Viral treatment for MRSA

Scott Ewan, BMN News

Treating bacterial infection with viruses might not be an obvious first line therapy. But Novolytics (http://www.novolytics.co.uk/) – a spin-off company from Warwick University, UK (http://www.warwick.co.uk) – is intending to do just that.

The potential of phages

The Warwick team intend to employ so-called bacteriophages, a type of virus that specifically targets and kills bacteria. The concept is not new – the potential of phages to treat infections has been recognized for over 80 years. Indeed, the Russians ran programs in the 1920s, successfully treating infections with phages. Phage therapy is still routinely used in the former USSR republic of Georgia.

Novolytics plans to target infections caused by MRSA – methicillin-resistant *Staphylococcus aureus* – a mutated bacterial strain that has developed resistance to most commonly used antibiotics. MRSA is responsible for an increasing number of deaths, particularly in already-compromized hospital patients.

Phages infect bacteria that have themselves infected host cells. They then use the host's cellular machinery to replicate up to 10,000 progeny. The host cell is then killed to release the viral progeny.

Phage therapy is primarily being studied with the aim of circumventing the problem of antibiotic resistance. Resistance can also develop to phages, but this is not such a problem. Bacteriophages bind to lipopolysaccharides on the surface of bacteria, and those bacteria can alter their polysaccharide make-up to become resistant. By coincidence, this alteration, although conferring resistance, also reduces MRSA pathogenicity. But it is unlikely this would occur in practice, say researchers, as double or multiple phage therapies would probably be used to optimize efficacy, and prevent the development of resistance.

Phages versus antibiotics

Efficiency is another advantage of phage therapy. With an antibiotic, large quantities of antibiotic end up circulating through the body, and only some of that reaches the site of infection. With a phage, if only one viral particle gets to the site of infection it can replicate and multiply at that site to fight the infection. Additionally, phages are far more discriminating than antibiotics, so the natural microbial flora of patients' guts should remain unaffected.

'In the short term, Novolytics plan to look at developing phage-containing wound dressings to stop MRSA infections,' says Chief Scientific Officer and Director Nicholas Mann. Long term, the company expects that the development of injectible preparations (to treat septicaemia, for example) could follow.

Geoffrey Hanlon at Brighton University, UK (http://www.brighton.ac.uk) agrees that the topical application of phage therapies is a 'very feasible prospect,' but remains unsure of the feasibility of parenteral treatments. 'There is the possibility of the phage being mopped up by the immune system or causing an allergic response,' he warned.

From an intellectual property perspective, says Mann, there is little scope for patents in this field. But Novolytics claims to have taken a creative route to sidestepping the problem. Normally a 'lytic' phage (phage that kills bacteria and the host cell) would be used for therapy, but these tend not be as successful at infecting MRSA as lysogenic or temperate phages (which do not kill the host cell). What Novolytics has done is select a mutated temperate phage into a lytic phage to infect MRSA.

Reduced colonization

Volunteer studies have proved successful in reducing nasal *S. aureus* colonization by over 75% in a single application. 'This is feasible,' said Charles Hart, Professor of Medical Microbiology at Liverpool University (http://www.liv.ac.uk), 'but depends on a number of variables. There are many strains of MRSA and frequent changes occur within them, he says. 'What is really needed is to prove the concept in clinical trials,' said Hart.