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“We have a chance to no longer be subject to the whims of the cosmos”

To become an interplanetary species, we may have to alter our DNA, says geneticist **Chris Mason**. He tells Joshua Howgego about his 500-year plan for life off-Earth

ROCIO MONTAYA

CHRIS MASON likes to think about the future. He isn't dreaming about a summer holiday, or even planning his retirement. His thoughts extend much further – to the point where Earth is no longer a suitable home for humans.

Alarmed at the prospect, Mason has sketched out a plan of action in the form of his book *The Next 500 Years: Engineering life to reach new worlds*. It covers some of the usual ground: how we will first establish bases on the moon and Mars, and later on the solar system's outer moons. Eventually, we will make an epic trip to a planet orbiting a different star.

What sets Mason's ideas apart, however, is that he realises that human bodies aren't well suited for life away from Earth, what with the radiation, toxic gases and so on. His programme for expansion comes with a detailed blueprint for the genetic improvements we will need to make to ourselves to boost our resilience off-world.

Mason is well placed to write such a plan. A geneticist at Weill Cornell Medicine in New York, he was a principal investigator on the NASA twin study, our most thorough look yet at what happens to the human body in space. The research focused on astronaut Scott Kelly, who spent nearly a year in orbit starting in 2015, and his identical twin, Mark, who remained on Earth for that period.

Mason is also actively exploring how to genetically modify human cells to help make them more resilient in space. Although his plan spans 500 years, he is laying the groundwork already.

Joshua Howgego: You say we have a moral imperative to find a way to live beyond Earth. Why do you think that?

Chris Mason: This is humanity's duty because of one simple fact: we're the only species that has an awareness of extinction. There could be some other species – dolphins or, who knows, maybe some primates – that think about this, but to our knowledge they don't. Plus, we're the only ones that can actually act on it.

Other duties you have are usually chosen. Maybe you've chosen to join the military and you have a duty to your country; or you've chosen a spouse and have a duty to your family. Those can often be abrogated and left behind. But I think a duty to life is something that is activated upon awareness. I think therefore we should enact it because otherwise no one else will.

Do we have to leave Earth to guarantee the survival of humanity?

When I was writing the book, I had a moment of stark sadness. I was projecting what happens over the next 5 billion years. It's estimated that the sun will become a red giant and eat up the inner planets and then slowly decay away and become a white dwarf. Most astrophysicists think we have got about 4.7 billion years before Earth becomes uninhabitable, which is a really long time. But the luminescence of the sun will increase to pretty intolerable levels in about a billion years. I suddenly realised we only had about one-fifth of the time that I thought we had. Earth is the greatest home we've ever known, but if we stay here it will be our last home.

What dangers will we face when we venture beyond Earth?

We have explored this quite deeply in the › work we've done with NASA on Scott Kelly. One of the biggest dangers is the radiation; we could see damaged DNA coming out of his urine. You could also see his body trying to adapt to zero gravity, struggling to maintain muscle strength and bone density. The atrophy of muscles, including the heart, is a well-known challenge. Scott's heart got a little smaller and some of his arteries got a bit inflamed.

There are also cognitive and mental health challenges. If you're in space for a year, that's one thing. Scott's cognitive abilities did slightly decrease in the six months after he returned to Earth. But if you're in a spacecraft for decades, that's another thing entirely.

I didn't realise that Scott's twin, Mark, was also an astronaut and has since become a politician. This is quite a family.

Could you imagine being at a dinner party and some parent saying: "Yeah, both my sons are astronauts and one's a senator too"? You would think they were lying.

How are we going to protect future astronauts from the harmful effects of space?

Engineering humans is complicated and controversial. It has to be done in the context of rigorous safety monitoring and clear regulation. So this is something that I think could begin to happen slowly in the coming decades. I'm proposing two ways of doing it. One is using the gene-editing tool CRISPR to modify specific genes. The second is epigenome editing, where you can transiently turn genes on or off. With these tools, we have this exhilarating opportunity to not be subject to the whims of the cosmos.

Do you have any ideas for which genes we should target first?

We can leverage the evolutionary lessons that every creature has demonstrated in its own biology. A tardigrade is one great example. This is a microscopic animal that can survive in the vacuum of space, it can be completely desiccated and then rehydrated – it's really an extraordinary creature. Its genome was sequenced in 2015 and the Japanese group that did the sequencing found an interesting catalogue of genes related to DNA repair.

> "The tardigrade genome has revealed a suite of genes related to DNA repair"

NECULA VALENTIN ANDREI/SHUTTERSTOCK

There is one gene in particular, called *Dsup*, which codes for a DNA damage suppressor protein. In my lab, we've now permanently integrated *Dsup* into a human genome and a new cell line in our lab. We can get up to 80 per cent reduction in DNA damage compared with unmodified cells when we fire heavy radiation at these cells.

Now, this is not an entire human body. But we think it's possible to stably introduce other organisms' genes into human cells and use that as a way to prevent radiation damage. Another example is a gene called *p53* – elephants have extra copies of this gene and it may explain why they so rarely get cancer.

Let's say we add these genes to our DNA. What could possibly go wrong?

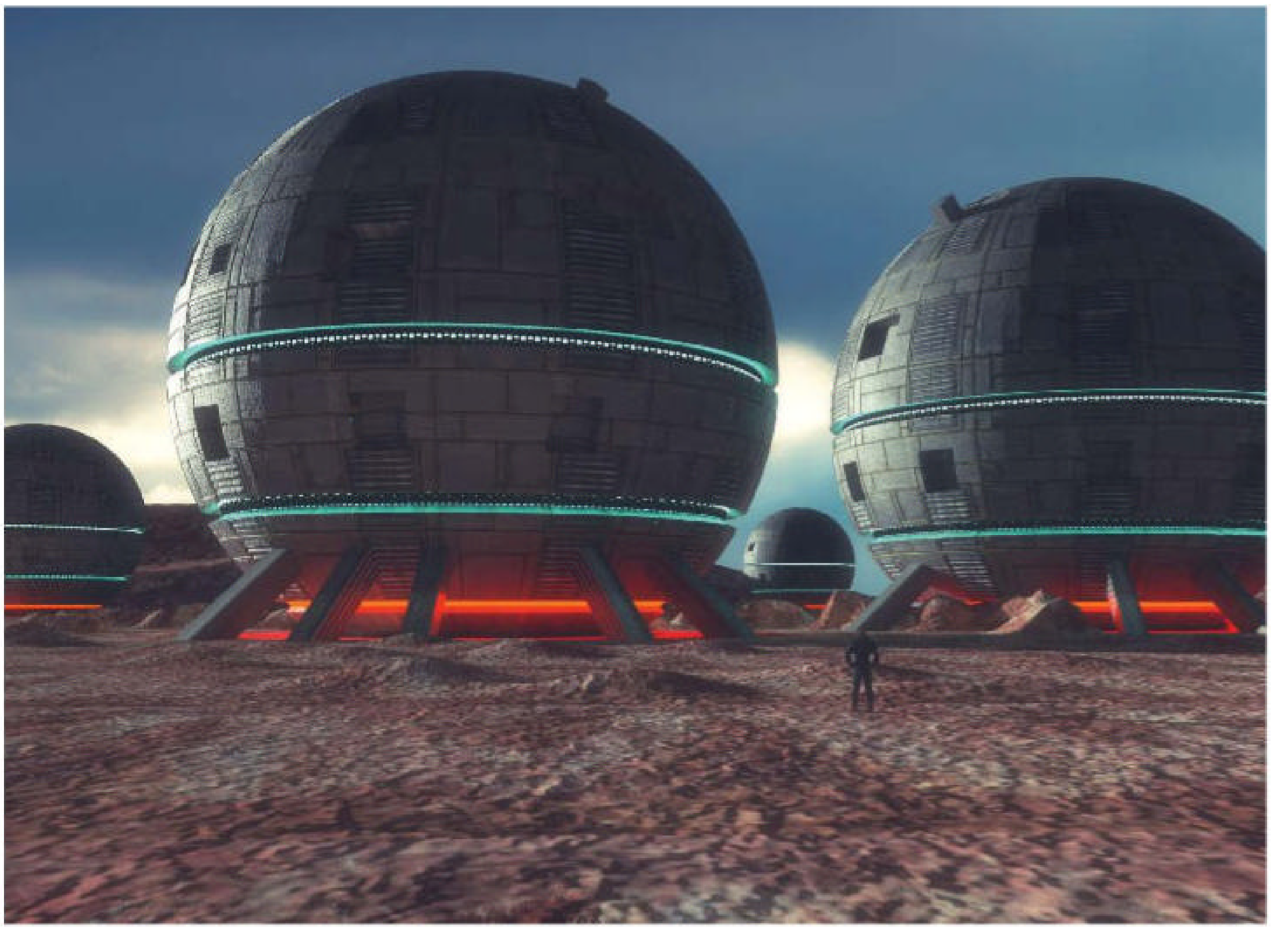
Whenever you add a gene to an existing biological system, you can create unexpected changes. We might see other mutations emerge, or alterations in the regulation of gene expression. There also could be a cancer risk. So you need to have proper oversight of all of this sort of work.

But we might also consider using epigenetic therapies, where you can temporarily turn things on and off. You change the structure of DNA and how it's regulated just for a little while. Imagine there was a burst of radiation coming at some astronauts – what if you could therapeutically activate additional radiation response machines in their cells and have them turn off afterward?

We know this is technically possible, and just needs to be optimised. These are the kinds of experiments I envision for the next 10 to 20 years.

Would we want to genetically modify other species to help us survive?

If we bring animal companions or plants, they will probably also benefit from genetic modification. Some of it may be just for survival – we might need nitrogen fixing bacteria modified so they can survive on Mars, for example. But eventually you could very well imagine it would be for food or pets, too.



MIGUEL AGUIRRE SÁNCHEZ/ALAMY

An artist's impression of what a Mars colony might look like

What about nutrition – is there a danger we'll struggle to grow enough of the food we need?
There are nine amino acids that humans need to consume to survive because we can't make in our own bodies. We have to get them from our diets, which is fine if you're living on Earth. If you go far away, you would have to bring them with you or manufacture them. But what if we could make them in our own bodies?

In my lab, we've done some work on how we might make humans more prototrophic, meaning we would be able to make all the molecules we need to survive within our own bodies with only simple food. We could co-opt pathways that are found in other organisms, integrating them into the human genome so we can make all of our amino acids. It has been demonstrated that this is possible for one or two amino acids, though again only in cells.

And you've looked at how we can make sure we get enough vitamin C…
If you don't get enough vitamin C, you'll get scurvy. We actually have the gene for vitamin C synthesis in our genome, it's just been degraded. Some call it a pseudogene. But with a small CRISPR tweak, you can reactivate it. If you're on some faraway planet, why not re-enable some genetic capacity or add other abilities? It would represent one of the largest genetic engineering projects ever performed to actually get this to work in full.

> "Multiple generations will have to live and die in the same spacecraft"

Can you tell me about the last phase of your plan, and particularly the idea of a generation ship?
There are now several hundred exoplanets that look habitable, meaning there might be enough liquid water there for humans to survive – maybe even without any protective gear. I propose that, by the year 2400, we should have enough knowledge about what happens to the body in long-term space flight, so we can actually put people on a ship that can make its way towards the best choice of our next home. It's called a generation ship because it will be a long trip; multiple generations will have to live and die in the same spacecraft.

Unless we figure out another way. We might be able to avoid the psychological stress of such a trip by having humans slow down their biology and go into stasis or hibernation. Studies of bears have already identified a suite of genes we might target to induce something similar in humans.

Speaking of new generations, one technology you say we might have in the future is an artificial womb. What makes you think we will need them?
Whenever possible, I describe in the book ways in which we should be able to increase not just planetary liberty, but cellular liberty. I'm not saying exowombs would replace biological wombs. It just gives you options. If, for any reason, pregnancy is too dangerous, it gives you an opportunity to have a child.

Of course, you and I won't be alive to see if all of this happens…
I'm very much planning to be dead for the vast majority of my 500-year plan. I think one of the most liberating states you can have is a healthy sense of mortality. That liberates you to think about what is going to come after you and how you can contribute to the future. What's striking is that a lot of people I've talked to about the book have never thought farther than 50 years ahead. ■

Joshua Howgego is a feature editor at *New Scientist*