based clinical trial conducted by an academic institution in the USA. The group will start a second trial this year.

However, more work is required on AAV vectors and the next step for Stilwell is to detect the cellular signature that result from infection with other serotypes of AAV and to test the AAV vector in other cell types. She also plans to reproduce her research *in vivo*.

Reference

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Moving forward with reverse vaccinology

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Reverse vaccinology is a valuable starting point when searching for novel vaccine candidates, says Rino Rappuoli, vice president and chief scientific officer at biotech leaders Chiron Corporation in Sienna, Italy (http://www.chiron.com/).

Using classical vaccinology, pathogens are grown *in vitro* and these, or components of these, are then used to develop vaccines. It is an approach that has led to the development of many important vaccines. But it cannot deal with pathogens that do not grow *in vitro*. Reverse vaccinology takes advantage of the growing number of genome sequences available for many microorganisms. These can be analysed to identify genes encoding various protein antigens on the surface of pathogens, which can then be used as targets for recombinant vaccine development.

Genome-based vaccine discovery

The genome-based vaccine discovery approach was first applied to meningococcus B, a bacterium that is a major cause of sepsis and meningitis and cannot be grown *in vitro*. Computer analysis of the meningococcus-B genome predicted over 600 potential vaccine candidates of which 350 were expressed in *Escherichia coli*, purified and used to immunize mice. Of these, 29 were found to induce bactericidal antibodies, thereby leading to protective immunity.

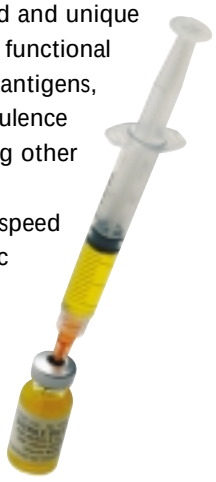
Similarly, reverse vaccinology enabled the development of vaccines against Hepatitis B and C viruses, which also cannot be tackled by conventional vaccinology. A recombinant vaccine against hepatitis B is now routinely used for universal immunization of children and a vaccine against hepatitis C is currently in clinical trials.

Proteins and polysaccaharides

Although reverse vaccinology is now becoming a standard technology, it does not provide a universal solution for vaccine development, says Rappuoli. 'Reverse vaccinology does not allow the discovery of vaccines which are not protein based,' he said, 'For instance, many infant vaccines are based on polysaccharides, which are conjugated to carrier proteins.'

The situation is different for protein antigens, says Rappuoli. 'Reverse vaccinology is a great tool in the early phase of vaccine development,' he told delegates at the 11th International Congress on Infectious Diseases (ICID) in Cancun, Mexico (http://www.isid.org/11th_icid/).

Biocomputing can be used to analyze the genome of a single pathogen, but it can also be used to compare multiple genomes to shed light onto conserved and unique families of proteins, functional domains of protein antigens, and evolution of virulence mechanisms. Among other advantages of this technology are the speed with which genomic sequences can be compared at a reasonable cost, in comparison with traditional strategies.



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