REGULATION OF THE HUMAN IMMUNE RESPONSE TO DENGUE VIRUS INFECTION BY AUTO ANTI-IDIOTYPIC ANTIBODIES

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PROBLEM : The technical objectives are :

1. To screen human hybridomas for production of naturally occurring anti-idiotypic antibodies directed against idiotypic determinants on anti-dengue immunoglobulins.

2. To produce and purify these anti-idiotypic antibodies in quantity.

3. To purify from serum the corresponding set of anti-dengue antibodies bearing these idiotypic determinants.

4. To develop immunoassays for detection and quantitation of both the set of idiotype-bearing anti-dengue antibodies and the corresponding anti-idiotype antibodies.

5. To determine the kinetics of both the idiotype bearing anti-dengue antibodies and the anti-idiotype antibodies during natural dengue infections in human.

6. To determine if exogenously added autologous monoclonal anti-idiotype can regulate the production of idiotype bearing antibodies by in vitro cultures of peripheral blood monoclonal leukocytes from humans with acute dengue virus infection. There is a military requirement for research leading to a better understanding of the antibody response to acute dengue virus infection. These infections represent a serious hazard to troops operating in tropical areas.

METHOD : Satisfactory conditions for production of stable hybridomas have been determined. Four fusions of continuous UC729-6 lymphoblastoid cells with peripheral blood mononuclear cells obtained from dengue hemorrhagic fever patients have produced 35 viable clones of hybrid cells. Nineteen of these hybrid clones produced IgM and one produced IgG. Eight of the IgM producing clones are stable and have been grown in continuous culture for more than three months. Antibodies produced by all eight of these clones do not react directly with intact virions. Further characterization of these antibodies, and additional fusions, are in progress.

FUTURE OBJECTIVES : This study is yielding interesting results and plans are to continue it for an additional year.