Immunodominant IgM and IgG epitopes recognized by antibodies induced in enterovirus A71-associated hand, foot and mouth disease patients

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ABSTRACT

Enterovirus A71 (EV-A71) is one of the main causative agents of hand, foot and mouth disease (HFMD). Unlike other enteroviruses that cause HFMD, EV-A71 is more frequently associated with severe neurological complications and fatality. Little is known about the immunogenicity of viral non-structural proteins in humans. Previous studies have mainly focused on characterization of epitopes of EV-A71 structural proteins by using immunized animal antisera. In this study, we have characterized human antibody responses against the structural and non-structural proteins of EV-A71. Each viral protein was cloned and expressed in either bacterial or mammalian systems, and tested with antisera by western blot. Results revealed that all structural proteins (VP1-4), and non-structural proteins 2A, 3C and 3D were targets of EV-A71 IgM, whereas EV-A71 IgG recognized all the structural and non-structural proteins. Sixty three synthetic peptides predicted to be immunogenic *in silico* were synthesized and used for the characterization of EV-A71 linear B-cell epitopes. In total, we identified 22 IgM and 4 IgG dominant epitopes. Synthetic peptide PEP27, corresponding to residues 142-156 of VP1, was identified as the EV-A71 IgM-specific immunodominant epitope; and PEP23 mapped at VP1 41-55 was recognized as the EV-A71 IgG cross-reactive immunodominant epitope. The structural protein VP1 is the major immunodominant site targeted by anti-EV-A71 IgM and IgG antibodies. These data provide new understanding of the immune response to EV-A71 infection, which benefits the development of diagnostic tools, potential therapeutics and subunit vaccine candidates.