PREFACE

This issue is the first of the series of the journal "Current Pharmaceutical Design" on antinfecive research. Serving as the lead off issue for the antinfecives, this issue consists of four invited in-depth reviews on recent developments of three major antinfecive therapeutic areas—antibacterial, antifungal and antiviral. It will serve as a survey of current advances in research in these important medical areas. Future issue in this series will consist of shorter and narrower reviews on antinfecive research in specific area.

From the study of early civilizations, we know that chemotherapy was in use long time ago. People used tribal and folk medicines to cure fever and constant coughs. However, it was not until Paul Ehrlich, who put forth the concept of selective toxicity in chemotherapy in 1913 that many antimicrobial agents were discovered. These agents are either isolated from natural sources such as plants, generated from microorganisms, or produced by synthetic means. It was not until after the discovery of penicillin by Sir Alexander Fleming in 1928 and its introduction into clinical practice in early 1940 for the treatment of bacterial infections that there was an enormous worldwide improvement in public health. However, as a result of selective pressure and the use of antibacterial agents, we have seen the rapid emergence of bacterial resistance to antibiotics.

The review entitled "Oxazolidinone Antibacterial Agents" by Dr. Steven Brickner addresses the issue of bacterial resistance. This paper provides the overview of the oxazolidinone antibacterial research with detail description on their synthesis, spectrum of antibacterial activity, mechanism of action, structure activity relationships as well as the toxicity issues. Oxazolidinones are active against important human pathogens, including multiple antibiotic-resistant strains of gram positive organisms.

The paper by Drs. Linus Shen and Daniel Chu on type II DNA topoisomerases as antibacterial target describes the biochemical aspect of DNA topoisomerases with particular emphasis on bacterial DNA topoisomerases II (DNA gyrase) and IV. These two enzymes are important bacterial targets for drug intervention. Inhibitors of these enzymes are useful antibacterial agents for a number of bacterial infections. Design of novel inhibitors can generate novel compounds with activity against multiple resistant bacteria.

Fungi can be considered as opportunity pathogens since most of fungal infections occur in immunocompromised hosts. In recent years, with the advance of medical technology and medical treatment such as organ transplantation, cancer chemotherapy, invasive medical techniques, and the increase of AIDS patients, there is a substantial increase in immunocompromised patients. Because of this increase, the incidence of life-threatening fungal infections has increased dramatically over the past ten years leading to an urgent need for better antifungal agents. The review by Dr. William Turner and Michael Rodriguez on recent advances in the medicinal chemistry of antifungal agents is a timely survey of the recent research in the antifungal area. Advances in polyenes, azoles, cyclic lipopeptide echinocarins, aureosidins as well as pradinicin antifungal agents are being described.

Human immunodeficiency virus (HIV-1) retrovirus has been implicated as the causative agents in AIDS by attacking the lymphocytes of the human immune system. Several potential targets for drug intervention on the replication cycle of the virus within the lymphocytes are actively being worked on by a number of laboratories. These include the prevention of virus' attachment and entry into the cell via specific cell receptor and inhibition of the function of viral reverse transcriptase or viral TAT regulatory protein as well as viral protease activity. The HIV protease is involved in the maturation of newly formed HIV particles through proteolytic processing of the gag and gag-pol gene products. The review entitled "HIV protease inhibitors" by Drs. Dale Kempf and Hing Sham described the current research effort on recent approaches to HIV protease inhibitor design and the identification of potent inhibitors of HIV protease for drug development. The preclinical pharmacokinetic properties of several inhibitors under clinical evaluation are also presented.

I like to thank the editor of this journal Professor Atta-ur-Rahman for his great leadership and invitation to be the guest editor of the antinfecive series. I deeply appreciate and acknowledge the excellent contributions from our authors Drs. Steven Brickner, Dale Kempf, Hing Sham, Linus Shen, William Turner and Michael Rodriguez. Without their sacrificing much personal time and immerse effort that the publication of this issue will not be possible.

Daniel T. W. Chu