

With the onset of winter and the danger of another outbreak of **SARS**, the search for a **vaccine** is becoming more urgent. Anjana Ahuja reports.

IT IS A GREY, drizzly day in Copenhagen and, frankly, Block 208 of the Technical University of Denmark doesn't look particularly inviting. But the low-level concrete bunker on the outskirts of the city contains a team of scientists working on one of the most promising leads for a **vaccine** against severe acute respiratory syndrome (**Sars**), which sent the world into panic last winter. By September the latest date for which the World Health Organisation (WHO) has global figures, **Sars** had infected more than 8,000 people, 774 of whom had died.

As temperatures drop, worries rise. Experts say that **Sars** could resurface, triggering the same global shutdown seen last winter. Even the WHO has warned governments to brace themselves for a possible outbreak.

Meanwhile, worldwide attention has focused on finding a **vaccine**. The Danish team, led by Professor Soren Brunak and Dr Ole Lund at the university's Centre for Biological Sequence Analysis, likes to think it is ahead of the game. The scientists have examined the genome of the **Sars** virus and pinpointed certain portions that might make a good **vaccine** target. They are sceptical about rumours that Chinese researchers have developed a **vaccine** ready for human trials. They point out that it has not, to their knowledge, been published in an accessible peer-reviewed journal. They point out that the WHO has also treated the claim with caution.

Brunak and colleagues have developed a sophisticated computer program that tries to mimic the human body's early warning system when a pathogen invades. When faced with a foreign organism, such as a **Sars** virus, cells shred the organism and attach some of the shards on their outer layer. These shards, called epitopes, slot into grooves on the outside of cells. They act like red rags to the immune system, inviting the body's immune cells to investigate the invaders and, if appropriate, mount an attack. Brunak is focusing on the immune response mounted by T cells, one particular class of immune cells. He is a bioinformatics expert, which means that his speciality is number-crunching. In a collaboration with Silicon Graphics, Brunak has developed a computer program that predicts how a virus and immune system will interact.

"For each stretch of the virus, the program predicts how well it will be presented to the immune system," Brunak explains. The program, a neural network, has been "trained" using a well-known database of pathogens and their effects on the immune system. "Within 48 hours of the **Sars** genome being announced, we had predictions for which epitopes could be involved."

There are estimated to be nine 'groove' shapes in the global population (groove shape is related to ethnicity). So for a **vaccine** to work globally, it would need to string together pieces that lock into these nine grooves.

The Danish team has identified a whole host of epitopes, and has come up with 112 permutations that might make promising **vaccines**. Now they need to test human samples, to check that at least some of the epitopes picked out by the program match those seen on the cells of real patients. **Sars** survivors are especially interesting - the epitopes, or shards of virus, locked on to their cells have obviously triggered a ferocious immune response. These epitopes are therefore ideal targets for **vaccines** and explains why the Danish researchers are so eager to get hold of them.

However, their efforts are being stymied by an inability to obtain blood samples from **Sars** survivors. The samples are a crucial step in checking whether the virus shards fingered by the team match those

lingering in the blood of survivors.

Requests to researchers working in the field worldwide have been met with silence.

The matter has also been tackled by Professor Soren Buus, of the University of Copenhagen, an immunologist who has joined Brunak's hunt for a **Sars vaccine**. He has approached researchers in America, China, Taiwan, Hong Kong and Singapore, to no avail. Buus has raised the matter with the WHO, which has circulated his request. Buus, who knows of other immunologists who have faced similar difficulties, is frustrated but tolerant: "The WHO has probably done as much as it can, because it does not have the authority to command anyone to collaborate. I suppose we have to understand that the needs of scientists are different from the needs of clinicians, whose priority is to stop their patients dying."

However, Buus says, the delay in getting samples means that a technology that could potentially produce **vaccines** within weeks of a pathogen being identified is being held up.

It is frustrating, Brunak says, because "we think we are ahead in terms of what to put into the **vaccine** because we think we have the best predictive tools".

Buus is now in contact with potential collaborators in Hong Kong and Toronto who have access to patients. Their blood is crucial to proving whether this number-crunching technique can turn the marathon of **vaccine** development into a refined sprint. "The most precious commodities are the **Sars** patients," Buus says.

"They are the remnants of what happened. Those who control them have a considerable advantage over those of us who don't.

"If (the computer program) turns out to be a viable strategy in the fight against infectious disease, it has every capacity to match the speed of DNA sequencing. A Canadian group sequenced the **Sars** genome in six days. If we invested the same resources into scanning for epitopes, we could have theoretical **vaccine** candidates in a similar time."

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