50 Years Ago

When spiders are given lysergic acid they construct webs of more than usual regularity; they become, like man in a similar situation, withdrawn from external stimuli so that their perceptive awareness is reduced, and they cease to adjust their webs to the irregularities of the surroundings. This example is used … to illustrate the importance of perception in ritualized behaviour. Psychedelic substances, as well as schizophrenia, distort perception to the extent that contact with external objects is prevented. Ritualization can be described broadly as the adaptive formalization of behaviour through the influence of natural selection. It seems to have occurred in animals as a means of improving signalling to other individuals; to serve as a more efficient stimulator of more efficient patterns of action in others; to reduce intra-specific damage, and to serve as sexual or social bonding mechanisms … During the evolution of vertebrates, ritualization has tended more towards the maintenance of efficient bonding and ceremonies have become more elaborate … Particularly in the primates, ritualized behaviour resembles to some extent that of humans.

From *Nature* 21 January 1967

100 Years Ago

In the thirtieth annual report of the Bureau of American Ethnology, Mr. M. C. Stevenson publishes an elaborate article on the ethnobotany of the Zuni Indians. This tribe had discovered the medicinal value of a large number of plants, one of the most important of which is the Jamestown weed (*Datura meteloides*), and the writer observes that from the symptoms caused by this drug, its homoeopathic adaptability to hydrophobia will be at once evident.

From *Nature* 18 January 1917

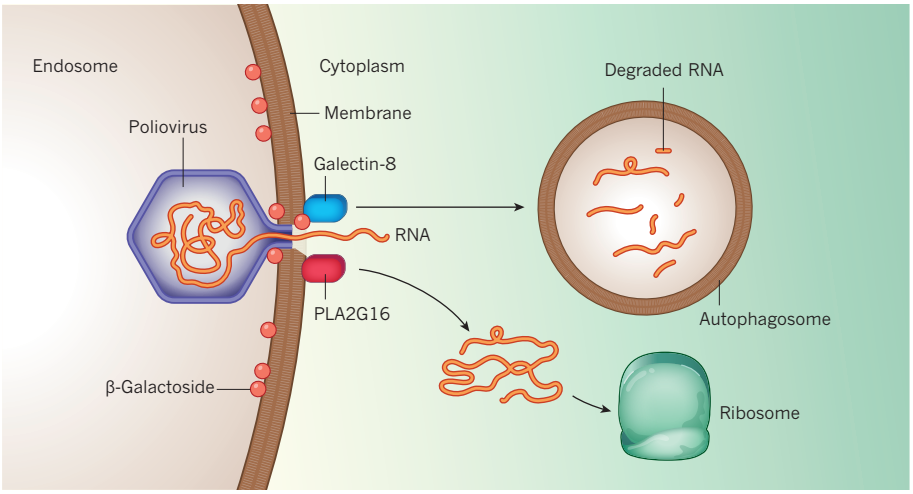

Figure 1 | Competition determines picornaviral entry. Picornavirusus such as poliovirus enter host cells inside membrane-bounded vesicles called endosomes. They then puncture the endosome membrane to release their RNA-based genomes into the cell cytoplasm. Staring *et al.*[1] report that the protein galectin-8 detects membrane rupture by binding β-galactoside ligands located on the lumenal (interior) side of the endosome membrane. These ligands become exposed to the cytoplasm following rupture. Galectin-8 restricts infection, probably by initiating a process called autophagy, in which the viral RNA is engulfed in vesicles called autophagosomes and destroyed. The authors find that the protein PLA2G16 counters this process, and suggest that it does so by moving to sites of membrane rupture and facilitating safe passage of the RNA away from galectin-8, enabling it to be translated into protein by a host structure called the ribosome.

of the *ATG16L1* gene restored the ability of poliovirus to infect *PLA2G16*-deficient cells in the authors' counter screen, but details of its precise role await further study.

This newly recognized facet of viral entry helps to explain why the particle-to-infectivity ratio of picornaviruses is so high[2] — 200 or more to 1. The viral RNA runs a gauntlet from its point of entry at the pore to the ribosome, and from there into the sheltering membranes of replication factories. It was already known that this route was laced with ribonuclease enzymes that degrade RNA, and the current study identifies autophagy as another obstacle. Only a small proportion of viral genomes are likely to successfully make the trip.

Little is known about this RNA trafficking and, although Staring and colleagues' work indicates a role for PLA2G16, the protein's exact contribution remains unclear. The authors demonstrated that the enzymatic activity of PLA2G16 is essential for viral entry, whereas its hydrophobic membrane-anchor domain is required for the formation of poliovirus-induced PLA2G16 puncta. But exactly how PLA2G16 recognizes picornavirus-induced membrane rupture, and whether this reflects a normal, previously unrecognized physiological function of PLA2G16, remain unknown.

How did picornaviruses come to depend on PLA2G16? Curiously, a few picornaviruses express proteins related to PLA2G16 (ref. 11) — perhaps they, too, facilitate viral entry. But if so, it is unclear how, given that entry must occur before the viral protein is synthesized by the host's ribosomes. How could expressing its own PLA2G16-like protein help a picornavirus? Questions such as these will keep picornavirologists busy for some time.

Finally, clinical considerations arise from these new findings. Effective antiviral therapies have been difficult to develop for this large virus family, in no small part because of their structural and genetic diversity. Staring *et al.* show that PLA2G16 facilitates the entry of several genetically distinct picornaviruses, suggesting that this is a broad target for host-directed antiviral development. ■

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