MONOCLONAL ANTIBODIES IN DERMATOLOGY

THESIS

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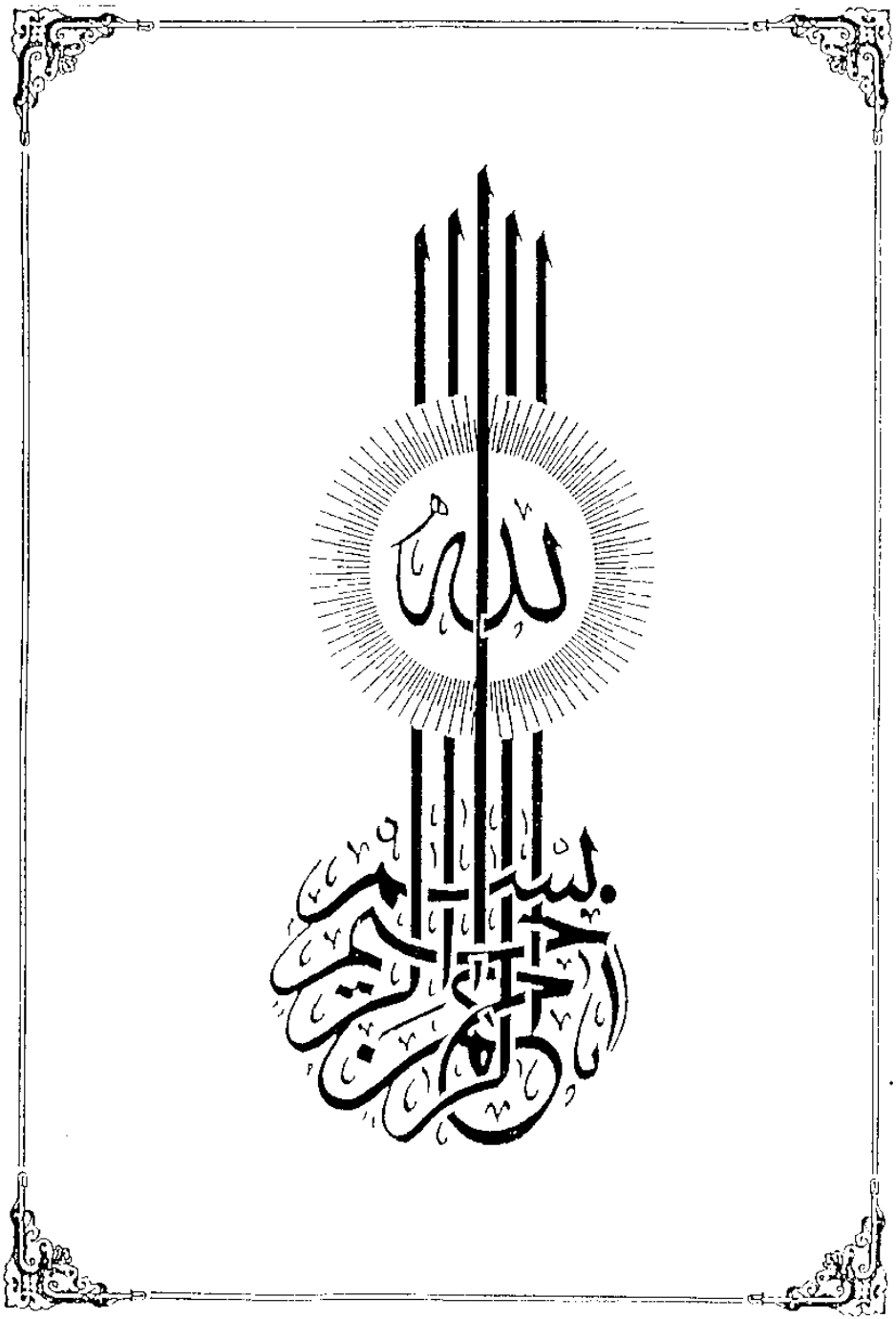

TO

MY FAMILY

AND

MY SON

ACKNOWLEDGEMENT

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C O N T E N T S

INTRODUCTION

I N T R O D U C T I O N

Monoclonal antibodies are antibodies which are produced totally specific for a single antigen. The most significant recent advance in immunology has been the "hybridoma method" of producing monoclonal antibodies (Chu et al., 1983).

It is possible to produce enormous amounts of purified antibody against any antigen that distinguishes human cells from mouse cells. The only ethical and practical means of producing antibodies against human cellular antigens was to immunize experimental animals with human material (Corte et al., 1982).

Available monoclonal antibodies react selectively with helper T cells, suppressor T cells, mature peripheral blood T cells, Langernans' cells and monocytes. Others react with activating antigens, a variety of cellular receptors (e.g. transferrin and sheep erythrocyte receptors), and immune-associated "Ia" antigens (Kung et al., 1980; Sutherland et al., 1981; and Van Wauwe et al., 1981).

Monoclonal antibodies may also serve as carriers of various agents that will destroy a targeted cell

type or as a part of combination chemotherapy protocols. Of great importance, is the development of monoclonal antibodies specifically reactive with malignant cells and non-reactive with normal cells. Such monoclonal reagents will allow selective destruction of neoplastic cells, while conserving normal cells and tissues (Corte et al., 1982).

Monoclonal reagents may also prove to be highly efficacious for immunosuppression therapy in organ transplantation and in the control of autoimmune problems (Kung et al., 1983).

One can anticipate that monoclonal antibodies will revolutionize our concepts of cutaneous diseases by providing a means of tissue analysis far more refined than any previously developed technology. Exactly how far this technology can take our clinical discipline is difficult to predict (Corte et al., 1982). Monoclonal antibodies have in recent years made an enormous impact on many areas of biomedical research but have not yet become widely used in diagnostic immunoassays. It will be necessary to produce and characterize a large number of monoclonal antibodies for a given antigen, in order to identify a few of exceptional properties and to consider various different ways of making use of these in diagnostic and therapeutic methods (Siddle, 1985).

The monoclonal antibodies have begun to assume a significant role in clinical research. The ability to label these agents has initiated research in the areas of radioimmunodetection and radioimmunotherapy. In the cases of antibodies directed against tumor antigens, imaging has been employed to help assessing location and extent of the disease, and to provide information concerning biodistribution to be used in subsequent dosimetric calculations. Careful attention to acquisition parameters and image processing options is needed if these goals are to be achieved (Spies et al., 1987).

B AND T LYMPHOCYTES

B- AND T- LYMPHOCYTES

There are two types of peripheral lymphocytes: T- and B-lymphocytes, both of which arise in the bone marrow. One type migrates to the thymus, where it differentiates to a lymphocyte, and then proceeds to the peripheral lymphoid tissues as a thymus-derived (or T-) lymphocyte. In lymph nodes, T-lymphocytes are located predominantly in the interfollicular cortex (paracortical areas). The other type of lymphocyte - the B-lymphocyte - matures in the bone marrow (Weissman et al., 1978). The term "B-lymphocyte" - meaning bursa-derived lymphocyte - originally was given because, in birds, the bursa of Fabricius is responsible for the maturation of B-cells. Its equivalent in man are probably the tonsils and the lymphoid tissue of the gut. In lymph nodes, B-lymphocytes largely occupy the lymph follicles, whereas, the T-lymphocyte is the effector cell for cellular immunity, the B-lymphocyte mediates humoral immunity. T-cells can exert important regulating functions on both T-cells and B-cells as helper T-cells and suppressor T-cells. Human T-lymphocytes have receptors for sheep

erythrocytes, so that, in the E-rosette assay, sheep erythrocytes [E] form rosettes around T-lymphocytes. The percentage of B cells among lymphocytes in normal adult blood is about 20%, whereas that of T-cells is about 75%. A small percentage of lymphocytes lack surface markers and are referred to as "unidentified" or "null" cells (Luckasen et al., 1974).

B- and T-cells differ as regards:

- The type of receptor they have: T-lymphocytes carry RBC receptors, while B-lymphocytes carry immunoglobulin and complement receptors.
- Their concentration in blood: T-cells are present in large numbers in peripheral blood, while B-cells are less.
- Their functions: In peripheral or secondary lymphoid organs (spleen and lymph nodes), they occupy different places where antigenic stimulation occurs. B-lymphocytes interact with the antigen and transform to plasma cells to form the antibodies. T-lymphocytes undergo a process of blast transformation (Macleod, 1984).

SUBPOPULATIONS OF T LYMPHOCYTES

SUBPOPULATIONS OF T-LYMPHOCYTES

T-cells may be subdivided into effector cells and regulatory cells. Effector cells are lymphocytes involved in delayed hypersensitivity and cytotoxic T-lymphocytes (which destroy cells infected with viruses). Regulatory cells are helper (or inducer) cells and suppressor cells.

The peripheral T-lymphocytes can be subclassified on the basis of "Ly" components on their surfaces (Shiku et al., 1975).

Ly 1, 2, and 3 are three separate surface antigens exclusive to "T" cells. Each one is expressed on immature "T" cells, but either 1, or 2 and 3 are largely lost as the cells mature and differentiate. "Ly" molecules have not been shown to play any part in cell function. The use of monoclonal antibodies (MoAb) has suggested that a similar system of surface antigens exists on human "T" cells (Playfair, 1984).

Approximately, 50% of peripheral T-cells manifest all three "Ly" components analysed (phenotype Ly 1, 2, 3). From these 50%, about 33% are only Ly_1 (phenotype Ly_1) and