Very exciting time to be in science!

Currently, the main problem I foresee is directing the DNA repair after the cas9 cut. I work with crispr in zebrafish and have read about a couple drugs that can lead to preferential non homologous end joining or preferential homologous recombination. Do you think understanding this mechanism (because at this point I see many variants of indels in the G0 of the fish I inject) would be crucial to reassuring people about its specificity for future therapeutic use?

Thank you for doing this!

round2ffffight

I have also seen that certain chemicals can tweak the CRISPR-Cas9 system in helpful ways. My lab is doing CRISPR work in mouse and human cells. It is very useful, but doesn't always work predictably. More depth of understanding of the mechanisms involved will be helpful both for us scientists and the public. Again as I mentioned earlier I'm not sure how much time we have before some try to make human genetic modifications that are heritable though. The world won't end if they do this, but it could harm individuals and also more broadly break public trust in science. It's an exciting, but crazy time in genetics research.

I personally have the feeling that gene editing/genetic modification technology has the same potential that nuclear technology has/had. It can be a source for a lot of good. But misused it could be the cause

for a lot of suffering.

Now to my question:
Did you ever think about not publishing a discovery because it would be to dangerous or the worst case scenario would be to grave? Is there any collaboration with lawmakers to create laws to nix or punish misuse of new discoveries before they get widely known?

G3sch4n

I have not personally avoided publishing a discovery because of potential dangers, but I know that has happened or been a dilemma for other scientists. The enhanced flu case comes to mind. I did avoid in my GMO Sapiens book and on my blog (ipscell.com) going into detail about how specifically one might make CRISPR-based genetic weapons. Terrorists probably can figure it out themselves via roping in scientists anyway, but I don't want to enable that in any way. I'm not aware of specifics on laws or regs against publishing on dangerous technologies, but I know again as mentioned earlier there have been cases where some work ran into that issue. Like you I see parallels between nuclear physics and human genetic modification as seen from a societal view. Some call the issues raised in a general sense to be "dual use dilemmas". Science can be used both for good and bad.

What areas of study (or even particular books) would you recommend to an autodidact who wants to understand more about the present and future of human enhancement?

Khiv_

I don't agree with many of its assertions and I think it downplays risks, but George Church's Regenesis is intriguing. Frankenstein's Cat is one focused on GM animals. Mara Hvistendahl's Unnatural Selection. Sorry if it sounds like self-promotion, but I'd recommend my new GMO Sapiens book too as it is targeted to a broad audience including autodidacts. Follow Antonio Regalado on Twitter as he is one of the best reporters in the world intensively covering this right now. Also check out #GeneEditSummit on Twitter for many more resources from last week's meeting at the US National Academy of sciences. I blogged extensively on that meeting as I was there: www.ipscell.com. You can also search for #CRISPR on Twitter.

Thanks to recent breakthroughs like CRISPR how far are we from therapies that correct single genetic errors in adult humans where the genetic cause has already been identified as a single gene? In other words, how far are we from treating diseases where, for example a recessive genetic flaw makes a person unable to produce a particular enzyme which can't otherwise be supplemented?

Do you think that our current regulations over drug and therapy development are adequately equipped to deal with what may arise out of recent breakthroughs? My understanding is that the development of genetic therapies has been greatly accelerated but the approval process has remained unchanged.

Thanks for doing this AMA!!

Seeker51

Hi Seeker, CRISPR-based gene therapies in adults are already in the works, but will have to go through clinical trials to assess safety and efficacy. I hope they work great. For the hypothetical scenario that you proposed for a rescue of enzyme function gene therapy in adults could work well. But every possible therapy again would need rigorous testing. Most are likely to fail. As to the regulatory system, the FDA has rules in place for gene therapy that seem to work reasonably well. They would need to be expanded or a new set implemented if we start talking about germline therapies. One concern is that some parties may do an end run around the FDA and go ahead and try

to produce GM babies even without approval and/or more efforts to countries with more permissive regs. Then again the US currently has no federal law prohibiting human genetic modification so maybe we are one of the permissive countries. How much can we count on a largely reactive (rather than proactive) FDA to handle heritable human genetic modification? I'm not sure...

Do you think there is a chance that, in the future, parents trying to modify their unborn children will end up adhering to a form letter for humans, the pinnacle of beauty and intelligence in order to give their child the best life possible, and in turn lose any uniqueness they would have had otherwise?

ImaginaryDemons

There is a temptation in culture to go for broad sense's of what is "better". Some call it in the US the "Ken and Barbie" view. I believe studies have shown that customers of sperm banks usually pick donors who are taller, viewed as more successful, etc. One reproductive company even offers a "celebrity look-a-like" service if you want your child to look somewhat like your favorite celebrity. I don't know how well that actually works, but it says something about human preferences and what some might call weaknesses.

How do you feel this technology will affect people of different classes? I basically see "designer babies" as a way for the very rich to get to not deal with the struggles of having an abnormal child, leaving poor folks to deal with lots of medical bills/problems. Do you/how do you plan on addressing this?

5firtrees

Class and social justice areas are highly relevant here. You are definitely asking some provocative, important questions. Genetic modification is likely to be very expensive and only available to some around the world. It could promote class strife and conflict if widely adopted in only certain socioeconomic classes. I'm not sure how this could be effectively addressed. If a genetic modification "therapy" was developed that was safe and effective, do you then make it available to all for an affordable price? Some say yes, but biotech companies need to make profits. This needs much more discussion. Thanks for raising these important issues.

How can a hopeful future parent be a part of these technological developments?

Let me explain. I'm 31, my fiance is 28. She had to have a hysterectomy at 22 due to severe endometriosis. She kept one ovary. My only chance for a child with her is for IVF using a surrogate. It's not impossible, but it will be hard. And there's a very real chance of passing the endometriosis gene along.

I've been interested in human gene editing as soon as I knew what my only chance at a biological child looked like. I'm worried the tech will come too late for me, though. I want to be involved, but I don't even know where to start.

patternfall

As you probably already know, you can contact any of a number of fertility clinics to help on the challenges. I'm not sure there is such a thing as an "endometriosis gene". It is possible that there are certain combinations of genes that predispose one to have an elevated risk for endometriosis, but surely this is not all genetic. The commenter below is likely right that genetic modification technology (at least that which is proven safe and effective and approved by regulators) is going to take a few decades to be even potentially possible in the clinic widely.

Could this technology be used to enhance or control Cell production within a person over the course of their entire lives? By this I mean could we potentially use this technology to make humans naturally produce more cells for repairs to our bodies, and could we use it to eliminate the production of Cancer/harmful cells within our bodies?

Bobaram

Interesting ideas, but tough to achieve safely. "Producing more cells" always brings cancer to mind for me. There's a fascinating and troubling relationship between cancer and aging/youth. Certainly there's a ton of interest in potential genetic manipulations to fight aging. I just think we need to keep risks of cancer in mind too as many anti-aging molecules are pro-cancer.

Hello Dr. Knoepfler, thank you for doing this AMA. Do you think that the rise in use of CRISPR will lead to a rise in genetic patenting? If so, how would this affect the progress of possible therapies?

neuronsandchemicals

This is a good point. You cannot patent naturally occurring genes, but you can CRISPR new versions of existing genes and try to patent those variants. I think this could be a hot topic in this arena.

As someone who works in the field, I'd like to hear your answers to these questions, or at the very least your perspective:

For instance, are we ready to make genetically modified people (what I call GMO sapiens as a mashup of Homo sapiens and GMO)? Is it OK to do this for trying to prevent genetic diseases? What about for human enhancement via designer babies? Could we draw the line between the two? How does this technology even work and what are the risks? Are past works of art like Brave New World and GATTACA now appropriate to discuss as human genetic modification appears to be marching toward reality? Or is that just going to scare people? What about eugenics turbo-charged by new technology? How do we find the right balance in discussion of this revolutionary issue so that we do not freak people out, but at the same time we have a real discussion that doesn't sugar coat things or dodge real potential issues?

Mason11987

Hi Mason, Nice to turn my questions back to me for answers! It definitely seems fair. Overall, I don't have good answers for all of them. I do believe that this technology has huge promise, but with its power comes equally high risk too. I don't think it is time to make heritable genetic changes in our own species. It's too dangerous for individuals and for society. I'm not convinced we can dodge eugenics and it could be a powerful eugenics turbo-charged by new technology. Check out my TED talk (see at the top for link) to get more of my concerns articulated kind of in story form in the talk. We need more dialogue and discussion that includes the public. Some of this stuff has potentially disturbing implications (e.g. designer baby attempts gone wrong, genetic weapons, ecological disasters via contagious gene drives) so it's going to be tricky to address the tough issues without being too dramatic that it is unhelpful. What are your thoughts?

What are some crops that you've seen get modified with CRISPR and what advantages do you see with them so far? Do you think we can revive the Enviropig project now?

How do we find the right balance in discussion of this revolutionary issue so that we do not freak

people out, but at the same time we have a real discussion that doesn't sugar coat things or dodge real potential issues?

Education, the people saying hold your horses don't even comprehend the basic's. If you could explain to Neil Young how his diabetes medicine that lets him live is the result of genetic modification, he might not be making songs against it.

kofclubs

I'm not a plant researcher so I will defer on the plants question in terms of CRISPR, but I do know that many research efforts in that area are underway. Certainly making GM animals (pigs, dogs, cows, etc) via CRISPR is a super hot area right now. In theory such efforts in agriculture could yield greater yields of more nutritious foods, but that's not my area of focus and some folks are strongly anti-GMO food/plants.

Hi Dr. Knoepfler, thanks for doing this. Great to have this subject brought into the public eye.

You obviously don't take issue with terms that are often used as anti-science fear-mongering such as "designer babies." Do you see any issue with framing the technology this way? Should we be trying to drive the conversation towards more accurate pictures of where the tech is right now that don't have built in cultural and moral connotations? Or is that futile, and we should just accept the terms handed down by reporters and dystopian novelists?

I see no problem with gene editing, even germ line editing, to correct genetic disease. A baby who had undergone this procedure would undoubtedly be called a "designer baby" by some. The term implies a commoditization of human life and a disrespect for human dignity. These things are cultural values which are completely separate from the technology, and should be addressed as such.

Your GMO sapiens term implies that a person who has had his genome edited in any way will no longer be human, but a whole new species, which is preposterous. To me it seems very dangerous to promote this kind of thinking.

What is your perspective on this?

JanSnolo

Hi JanSnolo, You raise valid points. I personally don't see GMO as a bad word and I don't have objections to GM plants/foods myself, but I realize that it has certain connotations.

At the same time we need to be accepting of the fact that to effectively reach the public we need to use a language that is approachable to them.

Scientifically, humans that have been CRISPR'd (have genetic modifications) would in fact be GMOs as the term is commonly used.

"Designer baby" is a phrase that for decades has seemed like sci-fi, but today it is within reach for some to at least try to achieve. That's my sense of the reality and I think that needs to be conveyed.

There are some, for example transhumanists, who embrace the idea of humans becoming a new species and actively want to make that happen, including in part via CRISPR. There's a push for a new eugenics. I don't know if society would still view a GMO sapiens as a human or not. To some degree it would depend on the scope of the genetic changes and how far they spread in our species.

I tried to tackle your questions in my new book too. I don't see enough discussion and debate out there so I've tried to spark that and that was another goal.

They way I see it, there are two things that can take humans to a new evolutionary level via us "upgrading ourselves" using technology. The **first** is a cyborg like path, where we build better hearts, organs, etc, a combination of man and machine. The second, **genetic modification**, is the more "natural" way, where we simply edit our genes so humans will be born with a better heart, organs, etc. Do you agree? And which do you see as a more likely path that will be accepted culturally?

ABC-DEF-GHI-JKL-MNO

Both the paths you mention are possible. I'm not sure frankly which might be more likely to be accepted. Both have potential positives and risks. I see that a lot of people are interested in each of these possibilities. In the first, some of the "building" is already ongoing via bioengineering and sometimes using stem cells. So the new parts could be biological or bionic (or a combo). As to the second path, of course technically the tricky part is what genetic modifications to "simply" make to get a better organ? It's not going to be a simple matter. In any case, if modifications can be shown to make people's lives better and society better, then cultural acceptance may follow.

As someone with a disease caused by a single errant gene (Neurofibromatosis Type II), the decision from the recent summit was quite upsetting. How do you feel the summit's decision will effect research on single gene diseases, in the near future?

YourWelcomeOrMine

What was upsetting about it to you? Did you get the impression that the summit wanted to restrict this research? I was there and I came away with the sense that they left the door open to proceeding cautiously in the future even if the focus for now should be on lab research.

Thank you for doing this AMA. My question is about genetically modifying adults to eliminate disease. I have Kennedy's Disease, basically I have about eight extra CAG triplets somewhere in my X chromosome that negatively effect my ability to absorb testosterone. The most noticeable effect is on the nervous system. My question is in your best guess how far away are we from being able o modify nerve cells in adults?

hummingfish333

Modifying nerve cells in the lab is doable, but very challenging. It can also be done in experimental animals for research. Doing it in people is possible, but would be challenging. It would come with risks too so it'd be a high-stakes gamble. For any given condition such as Kennedy's Disease, the patient and doctor would need to evaluate the potential risks and benefits if a gene therapy became available. Thanks for sharing your story and all the best to you.

This may mean we should reevaluate eugenics right?

Why shouldn't we make super babies? I get the first children will be at risk but we could use data they generate to improve the lives of billions, so long as we can assure them a free ride and the highest level of care we should probably try it.

As for gene therapy using viruses is it at all possible that these viruses could mutate into transmitable diseases?

If so does that mean we could end up with virulent aesthetic gene therapy, something that could

potentially change aliving persoms eye color or maybe their germ cells?

This last question is meant to be reaching quite far; could amad scientist enginere a diseato eradicate a specific ethnic group by killing them or changing their germ cells so they only produce offspring with the desired GM genes?

THE_BIONIC_DICK

It's time to revisit and talk more about Eugenics, yes. It's uncomfortable and even scary for some, but we are at a critical point in history where we shouldn't ignore this possibility. One of the inventors of CRISPR as a tool, Jennifer Doudna, recounted in a news article a dream she had about Hitler wanting CRISPR...so this is on the minds of the top scientists. It's not hyperbole. There is a concern that CRISPR, particularly in the form of viruses, could change or do harm. Some versions called gene drives are self-propagating so those are particularly risky. There has also been talk by serious scientists about the risks of rogues making genetic modification weapons. Even if these did not work as intended they could do terrible harm and could be contagious. I believe this is on the radar screen of people focused on national security.

Do you see any potential pitfalls with using CRISPR and our current sequencing technology. Does CRISPR have the potential to outpace our current analytic processes. (Which are already outpaced by how much data is out there.)

compbiol

CRISPR is on a blazing pace and there many pitfalls. It has great, positive potential too. How do we navigate all of this with things moving so fast?

Is there any chance we will achieve technology advanced enough to allow sucessful modifications in adults?

Khiv_

I think that is very likely in the form of CRISPR-based gene therapy. It will take some time though.

Thanks so much for your continued dialogue with the public in such a fascinating field.

Since CRISPR/Cas is a recent discovery that exploits a previously unknown biological process and improves gene editing applications from TALENs and ZFNs previously, do you think we will discover an even better gene editing tool in the future?

Has CRISPR rendered other gene editing systems obsolete?

SickLaughter

CRISPR is revolutionary, but I suppose it is possible that something even better could come along. However, CRISPR is so fast, cheap, and ubiquitous that I'm not sure what the "even better" tool might achieve. Perhaps even better accuracy? Some other systems are obsolete due to CRISPR, but for some things it is possible that TALENs, for example, could have unique applications

The idea of a moratorium on this technology sounds immensely appealing given all the potential risks. But do you think this could make the creation of "black markets" of designer babies, with even fewer

ethical bounds, more feasible? Should there be an entity in charge of specifically regulating human modifications? Who should define the members of this entity and how should they be defined?

gerp92

Yes, although I favor a moratorium, I realize it could lead to some unintended consequences. Further, even with a moratorium some people may just blow it off and do the attempts at making GM people anyway. The recent DC meeting that I attended at the National Academy of Sciences didn't even propose a moratorium so it may be a moot point.

Hello Dr Knoepfler, thanks for doing this AMA. I've been interested in CRISPR since hearing about it on Radio Lab a few months back, so it was exciting to see you here!

My question: Dr Stephen Hawking recently highlighted that we don't really have to fear robots in the future, but rather Capitalism and the societal structures that will create greater inequality, stating, "If machines produce everything we need, the outcome will depend on how things are distributed. Everyone can enjoy a life of luxurious leisure if the machine-produced wealth is shared, or most people can end up miserably poor if the machine-owners successfully lobby against wealth redistribution. So far, the trend seems to be toward the second option, with technology driving ever-increasing inequality."

Can you please comment on this related to CRISPR and the potential for it to create more inequality due the current structure of society?

frankstandard

This kind of concern is legit and it applies to any kind of technological advancement. A disruptive, powerful technology like CRISPR has already got the attention of investors to the tune of potentially $1-$2billion USD. They are going to want a return on their investment. Human modification, whether for disease prevention or enhancement, is unlikely any time soon after (or if) it is proven safe and effective to reach a diverse group of patients of different socioeconomic classes. There are risks for active class strife as well through eugenics too. These are issues we should be actively discussing, but too often they aren't on the table.

Hello Dr. Knoepfler, I've long thought genetic modification is really the only way humans will make it to the stars in a practical way.

Have you been approached by NASA or the private sector on persuing increased DNA resistance to radiation, increased bone-mass, or the like?

Keep up the great work!

Digitalneo

Transhumanists have one goal to be to leave Earth. It is very possible and some transhumanists have mentioned this, that CRISPR could be used to make better versions of humans that are "better" in the sense of being able to handle space travel more effectively (stronger bones, better resistance to radiation, etc). I would be surprised if NASA wasn't interested.

Hi Dr. Knoepfler. Thanks for taking the time to answer some of our questions. I have one for you.

Currently the NIH RAC (Recombinant DNA Advisory Committee) prevents the use of these type of

gene therapies for non-therapeutic purposes. There is pretty strict wording to ensure US government funded research isn't going towards eugenics.

Are the RAC guidelines an effective obstacle in advancements towards "designer" human genetic modification? Or can this research be carried by the private sector out relatively un-impinged? In other words, how important (or unimportant) will the NIH be in the totality (therapeutic and non-therapeutic) of human genetic modification?

shouldersofgiants

Great question. On the one hand, the NIH RAC has a lot of power to influence trends in innovative science involving recombination. On the other hand, the amount of private capital flowing into CRISPR is enormous and will be a booster rocket to a massive amount of NIH-independent research that could in principle include human enhancement. At the DC Summit last week it was mentioned that the total $ so far going into CRISPR biotechs is beyond $1 billion USD now. Someone said $2 billion. Clearly investors believe there is big money to be made and they won't be governed by NIH RAC regs. We need much more discussion of the commercial side of this story.

Can this be used to "cure" certain genetic syndromes like the Costello syndrome, by enabling/disabling specific protein or gene?

reddevilit

That is the hope, but rather than using the word "cure" which implies a pre-existing person/patient, I think the more accurate word to use is "prevent". If you make a designer baby with a corrected mutation then there was no disease to start with to cure. Just something that was prevented.

When we discuss designer babies and eradication of genetic disorders, when do we talk about the discussion of disability culture? I know you may be the wrong people to ask since you're on the technological end of this, but are we at risk of losing something culturally by eliminating heterogeneity through gene selection toward more preferred types?

We see much of this debate in the deaf community with the addition of cochlear implants and the risk it has of harming deaf culture in general. Do you ever become concerned about cultural impact of your own research along these lines?

Second, if I may have a follow up, is that while CRISPR seems to be a rather accessible method to modify genetic codes, are we still running the risk of a have/have not dichotomy when it comes to future genetic engineering? Should we not be rather careful to ensure that these technologies don't exacerbate class inequalities in the future? Are you concerned of class 'markers' being seen in genetic engineering?

FakeyFaked

Hi FakeyFaked, You raise some important points. Too often I think the disability culture is not discussed and social justice issues do not get enough attention as CRISPR-based human modification is pondered. Ablism is a real concern as well. As to your 2nd question, there are real concerns about the economics and class issues that could arise related to human modification, which is likely to be very expensive and only available to some and not others. Since this technology is potentially heritable too (e.g. it will be intended in some cases to be heritable) that could raise unique and troubling questions for society.

Why do you characterize an international, government enforced moratorium as "self-regulated"??

Sagacious_Sophist

It wouldn't be government enforced. It would be enforced within the scientific community. However, it is possible that government officials in the US could try to pass a law and I think that possibility is of deep concern to many scientists in this area. Such a law could do more harm than good.

What are the possibilities of creating a higher-order language, similar to how abstract computer languages build upon assembly, to preform basic DNA coding? I do understand that our knowledge of protein folding is still incomplete, yet the possibilities seem endless, such as true homogeneous catalysis via enzymes, biological chiral synthesis, &c. Forgive me if I'm being blunt, but the current level of genomic editing is just biochemists cutting genes, measuring gene expressions, calculating specificity... and it seems to be all too similar to hackers attempting to reverse engineer nature's systems.

Also, since CRISPR is fast yet sloppy, what are the possibilities for using CRISPR as a research tool and to develop TALENs for actual precise genetic modifications? I'd appreciate a long response!

lethe-wards

A higher order language could be made using DNA. Already some are working on that. It's a cool idea. Actually much of the CRISPR research is not just biochemical tinkering, but also studying biological outcomes so I disagree there. There are a lot of functional studies on development, health, etc. using CRISPR. Also CRISPR is getting more accurate by the day so I don't think we can call it sloppy today. Next generation CRISPR methods are at least as previous or better than past efforts at gene editing. In my lab we use CRISPR to study human disease like cancer and also stem cell functions. Thousands of labs are doing important research using CRISPR.

Would CRISPR be capable of same-sex couples producing children?

pumpkinsnice

Not CRISPR itself per se, but new stem cell and reproductive technologies (e.g. IPS cells) made this a real possibility in the coming decade.

Good afternoon Paul, Thanks for doing this AMA.

Given the GM spearhead provided by China let's assume that a governmental memorandum is ineffective at halting the expansion of CRISPR's application upon human fetuses.

Are there any mechanisms the scientific community have that could possibly cap the spread of new techniques that could limit the aforementioned application?

Do scientists have a weapon for curbing external usage of their own research and techniques is what I meant to ask.

TheSexMuffin

Good question. Generally the answer is nope. Scientists historically have seen the technologies that invent or work on be appropriated by others for various uses, some bad. With CRISPR, the dilemma that may emerge is that we have the community of science hypothetically get to the point where we can have a good expectation of safety and efficacy for gene therapies targeted at disease, but then we

see for-profit clinics around the world in permissive domains offer genetic enhancement that is unproven and dangerous. It's a serious dilemma.

I understand that a lot of questions you receive involve the technical and optimistic aspects of prenatal and postnatal genetic engineering, so I might as well voice a question in the context of automation and- at least in the US- the absence of universal coverage: Given how expensive medical treatments in the US are mostly inaccessible to working-class individuals, **what social safeguards will we have in place to ensure little Timmy and dear Sally are free from Huntington's, Tay-Sachs, and Down Syndrome?** The greatest fear here is not that the wealthy will have smarter and healthier offspring, but that those without the means to afford *any* corrective procedures will bear the brunt of bills and burdens of untreated genetic disorders.

CybernewtonDS

Socioeconomic issues are relevant and important here. As with any expensive medical produce (thinking for the moment only about non-enhancement uses for human genetic modification) there could well be disparities and issues of access.

Hi Dr. Knoepfler,

I am interested in your thoughts on the new GMO salmon that was recently approved for consumption by the FDA. If I understand correctly, the salmon that was approved only contains an insertion that increases growth hormone levels. The salmon have a natural advantage in mating but are less fit over time, so escaped salmon could cause a crash in wild populations.

Are there additional genetic tools that we could use to make GMO salmon safer for wild populations? For instance, adding male sterility genes or introducing positive selection for farming conditions?

Qytare

In terms of ecological risk, I believe the AquaBounty salmon are sterile and can only be grown in pens away from natural water sources. This doesn't eliminate risk entirely, but should keep it low. My sense is that the fish are likely to pose little if any risk to those who eat it, but I view all of these kinds of things as experiments so time will tell.

HI Dr. Knoepfler. I just wanted to say that your blog was a great resource back when I was trying to understand the whole STAP cell debacle and I really appreciated the way that you fostered collaborative efforts for post publication peer review and actual reproduction of results. I actually had to pass my ethics course during my PhD during that entire crisis, and had to study the similar scandal of Dr. Hwang.

I guess I don't have that much of a question, I'm just wondering if this yet-another-scandal has changed anything with respect to reproducibility and fraud or if just like the Hwang study it won't really change much because the frenzy of publishing is so enormous that people will always do this kind of thing. As such, how much time are you dedicating to the fight against misconduct, since you seem to be quite active in this area?

Come to think of it there was also that Voinnet siRNA fraud thing since.

canteloupy

Thanks for the feedback. In science we need a high level of trust (both internally and from the public)

for the research to function in a healthy, productive way. Every time there's a big scandal like STAP or the others you cited, there's a threat to trust. I do think that science as a whole handled STAP pretty well and despite the fallout from STAP, the healthy way that science grappled with it shows the public that we are serious about good science. But it wasn't all so perfect and some including me have been critical of journals for handling of certain misconduct situations such as STAP at Nature. The pressure to publish in big journals is still there today. I'm not sure how much has changed on that level. However, post-publication peer review has caught on and that (for all its challenges) may be having some impact.

In the latest Economist article, they talked a lot about the moral debate that needs to happen with this technology. Where do you stand in that debate, and who do you think should be holding it?

CarlosWeiner

I have mixed feelings. I'm in favor of a moratorium on clinical use of heritable human genetic modification technology. I don't think we are anywhere close to being ready technically or from an ethical level to go down that road. Others disagree and are eager to forge ahead ASAP. As to the moral debate, some people see human genetic modification as "playing God". Others have moral concerns about the manipulation of embryos and of our own DNA. I'm still trying to sort this out for myself at the moral level, but for me what is foremost in my mind are the technical and ethical issues at present. What do you think?

I work for a company that creates "conventional" crop GMOs. We're all jazzed up about CRISPR/CAS and the massive potential it provides for specific gene modification. Do you see the currently lower regulatory hurdle for cis-genic approaches being applied to the new gene-edited technologies?

Also, what ever happened to that whole stem cell political backlash from the previous US administration? Is that effectively over? I heard that labs had to segregate equipment based on which used public stem cell lines and which used non-gonvernment approved lines.

ih8dolphins

So far in the US on human genetic modification (e.g. gene therapy) there are a lot of regs to deal with (and I think appropriately), but as to how they will apply to heritable human modification I don't know. It's unlikely to be the low hurdle that you mention in the agro world. The stem cell controversies still exist, but things have calmed down for a few years. One still cannot use federal money for research that "destroys" human embryo, but fortunately one can do research on existing approved human ES cell lines.

Could we use Gene Drive, or Mutagenic Chain Reaction, to fix cystic fibrosis in patients? I'm assuming a viral vector needs to enter every cell, but shouldn't that be very doable?

Crestylia

Genetic chain reaction technologies such as Gene Drive are very powerful. I don't think we are ready to unleash them into patients or ecosystems quite yet though. They come with huge risks due to their self-propagating nature. You can think of what you are proposing for Cystic Fibrosis as a genetically contagious intervention. Getting anything into every cell is in fact not very doable unless you do the experiment starting with sperm, eggs, or 1-cell embryos.

As an aspiring undergraduate looking to pursue a career in Cell Biology, I take a lot of interest in your work. If you could go back in time to give your undergraduate self a piece of advice to lead you to an even more successful career, what would it be?

jnasta214

Great question. One thing I would tell younger myself is to reach out to faculty more to talk to them about their science. Be more bold. Take even more risks. That's easy for me to say now though...One thing I did right as a graduate student/postdoc was to do everything I possibly could to do research on stuff that I really cared about and that fascinated me.

Hey Dr. Knoepfler,

As a biomedical engineering student who is fascinated with the world of genetic engineering, what graduate specialization/companies do you think would enable me to have an impact on this industry?

Thank you so much for this AMA, I eat every word of this transhumanist stuff up.

SpecialEd17

Genetics and genomics!

Dr. Knoepfler thank you very much for this AMA and for your time. May I ask the following question .What do you mean by designer babies and what does that means for us - future parents ? That we will be able to come to you and for X amount of money be assured that are future children will be super strong and immune to , lets say , cancer ? Let me put it a little bit more straight forward - what can you actually do (or expect to be able to) in the next 5 years in this field ("enhansing humans")

archidoge

Hi Archidoge, For me a "designer baby" means a genetically modified person where the genetic modification was designed and introduced in the lab. I use the term "designer baby" more broadly than some, who limit it to GM babies made for enhancement purposes (height, looks, intelligence, etc.) Right now and even in the next few years, people cannot have any confidence that if they go to a company of scientist selling human genetic modification that they can have a safe, positive experience. Even so, some may make claims to offer enhanced children. The price tag could be in the millions of USD per attempt and with that kind of money on the line, I can't imagine that we won't see genetics clinics sprouting up. Real, safe applications are likely to take decades to be realized and there's a chance it won't ever be definitely safe or effective. There will always be risks. What are the risks versus benefits for any given future human enhancement procedure? Important, but tough question.

I want GMO Babies!
How long until this is available?

xlyfzox

Some want it to be in years, others measure it in a few decades. Depends on whether one would want a legit, proven safe and effective intervention or is willing to go to a clinic just trying to make millions of bucks.

Are you confident CRISPR edits designed to avoid the germ cell lines will be able to stay away from

them?

jsalsman

Not 100%. Of course many are contemplating CRISPR edits specifically in germ cells too to make GM humans that have dodged a genetic disease for example.

How long before these services are available to the general public?

theneonwind

In an approved, safe, effective form? A couple decades. And that's assuming a relatively smooth path. In a reckless, for-profit manner? Probably we'll see clinics selling it in a few years.

would it be possible to change a person gender thats already been born in the future?

balamory

Probably not.

Hello Dr. Knoepfler! I'm a recent college graduate, with my bachelor's in Biology, and the kind of work you guys do is what I've always dreamed of getting into. I would absolutely love to work on genetic modification and editing as a career, but unfortunately, I have no idea where to go from where I am. I've asked around with many professors at my previous college, and tried looking up what all I would need to do through the internet, but I've just gotten a lot of shrugged shoulders, misleading info, or dead-ends. So, I figure you would probably be one of the best sources to ask, since you're where I would like to be. What all did you do to get into the job you're doing now? What degrees did you need to acquire just to break into the field starting out? Did you need to get any certifications alongside those degrees, and if so, could you direct me in the general direction I would need to go in order to do so as well?

Basically, how could someone who's really passionate about genetics, but really lost on where to go next, go about getting into your line of work as well.

Taxtm

I took a long, non-linear path. Luck unfortunately/fortunately plays a role. At this point try to find a technician job or even volunteer internship in a lab doing the kind of work that excites you. All the best!

I'm a college biochemistry student and we actually just had a guest speaker, currently working on CRISPR CAS-9, tell us the basics and targets of his research. I find all of this research to be pretty unbelievable and definitely the future of medicine. Yet with medical advances such as these there are obviously inherent ethical concerns. I was wondering how often you run into ethical issues having to do with germline manipulation (as this will effect future unborn generations) or any other issues? As well as what direction do you see this research going in the future that makes you most excited? Thanks!

seth10miller

There are quite a few important ethical issues here, particularly when we talk about germline (heritable) modifications. One that has sparked debate is consent. The future GM person would not have consented to be genetically modified. Only their parents would have made that decision for them.

Of course some say that is not so different from other choices that parents make for their children...to me this seems fundamentally different. It's also true that it is not just the GM child affected and without consent, but also all future members of that family tree barring some risky attempt to reverse an undesired genetic modification.

Hi Dr. Knoepfler, I have cystic fibrosis and I'm wondering about CRISPR's ability to fix the disease in adults. It's an amazing time to be alive with CF with the potential for a cure on the horizon. Do you foresee clinical trials at any point in diseases where the specific faulty gene (F508Δ-CFTR in the case of CF) is already so well understood?

Tarzana_Banana

Thanks for sharing your story. CF is one of the top conditions discussed related to clinical use of CRISPR.

Some have proposed correcting the mutant CFTR gene in 1-cell human embryos.

It could potentially be done in adults or children too (e.g. in the respiratory system) via gene therapy using a viral vector containing CRISPR system components. A big challenge is getting enough cells genetically corrected properly (i.e. the delivery). Another challenge is safety as sometimes CRISPR could make the wrong genetic change.

Overall it's a very exciting time in the CF/genetics field! I think there is real hope, but it's going to take patience too.

All my best to you!

What are the limitations of intellectual property on genetically modified organisms. How could companies develop new or modify existing organisms while protecting their intellectual property. Could a company patent a multicellular organism? A humanoid? Companies already own certain life forms, i.e. Monsanto, with the current laws in place could a company own a complex life form such as a humanoid and make them work for nothing?

AndysPanties

Human beings cannot be patented, but it is possible that "invented" genetic variants created with CRISPR could be patentable. Certainly the CRISPR system itself is the subject of intense patent interest. While designer babies could not be patented, the genetic changes and methods used to make these GM humans could be patentable. You raise important issues!

Have people in your field thought about putting together any kind of formal rules on the ethical use of this and future technology, as Isaac Asimov did for robotics more than 70 years ago? What might those rules consist of?

Personally, I don't think it's too soon to start talking about a Gattaca-like future.

nosecohn

We had a big meeting last week in DC at the National Academy of Sciences to talk through some of these very issues. The end result was the sense that it is too soon for designer babies and that should be discoursed, but as a group nothing stronger was proposed such as a moratorium. Some there strongly advocated for going ahead and making designer babies so that was interesting. Others

thought that we do not need international consensus and in fact that a diversity of approaches to heritable human modification is a "good thing" in their view. What should the rules be? Great question without a clear answer. At the very least I'd like to see far more safety data in a variety of lab animals and that's going to take years to produce by the field. Another key, but very difficult question is where (or even if, for some people) to draw the line between CRISPR-based reproductive efforts to prevent disease versus those to promote human enhancement.

My mother has been studying CRISPR for years at Cal and I have to say it is absolutely strange to see CRISPR articles in the mainstream media.

Who (or what body) do you believe should be the holder of the ethical boundaries of what we**can** do in relationship to what we *should* do?

jagjagjagjagjag

I'm not sure there is any one governing body that should be the holder of what can/can't be done. Certainly the US National Academy of Sciences/the organizers of last week's meeting are strongly influential. Hopefully their words on people trying this clinical now will discourage dangerous and premature attempts at clinical use even though they stopped short of a moratorium. Every country may approach these kinds of questions differently too.

Why is the media so hyperbolic about CRISPR/Cas9? As of today, it is impossible to use it to turn horses into unicorns, resurrect dinosaurs or make a small dog large. Yet, this is what every story focuses on.

Mysterions

The media tend to focus on the most mindboggling stories, but CRISPR-Cas9 is so powerful that it lends itself to some pretty amazing future prospects. I did hear someone at a recent conference talking about making unicorns actually. They were semi-serious. As to dogs, just this year someone made super-muscled dogs via CRISPR and that was done with pigs too and cows. Another group in China made micropigs that you can buy as pets. They are the size of a cat. Crazy times...

I'm not attempting to fuel a debate about the impact of religion, but I seriously wonder what the reasons are that we wouldn't decide to move forward with a more "perfected" human being besides religion?

I guess more directly, and because I'm not up on the discussions, what are the objections of science to such advances?

tonusbonus

There are a lot of health risks to genetically modifying ourselves and our children. There are could also be larger, societal risks such as eugenics and class strife (what if only the rich could afford it?) I'm not a particularly religious person at all, but I do think we should pause to consider what it means to hack our own genomes as cool as that sounds.

I have great interest in gm because i see how powerful it will be to our future. gm algae could put an end to global warming etc. but I do worry about these practices causing genetic vulnerabilities.

edit on a more personal note. could these practices help people with ADHD, Tourette's, OCD,

Narcolepsy, and other conditions in this group?

urmamasllama

The best target diseases are those caused by a single, simple mutation. Some conditions such as those you mention may be only associated with certain genes rather than caused by them, and there could be dozens or hundreds of linked genes. Where do you start?

What do you think of George Church's ten modifications that show up a couple times in the press or the net? (i.e. ipscell) Do you think they are good examples of what we should do once the tech is safe enough?

DrXaverius

They are definitely interesting genes and worthy of attention. I'm not so sure about modifying them in people. I still worry about risks. One of his favorite genes, myostatin, has been the focus of a lot of attention in animals and already super-muscled pigs, dogs, cows, etc. have been made. I also wonder about how we will know if the tech is "safe enough".

I'm worried that CRISPR and tools like it could potentially spell the end of homosexuality. How would you suggest that I, as a gay man, fight this frightening possibility in the face of this technology?

Ontic

CRISPR does invoke social justice issues. I'm not convinced that homosexuality is a strongly genetically related trait so I'm not sure how it could be used in that area. A broader concern is that in the long run human genetic modification could reduce diversity in our species. We don't want to end up with a bunch of Ken-Barbie creations.

What are the possibilities for ecological modification? Could we do something like program a mosquito to only produce male offspring?

ZeroJoke

Yes, many people are excited and many people worried about ecological modifications that might come along via research experiments or accidents (e.g. release of a GM insect from the lab that can spread GM's to its relatives in a whole ecosystem). Keep in mind that mosquitoes don't exist just to cause other species including us trouble. If we eliminate them we could cause ecological harm.

Dear dr. Knoepfler,

as I understand, CRISPR is a new kind of 'toolbox' for 'genetic engineering' to manipulate and edit genes.

I have rare progressive brain disease named ADCA-SCA1, (shares the same genetic disorder that causes HD). Can CRISPR help in finding new 'mechanism' to cure or to minimize the effects of these kind of diseases?

obimk1

CRISPR may be helpful in defining the mechanisms, perhaps along with a stem cell technology called

iPS cells or induced pluripotent stem cells.

Have you seen the movie Gattaca? If so what did you think of it? (movie about future genetic modification)

fumbbles

I have seen it multiple times and it rings more and more true in terms of specific events in the movie such as human embryo selection, genetic modification, etc. I don't know that we are headed in the direction of a dystopia, but even if we aren't there might still be serious problems that could arise including social justice problems.

What is the largest threat CRISPR technology poses to humanity? I listened to a podcast where the speaker discussed the ability for people to potentially in the future design their children using CRISPR. Where do you consider the moral line for CRISPR technology?

much_thought

The biggest danger is heritable changes to our genomes that are harmful and cannot be reversed OR societal change such as eugenics

What's the difference between CRISPR and RNAi?

2ero

RNAi and shRNAs interfere with transcription and/or translation. CRISPR-Cas9 works generally by cutting DNA leading to a knockout or specific genetic changes. New forms of CRISPR can repress transcription instead of doing cuts though, which is more similar to RNAi

You should read "Beyond this Horizon" by Robert Heinlein- it takes in stride the ethics of gene selection

Quickbeam

I'll take a look. There's a lot of interesting, relevant fiction out there. YA fiction these days often touches on human cloning and genetic enhancement. Kids are fascinated by this.

Estimate on the cure of cancer? or any other life-threatening disease?

Rob4581

This would work by disease prevention in most cases rather than cure. Estimate is two decades in terms of timeline. I'm talking about heritable genetic modification. Gene therapy clinical trials are already ongoing.

Blue eyes are a genetic mutation right? How easy/hard would it be to change them back to brown?

Gadgetron94

Eye color could be controllable via genetic modification of embryos or germ cells. There might be side effects...

Can you make X-Men? People who have mutated genes that grant them special abilities?

Gamejunkiey

Some people have indeed talked about trying to make GM super heroes...seems unlikely to work, but who knows in the future.