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Treatment Of Lethal Lassa Virus Infection In Experimental Animal Model With Anti-TNF-α Serum.

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Lassa virus is a member of an Arenavirus family and the causative agent of hemorrhagic fever, an often fatal human disease in West Africa. The involvement of cytokines, such as interferon-α (IFN-α), tumor necrosis factor (TNF-α), and interleukin 1 play an important role in the pathogenesis of infection. 5-week-old mice (CBA/calac strain) inoculated intracerebrally with Lassa virus (Josian strain, 1000 PFU/animal) developed a characteristic disease and usually died in 9-10 days. High virus titers (4.5-5.2 log10/ml) were present in liver, spleen, serum, and brain near the time of death. Intravenous treatment twice with antitumour necrosis factor-α (anti-TNF-α) serum for 72 and 120 h after virus challenge significantly decreased mortality and reduced virus titers in organs. In addition, intravenous treatment with polyclonal TNF-α antibodies considerable influenced in levels of TNF-α and serum IFN activity. These results suggest a role for virus-induced cytokin activity, such as TNF-α in immunopathogenesis from arenavirus infections.

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Inactivation of Enveloped and Non-Enveloped Viruses by Ozone Induced Oxidative Stress. P. Lea, D. Klein, L. Lee, D. Adachi and W.J. Dermott, LifeTECH Corporation, 133 The West Mall, Toronto, Ontario, Canada M9C 1C2

Ozone has powerful oxidizing properties which may be applied to deactivate virus and bacteria. Attempts to sterilize biological substrates using other technologies and ozone methods have resulted in only partial deactivation of enveloped virus. For this reason, a non-enveloped and several enveloped viruses were selected to study ozone dependant virus inactivation using the *Life*TECH Sterinetics™ infusion System. Phosphate buffered saline containing increasing concentrations of ozone was infused into viral samples. For the enveloped viruses, Infectious Bovine Rhinotracheitis (IBR) and Bovine Viral Diarrhea (BVD) were used. More than 8.5μg/ml and 4.5μg/mL respectively of dissolved ozone was necessary for complete inactivation of log10^n of virus. Bovine Adenovirus type 7, a non-enveloped model, was totally inactivated at 2.2μg/mL of dissolved ozone. These results confirm that ozone is an effective agent for inactivating both enveloped and non-enveloped viruses when applied under carefully controlled conditions.

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Recognition and stabilization of single stranded adenine sequences by thymine base substituted-naphthalene diimide

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Nucleic acid assumes a variety of higher-order structures such as base bulge and hairpin, which are associated with many biological functions. Compounds recognizing these structures are important for studying the nucleic acid structure and may serve as new nucleic acid-targeting agents. Many compounds were synthesized from this viewpoint.

We synthesized novel naphthalene diimide **1** carrying two thymine moieties at the termini of both substituents and studied its interaction with several nucleic acids. Because of the steric bulk of thymine substituents, compound **1** shows a decreased affinity for double-stranded DNA and RNA. Instead, **1** showed an increased affinity for single stranded polyA and polydA, owing to the adenine-thymine hydrogen bonding. Furthermore, the binding of **1** is much more favorable for polyA than for polydA, making this compound truly specific for single-stranded RNA (polyA).

In the second step of this research, we studied the interaction of **1** with sA_3 oligonucleotide d(GCGAAACGC) which forms a hairpin structure under ordinary conditions. Surprisingly, a bulged duplex was induced on sA_3 in the presence of **1** as revealed by thermal denaturation studies. The competitive binding to sA_3 of **1** with ethidium bromide supported the notion that **1** interacts with the looped out adenine bases rather than the double stranded region of sA_3. The data obtained here are useful as a new strategy for developing molecules recognizing special structures of nucleic acids.