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The accidental crippler

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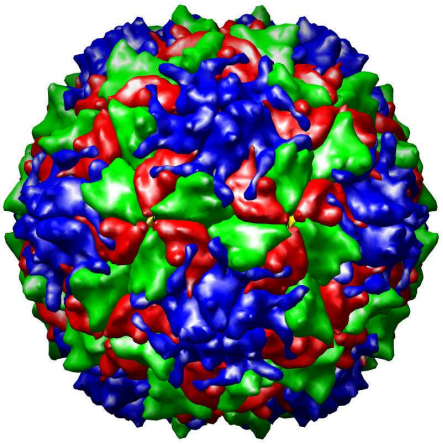
for Pat

All organisms need other organisms to survive. Flowers need bees. Frogs need flies. Humans need vegetables. And some viruses need us. Poliovirus in particular squats human cells preferentially, where it uses their machinery to replicate and multiply since it cannot do it on its own. In doing so, poliovirus – like all viruses – hinders not only the host cell's welfare but also any activity it should have undertaken. However, before a virus stands a chance of invading a cell, let alone propagating inside it, something has to let it in. For poliovirus that something is a protein receptor, known as the poliovirus receptor. These receptors are sprinkled on the surface of certain types of cells and are specifically recognised by poliovirus, which docks to them and subsequently finds a way to wriggle inside.



Poliovirus: the accidental crippler

Image produced with UCSF Chimera
(http:://www.cgl.ucsf.edu/chimera)

Poliovirus – or poliomyelitis virus – is highly contagious, and most probably spreads from one human to another via faecal or oral contamination. Upon ingestion, the virus multiplies in the epithelial cells of the intestine, from where it spills into the bloodstream and can then reach any other part of the body. As in all viral infections, our immune system is triggered off and the usual symptoms such as fatigue, fever or nausea will occur. In the event of poliovirus, over 98% of those infected manage to fight the infection off in the same way they would fight off the flu – it is the very unfortunate 2% who do not manage to do so. No one knows why. Could it be that their immune system is deficient in some way or another at the time of infection? The net result however is that poliovirus manages to reach their central nervous system, where it invades the nerve cells that control our muscles. And because its sole aim in life is to multiply, it will do so inside these cells, killing them off one by one, thereby causing muscle paralysis and the crippled postures a great majority of polio victims have to cope with for a lifetime.

From Egyptian stone carvings to the Bible, over the millennia depictions of people with crippled limbs are many but there is no telling whether they are the consequence of poliomyelitis. The first clinical description of polio dates back to 1789 when the British physician Michael Underwood referred to it as a 'debility of the lower extremities'. But a virus is microscopic and it was not until 1908 that poliovirus *per se* was identified by two Austrian physicians, Karl Landsteiner and Erwin Popper, and as a result polio became a reportable disease. Not much evolved until the 1920s when the future President of the U.S.A. – Franklin Roosevelt – is said to have been afflicted with poliomyelitis at the late age of 39. Not only did he and his wealthy family inject a fortune into polio research but his status helped to change public opinion, and cripples were no longer perceived as invalid humans to be withdrawn from society. Two polio vaccines were developed by the 1930s but both turned out to be a fiasco. Research was then brought to a near standstill during the 1940s because of World War II, and it was only in the 1950s that the first effective polio vaccines were developed almost simultaneously by Dr Jonas Salk and Dr Albert Sabin – the first given by injection, and the second oral. By the 1960s, polio had almost been eradicated from developing countries.

Viruses are hugely imaginative and have devised cunning strategies to invade a cell. Poliovirus uses a protein receptor, christened the 'poliovirus receptor' or CD155. The poliovirus receptor is a transmembrane protein found in different types of cells, and belongs to the immunoglobulin superfamily. Poliovirus recognises the extracellular domain of CD155 which lodges into 'canyons' that are formed on the virus's capsid. Once firmly attached, poliovirus can either enter the cell by way of endocytosis and use the infected cell's machinery to multiply, or it can inject its genome directly into the cell for the same purpose. The end result is viral propagation.

Curiously, the poliovirus receptor is expressed in many types of cell but not all kinds are infected. This could be explained by the fact that certain types of CD155 are not membrane-bound but secreted. The secreted forms could well baffle poliovirus by binding to them before it can actually dock to a cell, thus giving the virus no chance of survival.

Besides its ability to dock poliovirus, CD155 also seems to have a number of other functions. For instance, it may be involved in cell to matrix adhesion, or cell to cell adhesion, and it has been suggested that this could explain how poliovirus can glide unencumbered from the blood into the central nervous system, or even from a muscular cell into the central nervous system. What is more, CD155 is probably linked one way or another to dynein – a protein involved in cellular transport, not to mention axonal transport. Researchers do not bar the possibility that poliovirus could reach the central nervous system via the muscle itself. The virus would perform this by crossing the neuromuscular junction by way of endocytosis and actually hitching a ride up the axon in the endocytic vesicle thanks to dynein. More recently, CD155 has been shown to bind to cells of the immune system – the natural killer cells – thereby triggering off an immune response against not only certain viruses but also tumour cells that carry the receptor, which can be of great interest in the development of anti-cancer drugs.

Thanks to poliovirus, many processes involved in viral infection have been understood, which makes it all the easier to develop vaccines. Today though, scientists are worried that the eradication of polio may stunt further research because of the loss of funding. And it would be a loss not only for fundamental research but also for polio victims for whom it has taken a lifetime to accept their lame limbs and who – decades after their first encounter with the virus – are reminded of an ugliness they had forgotten, with the development of novel symptoms such as joint pains, exhaustion and muscular waste. Ailments which have been neatly stashed into a bag called 'post polio syndrome' and which, for polio victims, just feels like a stab in the back.

Words To The Virus Which Found Me In 1942

Pat Ingoldsby

How did you find me?
How in the name of God did you find me?
A tiny infant…down in the heart of old Malahide village…in the little house beside the coal yard.
Were you looking for me or what?
Jesus – I was only just born.
I knew nothing at all.
The name they put on you was bigger than me.
Infantile Paralysis.
That is what they called you.
You went around the place paralysing babies.
And you found me down there in that beautiful place
beside the village green
looking over to the island
looking out to the sea.
You came into me and you made me cry.
What time did you come in?
What day was it because I don't know?
What brought you down that way in 1942?
Which way did you come?
Was it down New Street past Bertie Boyle's
or did you come round from the Back Strand
under the railway arch past Lesley Riley's?
Was the tide full in?
I don't know that either.
Why did you go past Annie Daniel's house
and come into ours?
There was me and Michael, Ma and Da.
Why did you come into me?
Did I make a sound as you were going past?
Was that the way it happened?
Was the wireless on?
What could you hear?
I think it was a cowardly thing that you did.
To take the life away from my arm
and put hidden slow wasting in my legs
was a cowardly thing indeed.
Fifty years on
I am still finding the damage of you.
Fifty years on
you find new tears in me.

Are you still alive?
Are you still doing your virus stuff?
Are you still alive
or did something wipe you out?
I would like to know your name.
Mine is Pat.
I played soccer in spite of you
and I was good.

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