

## CHAPTER 32

### MEDICAL SCIENCES BIOCHEMISTRY

#### Doctoral Theses

295. TYAGI (Manoj)  
**Signalling Mechanism During the Expression of Proinflammatory Cytokines in Asthme : A Study on Role of Protein Kinase C in Macrophage Activation and Release of Interleukin-1Beta.**

Supervisors : Dr. S. K. Bansal and Dr. V. K. Vijayan  
Th 14707

#### *Abstract*

LPS and PMA activate rat peritoneal macrophages as evidenced by the expression of iNOS in a few minutes of exposure to it, and subsequent increase in the production of NO, though its production took about two to three hours after the expression of iNOS. Similarly, the generation of superoxide radicals, which also indicates the macrophage activation, took nearly the same time as taken for NO production. The kinetics of expression of iNOS is comparable to the expression and released minutes after the exposure of the macrophages to these stimuli. The changes may be associated to the changes in signal transduction mechanism, which also revealed the total activity of PKC to be increased in a few minutes after exposure to the stimuli. The changes in PKC activity could be further correlated with the changes in the isoenzyme profile of PKC and phosphorylation of its target proteins. The pattern of changes in this parameter by sphingosine and histamine did not show any definite pattern, but it appears with the analysis of the data that the release of PKC may be associated with the changes in the atypical PKC isoenzyme subtype. The changes observed in the release of IL-1 $\beta$  by healthy human alveolar macrophage in response to these stimuli showed its expression to take place earlier than that by the rat PM. In asthmatics, the release of IL-1 $\beta$  was comparable to its release by healthy human alveolar macrophage in response to these stimuli, suggesting that these stimuli act almost similarly in health and disease with respect to the release of IL-1 $\beta$ .

#### *Contents*

1. Introduction. 2. Review of literature. 3. Objectives. 4. Plan of work. 5. Material and methods. 6. Results. 7. Discussion. 8. Summary and Conclusions. 9. Appendix. 10. Bibliography.