Short Report

The Role of Monocytes and Prostaglandin E in the Regulation of Mitogen Response

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ENDO, F., SASAKI, T., SEKIGUCHI, Y., HARUYAMA, T., SATO, M., ABE, K, and YOSHINAGA, K. The Role of Monocytes and Prostaglandin E in the Regulation of Mitogen Response. Tohoku J. exp. Med., 1981, 133 (1), 119-120 —— The incubation of human monocyte rich fraction with PWM and SRBC revealed the production of significant amount of PGE in the supernate, suggesting the participation of PGE produced by monocytes in mitogen response. Con A-induced 3H-thymidine incorporation by lymphocytes was enhanced by addition of monocytes, and was further increased in the presence of indomethacine. These indicate that monocytes have helper effect in mitogen stimulation and are regulating the response through the production of PGE. monocyte; prostaglandin E; mitogen response

Prostaglandins (PGs) suppress lymphocyte transformation (Goodwin et al. 1977a) and antibody production (Webb et al. 1977), and it is known that blocking of PG synthesis recovers cellular immunity in tumor-transplanted mice and even leads to the tumor regression (Plescia et al. 1975). Goodwin et al. (1977b) reported that decreased 3H-thymidine incorporation in patients with Hodgkin's disease was restored by addition of indomethacine, a PG synthetase inhibitor. PGs were also demonstrated to be produced even without mitogen stimulation by glass-wool adherent cells, probably monocytes. However, it has not been clearly known if endogenous PG production by monocytes would significantly increase in mitogen-stimulated reaction. This experiment was carried out to examine the relation of monocytes and PGE in mitogen stimulation in man.

Monocyte rich fraction was separated from human peripheral mononuclear cells by adherence to a plastic dish coated with fetal calf serum and incubated for 48 hr (Kumagai et al. 1979). The culture fluids were assayed for PGE by radioimmunoassay (Abe et al. 1977). Marked production of PGE was observed by increasing numbers of adherent cells, especially in the presence of pokeweed mitogen (PWM) and sheep red blood cells (SRBC), showing increased synthesis of PGE by monocytes in antigen and mitogen stimulation (Fig. 1). Next, in order to investigate the relation of monocytes and PGE in concanavalin A (Con A)-induced lymphocyte transformation, monocytes were added in different numbers to constant non-adherent cells with or without indomethacine in the culture. Fig. 2 shows that the fraction of non-adherent cells, which contained 2.5% monocytes, incorporated approximately 7 x 10^4 cpm of 3H-thymidine. Addition of indomethacine did not induce the enhanced response to Con A in this fraction. On the other hand, increase in monocyte concentration significantly enhanced the incorporation as much as to 10 x 10^4 cpm. In parallel with this response PGE was detected increasingly in the culture (data not shown). Then, addition of indomethacine was observed to increase further the incorporation respectively, indicating that the immune regulation via PG was blocked. These data

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presented above suggest two lines of evidence. First, there is a significant production of PGE by monocytes in mitogen stimulation. Second, lymphocyte transformation is enhanced by the presence of monocytes and is further increased by addition of indomethacin. These facts show that monocytes have dual effects on mitogen stimulation, namely, while they enhance mitogen response of lymphocytes, their product, PGE acts suppressively on the reaction.

Fig. 1

Fig. 1. PGE production by monocyte rich fraction cultured for 48 hr with or without PWM and SRBC. Adherent cells contained 82% monocytes, determined by phagocytosis and esterase stain. •—•, with PWM and SRBC in the culture; ○—○, without PWM or SRBC in the culture.

Fig. 2

Fig. 2. Effect of indomethacin on Con A-induced ³H-thymidine incorporation by lymphocytes in connection with the concentration of monocytes. 1 X 10⁵ non-adherent cells were incubated for 72 hr with or without indomethacin (0.5 µg/ml) in the presence of Con A (10 µg/ml) and different concentrations of monocytes in the culture. Adherent cells contained 90% monocytes and non-adherent cells 2.5%, determined by phagocytosis, and ³H-thymidine incorporation was adjusted to cpm per 1 X 10⁵ lymphocytes. □—□, with indomethacin in the culture; □—□, without indomethacin in the culture.

References


