Decloaking the germ

The bacterium *Listeria* infects humans through contaminated food. Once in the gut, this pathogen can be life-threatening if contracted during pregnancy or by newborns and those with weakened immune systems. But for most people, an encounter with *Listeria* causes nothing more than vomiting and diarrhoea because our immune system recognises the long, propeller-like projections on the bacterial surface – called flagella – and mounts an assault on *Listeria* until it is wiped out. *Listeria*, however, has evolved a way to dodge this fate.

To anyone who has ever tried to cross enemy lines, this bacterium has an enviable ruse. After detecting the warmth of the human body, *Listeria* shuts down the production of flagella – the equivalent of enveloping itself in an invisible cloak. It does this by activating a protein called motility gene repressor, or MogR for short, which binds to DNA close to the flagella gene and suppresses it.

While thinking about how to rid humans of this irksome and sometimes serious threat, researchers Aimee Shen and Darren Higgins at Harvard Medical School in Boston, USA had the idea of stopping MogR from doing its job. This strategy would allow them to de-cloak the bacteria, leaving it exposed to the wrath of the immune system. But to do this, they needed to understand how MogR recognises its binding site.

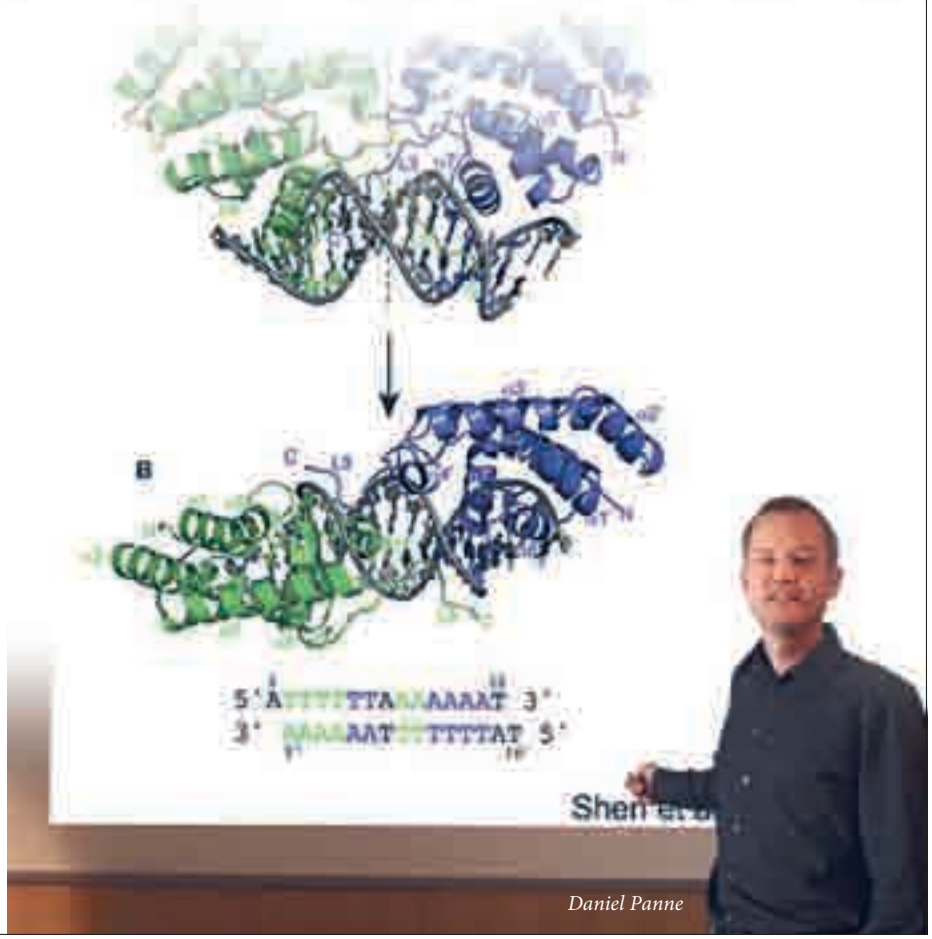
The scientists knew that the MogR protein regulates about 25 genes in the bacteria's genome. These binding sites are very rich in As and Ts, two of the four nucleotide 'letters' that make up the DNA alphabet, and are palindromic – that is, they read the same forwards as they do backwards. Knowing this, the researchers looked for where this particular motif occurred in the bacteria's DNA; to their dismay, they found more than 500 matches. This suggested that the DNA sequence of this regulatory motif was not sufficient to explain MogR's binding pattern. To understand how MogR selects for specific binding sites, the researchers turned to structural biologist Daniel Panne at EMBL Grenoble.

Daniel's lab was able to determine the crystal structure of the MogR protein bound to its DNA-docking site. From this, he saw that MogR recognises both the DNA's sequence and also its overall warped shape, which is created by the particular chemical properties of the AT-rich region that cause the DNA to bend to a 52-degree angle. This provided the first example of DNA shape-dependent recognition.

But this was not the whole picture: Daniel also noticed that MogR binding relied on specific electrostatic forces – similar to the static forces experienced by clothes just out of the dryer – that are generated by the different charges of the chemical bases that make up the docking site. Importantly, only the 25 MogR-regulated genes boast docking sites that rely on DNA sequence, shape and electrostatic forces for binding.

Scientists have since found more examples of proteins that use similar modes of DNA recognition to MogR. Daniel explains that these findings not only provide insight into a new mode of DNA recognition that is seemingly more common than suspected, but could also help bacteriologists develop a drug that offers protection against *Listeria* infection by disrupting MogR binding and thus stopping the bacterium from donning its invisibility cloak.

Shen A, Higgins D, Panne D (2009) Recognition of AT-Rich DNA Binding Sites by the MogR Repressor. *Structure* **17**: 769–777



Daniel Panne