are applicable to a broad-spectrum of pathogens. The acquisition of drug resistance might also be minimized since selective pressure is not directly placed upon the viral pathogen. Herein, we utilized this strategy of host-oriented therapeutics to screen small molecules for their abilities to block infection by multiple, unrelated virus types and identified FGI-104. FGI-104 demonstrates broad-spectrum inhibition of multiple blood-borne pathogens (HCV, HBV, HIV) as well as emerging biothreats (Ebola, VEE). We also demonstrate that FGI-104 prevents lethality from Ebola in vivo. Altogether, these findings reinforce the concept of host-oriented therapeutics and present a much-needed opportunity to identify antiviral drugs that are broad-spectrum and durable in their application.

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Derivatives of Tunicamycin as Effective Inhibitors of Classical Swine Fever Virus

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Classical Swine Fever Virus (CSFV) is often used as a surrogate model to elucidate the role of envelope glycoproteins of HCV. These two viruses are homologous in genomic organization, replication and protein function. Glycoproteins E2, E0 (E^{rns}) and E1 of CSFV play a major role in the initial stages of viral infection. They are detected on the external part of viral particles. It has been found that some glycosylation inhibitors, such as tunicamycin, which act at the early stages of glycan chain processing, can influence, not only glycosylation, but also the stability of E2 and E0 glycoprotein, effectively inhibiting the formation of glycoprotein complexes and the yield of the virus. Because tunicamycin is relatively toxic to the cells, we have synthesized a number of inhibitors mimicking tunicamycin structure or a part of this structure. The main aim of this work was to study the influence of tunicamycin derivatives on penetration and propagation of CSF virus, and on maturation of viral envelope glycoproteins. To this end we have investigated the formation of glycoprotein dimers by immunoperoxidase monolayer assay and by immunoblotting (Western blotting). Some of inhibitors effectively arrested viral growth without significant toxicity for mammalian cells. These inhibitors were further studied in order to elucidate the molecular mechanism of their antiviral effect using different mammalian and insect cell lines and it has been found that most of them inhibit N-glycosylation at the stage of glycan modification characteristic for mammalian cells. These results for CSFV were used in the initial characterization of the effect of the inhibitors on recombinant HCV glycoproteins.

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Anti-Picornavirus Activity and Other Antiviral Activity of Sulfated Exopolysaccharide from the Marine Microalga Gyrodinium impudicum Strain KG03

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The sulfated exopolysaccharide p-KG03, which is produced by the marine microalga Gyrodinium impudicum strain KG03, had a molecular weight of 1.87×10^6, and was characterized as a homopolysaccharide of galactose with uronic acid (2.96%, w/w) and sulfate groups (10.32%, w/w). Like other sulfated polysaccharide exhibited impressive antiviral activity in vitro against several enveloped viruses such as influenza virus and herpes simplex virus type 1 and type 2. It is a strong immunoinducer and showed antiviral activity against several picornaviruses such as encephalomyocarditis virus (EMCV) and Coxsackie B type 3 virus which are known as naked virus. Antiviral activities of p-KG03 against various picornaviruses and also other viruses will be reported and compared to other sulfated polysaccharides. The biological activities of p-KG03 suggest that sulfated metabolites from marine organisms are a rich source of antiviral agents. The p-KG03 polysaccharide may be useful for the development of marine bioactive exopolysaccharides for use in biotechnological and pharmaceutical products.

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Assay Development for Antiviral Drug Efficacy Evaluation Against Dengue Virus

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Dengue disease is an arthropod-borne disease, and Dengue virus is transmitted from person to person by Aedes aegypti in the domestic environment. Dengue virus (DENV), a NIAID Category A priority pathogen, is the most important mosquito-borne viral disease affecting humans currently. More than 2.5 billion peoples now live in areas at risk of infection. Annually, there are 50–100 million people being infected, with about 50,000 reported cases. The case-fatality rate of Dengue hemorrhagic fever is about 5%, and most fatal cases are among children and young adults. Currently, there is no efficient vaccine, no effective vector control measures, and no effective antiviral drugs against DENV diseases. With the rapid expansion of DENV disease in most tropical and subtropical areas of the world, it is urgent to develop antiviral drugs for Dengue disease control. To identify novel antivirals targeting DENV, we developed an assay for the evaluation of an antiviral efficacy against DENV, including serotype-1, -2, -3 and -4. This assay is a cytopathic effect (CPE)-based assay which has been used to evaluate the efficacy of recently identified antivirals against DENV-2 virus. The assay conditions, including the multiplicity of infection (M.O.I.) and cell density, were optimized and validated in 96-well plates. DENV-2-induced CPE can be observed and detected in BSR cells using CTG reagent (Promega) between 3 and 5 days post infection (d.p.i.) with M.O.I of 1. Antiviral efficacy studies were carried out using ten concentra-