96-well plates containing monolayers of primary human fibroblasts were infected at an MOI of 0.01 PFU/cell and the infection was allowed to proceed for 7 days. The level of luciferase activity expressed by the virus was assayed and used as a surrogate marker for viral replication. The assay yielded EC_{50} values that were comparable to those generated in standard assays for several compounds that are currently licensed for use against HCMV, but appears to offer significant advantages. Chief among them were reduced processing time, reduced incubation time (7 days instead of 14 days) and reduced sensitivity to colored compounds. This assay, paired with the CellTiter Glo® toxicity assay, promises to provide a rapid means to assess cytotoxicity as well as antiviral activity against HCMV.

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Carbocyclic L-Nucleoside Analogues as Potential Antiviral Agents

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The application of nucleosides in antiviral therapy has grown to a common process over the last three decades. There exists a huge variety of nucleosides, which show several modifications on the nucleobase or the sugar moiety. Due to these changes in nucleoside structure new antiviral activities were found. Beside the commonly used D-configurated natural nucleosides there is the important class of L-nucleosides which are the mirror-images of the natural ones. L-Nucleosides are known for their significant bioactivity, especially their antiviral activity towards Hepatitis B. There are several FDA-approved L-nucleoside analogues, e.g. lamivudinde (3TC), telbivudine (L-thymidine) and clevudine (L-FMAU). With regard to these derivatives we decided to connected the concept of carbocyclic and L-nucleosides within this work to obtain similar carbocyclic L-nucleoside analogues as potential antitumor and antiviral agents. As starting material, we chose a chiral cyclopentenol, which can be prepared from cyclopentadiene by alkylation and a subsequent asymmetric hydroboration. After protection of the formed hydroxy group, the remaining double bond can easily be hydroxylated by different methods, yielding a chiral cyclopentanol. Using a modified Mitsunobu protocol, heterocycles were condensed to this precursor leading to L-configurated pyrimidine und purine carbocyclic nucleosides, e.g.: L-*carba*-dT, L-*carba*-dA, L-*carba*-BVDU or L-*carba*-d4T. The obtained enantiomerically pure carbocyclic nucleosides can simply be converted into the corresponding *cyclo*Sal-pronucleotides or their monophosphate esters (nucleotides) with the aim to improve their activity.

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Immunoprophylaxis of Phleboviral Infection in Hamsters with Recombinant Eimeria Protozoan Surface Antigen

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Recombinant *Eimeria* antigen (rEA) has been shown to have potent anticancer and antiviral activity in respective mouse disease models, presumably through robust immune stimulation that occurs via TLR11, a pattern recognition receptor that recognizes profilin-like proteins expressed on apicomplexan protozoans. Comparable immunostimulatory activity in other species has yet to be demonstrated. Since rEA is known to be highly effective in treating Punta Toro virus (PTV) infection in mice, its ability to elicit protective immunity in the hamster PTV infection model was investigated. rEA was given alone, or in combination with IL-18 or IL-2, and virally challenged hamsters were observed for mortality. A dose of 100 μg of rEA, given once 4 h prior to viral challenge, and a second time on day 3 of the infection, was found to be the most effective prophylactic therapy protecting 60% of treated hamsters from mortality, compared to only 5–10% observed in animals receiving placebo. In addition, splenic cytokine transcript profiles for IL-12, IL-21, IFN-γ and TNF-α were assessed at various times after a single 100-μg dose treatment of rEA. Only IFN-γ and IL-12 were found to have remarkably increased expression following exposure. The data suggest that rEA does induce host antiviral responses in hamsters that result in significant protection from death, although determining the most appropriate dose for intervention in other species, including humans, will likely be very challenging.

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Novel Inhibitors of Orthopoxvirus Replication Target Vaccinia Virus P37 Envelope Protein

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Three compounds with antiviral activity against orthopoxviruses were identified through routine in vitro screening of over 1800 compounds from a chemical library utilizing cytopathic effect assays. Plaque reduction assays in human foreskin fibroblast cells confirmed the activity of three compounds against both vaccinia (VV) and cowpox (CV)