The SARS outbreak took the whole world by surprise in November 2002. It was the most unprecedented epidemic outbreak in recorded history and the first major new infectious disease of this century, unusual in its high morbidity and mortality rates and in strategically taking advantage of modern international travel to propagate itself around the world. What followed was a global havoc created by this disease, bringing the healthcare system of affected areas to a grinding halt, affecting healthcare providers, disrupting scheduled emergency surgeries and vital treatment to patients with serious conditions, overloading hospitals with infected cases, forcing public events to be cancelled, and schools, and borders to be closed. The economic impact on individuals and businesses was profound, downregulating tourism, education, and employment.

The epidemic was completely different from all known traditional atypical types of pneumonia because patients experienced lack of oxygen at the onset of the disease and hence required the aid of modern respiratory equipment to breathe. This syndrome was contagious enough to infect a substantial number of people widely and easily. In our days of medical advancement and high technology, which has subsequently led to increased life spans and longevity, a growing confidence had emerged in mankind that it had now achieved the ability to overcome the most complicated life-threatening situations. SARS shattered this confidence and made us realize once again that there are hundreds of dangerous and virulent microorganisms living on the other side of the border that can kill humans. What separates us from them is only the species barrier.

This is not the first time the species barrier has been crossed. The SARS outbreak was just another outbreak in South-East Asia, the breeding ground for notorious viruses. The current novel H1N1 swine-flu outbreak that emerged from Mexico, bird-flu H5N1 influenza in Hong Kong in 1996, human enterovirus 71 in Malaysia, Taiwan, and Singapore in 1977, 1998, and 2000 respectively, and the Nipah virus in Malaysia and Singapore in 1998, are all similar examples. The SARS outbreak was a short-lived near-pandemic situation that originated in the Guangdong province of south China in late 2002 and was efficiently contained by July 2003, with 8,096
known infected cases and 774 deaths (a case-fatality rate of 9.6%) infecting individuals from 37 countries worldwide (mortality by age group: below 1% for people aged 24 or younger, 6% for those aged 25–44, 15% for those aged 45–64 and more than 50% for those over 65). If SARS had not been fully contained, the world would have faced a full-blown pandemic. We must not forget that SARS has not been eradicated (e.g., smallpox). It is still present in its natural host reservoirs and carries the threat and potential to return into the human population any time.

We were able to subvert a potentially explosive spread of the new coronavirus (SARS-CoV) outbreak thanks to WHO’s global alert, getting together an emergency network of 11 leading laboratories from 9 countries to investigate this new virus. Within a short span of 1 month, these laboratories did a commendable job by tracing the viral etiology and developing a diagnostic test. Over the years, much has been learnt about this new SARS-CoV; however, our knowledge on the molecular biology of SARS-CoV, its life-cycle, infection, and pathogenesis still remain unclear. This virus is mysterious in its ways and this book looks at various molecular aspects of this virus which help us in understanding these complexities.

Prior to the SARS outbreak, human coronaviruses were only associated with mild diseases. SARS-related CoV became the first coronavirus to cause severe disease in humans. In April 2003, the complete genome sequence of the SARS-CoV was revealed. The genome contains unique 5’ and 3’ UTRs (untranslated regions) containing higher-order structures which play essential roles in viral transcription and replication, assisted by cellular proteins to perform RNA synthesis, a model elegantly reviewed by Liu and Leibowitz in this book. The SARS-CoV genome contains five major open reading frames (ORFs) that encode the replicase poly-protein, the spike (S), envelope (E), and membrane (M) glycoproteins, and the nucleocapsid protein (N). S binds species-specific host cell receptors and triggers a fusion between the viral envelope and the cell membrane. Lambert’s chapter clearly describes the basic cell biology of ACE2 and Pöhlmann’s chapter elaborates on the S-ACE2 interface. Receptor binding and the subsequent structural changes that result have been described in detail by Beniac and Booth. The S protein is the virulence factor in many different coronaviruses and the principal viral antigen that elicits neutralizing antibody on behalf of the host. To study this, Chow’s lab has undertaken whole transcriptome analysis of S transfected host cells and identified novel pathways that become altered. Replicase proteins have been extensively discussed in the chapters by Ziebuhr and Canard. Immediate early proteins, like the RNA dependent RNA polymerase (RDRP) and proteases, are responsible for preparing the infected cell for virus takeover. Dinman describes programmed -1 ribosomal frameshifting as an essential and unique feature of the virus for the translation of these proteins. The overlapping polyproteins 1a and 1ab are extensively cleaved by the internally encoded SARS-CoV proteases, Mpro, and PLpro and are extensively discussed by Chang in his chapter. The N protein forms the capsid and also plays several regulatory roles during viral pathogenesis which have been described by Surjit and myself. Cell type specific apoptosis induction of host cells by viral proteins has been elegantly described by Hermann Schätzl et al. Three chapters are dedicated to describe the current knowledge on accessory proteins by
Pekosz, Sun, and Tan. Sheahan and Baric’s chapter and Li and Xu’s chapter describe exhaustively the pathogenesis and protective immunity against SARS-CoV in humans. Cell signaling and associated lung fibrosis due to TGF-β/Smad pathways are discussed in the chapters by Mizutani and Chen, respectively. The importance and application of retroviral pseudotypes for highly pathogenic diseases like SARS, using surrogates of the live virus for neutralization assays, has been described by Nigel Temperton.

I wish to congratulate and thank all the contributing authors for the exhaustive coverage of their respective subjects and publication of this book. We hope the readers find this book a consolidated compilation of our current understanding of the molecular biology of SARS-CoV.

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