

## Cell screening

# Antibody discovery offers RSV hope

The lives of thousands of children and the elderly could one day be saved thanks to the discovery of a rare human antibody which targets a common virus that can be far more deadly than seasonal flu. The respiratory syncytial virus (RSV), which is frequently misdiagnosed as flu, is estimated to cause 1m hospitalisations annually – ten times as many as seasonal flu – and is the leading cause of pneumonia among young children. So far, there is no known treatment.

In as yet unpublished work, however, scientists at California, US-based Trellis Bioscience have found that their newly discovered antibody not only protects against the onset of illness but also kills the virus in rats and mice infected with RSV. Levels of the virus were almost completely cleared in mice and reduced by four orders of magnitude in rats after they were given the antibody treatment three days following RSV infection.

In addition, the antibody was also seen to be more potent than the commercial RSV preventive

*Synagis* in preventing the infection in rats and mice, according to Trellis' chief scientific officer Bruce Keyt. *Synagis* is currently the only commercial drug for preventing RSV infection and is given mainly to premature babies at monthly intervals throughout the RSV season. However, the drug has only a 50% success rate in reducing the incidence of severe disease while a typical treatment course costs \$5000/season, according to Keyt.

The Trellis antibody targets a different region of the RSV coat called the G protein, which is responsible for the ability of the virus to evade the immune system, Keyt explains. It also has the advantage of being fully human – derived from adults previously infected with the virus – which should make it extremely safe for use in therapy, he says.

Trellis' researchers discovered the antibody by using the firm's proprietary *CellSpot* technology, which allowed them to screen simultaneously as many as ten different parameters, such as



Microworks

**At risk: premature babies are vulnerable to RSV**

specificity, affinity and cross-reactivity, with other antigens. Using *CellSpot*, the researchers screened 20m cells from 30 donors to identify the best antibodies present at only a few cells per million, which are very difficult to detect and recover by conventional

screening techniques.

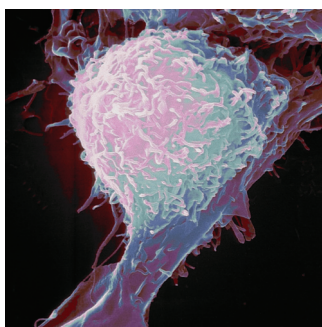
The company hopes to start clinical studies of the antibody in people in the next 12-15 months. If this and future trials are successful, Keyt expects the antibody treatment could be on the marketplace in the next five or six years.

## Biotechnology

# Weed clearing to improve cancer treatment

An enzyme that degrades a bulky sugar-like substance surrounding certain solid tumours could hold the key to new and improved therapies for cancer. The enzyme hyaluronidase targets and degrades the glycosaminoglycan molecule hyaluronan (HA) that coats subsets of solid tumour cells including prostate, breast, lung, pancreas, stomach and colon cancer cells. In as yet unpublished work in rats and mice, researchers at Halozyme Therapeutics in San Diego, US, discovered that the enzyme not only improves access to the cells by other anti-cancer agents but also directly slows tumour growth.

'Clearance of HA in the tumour cell environment results in a drop in interstitial fluid pressure that makes it easier for other anti-cancer agents to target tumour cells,' explains



**SEM: of prostatic cancer cell**

Jonathan Lim, Halozyme president and ceo.

Tests in small animal models showed that the enzyme reduces the fluid pressure by up to 80% in the first hour of administration, which is double the drop seen with other anticancer drugs, even after several days, Lim

says. 'No other therapy reduces the interstitial fluid pressure through this mechanism, which presents us with a unique therapeutic opportunity.'

The preclinical studies also demonstrated that the enzyme was useful as a combination therapy to improve the activity of the anticancer agent *Taxotere*. However, the fact that the enzyme demonstrates an anti-tumour effect even in the absence of other anticancer agents also shows that another mechanism of action as well as the pressure effect may be in play, Lim notes.

At a conference in April 2009, Halozyme researchers reported that the enzyme inhibited the growth of prostate cancer and breast tumours by up to by up to 46% and 61%, respectively, in mouse models. Used with chemotherapy or radiation, the enzyme also improved survival

rates among mice with brain tumour metastases by up to 45% relative to the control animals.

The first clinical trials, in cancer patients with refractory solid tumours, got under way earlier this year, with results expected by the middle of 2010.

The hyaluronidase enzyme used in the anticancer studies is a soluble recombinant version of a naturally occurring human enzyme, which is pegylated, or attached to a molecule of polyethylene glycol, to allow the enzyme to survive in the bloodstream. A non-pegylated version is already marketed by pharma firm Baxter as *Hylenex*, which is used to improve delivery of injected drugs through the skin. Halozyme is also in Phase II trials with another formulation of the enzyme for improved insulin delivery.