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> ONE MONTH, ONE PROTEIN <

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twisting fate

Vivienne Baillie Gerritsen

Life strives on reproduction. Over time, it has found very imaginative ways to proliferate in multitudinous forms – from protozoa wriggling in the bottom of pools to big cats racing across the African plains and birds flying swiftly through the air. All forms of life – or certainly the great majority – require help of some sort to reproduce: mammals need a partner, plants rely on insects for pollination and many amphibians are dependent on favourable conditions for spawning. There are life forms, too, that not only count on others to multiply but also damage them in the process, frequently to the extent of killing them. This is the realm of infection. Though their ultimate aim is not to kill their hosts, pathogens such as viruses, bacteria or fungi invade other organisms to take advantage of their resources – in so doing, if left unchecked, they can destroy their hosts. In this way, the AIDS virus diminishes our immune cells, the poliovirus attacks our motor neurons and a variety of fungi infect plant cells, ultimately wiping out complete crops. One such fungus is *Phytophthora infestans* that invades potato plants in particular. Scientists are slowly unveiling how *P.infestans* uses potato cells to develop, and which molecules are involved. Notably: a protein known as PexRD54.

©Jo Bradney, *Spudnik, charcoal on paper*

courtesy of the artist

Potatoes. These rounded vegetables – of which there are approximately a thousand varieties today – have become part of Europe's culinary culture within the last 150 years. Though it is difficult to imagine Europe without its stews, baked potatoes and fries, potatoes did not grow on the old continent before the 16th century. Potato plants come from South America, where the Peruvians and Bolivians domesticated them between 8000 and 5000 BC. The first potato arrived in Europe on a ship just back from the Spanish conquest of the Inca Empire. It took a further two centuries before European farmers actually began to grow it on an industrial level, and their families to add it to their dishes. A few countries – in particular Western Ireland and parts of the Scottish Highlands – eventually became economically dependent on potato crops besides them being the staple diet of farmers and their families. This turn of events became a tragedy in Ireland when, over the course of several consecutive years, whole crops were killed by the fungus *Phytophthora infestans,* a disease now known as late or potato blight. The poor began to starve and, weakened, became ill and died. Between 1845 and 1849, about one million Irish farmers and their families died, and as many fled the country sometimes perishing in wild seas as they emigrated.

Like potatoes, *P.infestans* also travelled by ship from the Americas to Europe. Potato blight had already hit North America in the early 1840s. Ireland was particularly unfortunate in that the fungus loves cold and humid weather – conditions these parts of Europe are particularly accustomed to. What is more, the Irish potato crops lacked variety, making them even more susceptible to infection. Had the genetic diversity been greater, less crops would have been lost. Farmers, also, would have lost less besides the fact that they had to endure questionable decisions taken by those governing Ireland at the time. Interestingly, after the Great Irish Famine, Charles Darwin exchanged letters with James Torbitt, an Irish merchant seeking to produce plants that would be resistant to *P.infestans* by selecting those that had survived – a procedure based on Darwin's then recent theory of natural selection.

P.infestans is a filamentous fungus. It infects potato cells by penetrating the cell wall with its haustorium – a long narrow protrusion, like a long slender finger pushing through crust to reach the pie. Once inside, *P.infestans* releases myriads of effector proteins whose role is, literally, to hijack major pathways in the plant cell for the fungus' own benefit. One of these pathways is the potato's autophagy pathway – in particular: selective autophagy. Autophagy and selective autophagy: what is the difference? Under stress – such as starvation or drought for example – certain cells can decide to degrade parts of themselves and redistribute the resulting catabolites to where they are most needed. This is called autophagy. Some cells use a similar process to degrade parts inside them that are foreign, i.e. that are the result of infection for instance. Thus, selective autophagy acts like an immune system, a means of defence.

PexRD54, secreted into plant cells by *P.infestans*, takes over the selective autophagy pathway, subsequently twisting it to its own advantage. Although metabolic pathways are the result of networks of interconnecting proteins or protein complexes, one protein is bound to light up like a beacon because it has a decisive role in the matter. In *P.infestans*, one such protein is PexRD54. Following infection, PexRD54 binds to ATG8CL in the plant cell. In doing this, PexRD54 steals the place of Joka2, a potato protein, whose role is to cargo molecules. When Joka2 binds to ATG8CL, binding triggers off the formation of autophagosomes – vacuoles that degrade selected metabolites. If PexRD54 gets there first, the plant loses its means of defence. The fungus can then proceed to infect and multiply in its host, while taking advantage of the plant's nutrients. If infection goes unchecked, the plant will eventually wither and die.

PexRD54 and Joka2 both bind to ATG8CL. This implies that they share a domain capable of recognising ATG8CL. Indeed they do, and the domain is called AIM for ATG8CL-interacting motif. In short, PexRD54 is an elongated protein with sixteen helices along its sequence. Fifteen of these pack into five distinct bundles of three helices each, thus forming a stable core. A flexible C-terminal domain punctuates the lot with a pentapeptide at its very tip: the AIM. AIM recognises ATG8CL in an extended conformation forming a beta-sheet parallel to a beta-sheet in ATG8CL. Once bound, autophagosomes form but instead of digesting parts of *P.infestans*, they help it grow. Like Joka2, PexRD54 may also act as a cargo receptor but for the sake of *P.infestans* and not potatoes.

Infection is always a case of one organism taking advantage of another, usually by diverting the host's nutrients and replicative machinery to its own advantage – from a biological point of view, the imagination that Nature has put into the infective process is staggering. Potato blight continues to be a threat, and still causes the loss of crops that could feed hundreds of millions of people around the world. The damage that a fungus such as *P.infestans* is able to cause is so great that in the 1940s and the 1950s, several countries – namely France, Canada, the USA and the Soviet Union – considered using it as a biological weapon before they the program was finally suspended. Understanding exactly how *P.infestans* infects potato plants and what is involved exactly where the fungus meets the host cell will give scientists the means to develop methods that should help to save crops and supply food to human beings.

Cross-references to UniProt

RxLR effector protein 54, *Phytophthora infestans* (Potato late blight fungus) : D0NBE6

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