Spodoptera frugiperda rhabdovirus, which was unexpectedly found in Sf9 cells lines (substrate for biological products) in 2014, as a coinfection in SARS-Cov2 patients in China

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Letter

The identification of a novel rhabdovirus in Spodoptera frugiperda cell lines in 2014 [1] - used since 1977 as a cell substrate for biological products [2] - was ‘after decades of safe and beneficial use, it was a surprise to the biotechnology industry to discover an endemic rhabdovirus in Sf9 cells’ [3]. This gains more importance since Sf9 cells lines are used for ‘commercial-scale production of vaccines, biobetters, and other recombinant proteins’ [3, 4]. Furthermore, Sf9 cells line are derived from a moth whose larvae feed on food used in human consumption. It was said that there was no ‘overt risk from exposure to Sf-RV’ [3] and no persistent infections in mammalian or insect cells [5].

Spodoptera frugiperda rhabdovirus genome

Currently, there are only 6 known genomes of Spodoptera frugiperda rhabdovirus (SFR). Interestingly, the genome of SFR has no homology to any other genome. However, encoded proteins show that they are viruses from the large family Rhabdoviridae (Fig 1) that infect invertebrates, animals, and plants [6]. Parts of the viral genome seems to have integrated in the insect genome [7], thus making it necessary to generate ‘Sf-rhabdovirus-negative Spodoptera frugiperda cell line as an alternative host for recombinant protein production’ [5].

Spodoptera frugiperda rhabdovirus in the bronchoalveolar lavage fluid of Covid19 patients

The metagenome from the bronchoalveolar lavage fluid of 5 Covid19 [8–10] patients from Wuhan (Accession: PRJNA605983) shows SFR infection in all 5 patients (SI:SI.sf9). Many of these reads show integration with chloroplast or mitochondria (Fig 2). Some of these patients also had a Nipah virus infection [11].

References

1. Ma H, Galvin TA, Glasner DR, Shaheduzzaman S, Khan AS (2014) Identification of a novel rhabdovirus in spodoptera frugiperda cell lines. Journal of virology 88: 6576–6585.
2. Vaughn J, Goodwin R, Tompkins G, McCawley P (1977) The establishment of two cell lines from the insects spodoptera frugiperda (lepidoptera; noctuidae). In vitro 13: 213–217.
3. Schroeder L, Mar T, Haynes J, Wang R, Wempe L, et al. (2019) Host range and population survey of spodoptera frugiperda rhabdovirus. Journal of Virology 93.
4. Felberbaum RS (2015) The baculovirus expression vector system: A commercial manufacturing platform for viral vaccines and gene therapy vectors. Biotechnology journal 10: 702–714.
5. Maghodia AB, Jarvis DL (2017) Infectivity of sf-rhabdovirus variants in insect and mammalian cell lines. Virology 512: 234–245.

6. Jackson AO, Dietzgen RG, Goodin MM, Bragg JN, Deng M (2005) Biology of plant rhabdoviruses. *Annu Rev Phytopathol* 43: 623–660.
7. Geisler C, Jarvis DL (2016) Rhabdovirus-like endogenous viral elements in the genome of *Spodoptera frugiperda* insect cells are actively transcribed: implications for adventitious virus detection. *Biologicals* 44: 219–225.
8. Perlman S (2020). Another decade, another coronavirus.
9. Wu F, Zhao S, Yu B, Chen Y, Wang W, et al. (2020) Complete genome characterisation of a novel coronavirus associated with severe human respiratory disease in Wuhan. *China bioRxiv* 24.
10. Chen L, Liu W, Zhang Q, Xu K, Ye G, et al. (2020) RNA based mNGS approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 Wuhan outbreak. *Emerging Microbes & Infections* 9: 313–319.
11. Chakraborty S (2020). There was a simultaneous outbreak of the zoonotic Nipah henipavirus in Wuhan - 4 out of 5 patients have the virus in Jinyintan hospital , along with SARS-Cov2, in their metagenome - which seems to have resolved by itself. doi:10.31219/osf.io/s4td6. URL osf.io/s4td6.

Organism	Blast Name	Score	Number of Hits	Description
root			701	
• Viruses	viruses		694	
• • Riboviria	viruses		692	
• • • Negamaviricota	viruses		666	
• • • • Mononegavirales	viruses		665	
• • • • • Rhabdoviridae	viruses		664	
• • • • • • unclassified Rhabdoviridae	viruses		80	
• • • • • • • Spodoptera frugiperda rhabdovirus	viruses	4412	7	Spodoptera frugiperda rhabdovirus hits
• • • • • • • Lepidopteran rhabdo-related virus OKIAV34	viruses	1905	1	Lepidopteran rhabdo-related virus OKIAV34 hits
• • • • • • • Lepidopteran rhabdo-related virus OKIAV32	viruses	1824	1	Lepidopteran rhabdo-related virus OKIAV32 hits
• • • • • • • Lepidopteran rhabdo-related virus OKIAV35	viruses	1698	1	Lepidopteran rhabdo-related virus OKIAV35 hits
• • • • • • • Lasius neglectus virus 2	viruses	1083	1	Lasius neglectus virus 2 hits
• • • • • • • Wuhan Ant Virus	viruses	1075	2	Wuhan Ant Virus hits
• • • • • • • Hymenopteran rhabdo-related virus OKIAV109	viruses	1051	1	Hymenopteran rhabdo-related virus OKIAV109 hits
• • • • • • • Hymenopteran rhabdo-related virus OKIAV38	viruses	1045	1	Hymenopteran rhabdo-related virus OKIAV38 hits
• • • • • • • Atrato Rhabdo-like virus 3	viruses	1029	1	Atrato Rhabdo-like virus 3 hits
• • • • • • • Hymenopteran rhabdo-related virus OKIAV40	viruses	952	1	Hymenopteran rhabdo-related virus OKIAV40 hits
• • • • • • • Lepidopteran rhabdo-related virus OKIAV33	viruses	840	1	Lepidopteran rhabdo-related virus OKIAV33 hits
• • • • • • • Agrotis ipsilon virus	viruses	691	1	Agrotis ipsilon virus hits
• • • • • • • Blacklegged tick rhabdovirus-1	viruses	652	1	Blacklegged tick rhabdovirus-1 hits
• • • • • • • Blattodean rhabdo-related virus OKIAV14	viruses	651	1	Blattodean rhabdo-related virus OKIAV14 hits
• • • • • • • Coleopteran rhabdo-related virus OKIAV20	viruses	648	1	Coleopteran rhabdo-related virus OKIAV20 hits

Figure 1: Taxonomy of *Spodoptera frugiperda* rhabdovirus:

Figure 2: *Spodoptera frugiperda* rhabdovirus reads are often merged with mitochondrion or chloroplast