A high-resolution temporal atlas of the SARS-CoV-2 translatome and transcriptome

Doyeon Kim*, Sukjun Kim*, Joori Park*, Hee Ryung Chang*, Jeeyoon Chang*, Junhak Ahn*, Heedo Park*, Junehee Park, Narae Son, Gihyeon Kang, Jeonghun Kim, Kisoon Kim, Man-Seong Park#, Yoon Ki Kim#, Daehyun Baek#

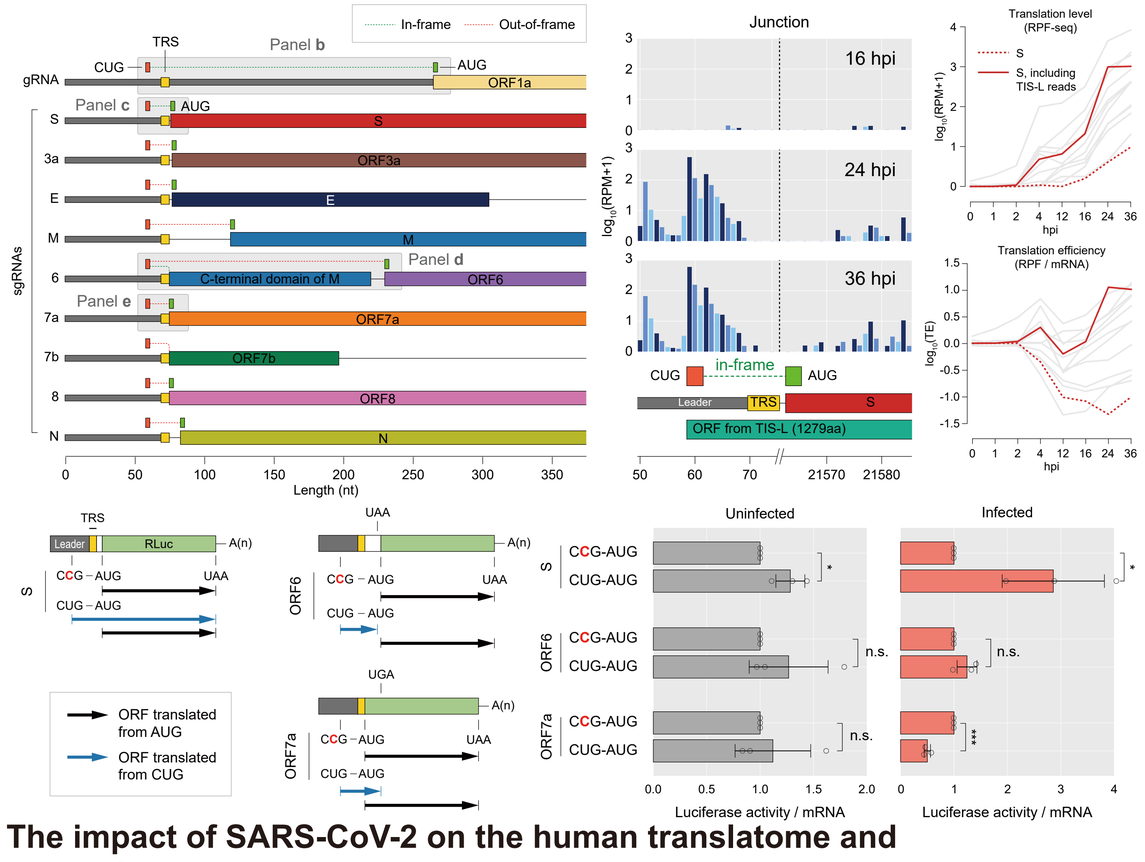
School of Biological Sciences, Seoul National University, Seoul, Republic of Korea., Division of Life Sciences, Korea University, Seoul, Republic of Korea., Department of Microbiology, Institute for Viral Diseases, College of Medicine, Korea University, Seoul, Republic of Korea.

*Equal contributions., #Correspondence should be addressed to M-S.P. (manseong.park@gmail.com), Y.K.K. (yk-kim@korea.ac.kr), and D.B. (baek@snu.ac.kr).

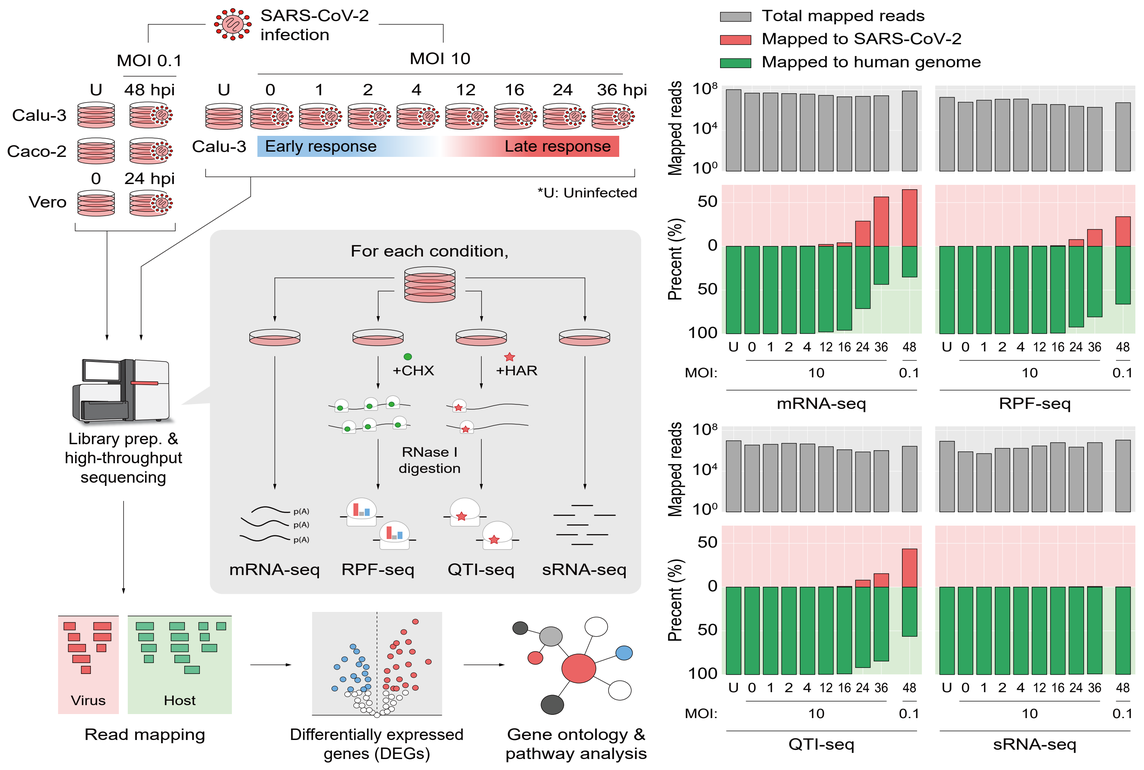
Abstract

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which infected >200 million people resulting in >4 million deaths. However, temporal landscape of the SARS-CoV-2 translatome and its impact on the human genome remain unexplored. Here, we report a high-resolution atlas of the translatome and transcriptome of SARS-CoV-2 for various time points after infecting human cells. Intriguingly, substantial amount of SARS-CoV-2 translation initiates at a novel translation initiation site (TIS) located in the leader sequence, termed TIS-L. Since TIS-L is included in all the genomic and subgenomic RNAs, the SARS-CoV-2 translatome may be regulated by a sophisticated interplay between TIS-L and downstream TISs. TIS-L functions as a strong translation enhancer for ORF S, and as translation suppressors for most of the other ORFs. Our global temporal atlas provides compelling insight into unique regulation of the SARS-CoV-2 translatome and helps comprehensively evaluate its impact on the human genome.

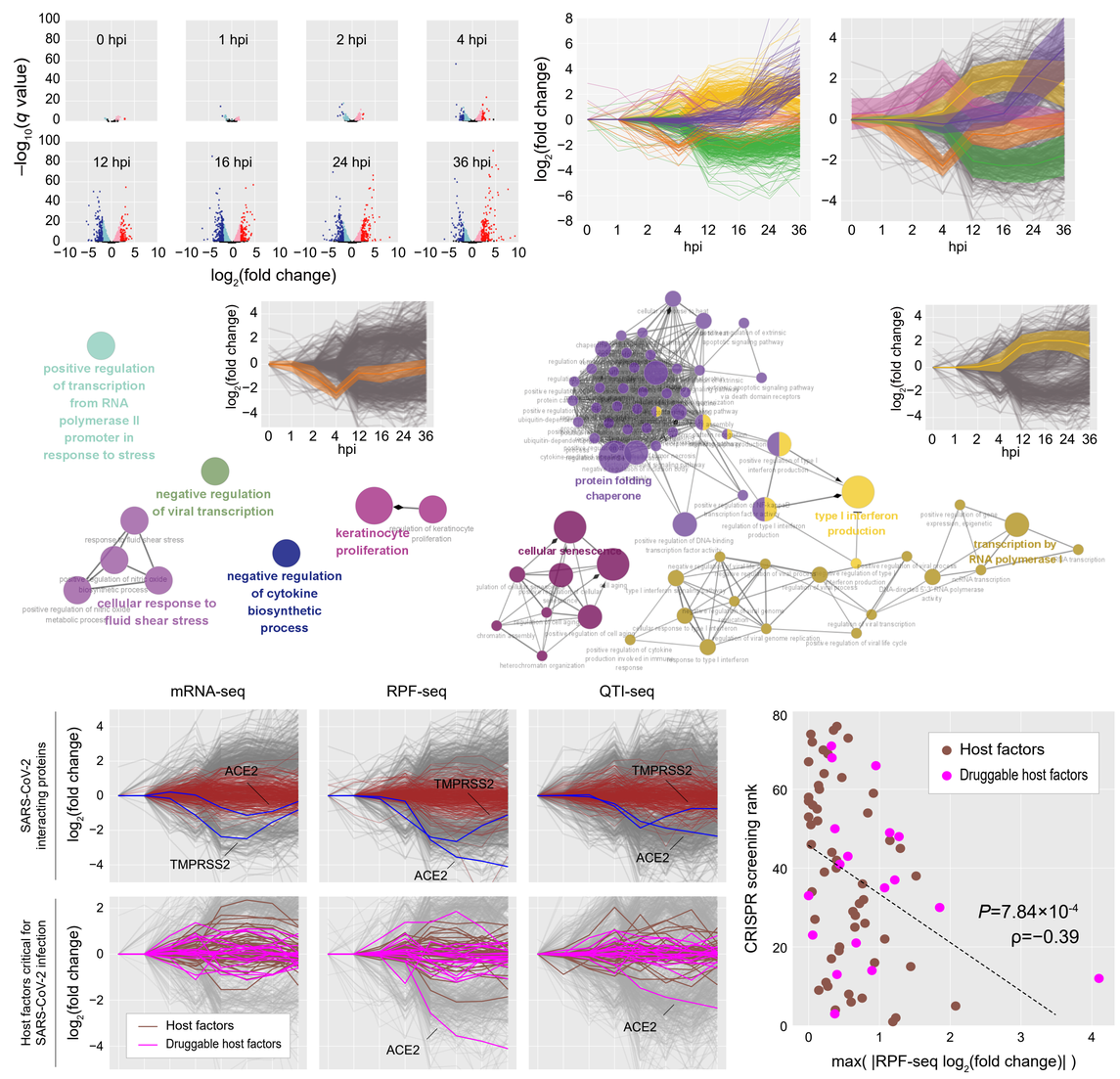
TIS-L functions as a global regulator of the SARS-CoV-2 translatome



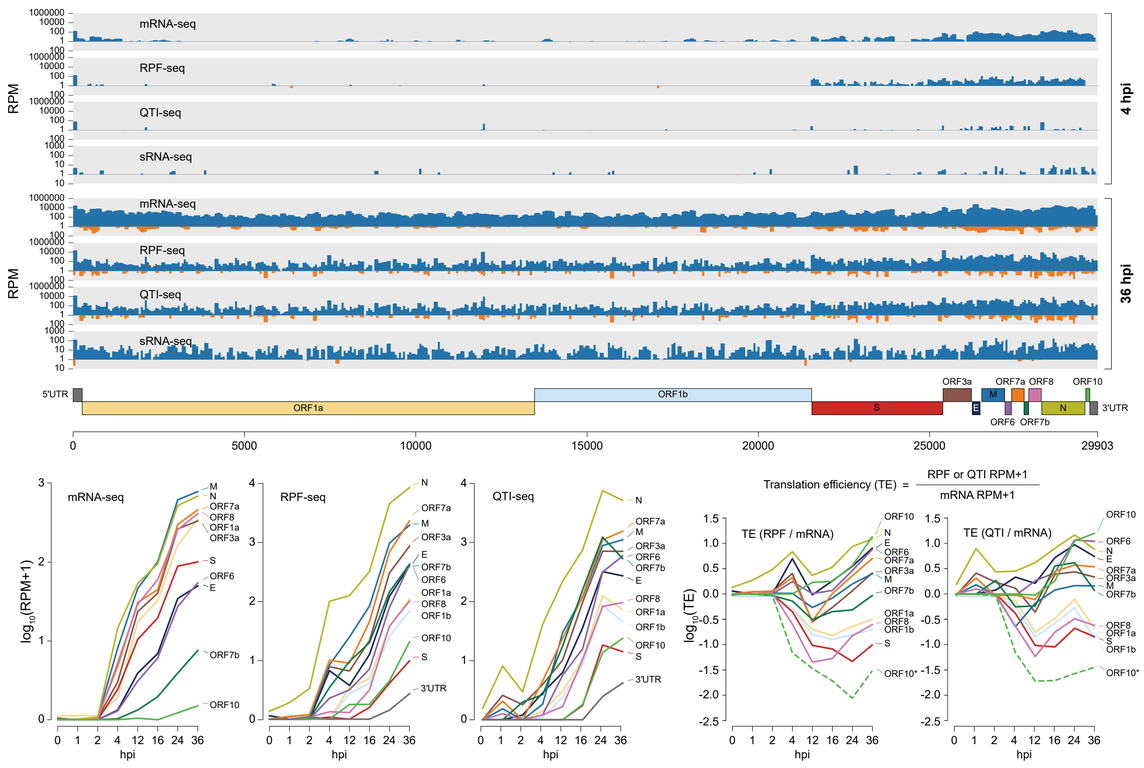
Generation of massive-scale datasets of the SARS-CoV-2 translatome and transcriptome



The impact of SARS-CoV-2 on the human translatome and transcriptome



Temporal landscape of the SARS-CoV-2 translatome and transcriptome



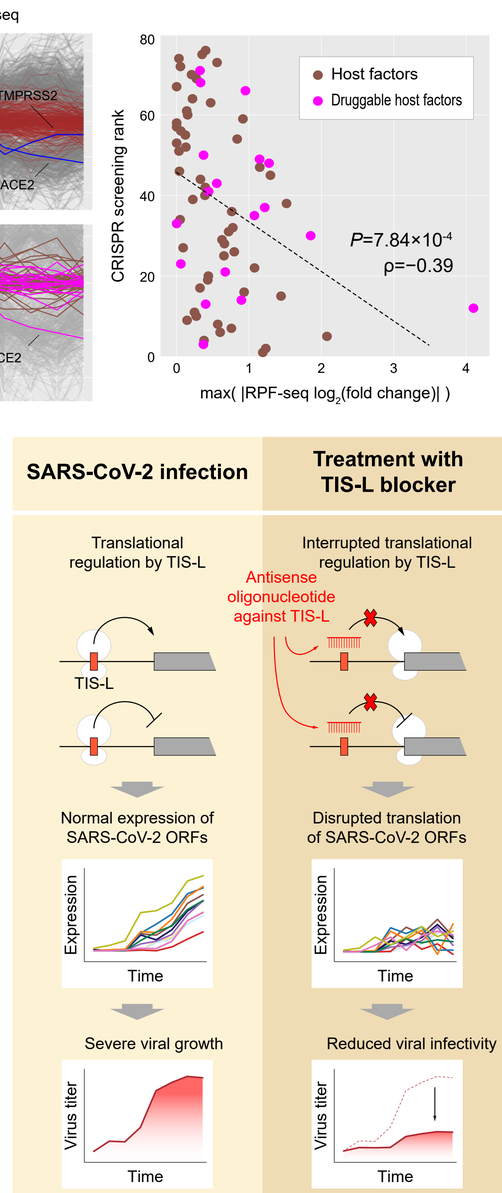
Translation initiation site located in the leader (TIS-L)

Conclusions

- We have constructed massive-scale datasets of mRNA-seq, RPF-seq, QTI-seq, and sRNA-seq at various time points in order to observe the translatome and transcriptome dynamics upon SARS-CoV-2 infection.

- A large fraction of SARS-CoV-2 RPF-seq and QTI-seq reads were mapped to a translation initiation site located in the leader (TIS-L), which may function as a global regulator of the SARS-CoV-2 translatome.

- Our temporal atlas of the translatome and transcriptome of the SARS-CoV-2 and its human host will serve as a useful resource to reveal the molecular basis of the SARS-CoV-2 pathogenicity and to discover effective therapeutic strategies.



Acknowledgements

This study was supported by the National Research Foundation of Korea (NRF) funded by the Ministry of Science and ICT, Republic of Korea and from Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health and Welfare, Republic of Korea.