

Transcriptomic Characterization Reveals Attributes of High Influenza Virus Productivity in MDCK Cells

Qian Ye¹, Thu Phan², Wei-Shou Hu³, Xuping Liu⁴, Li Fan⁴, Wen-Song Tan¹, and Liang Zhao¹

¹East China University of Science and Technology

²University of Minnesota Twin Cities

³University of Minnesota

⁴Shanghai BioEngine Sci-Tech Co., LTD

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Abstract

Madin-Darby Canine Kidney (MDCK) cell line is among the commonly used cell lines for the production of influenza virus vaccine. As cell culture-based manufacturing poses to replace egg-based process, increasing virus production is of paramount importance. To shed light on factors affecting virus productivity, we isolated a subline, H1, which had twice the influenza virus A (IAV) productivity of the parent (P) through cell cloning. Transcriptome analysis revealed that within a few hours after IAV infection, viral mRNAs constituted over one fifth of total mRNA, with several viral genes more highly expressed in H1 than P. Functional analysis of the transcriptome dynamics showed that H1 and P responded to infection similarly, were both subjected to host shutoff and inflammatory responses. Importantly, H1 was more active in translation and RNA processing intrinsically and after infection. Furthermore, H1 had more subdued inflammatory and antiviral response. Taken together we postulate that high productivity of IAV hinges on the balance between suppression of host functions to divert cellular resources and sustain sufficient activities for virus replication. The mechanistic insights on virus productivity can facilitate the process optimization and cell line engineering for advancing influenza vaccine manufacturing.

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