INDUCTION AND PRELIMINARY CHARACTERIZATION OF A TNF-INDEPENDENT TUMORICIDAL ACTIVITY IN SERA OF MICE TREATED WITH *P. ACNES* AND CHALLENGED WITH LPS

G. Schwamberger,E. Ferber, M. Freudenberg, C. Galanos
Max-Planck-Institut für Immunbiologie, Freiburg, Germany

Sera of mice infected with certain bacteria and subsequently challenged with LPS promote hemorrhagic necrosis of some tumors in vivo and display tumoricidal activity against a variety of tumor cell lines in vitro. This activity has been associated with the induction of TNF-α, which is regarded as the central antitumor mediator both in vitro and in vivo. However, discrepancies exist concerning the role of TNF-α as the primary cytotoxic mediator in these processes, since the in vitro cytolytic activity of TNF-α is restricted to a very small number of highly sensitive tumor cell lines. This leaves the possibility that other mediators apart from TNF-α may be operative in the destruction of tumor cells by these sera. We therefore have analyzed such sera for in vitro cytolytic activity against TNF-α resistant murine tumor cell lines and compared this activity to TNF-α. Cytolytic activity was induced in sera of mice treated with *P. acnes* within 2 to 8 hours after LPS-challenge, whereas TNF-α approached a peak value at about 90 min. after LPS injection, and rapidly declined thereafter. Sera, collected 6 to 8 hours after LPS-challenge, containing virtually no detectable TNF-α, displayed cytolytic activity against a variety of tumor cell lines, whereas normal nontumorigenic cells were not affected. In contrast to TNF-α, this activity was inactivated by preincubation at 56°C but could not be inhibited by neutralizing antibodies against TNF-α. We thus conclude, that these sera contain a previously unrecognized tumoricidal activity distinct from TNF-α, which may also constitute a mediator for LPS-induced tumor regression in vivo. Based on preliminary biochemical data as well as functional criteria, this activity is also distinct from other known cytokines, but seems to be closely related to a novel high molecular weight tumoricidal activity of murine macrophages termed MTC 170, which constitutes a major effector pathway for the specific destruction of tumor cells by activated macrophages.

Eur Cytokine Netw **5**:220. 1994