VI. SUMMARY

In an attempt to evaluate the in situ antitumor response of TAM in S-180 ascites tumor of mice the killing activities of the TAM against ATG were studied in vitro. Evaluation of phagocytosis and lysis of ATC by the TAM at different days of tumor growth constituted a major aspect of the study. At the early period of tumor growth the TAM revealed highly phagocytotic and cytolytic activities against ATG. The lysis of ATC was effectively mediated by the antibodies present in the serum of tumor bearing mice which was used to coat the tumor cells. At day 2 of tumor growth the phagocytosis of ATC by the TAM was observed to be at its peak, but the ADCC extended by the cells was negligible and at day 3 the reverse was observed. This suggested presence of different subpopulations of TAM responsible for phagocytosis and ADCC and a differential time course for activation of the subpopulations following tumor inoculation. Both the tumor killing activities were observed to be inhibited with advancement of tumor growth. The heightened phagocytotic and ADCC activity of the TAM were correlated with the target binding ability of the TAM, particularly with the enhanced Fc receptor expression by the TAM. Elevation of in vitro lytic and phagocytotic activities of the functionally
depressed as well as activated TAM was achieved with suitable doses of IMS and Poly 1.8. It was observed that the selection of the potentiating dose of the modulators critically depended on the functional status of the effectors. At proper dose level the modulators could augment both initial target binding and final events of phagocytosis and ADCC by the RM and functionally depressed TAM, but only the later event by the activated TAM.

The lectins, Con A and WGA, were found to be active inducers of LDCC to tumor cells by the TAM at both early and late period of tumor growth. The lectins also additively potentiated the lysis of tumor cells in ADCC and augmented phagocytosis of ATC-mediated by the TAM and RM. Increased target binding by the effectors due to the lectins though could be correlated with the augmented activity of the effectors, was not the sole factor responsible for cytolysis.

The ADCC to ATC mediated by the TAM or RM was totally abrogated with 25mM of D-Mannose, NAcGlc and NAcGal. Glucose at 25mM had a marginal potentiating effect. The preincubation studies indicated that the effects of the sugars were predominantly on the effectors. Though Mannose NAcGlc and NAcGal inhibited target binding
by the effectors, which correlated well with the abrogated ADCC, the phagocytosis mediated by these cells was either enhanced or unchanged in presence of the sugars. Pretreatment of the TAM with Mannose and NAcGlc also inhibited LDCC due to Con A and WGA, respectively.

The observations lead to speculation that lectin like receptors present on the surface of the effector, might be involved in the lytic event of ADCC and LDCC. The sugars might block the receptors and inhibit lysis. Inhibition of binding of antibody coated targets and LDCC might also be a result of steric hinderance of the Fe receptors and the lectin receptors involved in binding antibodies and LDCC, respectively.

Elutrition of TAM subsets on Percoll gradient resulted in four subpopulations of TAM. The ADCC activity of the subpopulations though slightly overlapped, was mainly expressed by the subset 2 obtained at the interphase of 20-40% Percoll. The activity was associated with large, granulated and well differentiated macrophages.