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An Integrated High-Throughput Approach to Study Proteomes of Infectious Agents: A Case Study of the Severe Acute Respiratory Syndrome Coronavirus. Saikatendu Kumar, Jeremiah Joseph, Vanitha Subramanian, Benjamin Neuman, Michael Buchmeier, Raymond Stevens, Peter Kuhn, Depts. of Cell Biology and Molecular Biology, The Scripps Research Institute, 10550 N. Torrey Pines Rd, La Jolla, CA 92122, USA.

We have developed a biology-driven, high-throughput approach to study emerging infectious agents like the Severe Acute Respiratory Syndrome coronavirus (SARS-CoV). The 28 mature proteins encoded by the ~29kb viral RNA genome have been subjected to a miniaturized crystallomics pipeline. We have successfully obtained soluble high-yield expression of 20 proteins (71%) in *E. coli* and one in baculovirus system. 13 structures have been determined by a combined global effort, covering ~21% of the proteome. The structure of a conserved domain of nsp3 (nsp3b) has shown it to be a macro domain phosphatase specific for Appr-1"-P, pointing to its role in RNA maturation pathway. The structure of nsp10 revealed a new fold with two novel zinc fingers. The structure of the nsp(7/8)₈ supercomplex along with the those of nsp9 and nsp10 are beginning to provide important details on the supramolecular organization of the SARS replicase complex and its role in viral genome replication. This study was supported by NIAID/NIH Contract #HHSN266200400058C "Functional & Structural Proteomics of the SARS-CoV".