Preface

Fig. 1. From the left to the right. First row: Dr. A. Zeevi, Dr. S. Michelson, Dr. I. Lautenschlager, Dr. N. Davis-Poynter, Dr. M.-P. Landini. Second row: Dr. S. Prösch, Mrs. F. Claus-Hahn, Dr. L. van Renterghem, Dr. L. van Poucke, Dr. C. Bruggeman, Dr. A. Ramon, Dr. D. Sedmak, Dr. H. Thé. Third row: Mrs. G. Grauls, Dr. V. Emery, Dr. J. Middeldorp, Dr. J. Neyts, Dr. R. Blok, Dr. C. Söderberg, Dr. V. Goossens, Dr. M. Scholz, Dr. T. Mertens, Dr. F. Kern. Fourth row: Dr. G. Jan, Dr. C. Vink, Dr. J. Waldman and Dr. J.-U. Vogel.

Cytomegalovirus (CMV) is usually harmless and without clinical significance. More than 50% of the world's population are carriers of CMV and therefore host the virus their whole lives, most of them not even knowing that they are infected. So, what keeps us busy and curious is the fascination exerted by CMV, a herpesvirus that is significantly implicated in morbidity and mortality in immunocompromised patients, such as transplanted or AIDS patients. Moreover, evidence is accumulating that

CMV may also be pathogenic in nonimmunosuppressed persons (autoimmunity?).

The management of CMV disease may be an enormous challenge for every clinician when antiviral agents prove to be inefficacious in controlling viremia. It has been suggested that CMV induces aberrant immune reactions that are necessary for its survival and contribute to pathogenesis. However, we still do not know how CMV triggers the immune system in an obviously 'intelligent'

way that enables its escape from the immune system and lifelong persistence in the host. Moreover, in order to disseminate, CMV seems to drive white blood cells to attach to infected host cells, which allows it to live and to 'grab' a comfortable carrier leukocyte within the blood stream. The living and transportation costs of CMV are paid for by the host through modifications of immune responses, which may be subclinical in immunocompetent hosts but highly critical in hosts with naturally or iatrogenically modified immunity. Of course, the concept of unlimited virus production leading to disease (progression) as a result of a decrease in 'controlling' immune cells induced by immunosuppression is generally accepted. But besides the viremia-associated disease, CMV probably also acts 'incognito' through the 'back-door'. More specifically, it has been proposed by several researchers that CMV manipulates the immune system during latency or the immediate early phase of replication. It may be speculated that this (prolonged?) immediate early phase drives the host cell and the immune system to support the persistence and dissemination of the virus. As it leads to tolerance or to aberrant immune responses – both predominant factors in pathogenesis – this modified behavior may be of immunological relevance.

This novel philosophy on the impact of CMV on the host, and the frequent failure of standard antiviral drugs to halt the disease, led us to look for novel therapeutic agents. These drugs should be able both to stop viral replication and inhibit virus-induced immunomodulation. Since CMV immediate early proteins have transactivating properties for viral and cellular genes, it may be important to develop drugs that target CMV immediate early expression.

To obtain clinical success in the treatment of CMV disease, one cannot restrict oneself to inhibiting pathomechanisms in experimental models. It is essential to combine the knowledge and know-how of scientists working in the areas of diagnosis, antiviral therapy, clinical and basic research to solve CMV-related problems in close collaboration.

Two years ago, a small group of researchers from different disciplines gathered for the first time in Frankfurt, Germany, to discuss the multifold aspects of CMV-related immunopathology. The contributions to that meeting were published in *Monographs in Virology*, a Karger book series. To ensure continuity not only in our scientific work, we are pleased to publish the proceedings of this year's meeting in *Intervirology*, which is also published by Karger publishers, whose extended and valuable cooperation we would like to acknowledge.

Furthermore, we would like to express our appreciation to all the scientists who came to Maastricht: first of all, to those who already participated in the Frankfurt meeting and who came in order to discuss the progress accomplished during the past two years, as well as to the 'new' participants. A lot of new data and interesting findings were presented in this meeting, giving us new insights in this complex virus. We learned that during stress situations the virus reactivates, but also some new aspects of the effect of CMV infection on interferon signal transduction. New detection methods for the virus diagnostic laboratories were presented for detection of active CMV infection in transplant recipients and for the detection of congenital infections. Using basic experimental models (in vivo and in vitro) new insights in the pathogenesis of CMV disease and interaction with the immune system were given. Especially, immune escape mechanism of this virus is an intriguing topic. Important findings in the field of antiviral therapy are under development giving promising results for the near future. Some of these new antivirals were presented during this meeting. All these contributions can be found in this issue of *Intervirology*. We thank all contributors for the interesting discussions we had, and are looking forward to the next meeting in 2001.

The sponsors who made this meeting possible are listed on a separate page. We would also like to sincerely thank them and hope that the collaboration between biomedical science and industry will be successful in developing novel strategies in fighting against CMV disease.

Cathrien A. Bruggeman, Maastricht
Albert Ramon, Maastricht
Martin Scholz, Frankfurt/Main