# Science AMA Series: This is Chris Deeg of the University of British Columbia (Canada). I do research on Giant Viruses that infect microscopic organisms and I'm here today to talk about it. AMA!

eLife$_AMA$[1]$andr/ScienceAMAs$[1]

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April 17, 2023

**Abstract**

hi reddit! I'm a graduate student in Curtis Suttle's lab at the University of British Columbia (Canada) where our research focuses on aquatic microbiology. I study pathogens that infect protists – microscopic organisms living in aquatic environments. Amongst them are Giant Viruses that have challenged concepts of what constitutes a virus due to their enormous size and complexity. My research aims to explore the diversity and environmental role of these overlooked viruses. Further, I am interested in the evolutionary processes that have led to Giant Viruses reaching a complexity comparable to cellular organisms. In a recent paper published in the journal eLife, my colleagues and I isolated and characterized the giant Bodo saltans virus (BsV) that infects the protist Bodo saltans. Sequencing the genome of BsV revealed many previously unknown genes, a putative mechanism for genome expansion, and several unusual features, such as movable genetic elements that might help to fend off other Giant Viruses by cutting their genomes. You can read a plain-language summary of our findings. I'm here to answer questions related to our eLife paper or our research more broadly. I'll start answering questions at 1pm EDT. AMA!

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REDDIT

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ELIFE_AMA R/SCIENCE

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CORRESPONDENCE:

DATE RECEIVED:
May 17, 2018

DOI:
10.15200/winn.152647.75054

ARCHIVED:
May 16, 2018

CITATION:
eLife_AMA , r/Science , Science AMA Series: This is Chris Deeg of the University of British Columbia (Canada). I do research on Giant Viruses that infect microscopic organisms and I'm here today to talk about it. AMA!, *The Winnower* 5:e152647.75054 , 2018 , DOI: 10.15200/winn.152647.75054



What was it that first got you interested in studying giant viruses?

StuartRFKing

Hi StuartRFKing,

That goes back to the controversy about the fourth domain of life and whether or not you should consider viruses to be alive.

I started working on influenza virus during my master's thesis and when I read the first papers on the mimivirus it blew my mind. I could not believe the complexity of these viruses and the potential implications that this had for our understanding of what it means to be "alive". After spending several years of my life studying giant viruses I am left with more questions than answers. We might never be able to satisfactorily answer the question if giant viruses are alive or not because they sit on a continuum from the living to the non-living and no matter where we draw the line it will always have some uncomfortable consequences. For instance, if we say giant viruses are not alive, then we would also have to take the living status away from several parasitic intracellular bacteria that are as or less complex than these viruses. Vice versa, if we say giant viruses are alive, then where do we draw the line amongst viruses? Surely we wouldn't consider the tiniest of viruses alive.

Thinking about this just blows my mind and I am more fascinated than ever!

Chris

im not a science person, but i heard that some scientist is breeding some giant virus or whatever single large cell thinggy that is capable to eat up the HIV virus.

Is that true? or horseshit?

UnlovableVisor

Hi UnlovableVisor,

I would call mostly horseshit on this story and I have not heard of it in this way. However, there are a few elements in there that by themselves are somewhat correct, let's see if can make some sense of it:

First, science is miles away from " breeding ... giant virus or whatever single large cell " from scratch. The best we can do, and that is crazy in itself, is to make a replicate genome copying the natural version in the test tube and put that back into a cell and it works. But for most applications, we have to stick to modifying natural systems.

There are cells of the immune system who literally eat pathogens such as bacteria, they are called macrophages. In theory, it could be possible to manipulate those to "eat" HIV, but I am not aware of any studies like that. Further complicating the matter is the fact that HIV itself infects cells of the immune system, this is what makes AIDS so nasty. So macrophages themselves can get infected by HIV, which means they would not be very useful in combating the virus unless we could stop them being infected in the first place which would probably be a major breakthrough in it self.

**Disclaimer: Take all this information with a grain of salt since I am not an HIV researcher myself.**

I hope this made sense.

Chris

Hey not much going on right now. Let´s see if we can change this :)

- What would you say are the main points making giant viruses different from "normal viruses"
- What groups of giant viruses are known right know and is there a patternw here they occur?
- If you would have to look for new giant viruses where would you look?
- Are there high quality electron pictures of giant viruses outthere? Can you show some?
- What´s the most complex giant virus you know of?

Thanks for doing the AMA! Really interesting stuff!

Milvolarsum

Hi Milvolarsum,

Let me address these questions individually:

*What would you say are the main points making giant viruses different from "normal viruses"*

I don't think there is such a thing as "normal viruses', but you could easily point out the genomic complexity compared to "normal sized viruses" and the unusual functions that are encoded by such big genomes. Especially the genes involved in producing proteins are not usually found in smaller viruses. What also sets giant viruses apart is that some of them are themselves parasitized by smaller viruses called virophages.

*What groups of giant viruses are known right now and is there a pattern here they occur?*

This is a very good question! There is one large group of giant viruses emerging that is called the Mimiviridae, represented by the first giant virus mimivirus as well as BsV and has several sub groups. However, giant viruses are not necessarily closely related, since other giant viruses, such as the pandoraviruses are more closely related to comparatively smaller viruses infecting algae. So basically it looks like several branches of a very diverse group of DNA viruses have independently become very large and are together referred to as giant viruses. It appears that it is the lifestyle of infecting single-celled organisms that feed on bacteria, such as amoeba, that causes the viruses to become so large, in regards to both, their particle and genome size.

*If you would have to look for new giant viruses where would you look?*

You will find giant viruses everywhere you can find their hosts. They are very abundant in aquatic and soil environments but have also been found under rather surprising setting. One of my favorite examples is a giant virus that was isolated from an amoeba that caused a keratitis in someone's eye. The main problem with isolating giant viruses is growing their hosts and then finding the matching virus. The fact that there are virophages that can infect the giant make it even more challenging to propagate them in the laboratory. A new promising field is single virion genomics, which basically means sequencing the genome of a single virus particle from the environment. This way one can bypass the need to culture the host and this will surely provide some very interesting new giant viruses int he near future.

*Are there high quality electron pictures of giant viruses outthere? Can you show some?*

Here is a nice study on mimivirus: http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1000092

The recently discovered tupanvirus also has a really funky tail:https://www.nature.com/articles/s41467-018-03168-1

And of course don't forget my friend, the Bodo saltans virus which is the prettiest one ;) : https://elifesciences.org/articles/33014

*What´s the most complex giant virus you know of?*

That depends on what you define as being complex. The largest virus by quite a margin is Pandoravirus salinus, but it has a rather low density of genes (http://science.sciencemag.org/content/341/6143/281). Tupanvirus has the most genes involved in translation (making proteins from RNA), and a really interesting tail structure that makes it complex both in its structure and coding potential.

Chris

Hi there!

Do you think any of the unusual features of this giant virus have the potential to be utilized for some research and/or medical applications (e.g. genome editing, drug delivery...etc)?

hasslemind

Hi hasslemind,

This is indeed a good point! Almost half the genome encodes for proteins that we have never seen before. Another 10% encodes ankyrin-repeat domain proteins. Those are a class of poorly characterized proteins that mediate interactions with other proteins. Together, I would assume that

these and most of the unknown proteins are involved in modifying the host cell to make it more suitable to viral replication, or fending off any competing parasites that might infect the host cell. So we have two very interesting classes of factors. One is modifying eukaryotic cells, just like ours, and the other is inhibiting bacteria or viruses. So I would predict that at least some could be utilized as pharmaceuticals to treat metabolic disorders and as antimicrobials. To test this, one would need to isolate the individual genes and express them in eukaryotic cell lines or yeast cultures to see how they manipulate the cells. The produced factors could then also be tested against different microbes to test for antibacterial effects.

So to summarize, I do think there is big potential for medial applications, but given that we are in the infancy of understanding the function of these genes, there is a lot of work to be done before any potential applications can be found.

Chris

Off topic layman here. I have heard of interesting phage therapies being conducted in, well, formerly communist countries. And that these treatments are particularly well suited to antibiotic resistant infections.

Has any of you work involved studying this? Is phage therapy too risky to be tried in the "western world"?

Next question, do viruses infect fungi? Or slime moods?

Srynaive

Hi Srynaive,

While I have worked with phage a little bit, I have not been involved in any actual phage therapy work. You are absolutely correct that there was a lot of work on phagetherapy in the former soviet union. This work has slowed down quite a bit since the discovery of antibiotics, but is currently experiencing a bit of a revival due to the emergence of antibiotic resistance. There are a few institutes that never stopped working on phage therapy and specifically one institute in Georgia offer phage treatment to patients today.

The problem that phage therapy has in the western world is, to my knowledge, more of a regulatory one. The respective authorities (like FDA) can not approve phage therapy due to the restrictive regulations. This has, and again I might be wrong about this, to do with the fact that phage are an evolving multiplying population that could replicate and spread to other individuals, which is something that can not be approved. However, given the looming antibiotic crisis, I think it wont be too long until those rules we be adjusted.

Given you final question, yes fungi have viruses too! I am willing to go out on a limp here and claim that all lifeforms have viruses, we just haven't found them all.

Chris

This sounds amazing and very compex! Just wanted to say I'm glad there are brilliant people like yourself out there doing this vital research and dedicating their lives and minds to this kind of thing.

My question is this: what kind of positive impacts do you think this will have on society and how can your research be applied to improving medicine and healthcare, if at all?

Thanks for doing the amazing work you do!

climbman957642

Hi climbman957642,

Thank you for the kind words!

This is admittedly very basic research with no apparent direct application for healthcare. But that doesn't mean that it is not important. You might have heard about the recent hype around CRISPR, the gene editing system that is already transforming how we do scientific research and most likely will have massive implications in health care, the first clinical trials being just under way. Now CRISPR was discovered by a group studying bacteria and phage in yogurt for totally unrelated reasons. I like this example and there are many like it, because it shows what is so great about fundamental basic research: You never know what you will get in the end! Sometimes it takes years for the scientific community to realize how important some of the very basic findings are and just because there is no immediate use doesn't mean you should't do the research.

That being said, I do think there could be some applied used of many of the genes encoded by the giant viruses further down the road. But those certainly need some detailed follow up studies. Check out my answer to hasslemind above for a more detailed account.

Chris