

Molecular evolution of SARS coronavirus tracked

An investigation of the molecular evolution of the severe acute respiratory syndrome (SARS) coronavirus in Guangdong Province, China, provides additional insights into how the virus adapted to life in people after shifting from animals. These results, says Guo-Ping Zhao (Chinese National Human Genome Center and Chinese Academy of Sciences, Shanghai, China), "confirm that this disease is not as infective when it first enters people as it is later in its evolution".

Many genetic variants of SARS coronavirus have been described since its identification as the SARS causative agent in May 2003. The study of these variants in combination with the epidemiology of the disease, explains Zhao, can provide clues to the biological significance of these variations and may enable us to "take sufficient measures to prevent human transmission from the very beginning of any future outbreak, and then we should be able to prevent an epidemic of the scale we saw in early 2003".

In its study of 63 SARS-coronavirus sequences (including two from palm civets) from the 2003 epidemic, the consortium divided the epidemic into

three phases. In the early phase (Nov 16, 2002–Jan 31, 2003) scattered cases were reported in Guangdong Province. The middle phase (Jan 31–Feb 21) started when a patient admitted to hospital in Guangzhou infected more than 70 people. In the last phase (Feb 21 onwards), a doctor from the hospital apparently carried the virus to Hong Kong.

The researchers report that although single nucleotide variants occurred throughout the epidemic, variants that changed the amino acid sequence of coding regions arose mainly at the start of the epidemic as SARS coronavirus became adapted to life in its new host. In particular, the sequence of the spike protein, which is important in viral-host recognition and internalisation, was under strong selective pressure early in the epidemic but then stabilised (*Science*; DOI 10.1126/science.1092002).

"This informative paper provides compelling molecular evidence for animal-to-human transmission of SARS-coronavirus", says Wayne

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Guangdong Province

Marasco (Dana-Farber Cancer Institute, Boston, MA, USA), "and supports the idea that targeting the spike protein with antibody and vaccine therapies may be possible".

Marasco has recently isolated a human monoclonal antibody directed against the spike protein that can neutralise SARS-coronavirus infection in vitro (*Proc Natl Acad Sci USA*; DOI 10.1073/pnas.0307140101). "Initial results in animals are encouraging", he says, "but more experiments are needed to determine whether the antibody will be useful for SARS prophylaxis or early treatment".

Jane Bradbury

Doubts cast on Thai HIV vaccine trial

The Thai government has dismissed criticism that the world's largest HIV vaccine trial underway in Thailand is bound to fail (*Science* 2004; 303: 316). 22 leading HIV/AIDS experts have criticised the trial for its use of vaccine preparations with only modest immunogenicity, which are not likely to generate the host defences needed to protect against HIV infection.

"While we welcome constructive input, we find the underlying premise of the article flawed in that it uses data from efficacy trials of a single vaccine concept to predict the results of a prime-boost combination vaccine study", Charal Trinvuthipong (Disease Control Department, Public Health Ministry, Bangkok) told *TLID*.

The prime-boost HIV vaccine contains AIDS VAX (manufactured by VaxGen) and ALVAC (Aventis Pasteur)

which, when used alone in clinical trials, were ineffective in preventing the development of HIV infection. The researchers argued that "there are no persuasive data to suggest that the combination could induce better cellular or humoral responses than either component can alone". "We seriously question whether it is sensible now to conduct a third trial that, in our opinion, is no more likely to generate a meaningful level of protection against infection or disease", the authors pointed out.

The US\$119 million trial, which began in Sept 2003, would recruit 16 000 volunteers over the next 3 years. "We fear this study will not achieve its objectives", Michael Lederman (AIDS Clinical Trials Unit, University Hospitals of Cleveland, OH, USA) told *TLID*.

Trinvuthipong disagrees: he explained that regardless of its outcome, the trial has helped strengthened Thailand's capacity to conduct HIV vaccine research. "There is only one way to know if a combination of two candidate vaccines as a way of inducing both cellular and humoral immunity will protect against HIV infection and that is to do this trial", he noted.

According to Peggy Johnston of the US National Institutes of Health, although there were better vaccine candidates under development, it was hard to assess when they would be ready for trials in human beings. "Given the urgency of the epidemic, we don't want to sit back and wait until we have complete consensus that we have something that's perfect", she concluded.

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