

Hi, this is Duranee for Cheap Astronomy, www.cheapastro.com. This is SISS, Science on the ISS – and today's episode is *DNA in space*.

Given everything else we've already flown into space, it should come as no surprise to learn that we've now flown up a gene sequencer. And of course, it was a gene sequencer able to work in microgravity, but this was one of those rare moments when we flew up a COTS product – that is, a commercial off-the-shelf product, that was actually developed for use on Earth, but which could work just as well on the ISS.

This COTS product, MinION, is about the size of a harmonica and plugs straight into a USB port and uses ion-flow nanopore sequencing – where a very, very small hole, a nanopore, will only allow the passage of a single molecular strand – which might be DNA, RNA or even a protein. That strand is drawn through the nanopore by a flow of ions – that flow being driven by a charge differential created on each side of the nanopore.

But remember, this is a nanopore. It's so narrow that every time a polymer unit of a molecular strand squeezes through it, there is a tiny hiccup in the accompanying flow of ions. These tiny hiccups vary according to the exact geometry of each polymer unit and produce a characteristic electrical pulse – which means you can accurately identify each individual polymer unit as it passes through. This is how a ion-flow nanopore DNA sequencer works. Cool, huh?

The MinION sequencer (where MinION is a contraction of the words mini and ion) was designed and built for use by scientists trekking through a Brazilian rainforest or bouncing around in a land rover in central Africa. For a gene sequencer to operate under such conditions it has to be largely immune to various bumps and knocks and changes in its orientation. And as a consequence of that, it ends up being exactly the right kind of gene sequencer to operate in the microgravity environment of the ISS.

So, the ISS has a space-compatible, as well as USB-compatible, gene sequencer. But, so what? Well, for a start, we could put a petri dish on stick and wave it around outside the ISS and see what sort of microbiota are making a go of it at 400 km altitude – determining their species as well as looking for any unique genomic features that may distinguish their space-faring sub-species.

Of course, waving a petri dish on a stick outside the ISS might only manage to grab a tiny biological sample for testing. But, in addition to MinION we are steadily adding all the requirements of a space-based DNA research laboratory. A lot of DNA research often starts with a tiny trace of something that needs to be copied repeatedly in order to give you a large enough sample for analysis. So, most working DNA research laboratories have a polymerase chain reaction thermal cycler. This is a machine that adds a small DNA sample to a solution containing a mixture of enzymes. The machine then runs that solution through a cycle of changing temperatures – which is why it's called a thermal cycler. Since the different enzymes in the solution work optimally at different temperatures, you can run a staged biochemical process that creates multiple copies of the DNA sample, producing a final sample that is orders of magnitude bigger than the trace sample you started with. The machine now being used on the ISS is called MiniPCR, which, like MinION, is also a COTS (commercial off-the-shelf) product that also happens to work just fine in microgravity.

So, what else can we do with a working DNA laboratory on the ISS? Well, we could also wave a petri dish on a stick around the inside of the ISS. Since the ISS is full of people – and food and water and a

dense atmosphere – over time, various microbes have snuck aboard and made it their home. Such organisms are mostly benign, but some might represent a risk to human health and others could even damage to internal infrastructure, eating away at electrical wiring insulation or pressure seals. The ISS gives us an opportunity to do a stocktake of all the Earth-based microorganisms that might establish themselves on a spaceship. We can then assess the risk they pose to astronaut health and spacecraft integrity and devise various biological countermeasures to control their growth. Back on Earth we sometimes refer to such biological countermeasures as cleaning. Diligent cleaning is something you don't have to worry about on a 3 day flight to the Moon, but you really have to worry about on a 7 month flight to Mars.

And speaking of Mars, since the MinION sequencer and the MiniPCR thermal cycler survived a trip to the ISS, they could just as well survive a trip to Mars. So, whenever that trip happens, we can expect Mars astronauts will have the technology at hand to sequence DNA. If we can isolate a microbial life form on Mars, we might be able to determine from it whether life on Earth and Mars have a similar biomolecular origin. Alternatively, if we just get garbled nonsense back from our sequencer, we'll be able to say that life on Mars really is alien.

And, even if we aren't going to Mars anytime soon, there is still plenty of work to do. There is clearly something about being aboard the ISS that has epigenetic effects on test samples and even test people. It might be microgravity – but it might also be something else entirely. DNA samples flown to the ISS have to undergo several Gs of acceleration to get there. Once on board they are handled by astronauts in different ways from how they are handled by lab technicians on Earth. And, once aboard the ISS, any biological material, including human beings, are exposed to higher levels of cosmic rays – and there are always slightly higher CO₂ levels on the ISS than there are back on Earth. This is because the best air scrubbing technologies available still can't fully compensate for the impact of having six to seven people exhaling CO₂ within the same enclosed space.

Anyhow, whatever the cause may be, here's a list of unusual DNA-related things that happen aboard the ISS:

- 1) Stem cells appear to proliferate at a faster rate on the ISS than they do on Earth. Proliferate means they divide and grow more rapidly within a cell culture. Understanding why this happens might help us to better mass produce therapeutic cell lines back on earth.
- 2) The rate of random mutations in cell lines, including bacterial cell lines, is faster on the ISS than it is back on Earth. This may help us track the development of bacterial resistance to antibiotics over generations of bacterial cell lines – and if you can determine what speeds up random mutations, perhaps you can determine what slows them down as well.
- 3) The Scott Kelly / Mark Kelly twins study has found that Scott Kelly's telomeres grew longer while he was aboard the ISS, but then shrunk back to the same size again after his return to Earth. Telomeres are involved in the repair of damaged DNA and manipulating them in the right way might slow down the ageing process.

The fact that we've discovered these interesting things happening on the ISS, doesn't mean that the ISS is the only place we'll ever be able to make these things happen. We just have to understand why these things happened on the ISS and then try to mimic those same conditions back on Earth. For example, it's unlikely that spending long periods in microgravity to extend your telomeres will

extend your lifespan. Indeed, the opposite is more likely given the number of unhealthy things microgravity does to your body – skeletal erosion, muscle degradation, et cetera.

And there's something else we've learned from the ISS. As well as learning that living in space can affect people's DNA, it seems that people's DNA may affect how well they can live in space. Polymorphisms are minor variations in a genome that have never really mattered in natural selection, so evolution has never weeded them out. A good example is blood groups. They have a genetic basis, but their minor differences don't affect your survival – at least not until we invented blood transfusion. In a similar way, polymorphic variations may explain why some astronauts' visual acuity is affected by long duration in microgravity, while other astronauts are not so affected.

These visual changes are something that has made no difference so far in our evolutionary history, but might now affect how well we succeed in space. But of course, gaining a better understanding of the polymorphic basis of these vision changes may show a way to prevent anyone from being affected in the first place. We don't fully understand all the details yet – but that is why we do science on the ISS.

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