Monday April 11

Poster Session I
Antiviral Agent Targeting, Synthesis and In Vitro Testing

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Specificity of Viral Proteases:Target for Therapy of Infectious Diseases, Bruce D.Korant, DuPont Experimental Station, Wilmington, Delaware 19898, U.S.A.

Viral diseases are currently a source of extreme concern for those involved in the epidemiology and control of infectious diseases. Compared with antibacterials, the history of viral chemotherapy is a brief one, and not very successful. In part, this is a consequence of the intimate association between viral parasites and the human host cell. Specific chemical intervention becomes very difficult to attain starting with a discovery process dependent on standard viral assay or screening procedures. A more optimistic outlook is possible as studies of the molecular biology of viruses have become increasingly detailed and new targets among viral molecules continue to be identified and described. For example, we have investigated the structure and function of a protease specified by picornaviruses, which is essential for the assembly of new virus particles inside infected cells. The picornavirus protease is a member of the well-known class of thiol active site proteases, but is very selective for a few cleavage sites in viral precursor proteins. The enzyme can be inhibited by compounds reactive with thiol proteases or by peptide structures which mimic the viral cleavage sites. Combining the two classes of compounds yields very potent inhibitors of picornavirus protein processing which are antiviral both in vitro and in vivo. Extending these results may provide a new family of antiviral drugs, if the viral protein cleavage events are programmed by the virus. Recent evidence indicates that, for a series of viral diseases ranging from the common cold to AIDS, our approach is valid.