Oral Session VI: Other Viruses and Late Breaker Presentations

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Comparative Activity of Anti-Enteroviral Agents Against Poliovirus Replication In Vitro
Implications For the End Phase of the Polio Eradication Initiative

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In 1986, the World Health Assembly launched the Global Polio Eradication Initiative with the aim to eliminate polio worldwide by the year 2000. So far, large-scale vaccination campaigns with the oral live attenuated (Sabin) vaccine (OPV) resulted in a dramatic reduction of the total number of poliomyelitis cases and the number of countries in which polio is endemic. However, the end stages of the eradication appear to be much more difficult than was anticipated. In this context, a panel convoked by the National Research Council concluded that it would be appropriate, and possibly essential, to develop antiviral drugs against poliovirus, to facilitate risk management in the post OPV-era. We performed a comparative study on the in vitro activity of a selection of anti-enterovirus compounds against the three poliovirus Sabin strains. Drugs with different targets were selected: capsid binding agents (pleconaril, pirodavir and its analogue R78206), a protease inhibitor (ruprintrivir), polymerase inhibitors (2′-C-methylcytidine and related analogues), a 3A inhibitor (enviroxime), 2C inhibitors (MRL-1237 and HBB) as well as ribavirin and a compound with an unknown mechanism of action (MDL-860). In particular, ruprintrivir and the pirodavir analogue R78206 exhibited potent antiviral activity against all three strains. Compounds such as ruprintrivir or pirodavir, that have been evaluated in the clinical setting for the treatment of rhinovirus infections, or analogues thereof, may have the potential to be used in the control of polio in the end phase of the eradication campaign and in the post OPV-era.

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Carbohydrate-Binding Agents (CBAs) Selectively Target the Glycoproteins of the HCV and HIV Envelope to Prevent Viral Entry

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HIV and HCV are human pathogens that often co-infect the same hosts. Virus capture and transmission may occur through SIGN-positive carrier pathways. Both HIV and HCV are enveloped viruses that contain extensively glycosylated envelope glycoproteins, which are crucial for cellular attachment and infectivity. We studied the anti-HIV and -HCV activity of carbohydrate-binding agents (CBAs) such as plant lectins (i.e. mannose-specific agglutinins of Galanthus nivalis (GNA), Hippeastrum hybrid (HHA) and Cymbidium sp. (CA); the GlcNAc-specific agglutinin of Urtica dioica (UDA)) and the mannose-specific non-peptidic antibiotic Pradimicin A (PRM-A). The CBAs efficiently prevent HIV and HCV infection of target cells in the nanomolar range (plant lectins) or lower micromolar range (PRM-A). The CBAs also prevent HIV-1 capture by DC-SIGN-expressing cells. Other enveloped viruses (i.e. herpes simplex virus, respiratory syncytial virus, vesicular stomatitis virus, parainfluenza-3 virus) did not show marked, if any, sensitivity to the inhibitory effect of the CBAs, pointing to a pronounced antiviral selectivity of these agents. Mannan is able to reverse partially the antiviral effect of the CBAs. Infection studies with pseudotyped HCV and HIV particles revealed that virus entry is the principle target of therapeutic intervention of the CBAs. A close correlation ($r = 0.93$) was observed for the antiviral activity of the CBAs against both HIV and HCV replication. CBAs should be considered as novel tools to prevent transmission and entry of HIV and HCV into target cells. The discovery that the non-peptidic antibiotic PRM-A is effective against HIV and HCV proves that development of CBAs as therapeutic agents may become an achievable goal in the clinical setting.

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