proteinspotlight
> ONE MONTH, ONE PROTEIN <

Issue 90, January 2008

www.proteinspotlight.org

I'll have you for supper

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When there is nothing left to eat, we do not eat our parents or our children. We go down to the closest supermarket for food. Supermarkets, however, are not an option for bacteria. When they are short of nutrients, they are faced with a number of fates amongst which are sporulation, starvation or, for some, cannibalism. Indeed, *Bacillus subtilis* – a sporulating bacterium – has devised a way to feed on its sister cells in order to prolong its non-spore life. It does this by way of toxins which it produces itself and from which it must be protected to avoid committing suicide inadvertently… Needless to say, the molecular pathway is intricate and still obscure. However, hosts of proteins are being discovered, two of which are known as SkfA and SpdC whose actions result in *B.subtilis* sister cell lysis, from which the non-lysed cells will feed.

Why make a meal out of your kin when you have the option of surviving – albeit in a slow-motion form – as a spore? Sporulation occurs when the environment does not provide sufficient nutrients for micro-organisms such as *Bacillus subtilis*, for example, to survive. Though the aim of sporulation is to prevent cell death by enclosing it in a micro-environment in which the minimum is provided for a creature living at a minimum pace, the process is extremely energy-consuming. Sporulation calls on the activity of over five hundred genes, involved in complex molecular pathways. Once the first steps have been completed, the morphogenesis of sporulation is irreversible. When the environment becomes plentiful again, unraveling the doings of sporulation is just as energy-consuming before *B.subtilis* can settle down and feed. So if sporulation can be sidestepped, it is.

One way of doing it is to make sure *B.subtilis* has enough to live on. If it doesn't, the next step is to delay sporulation as long as possible, just in case the conditions get better. Indeed, a non-sporulated bacterium will profit from bountiful surroundings much faster than a sporulated one. As a consequence, non-sporulated *B.subtilis* are far more favoured. In stark conditions, one gruesome way of putting off sporulation is by eating those closest to you. Though unicellular, *B.subtilis* is relatively sociable and frequently evolves in small colonies. When conditions become life-threatening, a number of the cells in the colony are thrust into the process of sporulation while the fate of the others – over two thirds of the whole colony! – is to be lysed and digested.

Two proteins directly involved in this peculiar homicide are the sporulation killing factor, SkfA, and the sporulation delaying protein, SpdC. Cells which are not directed towards sporulation and whose fate is to become bait, produce neither SkfA nor SpdC. Both toxins are produced when *B.subtilis* enters the first steps of sporulation – steps which are not yet irreversible. Very little is known about the two proteins and their mode of action, besides the fact that without them, there would be no cell lysis, and hence no food supply.

Both proteins are toxic and secreted into the environment. SkfA is secreted by way of a

pump which also only appears in sporulating cells. Being specifically pumped out of a cell may be one way of shunning suicide. Indeed, if SkfA can kill off identical cells, it can also kill the one which made it. It's like turning your own weapon onto yourself. SpdC is also secreted. It is still unknown how but more importantly its existence seems to stimulate the production of an immunity protein known as SpdI which protects the sporulating cell from doing itself any damage.

How SkfA and SpdC lyse the sister cells remains a mystery. It may be that they are merely intermediate and that it is another molecule that is actually responsible for lysis. Perhaps they disrupt the cell membrane some way or another, either by lodging themselves inside it and causing molecular chaos. SpdC acts as a ligand and the attacked cell may have an SpdC receptor on its membrane. SpdI – which is only stimulated in sporulating cells – may act as an immunity molecule, either by binding directly to SpdC in the sporulating cell so that it doesn't get the chance to bind to its receptor, or by binding to the SpdC receptor so that there's no room for SpdC. Either way, the sporulating cell is saved from self-attack.

There are many unknowns in this peculiar bacterial cannibalism. Since *B.subtilis* assembles in colonies, the process can be seen as a form of programmed cell death where – in close proximity – a number of cells are sentenced to death in order to save others. It is also a singular case of chemical warfare – a very well documented event amongst distinct bacterial populations. In fact, SpdC and SkfA may enjoy a far broader toxicity than their own species. Especially if they can disrupt a cell just by squeezing into its membrane. Evidently, more time is needed to unravel the mystery of *B.subtilis* vs *B.subtilis*. And why see it as a way of avoiding sporulation? Perhaps feeding on sister cells is less to delay the process than simply to make sure that sporulation is completed – since it takes up so much energy. You wouldn't want to find yourself half-sporulated with no nourishment to finish off the job… In which case, is it not more a case of altruistic martyrdom than cannibalism?

Cross-references to Swiss-Prot

Sporulation killing factor skfA, *Bacillus subtilis* : O31422
Killing factor sdpC, *Bacillus subtilis* : O34344
Immunity protein sdpI, *Bacillus subtilis* : O32241

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Protein Spotlight (ISSN 1424-4721), http://www.proteinspotlight.org, is published by the Swiss-Prot group at the Swiss Institute of Bioinformatics (SIB).