Introduction

Dengue fever (DF) and its more severe manifestations, namely, dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), are caused by infection with the mosquito-borne dengue viruses, which are members of family Flaviviridae. There are four closely related, antigenically distinct, serotypes (1-4) of dengue viruses, each of which can cause a severe disease. In recent decades, there has been a dramatic increase in the incidence of dengue infections, with about 100 million cases of DF occurring each year. Globally, about 2.5 billion people are estimated to be at risk from dengue. The lack of a licensed dengue vaccine, in conjunction with predicted climatic changes and population growth is projected to place 5-6 billion people at risk of dengue transmission in the coming decades.

Dengue infections may be clinically inapparent or may result in non-specific febrile illness, DF or DHF. Severe plasma leakage can lead to fatal DSS and mortality rates for untreated patients can be as high as 40-50%. The high mortality associated with DHF and DSS can be significantly minimized through timely medical care, which in turn depends on accurate diagnosis of dengue infections. Several dengue diagnostic kits are available in the market. Currently available commercial dengue diagnostic kits rely on the use of whole virus antigens, and are consequently associated with false positives, due to serologic cross-reactivity, high cost of antigen production, and biohazard risk.

There is a need to develop inexpensive dengue diagnostic intermediates, of high sensitivity and specificity. This thesis describes the design, expression and purification of two novel multi-epitope recombinant proteins, namely, r-DME-G and r-DME-M, along with preliminary evaluation of their utility, for the detection of anti-dengue IgG and IgM, antibodies, respectively, in dengue infected patients. The high epitope density, careful choice of epitopes, and the use of E. coli expression system for their expression, coupled to simple purification, jointly have the potential to lead to the development of an inexpensive dengue diagnostic test, with a high degree of sensitivity and specificity.