Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Editorial

SARS – Unprecedented global response to a newly emerging disease

Severe acute respiratory syndrome (SARS) is a life-threatening form of pneumonia that is characterized by fever, chills, myalgia, dry cough, and progressing lung infiltrates (Nicholls et al., 2003; Peiris et al., 2003a). In a substantial number of patients, diarrhea develops in the course of infection. The disease-associated hypoxemia often requires mechanical ventilation. Both the high mortality rate associated with the disease and the ease of transmission by aerosols (and likely also the fecal-oral route) requires extreme infection-control measures to prevent further spread of the disease. Within only few weeks (February-April 2003), SARS spread from its likely origin in Guang Dong Province, China, to as much as 32 countries. Like in many other infectious diseases, the rapid spread was facilitated by the mobility of contemporary society (including air-travel) and densely populated urban areas. As of June 11, the World Health Organization (WHO) reported 8435 cases with 789 deaths. In contrast to the initial phase of the outbreak in which there was a serious danger of a worldwide pandemic, there is now cautious optimism that the outbreak may be contained. Without doubt, this is the result of heroic public health efforts to reduce transmission, particularly in the most affected countries, such as China and Singapore. However, even though the numbers of new SARS cases have dropped substantially over the past three weeks, there is no reason for complacency or negligence.

The ongoing epidemic is only the latest in a long list of emerging viral diseases, which all teach us lessons. The current epidemic, however, is unprecedented in several respects. Thus, thanks to the advances in molecular diagnostics and the joint efforts of an extraordinary network of 13 laboratories coordinated by the WHO, the identification of the causative agent of SARS, a novel coronavirus designated SARS coronavirus (SARS-CoV), was achieved within only two weeks (Drosten et al., 2003; Ksiazek et al., 2003; Peiris et al., 2003b). Again two weeks later, the genomes of two SARS-CoV isolates, Toronto-2 and Urbani, had been completely sequenced (Marra et al., 2003; Rota et al., 2003) and, to date, many other SARS-CoV sequences have been deposited with public databases. Cell culture-grown SARS-CoV was subsequently shown to cause lower respiratory tract disease in monkeys, fulfilling Koch's postulates and providing strong evidence for the novel coronavirus being the cause of SARS (Fouchier et al., 2003).

Because of the large phylogenetic distance to previously known coronaviruses, SARS-CoV cannot easily be assigned to any of the established coronavirus groups, and recombination between known coronaviruses could be excluded as a possible source of SARS-CoV. It rather seems likely that the ancestor of SARS-CoV is an animal coronavirus. Consistent with this hypothesis, Yuen and colleagues recently isolated a coronavirus from masked palm civets sold in a market in Guangdong (Enserink, 2003). Apart from a 29-nucleotide insertion converting two small ORFs in the 3′-region of the SARS-CoV genome to one continuous ORF, the civet virus was almost identical to SARS-CoV. More samples are needed to answer the question of whether or not civets are the true origin of the human virus or just got the virus from yet another species, for example by food. Interestingly, there is one human isolate, GZ01, that also carries the 29 extra nucleotides (Ruan et al., 2003). The patient from which this virus was isolated may have been an early SARS case, and it is possible that the deletion found in all other isolates is a result of adaptation of the ancestral virus to humans.

Despite considerable progress in recent years, the molecular characterization of the coronavirus life cycle is still at a relatively early stage. This is mainly due to the unparalleled size of the coronavirus RNA genome which, until recently, has made the devel-

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opment of reverse genetics systems a major challenge. Coronaviruses feature an (among RNA viruses) unparalleled complexity in the regulation of their gene expression and they encode a series of (mainly uncharacterized) enzymes not found in other virus families. It can be anticipated that our general understanding of the unique features of coronavirus replication will benefit from the numerous ongoing studies on the biology of SARS-CoV.

Only few weeks after the outbreak, the concerted global efforts have resulted in the identification of first coronavirus enzyme inhibitors (Anand et al., 2003; Xiong et al., 2003) that are hoped to be useful for the development of anti-SARS drugs. In the future, coronavirus-specific antivirals might also be used to treat common colds in humans and severe animal coronavirus infections, such as feline infectious peritonitis, a fatal disease of cats for which no safe vaccine or therapy is available. Obviously, there is also an urgent need to develop SARS-CoV vaccines, and corresponding efforts are already well underway. In this respect, it should be noted that sequence analysis of multiple SARS-CoV isolates revealed a remarkable genetic conservation of SARS-CoV since the outbreak was first documented in February, indicating that the development of vaccines is feasible (Ruan et al., 2003). However, there is also a number of potential problems that might complicate the development of vaccines, such as the lack of protective immunity in some coronavirus infections, persistent infection and antibody-mediated enhancement. It remains to be investigated to which extent these issues also apply to SARS-CoV or even contribute to the high mortality rate associated with SARS. In fact, evidence is now accumulating that, later in infection, lung damage may be caused primarily by the host immune response rather than uncontrolled viral replication (Peiris et al., 2003a). The direction of SARS research is now increasingly changing from identification and sequence analysis to other topics, such as the origin of SARS-CoV, routes of transmission, mechanisms of virulence, viral gene expression (Thiel et al., 2003), and development of vaccines and antivirals. The period of grace until the next major outbreak will hopefully provide answers to the most urgent questions, which may then allow to combat SARS successfully.

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