La Jolla, CA
April 17- 21
2016

hosted by the
INTERNATIONAL
SOCIETY FOR
ANTIVIRAL
RESEARCH
(ISAR)

29th International Conference on Antiviral Research (ICAR)

Program AND Abstracts

of antagonizing viral countermeasures. Our lead antiviral series demonstrates host-mediated protection from multiple respiratory and systemic viruses in vitro including influenza, RSV, dengue, and ebola. Administration of lead compounds provides significant reduction in viral titers resulting in a reduction in morbidity and mortality in murine models of influenza and RSV infection, even when administered up to 24 hours post-challenge. In summary, scaffolds identified using Kineta's AViiD™ platform are being developed as non-direct acting antivirals that potentiate a cell autonomous effector response active against diverse RNA viruses, are less likely to elicit emergence of resistant viral variants, and have potential to be therapeutics for viral infections of undiagnosed etiology.

171 Emerging Tick-Borne Phleboviral Diseases Modeled in Genetically Engineered Golden Syrian Hamsters Highlight the Importance of STAT2 in the Control of Infection and Serve as Novel Models for Antiviral Drug Development

Brian Gowen, Ph.D., Jonna Westover, Ph.D., Brady Hickerson, B.S., Brittney Downs, B.S., Skot Nielson, M.S., Zhongde Wang, Ph.D.
Utah State University, Logan, Utah, USA

Severe fever with thrombocytopenia syndrome virus (SFTSV) and Heartland virus (HRTV) are emerging tick-borne viruses (*Bunyaviridae* family, *Phlebovirus* genus) present in Asia and the Unites States. SFTSV has caused significant morbidity and mortality in China, Korea and Japan, while HRTV is an emerging disease threat with reported cases in Missouri, Tennessee and Oklahoma. Key features of disease associated with infection are intense fever, thrombocytopenia, and leukopenia, with case fatality rates up to 30%. The development of small animal models for early stage antiviral drug evaluations has been hampered by the lack of susceptibility of immune competent laboratory mice and hamsters to SFTSV and HRTV challenge. Here we show for the first time uniformly lethal disease in STAT2 knock-out (KO) hamsters, deficient in type I interferon antiviral signaling, with as little as 10 plaque-forming units of either virus. Notably, the STAT2 KO hamsters were acutely affected by SFTSV infection with all animals succumbing within 5-6 days after subcutaneous challenge. In contrast, hamsters challenged with HRTV succumbed 9-15 days post-infection. In several moribund animals infected with HRTV, infectious virus was detectable in the serum, spleen, liver, and kidney, but not brain tissue. Studies characterizing the natural history of disease in both models and the use of these novel phlebovirus infection models in the evaluation of candidate antiviral therapies will be presented. *This work was supported in part by the National Institutes of Health (HHSN272201000039I).*

172 Expression of CCR5 and CXCR4 on CD4+T-Lymphocytes in HIV-Positive Patients in Dependence on HIV-1 Subtype A Tropism

Natallia Matsiyeuskaya, M.D., Ph.D.[1], Irina Tokunova, M.S.[1], Dmitriy Kireev, Ph.D.[2], Andrei Hancharou, Ph.D.[3]
[1]*State Medical University, Grodno, Grodno, Belarus;* [2]*Central Research Institute for Epidemiology, Moscow, Moscow, Russian Federation;* [3]*Republican Research & Practical Center for Epidemiology & Microbiology, Minsk, Minsk, Belarus*

Aim of study was to establish expression of CCR5 and CXCR4 on CD4+T-lymphocytes in HIV-positive in dependence on HIV-1 subtype A tropism.

MATERIAL AND METHODS: 29 HIV-positive patients with subtype A without antiretroviral therapy (mean age - 33,5+7,2 yr., women – 16) were divided in 2 groups: the 1st – 17 patients with R5-tropic virus (AIDS was in 3/17,6%) the 2nd – 12 ones with non R5-tropic HIV (AIDS was in 4/33,3%). HIV tropism was detected by sequencing of V3 loop of gp120 gene («AmpliSens HIV-Resist-Seq», Russia), FPR – 20%. «FACSCalibur» flow cytometer («Becton Dickenson», USA), monoclonal antibodies CD184, CD195 (Abd Serotec) were used.

RESULTS: In the 1st group expression of CXCR4 on T helper were significantly decreased in patients with AIDS in comparison with non AIDS ones (cells/mkl): 7,10 (1,1-78,4) and 107,43(30,7 -331,7), p=0,02, respectively, Mann-Whitney test. Expression of CCR5 on T helper did not differ significantly in AIDS and non AIDS patients of the 1st group: 31,36 (10,6-31,5) and 54,84 (21,9-84,6), p=0,06, respectively.

In the 2nd group expression of CCR5 on T helper were significantly decreased in AIDS patients in comparison with non AIDS ones: 20,81 (8,5-32,6) and 61,90 (13,3- 129,0), p=0,03, respectively. Expression of CXCR4 on T helper did not differ significantly in AIDS and non AIDS patients of the 2nd group: 16,94 (10,6-510,0) and 60,60 (0,0-166,3), p=0,4, respectively

CONCLUSIONS: Different patterns of CCR5 and CXCR4 expression on CD4+T-lymphocytes in study groups may reflect the different mechanism of AIDS formation in dependence on HIV tropism.