Science AMA Series: Hi Reddit, I'm Gary Gorbsky and I study cell division and how errors in the process can lead to cancers and birth defects. My lab was the first to reverse the process of cell division. Ask me anything!

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GARY_GORBSKY R/SCIENCE

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What does "reversing cell division" mean? Cell fusion? What does that accomplish?

ncohrnt

Joev714 is correct about what we mean by "reversing cell division." Ok, this was a set of experiments where we essentially hacked the signals controlling the process of cell division. Normally cell division is a one-way street. One cell divides into two. Scientists have been studying this process for well over a hundred years. What we did was to use drugs to manipulate the process. We gave cells that were in the middle of division a drug that caused them to finish the process and split in two. Normally when that happens there is a protein, termed a Cyclin, that is destroyed after cell division. The destruction of the Cyclin protein normally prevents the cells from going backwards. So in our experiments, in addition to the first drug to push the cells to divide in two, we also applied a second drug that blocked the destruction of the Cyclin protein. After the cells had divided, we removed the first drug. Since the Cyclin protein was still present the divided cells reversed back to becoming one cell. We did not do this just for fun (although it was tremendous fun). We did it because it told us a great deal about the biochemical pathways that control the directionality of cell division. We figured out a lot about what depends on what in regulating the process of cell division.

Hi Gary. We have read about Leukemia in girl being completely reversed in UK with Cell modification or gene editing. Is that what you can do? And can all cancers be treated the same or do they require different therapies?

Psalms137-9

I am sorry I am not familiar with the specific person you are writing about. We do use gene editing in manipulating cells but all of our work is done on cells in culture (cells grown in dishes). It is likely that different types of cancer will require different therapies. What we are trying to do in my lab is to figure out pathways by which cells become abnormal and how that contributes to the aggressive properties of cancers.

If cancer cells can avoid the problem of telomere degradation to "immortalize" cell lines, how come we can't make use of that to prevent ageing? What's stopping us?

ThermalFlask

Ageing is a complicated issue. Loss of telomeres in our stem cells may be one contributing factor but there is lots more going on including damage to our DNA and defects in the mitochondria, which make energy for the cell.

My stepmother is now cancer free after T-cell gene therapy. This stuff works rather well. It is truly an amazing time to be alive, and it must be an incredible feeling to be on the science and innovation side of this.

I have heard that these kinds of treatments are being applied to Leukemia (like my stepmother) as well as to lung cancers. From what I understand T-cell gene therapy trains white blood cells to recognize cancerous cells that your immune system normally would miss. And this is an approach that makes immediate sense to laypeople when you explain it.

Can you explain how "reversing the process of cell division" works on treating cancers? Do cells literally merge back together, or do the cells just implode on themselves achieving the "cell death" result that chemo currently provides?

Are you using CRISPR to trigger the reversal process? And do you see a cell division reversal process as being a component in the genetic "fountain of youth" problem?

Lastly, do you see other applications for cell division reversal outside of the cancer space? Can it be used for nerve damage, for instance, or cirrhosis? What are the other likely treatment candidates that you'd like to see being studied with this technique?

ahoogen

Great that the T-cell therapy worked for your stepmother. That is one where basic science in immunology was applied to generate a specific tool for cancer treatment and is paying great dividends. Our studies on controlling the directionality of cell division are still in basic science realm. We are confident that someday they will impact new therapies for cancer and other diseases but at the moment they do not provide a direct link to therapy.

Hi Gary. Does your research touch on issues of ageing and how it might be mitigated or eliminated? Are there any organisms that don't experience breakdowns in the transfer of their DNA over time?

Jericrich

We don't work on ageing directly but is likely that defects in chromosome segregation do contribute to this health issue. Interestingly there are a few species that do not seem to age, although this depends on how you define aging. Two of the most common species that do not seem to age are two invertebrates, hydra and planaria (flatworms). People are studying them to try to figure out how they escape aging.

Hi Gary. Outstanding work by your team and congratulations on the accomplishment. Can i ask how you are thinking of applying this to cancer and congenital birth defects? Are you thinking of reversing

tumor cells back to their original state?

Thank you!

TornHomoSapien

Thanks for the compliment. We are basic cell biologists trying to understand how cells divide and how the division process can go awry. Basic biology is extremely important as is our work. Many human health problems, for example cancer and likely aging, are problems with cells. To fix these problems we have to know how cells work. Just like your mechanic trying to fix your car has a shop manual to refer to, cell biologists are trying to write the shop manual for cells, so we can fix them when they malfunction. Unfortunately, cells are millions of times more complicated than cars so it will take the efforts of many people to complete the shop manual for the cell.

My local university offers a bsc course on 'Computational Biology'. Is this worth taking if I want to pursue a career in research? How would it compare to a convention degree in life sciences? What areas of research in biology would I be looking at with this degree?

WarmUpHere

My suggestion is to take the course. When I first started in biology, it was very descriptive, with little math. That has been changing rapidly and we have had to adapt. So now having a background in mathematical approaches to biology is essential. Almost all fields will eventually need to embrace this but currently if you are interested in cancer for example it is essential because of the huge amount of data being generated.

My mom is almost done with her cancer treatment. I have an undergraduate degree in chemical engineering, but I'm really compelled to contribute to cancer research. How do I go about joining a lab like yours?

sinekrah

Hope your Mom is doing well. We need chemical engineers in biology so I encourage you to keep with your goal. Depending on your academic background you could apply to grad school or to an MD/PhD program. Alternatively, get yourself into a research lab anyway you can. Wash dishes, whatever. Then prove to your boss that you are really passionate about research. From there just keep following your nose and keep advancing. At some point you will need an advanced degree to move up to positions of leadership.

What couple pieces of advice would you suggest to a new graduate student? I'm constantly worried that I'll never be able to attain the level of knowledge of my peers let alone my mentor and other colleagues. Thanks.

ljhmigeggds

My best advice is to develop your skills and choose your field accordingly. I am not as smart as a lot of other scientists and I have a horrible memory. What I do think I have is great pattern recognition and some level of ability to synthesize disparate pieces of data. So much of my work focuses (pardon the pun) on microscopy and analysis of visual data. It is also what I love to do. That is the second most important. Being a scientist provides a certain type of reward, seeing new stuff. That has to motivate you. Figure out what stuff it would be most exciting to discover.

Where do you align yourself on the handcuff vs embrace cohesin model debate?

apjoijfou

Ok, this is pretty deep into the weeds but our studies of cohesion fatigue, the separation of chromosomes induced when cells are arrested at metaphase, suggest that the handcuff model may be more likely.

Do all kinds of cells have defective cell division in the same way? Are some types of cells more likely to have defective cell division?

firedrops

This is a great question for which I am going to have to speculate. The short answer is that we see lots of defects during cell division and the seem to exist in all kinds of cells. Certain of the controls of cell division are widely shared even among lower organisms such as yeast. Others are more specialized. Cells that undergo lots of division in adults such as skin and intestinal cells may then have a higher incidence of defects.

Hi Gary, thanks for doing this AMA.

I understand that if there is an error in any stage of cell division, there are these "cell checkpoints" which can lead to apoptosis. What is a cancer cell doing that evades apoptosis, or any regulatory process for that matter?

RMNDK4Life

Yes, great question. Cell cycle checkpoints are very important in keeping normal cells normal. They work at many stages of the cell division cycle including DNA replication. They also keep track of damage to the DNA and start repair processes. There is an important checkpoint that functions during cell division. It prevents the chromosomes from separating before they are lined up in the middle of the cell. This checkpoint is signaled from chromosomes that have not yet aligned, basically a “wait for me” signal. Once all the chromosomes are properly aligned, the checkpoint signal decays and allows the cell to progress to the next stage where the chromosomes are separated into the two new cells. If the checkpoint fails to work, which can happen, then the chromosomes will segregate too early and the progeny cells will end up with different numbers of chromosomes, a bad outcome. Recently we have been working on a situation where the checkpoint is too active. The chromosomes spend too long lined up in the middle of the cell and can eventually be ripped apart, another bad outcome, so there is a goldilocks “just right” time for the chromosomes to be waiting to separate when they are aligned in the middle of the cell. The checkpoints can either induce repairs or cell death, apoptosis. Cancer cells do develop ways to evade apoptosis by turning off certain pathways.

Mr. Gorbsky, what does your average day look like?

ti_lol

Ok, I get up pretty early usually about 4 am. Spend an hour waking up then either go for a run or other exercise. Then I spend the day in the lab, actually mostly at my desk. Unfortunately as you move up the ladder, you have less time in the lab. But I do keep my hand in. My current personal project is to develop new cell lines from amphibians, frogs and salamanders.

I'm learning about Mitosis in biology class. I'm in 9th grade and I am learning about intersex chromosomes. Do you know anything about that?

alexfierro88

I am not really sure what you mean. Do you mean when an organism has a atypical complement of sex chromosomes?

Thank you for doing the A2A! What is one of the biggest challenges you face in your work?

TheRealAelin

Hard to separate out just one but since this is on my mind in this session, I think convincing people of the value of basic science is really important. Actually I don't really find it hard. Most people are really into the importance of basic science and the adventure of exploring things no one has seen before. I really feel priviledged to have this job.

If your lab can reverse/stop excess cell division, why is curing cancer so difficult? Sounds flippant, but i wanted to ask in an ELI5 way.

annie_niwhdin

Ok, my best ELI5. Getting cancer is like having a new species of organism appear in your body. And each cancer can be completely different. If you find a way to kill it without killing all the normal dividing cells in your body, great. But unfortunately, lot of times when we think we have killed it there are a few survivors. These can come back with a vengence and are now resistant to the original therapy. Cancer is a bunch of diseases with similar symptoms. Whle there have been a lot of successes, much more research will be needed to get them all.

I'm a student in research aspiring to make a contribution like you have, but I know it will take much time and effort. How many times did your lab fail before succeeding and what was the point you realized how to acheive this?

DuchessOfDesserts

If you stop failing that means you have stopped trying. In terms of career I can't even remember how many grant applications I have written that have failed. In terms of experiments in the lab it is a different story. Often experimental "failures" tell you more than experiments that succeed. A failed experiment tells you your fundamental assumptions were wrong and need to be revised. That is when you make the biggest breakthroughs.

Hey Gary, I'm a genetics student at the University of Georgia, hoping to do exactly what you do! How did you attain your position in your lab, and what made you decide to stay in your lab? I intend to research (as a career) genetics as it pertains to psychology, and any info would helpful! Thanks for doing this AMA, I look forward to reading your responses!

sam_destef

Well, kind of a corny answer but I just tried to do what I loved. I have been trying to be a biologist since

I was a little kid. Then just found interesting things to study in school then in doing research as an undergrad student on. Keep up your studies. Genetics is cool and applying it to psychology sounds exciting.

Can you tell us more about Chi running?

ncohrnt

I love talking about Chi running so am happy to answer this. Sometimes I jokingly refer to Chi running as a cult because of the enthusiasm of many of its proponents. Chi running is a style of running developed by Danny Dreyer where the principles of Tai Chi, of which I know very little, are applied to running. The result, to which I can testify, is a more gentle, less pounding experience. I am 62 now and have been running races for about 15 years. In 2015 I ran my personal best marathon which qualified me for the 2016 Boston marathon, which I ran last Spring. Actually I have become something of an exercise fanatic, mostly because from the biology of what I read, it seems to be preventative of many human health issues, including aging. My favorite exercise story is as follows. After a run, wearing an Oklahoma Medical Research Foundation t-shirt, I went into the grocery store. While standing in line a gentleman said to me, "When are you scientists going to figure out the secret to eternal youth?" I thought for a second and said, "Oh, we've got that already." He replied, "Really, what is it?" I said, "Exercise." I don't think that is the answer he wanted.