a small, cytokine-like protein capable of inducing an anti-DEN-2 response in Vero cells.

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**74**

## The Susceptibility of Isolates of Pandemic 2009 H1N1 Influenza A Virus to Russian Domestic Antivirals

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The antiviral drugs rimantadine, arbidol and ingavirin produced and widely used in Russia are licensed for the phrophylaxis and the treatment of influenza A and B. Ribivirin has been long recognized as a broad-spectrum antiviral agent with particularly distinct activity against orthomixoviruses (that is, influenza) and paramyxoviruses. The purpose of this study was to provide detailed information on Russian domestic drug susceptibility of the pandemic 2009 H1N1 influenza A virus. A/California/04/2009 and A/California/07/2009, that were obtained from CDC, and 4 viruses that were isolated in Russia from patients infected with 2009 H1N1 virus were used in this study. The results of experiments have shown that arbidol and ribavirin inhibited selectively the reproduction of studied viruses in MDCK cells. All 6 tested 2009 H1N1 viruses exhibited $IC_{50}$ values characteristic of other laboratory and epidemic strains of influenza viruses. The $IC_{50}$ for arbidol ranged from 4 to 8.5 μg/ml, whereas those for ribavirin ranged from 1.5 to 3 μg/ml. Rimantadine in nontoxic for cells concentrations does not affect the reproduction of all studied isolates of pandemic 2009 H1N1 influenza A virus. We revealed no significant antiviral activity of ingavirin in cell culture in nontoxic concentrations (up to 200 μg/ml) against all studied 2009 H1N1 influenza viruses. Sequencing of viruses with the further analysis on mutations which are responsible for resistance to anti-influenza drugs were conducted. The data obtained in cell culture have been confirmed by the results of genome analysis of all 6 studied viruses. It was shown previously that resistance to arbidol-resistant mutants generated in vitro has been due to substitutions in different positions of HA2 subunit of HA protein. The sequence of genes of all studied viruses did not reveal the replacements defining resistance to arbidol while both viruses contained a mutation in position 31 of M2-protein which is responsible for resistance to adamantanes.

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**75**

## Small Molecule Inhibitors of *De Novo* Cell-free Capsid Assembly Effective against *Flaviviridae* and *Togaviridae*

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We have established separate cell-free protein synthesis (CFPS)-based screens for small molecules that block any step in the pathways of host-catalyzed capsid assembly of Hepatitis C virus (HCV) and Venezuelan equine encephalitis virus (VEEV), members of the families *Flaviviridae* and *Togaviridae*, respectively. For HCV, over 80,000 small molecules were screened and approximately 400 initial hits were counter screened to exclude inhibitors of protein synthesis, thereby narrowing hits to approximately 90 molecules representing over 20 distinct pharmacophores with molecular weight <500 Da. Approximately 75% of these chemical classes (16 of 21) have been demonstrated to be active against infectious Hepatitis C virus. For VEEV, a screen of approximately 20,000 compounds yielded a large number of shared hits with the HCV screen as well as some with activity against VEEV but not against HCV. Several of the compounds active against live HCV in cell culture are active at similar doses against infectious Dengue virus in cell culture but are not active against VEEV. Thus it appears that a substantial subset of the novel small molecules that emerged from the HCV screen are relatively specific for flaviviruses, having activity against two different members of family *Flaviviridae* and no activity against a member of the *Togaviridae*. Data will be presented on a small molecule active against each of these two viral families. Together these findings suggest the potential for a new generation of broad-spectrum antiviral therapeutics active against whole families of viruses. Other data suggest that many of these drugs target host factors and thus, the breadth of their activity raises the possibility that they may be less susceptible to the development of virus resistance.

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