proteinspotlight
> ONE MONTH, ONE PROTEIN <

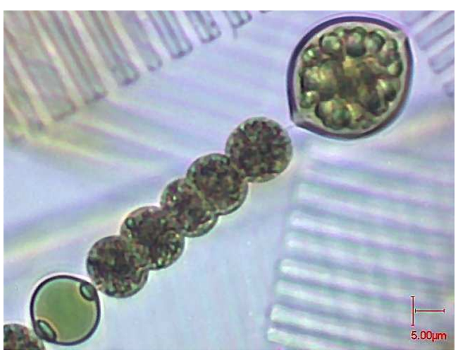
Issue 23, June 2002
www.proteinspotlight.org

Heterocyst or not heterocyst?

Vivienne Baillie Gerritsen

What is it in a cell that drives it to become one type of cell rather than another? Conversely, what is it in a cell that summons it not to budge? It is the fascinating world of cell fate, one of the most intriguing questions developmental biologists have pondered on for centuries. The blue-green cyanobacteria *Anabaena* is a perfect illustration of one developmental model: cell differentiation occurs thanks to the diffusion of molecules, which creates a cell gradient. Hence, cell differentiation becomes an issue of 'more or less'. One illustration resides in a very small peptide - barely 17 amino acids long - known as patS. A difference in concentration of patS is not only the sign that an *Anabaena* cell is about to undergo a major change but that neighbouring cells will too.

Anabaena are filamentous cyanobacteria, meaning that they grow in colonies. Cyanobacteria have been around since the first bubbles of life and have always lived in the most diverse and extreme ecological habitats. Without them we would most probably not be here. Indeed, they are the ones who spat oxygen into the atmosphere over 3 billion years ago and paved the way for those whose breathing depends on it.



Anabaena

Anabaena has only two types of cells which make it a simple 'organism' to study: vegetative cells and larger cells termed heterocysts. What is the difference? The vegetative cells carry out photosynthesis and that is why cyanobacteria were called blue-green algae in the first place. Heterocysts fix atmospheric nitrogen, something the vegetative cells cannot do. When there is an insufficient supply of fixed nitrogen (NH4 and NO3), heterocysts can actually produce some and distribute it to the neighbouring vegetative cells which, in turn, offer oxygen products. And since oxygen is fatal to nitrogenase, heterocysts are surrounded by a thick protective cell wall which makes them easy to distinguish from their vegetative counterparts.

Anabaena starts off as a filament of vegetative cells. When there is not enough fixed nitrogen to go around, one of the vegetative cells becomes a heterocyst. Heterocyst differentiation takes approximately 24 hours. But they are dead end cells: unlike their vegetative counterparts they can no longer multiply. However, the vegetative cells surrounding them continue to do so. As a result, the supply of fixed nitrogen is soon depleted and another heterocyst appears. And so on. The outcome is a string of vegetative cells interrupted by heterocysts at regular intervals – the appearance, the maintenance and the regularity of which are orchestrated by patS.

When fixed nitrogen becomes scarce, patS is expressed in every cell where it increases gradually, save in one where its abundance is far greater. This particular vegetative cell is destined to become a heterocyst. But the other vegetative cells would too were it not for patS which seeps from the pre-heterocyst, via the periplasm, into the contiguous periplasms of the neighbouring vegetative cells, where it switches off the cell's power to differentiate. So the role of patS is not so much cell differentiation but in fact inhibition of cell differentiation. PatS –

being only 17 amino acids long – is already small, yet it has been demonstrated that only five consecutive amino acids are necessary to inhibit differentiation.

On the molecular level, no one knows how patS works. An increase in the expression of patS triggers off a response. As its concentration diminishes – and hence its power to inhibit – differentiation can again occur within a vegetative cell, about 10 cells downstream or upstream from the heterocyst. So, patS not only inhibits heterocyst differentiation but maintains it and establishes heterocyst spacing. This is important since heterocyst formation is a costly business; not only is it energy-consuming but it also spells no more reproduction. And no living species can afford to do this too frequently.

To say that patS inhibits heterocyst differentiation on its own would be telling a fib; the nitrogen products supplied by the heterocysts themselves also have a direct role. Once formed, they are distributed to the neighbouring cells, where they also create a fixed-nitrogen gradient. As this gradient – together with the patS gradient – diminishes on either side of the heterocyst, a new heterocyst forms. And the cycle continues.

One interesting question, which remains unanswered to date, is the pre-heterocyst's acquired immunity to patS. Something within the differentiating cell must make it immune to patS while all the other identical vegetative cells are sensitive to it, so that heterocyst differentiation is hindered. To sum things up, we have a pentapeptide which has a direct role in a cell's fate, raises the question of acquired immunity, and offers the spatial separation of two biochemical processes – photosynthesis and nitrogen fixation – which are usually incompatible in one same organism!

To date, patS and its role in cell fate has not been grabbed by any chemical industry. *Anabaena* itself has not really met with much enthusiasm either – unlike its cousin, *Spirulina*, which is added to trendy diets. *Anabaena* is more likely to give you swimmer's itch or even kill you. Recently however, there has been a call for investors for the Lake Erie-based (USA) *Anabaena*, and an Initial Public Offering has already been made. *Anabaena* was described as a worthy investment since it supplies a great portion of the earth's oxygen and with the rate of population growth, humans will be needing more and more of it…. *Anabaena*'s official advertising slogan read '*Anabaena* – We didn't make the atmosphere, we just made it breathable.'

Cross-references to Swiss-Prot

Heterocyst inhibition signaling peptide, *Anabaena sp.* : O52748

References

1. Yoon H.-S., Golden J.W.
   PatS and products of nitrogen fixation control heterocyst pattern
   J. Bacteriol. 183:2605-2613(2001).
   PMID: 11274121

2. Yoon H.-S., Golden J.W.
   Heterocyst pattern formation controlled by a diffusible peptide
   Science 282:935-938(1998).
   PMID: 9794762