REVIEW ON

# HETEROGENEITY IN MACROPHAGE CELL LINE

THESIS

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By

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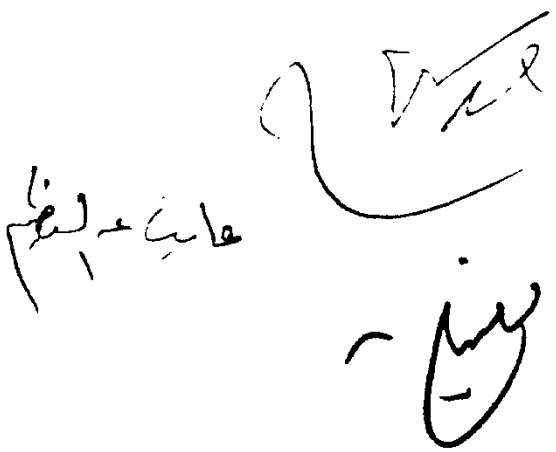

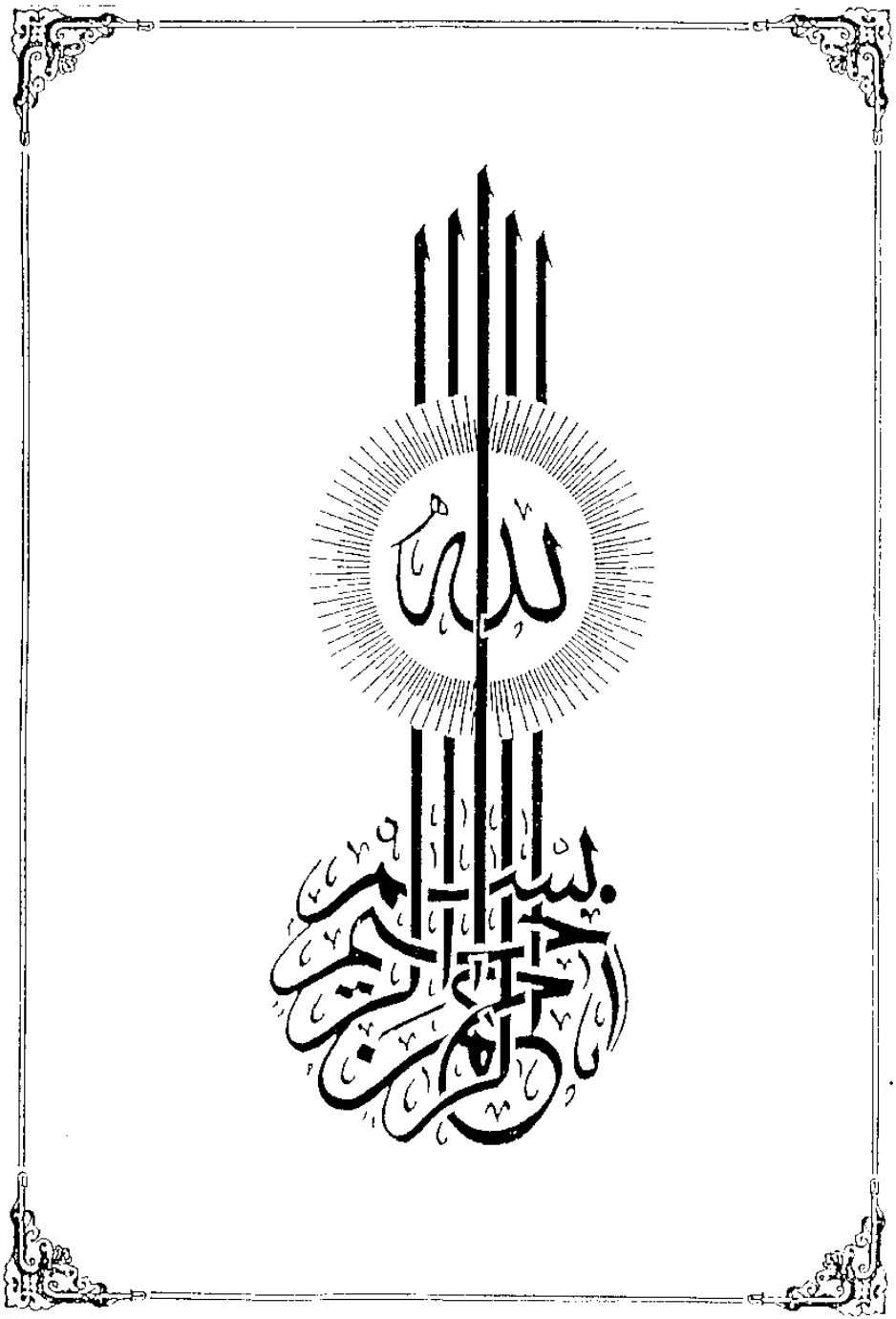

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# INTRODUCTION

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## . Heterogeneity in macrophages:

Populations of macrophage are functionally, morphologically, and cytochemically heterogeneous, but the basis for this diversity has yet to be resolved (Walker, 1982).

Some examples of heterogeneity could be attributed to the effects of the local tissue microenviroment (Ron et al., 1981) while others were best explained by stage of maturation and differentiation of cells belonging to a single lineage (Van Furth et al, 1972).

Finally, data have been obtained supporting the view of multiple lineages of macrophage (Bursuker, 1979)including the existence of self renewing populations (Volkman, 1976).

## . Source of inflammatory macrophages:

Peripheral blood monocytes are the principal source of the heterogenous populations of infl mmatory macrophages found in chronic inflamatory exudates (Van furth , 1975).

Monocytes and macrophages may undergo a variety

of metabolic and functional changes (activation) in responce to different local and systemic stimuli (Cohn ., 1978).

. Function of macrophages:

Several agents that promote the development of chronic inflammation inviv activate monocytes and macrophages invitro to display some characteristics associated with inflammatory macrophages.

An important function of inflammatory macrophages is secretion of biologically active substances. Stimulated macrophages secrete substances in vitro that may mediate inflammatory processes.

. These secretions include:

- Collagenase (Wahl et al., 1977).
- Plasminogen activator (Unkeless et al., 1974).
- Lysosomal enzymes (Schuyler et al., 1978).
- Complement (c) components (Einstein et al., 1976).
- Fibroblast growth factor (Glenn et al., 1981).
- Bone resorbing factor and metabolites of arachidonic acid, including prostaglandin (Goldyne et al., 1981).
- Several agents, including some that interact with specific mononuclear phagocyte surface receptors, induce secretion (Passwell et al., 1979).

# HISTORY

## HISTORY

The history of macrophage is complex. The immunalogical importance given to this cell has varied throughout the years. ( [illegible] )

In 1920 when the understanding of lymphocytes and antibody formation was poor, it was thought that macrophages themselves were responsible for both uptake of antigen and synthesis of antibody (Sabin, 1923). As a consequence, a great part of research in immunology employed techniques which evaluated uptake of antigen or physiology of the macrophage system. Following the recognition that lymphocytes and plasma cells were the cells involved in antibody responses, the interest in macrophage dwindled for a time only to be renewed by Fishman and Adler's provocative observations in the early 1960 (Fishman and Adler 1963) . These authors demonstrated that under certain conditions antibody responses by lymphocytes did not occur upon exposure to antigen alone but rather upon interaction with extracts of macrophages which had previously phagocytized the antigen.

These early experiments were interpreted as denoting that a special processing of antigen by

macrophage was an essential step in immune recognition. The macrophage again was the centre of attention, but only for a short time. Later, as more experimental data became available, it was clear to many that this early interpretation might not be entirely correct.

Subsequent experiments have shown that lymphocytes do interact with antigens bound to macrophages but that this interaction on occasion may not be absolutely necessary and, moreover, may not involve processing of antigen molecules.

A part from its role in the induction of immunity, the macrophage has held the interest of those studying delayed hypersensitivity (or cell-mediated immunities) (Benacerraf and Green 1969). Now macrophage is recognised as one of the cells involved in the nonspecific components of these reactions, playing an essential role in resistance to some bacterial and viral infections (Mackaness and Balden, 1967).

# MACROPHAGE HETEROGENEITY

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It was found that, in rat appropriate stimulation of the peritoneal cavity caused a rapid increase in the absolute number of mecrophages and dramatic change in the proportions of different macrophage subpopulations (Cohn and Benson, 1965).

Because of the heterogeneity of these elicited populations dynamics of peritoneal exudate development was studied. These heterogenous populations differ in many ways (Nelson, 1976) :

I. Heterogeneity in Cytochemestry.
II. Heterogenous morphology.
III. Heterogenous surface properties.
IV. They perform different functions.

### I. Cytochemical heterogeneity:

Quantitative and qualitative changes in rat peritoneal cavity cell population as a function of time following intraperitoneal injection of thioglycollate (TG) broth, an agent commonly used to elicit peritoneal exudat cells (PE) (Bianca et al., 1975).

Comparison between (a) normal steady-state, and (b) TG elicited macrophage populations for their content

of four subpopulations was studied (Forster and Landy, 1981). These subpopulations had distinct ultrastructural peroxidate staining patterns (Unanue et al., 1976) and undergo marked and rapid changes during the course of exudate development. These changes were, studied on suspentions of steady state peritoneal cells and the 4-day TG elicited cells or their content of cells:

1. Cells bearing Fc reseptors (FCR).
2. Complement receptors CR.
3. Cells expressing Ia antigen.
4. Progenator cells that give rise to macrophage colonies invitro.

. Characters of steady State: (Resident macrophages)

The steady state population consisted primarily of macrophages with peroxidatic staining limited to the nuclear envelop (NE) and endoplosmic reticulum such cells are called Resident macrophages (Robert et al., 1983).

. Characters of 4-days TG induced macrophages (Elicited):

- Within hours of TG injection, there was an influx of monocyte-derived exudate macrophage, the number of which reached a maximum, by 24 hr.
- During the next 24 hr the proportion of exudate

macrophages decreased with a concomitant increase in peroxidatic activity (PA)-negative macrophages.

- These two cell types continued to predominate for the next 48 H., during which there was a gradual increase in resident macrophage and so called "exudate-resident" macrophages, the latter of which exhibits both exudate and resident peroxidatic activity (PA) patterns.

- 4-days TG-induced population consisted of four cytochemically distinct macrophage subpopulations :
  1. 50 % PA-negative macrophages.
  2. 25 % exudate macrophage
  3. 15 % resident macrophage
  4. 10 % exudate-resident macrophages

  Sited by (Robert et al., 1983).

II. Morphological heterogeneity:

(a) Normal steady state rat peritoneal cavity cell population consists primarily of:
- 70 % morphologically identifiable macrophages
- 20 % eosinophilic granulocytes.
- small proportion, mast cells and lymphocytes (Beelen et al., 1978).

Macrophages are morphologically heterogeneous, normal steady state macrophage were mature and fully differentiated macrophages (Rhec et al., 1977). Four hours after TG injection, there was a five-fold increase in cell over steady-state levels with a maximum number being reached by 24 hr. (Robert et al., 1983).

(b) The TG-elicited populations: were morphologically heterogenous, the degree of which depended on when the cells were harvested following initiation of the inflamatory response (time factor).

- The majorty of cells present early after the onset of inflammation (16-24 hr) were small, immature monocyte like macrophages.

- During the midphase of the response, larger macrophages containing numerous cytoplasmic inclusions of amorphous material.

- The late phase of response (15-30 days) was characterized by gradual return to a population of macrophage with ultrastructure identity to that of cells in the normal steady state peritoneal cavity. (Robert et al., 1983).