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Microbiology

The unexpected partner(s): a billion viruses

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What constitutes a human body? What is it that makes your body, your own? If we begin to break it down, you can easily see that your body is covered with a layer of hair and skin. Beneath that lie your circulatory systems, bones and organs, such as your lungs, kidneys, and brain, which form large functional units within your body. If we start to go smaller we can begin to look at your individual cells. These cells form large fluid-filled sacks that are responsible for many of the processes and functions that your body performs. Smaller still and we begin to see the trillions of microorganisms that coat and inhabit every twisting corner of your body. Among these microorganisms are the bacteria; tiny single-celled creatures that peacefully live upon and inside of you. These bacteria perform critically important functions, such as helping you digest your food or regulating the time that you fall asleep at night. But the journey does not stop there, smaller still and we find infinitesimally small viruses; yet these viruses do not infect us, they're the good kind of virus.

Bacteriophages, or simply phages for short, are tiny viruses that only attack bacteria. Phages thrive throughout your gut where they "feed" upon the bacteria that live there. They can even act as part of your immune system by protecting you from bacterial diseases. Importantly, phages don't infect human cells and they don't cause disease – as a matter of fact, biology books tell us that they don't interact with us at all.

Yet, contradictory to these teachings, scientists have observed phages in parts of the human body where they shouldn't. Phages have been found within the bloodstream, kidney, liver and even within the brain – all organs of the human body that are considered to be 'sterile'. If phages cannot interact with human cells, then how are they able to get inside of our bodies and organs?

In an attempt to answer this question my lab at Monash University designed a simple experimental system. We grew a layer of human cells that were isolated from the gut in a small, two-sided, plastic dish. These human cells grew closely together and after about three days of growth, they formed a tight cellular layer. To show that this cell layer had no gaps or holes, we added a blue dye to one side of the cells and measure if any dye was able to leak across. Next, we added phages to one side of the seemingly impermeable cell layers and shockingly found that they were somehow able to cross it.

These human cells were using a process known as 'endocytosis' to engulf the phage particles. Using powerful microscopes we were able to visualize the tiny phages particles inside of comparatively enormous human cell: the phages were shuttled around the cells inside of membrane-bound vesicles. Most of phages remained trapped inside the human cell and were eventually degraded, but a select few continued their transport and were eventually released on the opposite side of the cell.

Based on these discoveries we collaborated with the Luque lab at San Diego State University to develop a mathematical model to estimate just how many phages the average human body absorbs by this mechanism each day. From microscopy counts, we know there are roughly five billion phages in each gram of human faeces. We were also able to find some very obscure old measurements of the size, volume and surface area of the average human colon (which has a volume of 409 ml if you ever wanted to know). We combined these measurements and estimated a total of two trillion phages living within the gut. With this number, we calculated that the average human body absorbs approximately 31 billion phage particles every day, with these phages being transported through the circulatory system and organs of the body.

We called this mechanism 'phage transcytosis' and propose that this is how phages are able to enter into the 'sterile' regions of the body; solving the decades-old mystery appearances of phages within the body. This research opens up many more questions than it answers–namely, why do our cells transport phages and what is their function, if any, within the body? These intra-body phages could be protecting us from opportunistic bacterial infections, may regulate our immune systems or even control the cellular processes within our body. At the very least, hopefully, these phages have shown you that your body is much more viral than you had previously thought.