Monoclonal Antibodies Against Five Structural Components of Measles Virus

II. Characterization of Five Cell Lines Persistently Infected with Measles Virus

By

H. SHESHBERADARAN\textsuperscript{1}, E. NORRBY\textsuperscript{1}, and K. W. RAMMOHAN\textsuperscript{2}

\textsuperscript{1} Department of Virology, Karolinska Institutet, School of Medicine, Stockholm, Sweden
\textsuperscript{2} Division of Neurology, University Hospitals, The Ohio State University, Columbus, Ohio, U.S.A.

With 2 Figures

Accepted June 28, 1984

Summary

Groups of monoclonal antibodies against measles virus nucleoprotein (NP), phosphoprotein (P), matrix (M), hemagglutinin (H) and fusion (F) components were used for characterization of 5 persistently infected cell lines. In four of these lines (Lu106 carrier, MaSSPE, MaPi, HEpPi) all cells were infected but the cells mostly produced noninfectious virus products. The fifth line (HNT in vero cells) did not produce any infectious virus and only a fraction of the cells were infected in most passages. In agreement with earlier findings the virus strains showed marked variations in the M epitope pattern and also some variation in the H epitope pattern. In addition epitope variations were found in both NP and P protein, which contrasted with conserved antigen characteristics of these components in lytically replicating virus.

Restriction of fusion in the persistent infections was studied further. HNT and Lu106 cells showed selective quantitative restriction in F protein synthesis. Lu106 cells were found to contain distinct epitopic F species. In contrast MaSSPE cells produced readily detectable cleaved F protein and in addition extracellular virus products carried hemolytic activity. The fact that no cell fusion occurred was interpreted to be due to particular properties of the Ma106 cells, a concept supported by the absence of fusion of these cells when infected with syncytioegenic measles virus. It is concluded that (a)
under conditions of persistence of measles-virus without requirement for synthesis of complete virions a more pronounced variation in epitope characteristics of virus components is encountered than in lytic infections; and b) that persistence of measles virus shows individualistic characteristics which may reflect changes in the virus and/or innate properties of the host cells.

Introduction

Measles virus has been shown to readily establish persistent infections in a variety of mammalian cell systems (22, 28). Interest in these in vitro systems has been prompted by the established causal relationship of chronic measles virus infection to subacute sclerosing panencephalitis (SSPE). There is however a wide degree of variation in the conditions of virus-cell interaction in different in vitro systems. Consequently, the proposed major mechanism(s) involved in the establishment and/or maintenance of these persistent states are at variance. Some studies emphasize the role of temperature-sensitive (ts) mutants (6, 9, 16, 29), others defective-interfering or incomplete virus particles (23, 25) and still others host cell factors (12, 21, 30). Analysis of individual viral proteins in persistent infections has mainly involved use of polyvalent sera which fails to reveal fine changes. More recently monoclonal antibodies have been employed with promising results in studies on the hemagglutinin and matrix protein in two persistent measles virus infections (5, 27).

We have recently prepared monoclonal antibodies against 5 of the 6 structural proteins of measles virus (18) and used them to characterize epitopes on 9 strains of measles virus in productive infections in vitro (26). Using the same bank of hybridomas, in this study we have characterized the viral proteins in 5 persistent measles virus infections in vitro. The persistently infected cell systems were selected to include different viral and cell origins; ts and non-ts virus: systems producing moderate amounts of virus particles which are mainly non-infectious and a highly defective system producing no virus particles. The results indicate that compared to each other and to virus causing lytic infections, virus in persistent infections had accumulated mutations (detectable as epitopic variations). The degree of epitopic variations within and between individual proteins, however, varied between different persistent systems.

Materials and Methods

Virus Strains

The LEC strain, propagated for several years in our laboratory (referred to as LEC-KI), the dilute passaged laboratory Edmonston (EDM/DP) strain and a fresh isolate Hu2 strain was kindly provided by Dr. B. K. Rima, Belfast, Northern Ireland. All strains have been described previously (26).