

Conclusion: The findings of the study reveal the need of the establishment of a arbovirus surveillance and monitoring program in the zoological parks for the appropriated control of the mosquitoes thriving in the parks and consequently reduce the risk for the emergence of zoonotic mosquito-borne virus infection in animals and humans.

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The Effect of Dengue Viral Infection on the Unfolded Protein Response in Primary Macrophages

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Purpose: The unfolded protein response (UPR) and ER stress play a significant role in determining the outcome of DENV infection. The activation of UPR is cell-type dependent. There are no data available on the effect of DENV infection on the UPR in human primary cells. We conducted *in vitro* experiments on human primary macrophages to identify the effect of DENV on the IRE1 α -XBP1 and PERK-eIF2 α -ATF pathway.

Methods & Materials: Human peripheral blood monocytes were differentiated to macrophages and infected with DENV 16681 at a multiplicity of infection 1. Cells were harvested, lysed and western blots were performed using antibodies against PERK, eIF2 α , p-eIF2 α , and ATF at selected time points. Cells were harvested and RNA extraction was done to identify XBP1 RNA by qRT-PCR at selected time points. Secreted viruses from cells were quantified by a qRT-PCR assay and infectious virus levels were identified using a plaque assay. Secreted TNF α and IFN α were measured using a functional assay. GSK2606414 and 4 μ 8c were used to inhibit the PERK and IRE1 α -XBP1 arms, respectively. Tunicamycin, an ER stress inducer was used as the control.

Results: A non-significant increase in ATF4 protein was seen at 12 hours post infection (p.i.) with no change in ATF4 mRNA levels at 6 and 12 hours p.i. in macrophages. Activation of the PERK arm although minimal was seen early at 6 hours p.i. and a robust IRE1 α -XBP1 arm activation was seen at 48 hours p.i.. DENV infection increased the XBP1t and XBP1s levels with an increase in the XBP1s/XBP1t ratio. Inhibition of the IRE1 α -XBP1s pathway resulted in a significant reduction in secreted and infectious virus from macrophages in addition to reduced secretion of TNF α and IFN α levels. PERK arm inhibition did not have an effect on secreted virus or secreted IFN α . However, secreted TNF α levels were reduced by PERK inhibition.

Conclusion: Activation of PERK and IRE1 α -XBP1 arms were time-dependent. The IRE1 α -XBP1 pathway was pro-viral and chemical inhibition of XBP1 splicing resulted in low DENV secretion and reduced TNF α and IFN α secretion from primary human macrophages. DENV activates the pro-viral IRE1 α -XBP1 pathway preferentially over the PERK arm in primary macrophages.

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Review of the incidence of Crimean-Congo hemorrhagic fever for 16 years in 2005-2020 based on ProMED-RUS reports

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Purpose: The ProMED service in Russian (ProMED-RUS) informs its readers about new infectious diseases in 16 countries of the former Soviet Union (FSU). Among the regions where monitoring is carried out, there are several territories endemic for Crimean-Congo hemorrhagic fever (CCHF).

The aim of the study was to assess the epidemiology of CCHF in the territory of the FSU over the past 16 years based on data from ProMED-RUS.

Methods & Materials: We reviewed 289 ProMED-RUS reports on CCHF published in the period from 2005 to 2020 inclusive. The moderators' comments were also taken into account.

Results: According to ProMED-RUS, during 2005-2020, cases of CCHF were registered in Russia (Rostov, Stavropol, Volgograd, Astrakhan regions, the Republics of Kalmykia, Kabardino-Balkaria, Dagestan, Ingushetia), Kazakhstan, Georgia, Kyrgyzstan, Uzbekistan and Tajikistan. In Russia during this period 1,919 cases of the disease were registered, including 43 deaths (CFR 2.8%).

The ProMED-RUS service reported about the cases of CCHF in the South of Kazakhstan (Zhambyl, Kyzylorda and Turkestan regions) since 2008. The largest number of cases (26) registered in 2009. Later, from 6 to 20 cases of the disease with a CFR of 20-30% are registered annually. The ProMED-RUS service first reported 5 cases of CCHF in Tajikistan in 2009, 3 of them were fatal (CFR 60%). Later, there was no information about cases of CCHF in the Russian-language mass media (RLMM).

ProMED-RUS first reported cases of CCHF in Georgia in 2009. In 2010-2012, sporadic cases of the disease were registered in this country, and since 2013, more than 10 cases of CCHF are diagnosed annually. In 2020, only 9 cases of CCHF were registered in Georgia, which 1 ended fatally (CFR- 30%).

In 2019, ProMED-mail first reported a case of CCHF infection in Kyrgyzstan, imported to Kazakhstan. In 2020, no cases of CCHF were registered in this country

The ProMED-RUS service first reported 13 cases of CCHF in Uzbekistan in 2013-2015, 10 of them were a fatal, and 2 - in 2017.

Conclusion: ProMED-RUS reports on CCHF in the FSU provide up-to-date and useful information that allows to monitor the epidemiological situation in these regions.

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