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Oxford Vacmedix Ltd.: harnessing the power of immunotherapy to treat and monitor cancer

A new platform built around recombinant overlapping peptides (ROPs) promises quicker and cheaper production of more effective therapeutic vaccines and diagnostics for cancer and viral infections.

Immunotherapy is a fast-growing approach for cancer treatment and the prevention of infections based on manipulation and direction of the patient's immune system. It is a targeted therapy that is less toxic than chemotherapy and is usually suitable for combination with other treatments.

Vaccination against a cancer or pathogen can be achieved through injection of a preparation containing antigens that direct and stimulate T cells to attack anything bearing those antigen markers. However, there are two immune responses: one that produces antibodies and helper T cells, and another that produces killer T cells. For cancer, the killer T cell approach has been found to be much more effective. Unfortunately, many cancer vaccines are based on full-sized proteins produced by a tumor, which tend to generate antibodies and helper T cells rather than killer T cells.

Enter Oxford Vacmedix and its ROPs. Back in 2000, while at Harvard University, the company's founder and CSO Shisong Jiang proposed that breaking a whole target protein into short but overlapping linear fragments would be much more effective for cellular immunity.

Although this approach is very effective, it requires the production of many different peptides. So in 2004, Jiang (then at Oxford University) and his team worked out a way to grow all the overlapping peptides together in bacteria, and in 2012 they spun out Oxford Vacmedix to exploit the technology.

The fragments, with an enzyme cleavage site between them, are linked into a single molecule encoded by a single gene for expression as a single protein. Once expressed, the protein can easily be split into the individual ROPs by enzyme cleavage (*in vitro* or inside cells), which makes it easy to both deliver and manufacture.

The peptides can be produced synthetically but this can be slow and expensive. ROP production takes only 2–3 days at a time—a great improvement on synthetic production. "Vaccine can be designed and scaled up much more quickly, it is also more suitable than the pooled peptides strategy for applying for FDA [US Food and Drug Administration] registration," said Jiang. "I have calculated that manufacturing overlapping peptides using a natural expression system is a thousand times cheaper and has the potential to significantly reduce the cost of vaccine development."

Oxford Vacmedix is currently developing two therapeutic vaccines. OVM-100 is a first-in-class human papillomavirus (HPV) vaccine aimed at cervical cancer, with an estimated market size of over £1 billion. OVM-200 is a first-in-class cancer vaccine that targets survivin, a protein that is expressed at high levels in many solid tumors, such as breast, lung, ovarian and colorectal, as well as blood cancers—a huge potential market. Data so far are compelling, with vaccinated mice showing greatly extended survival in tumor model systems. OVM is developing a large-scale good manufacturing practice (GMP)-compatible production process in China prior to transferring production to a contract manufacturing organization (CMO) in Europe.

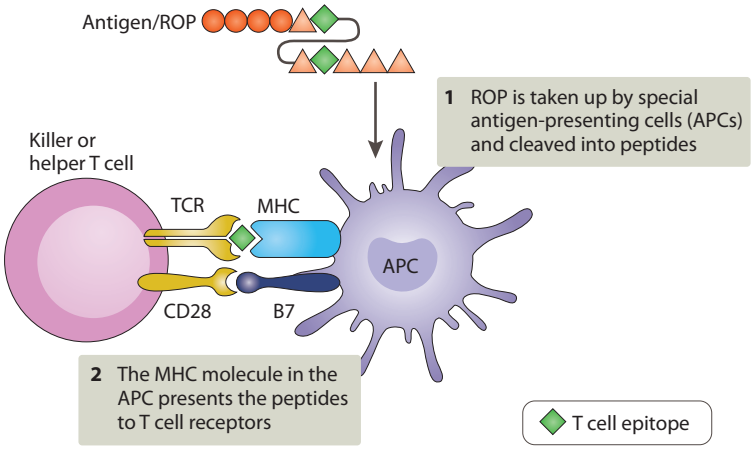

Figure 1: Antigen presentation of ROP. MHC, major histocompatibility complex.

Additionally, using ROPs as diagnostic reagents, Oxford Vacmedix in China is developing companion diagnostics for monitoring its therapeutic vaccines, and a test to identify chronic/latent infection in tuberculosis (TB). In the Elispot test (a widely used way of monitoring cellular immune responses), ROPs are added to a blood sample; if the subject already has strong immunity, the T cells respond vigorously by producing a cytokine that can be readily assayed. Tests of the TB prototype on more than 200 people have shown that it is comparable to gold-standard reagents and is early proof of the platform. "T cell immunity is instrumental in containing infections and tumors but, apart from TB, which is expensive, there are currently few diagnostic kits commercially available," said William Finch, CEO of OVM. "This is a great medical need and we believe diagnostics for T cell immunity have a vast market.

Partnering outlook

Oxford Vacmedix is looking for a large pharmaceutical firm to codevelop its ROP technology, a suitable CMO for GMP-level production for its preclinical/phase 1 vaccine trials in Europe, and firms that can sequence tumor mutations against which it can design personalized vaccines (neoantigens). The company is also interested in collaborating with organizations that can provide checkpoint inhibitors suitable for combination with ROP vaccines.

"We are the first company to not only prove that overlapping peptides stimulate both helper and killer T cells, but also propose using them as vaccines to stimulate T cell immunity," said Jiang. "Our high-performing ROP vaccines are easier and cheaper to design, scale up and quality-control than existing approaches—the potential impact on health care is enormous."

Oxford Vacmedix is also looking to combine ROPs with other treatments, e.g. checkpoint inhibitors. As Jiang explained, "If you liken immunotherapy to a car, ROPs would be the steering wheel and checkpoint inhibitors like releasing the brake—the combination enables you to go very fast in the right direction."

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