Short Communications

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Disodium Cromoglycate Inhibits Immunoglobulin Production in vitro without Affecting Cell Growth in Human B Cell Lines

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Abstract

The effect of disodium cromoglycate (DSCG) on human B cell lines (IM-9, GM-1056, and AF-10) was studied. DSCG inhibited immunoglobulin production by these B cell lines without affecting thymidine uptake or cell number. Thus, in addition to its antiallergic function, DSCG may also act as a B cell-modulating reagent in vitro.

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Disodium cromoglycate (DSCG) has been reported to inhibit histamine release from mast cells [1], activation of inflammatory cells including neu-trophils, eosinophils, and monocytes [2] and antibody-dependent granulocyte-mediated cytotoxicity [3]. We have previously reported that topical application of DSCG solution was effective in the treatment of atopic dermatitis [4]. Moreover, DSCG inhibited human allergic skin reactions in vivo [5]. These results indicate that DSCG can modulate immune responses both in vitro and in vivo. However, the effect of DSCG on B cell response in vitro has not previously been studied. Thus, the effect of DSCG on human B cell immunoglobulin (Ig) production and thymidine uptake has been studied by using human B cell lines, IM-9 (obtained from the Japanese Cancer Research Resources Bank), GM-1056 (obtained from the NIGMS Human Genetic Mutant Cell Depository, Camden, N.J.) and AF-10 (a kind gift from Dr. Andrew Saxon, UCLA, Los Angeles, Calif.) [6]. These lines produce IgG, IgA, and IgE, respectively [6]. Each cell line was cultured (1×10^3 /200 μ l/well) in 96-well U-bottom microtiter plates (Coster, Cambridge, Mass.) for 4 days with various concentrations of DSCG in RPMI-1640 medium containing 10% fetal calf serum, 2 mM glutamine, 50 U/ml penicillin, and 50 μ g/ml streptomycin. The amount of Ig in the culture supernatants was measured by ELISA [7], and cell numbers were counted simultaneously. Cells were also pulsed with 1 μ Ci [3 H]-thymidine 8 h before harvest, and thymidine uptake was measured [7].

As shown in figure 1, DSCG inhibited Ig production from IM-9, GM-1056, and AF-10 at 10^{-6} and 10^{-5} M ($p < 0.01$). In contrast, neither thymidine uptake nor cell number was affected by DSCG at any concentration tested (fig. 2). Thus, inhibition of Ig production by DSCG was not due to a decrease in cell growth. It has been reported that in patients on DSCG treatment, IgA concentrations in bronchoalveolar lavage were decreased while there was no decrease in lymphocyte number [8]. This is in agreement with the results of this study: inhibition of IgA production without affecting cell growth. We have previously reported that Ig production from these cell lines was not inhibited by various cytokines including IL-1 β , IL-2, IL-4, IL-6, TNF- α ,

GM-CSF, IFN- α , IFN- β , and IFN- γ [7]. The mechanisms of this inhibition are now under investigation. DSCG may have acted directly on B cell lines and inhibited Ig production. Alternatively, DSCG may act on B cell lines to produce some inhibitory cytokines, which then inhibit Ig production.

Taken together, these data may indicate that, in addition to its antiallergic function, DSCG may act as a B cell regulatory reagent.

Disodium Cromoglycate Inhibits Immunoglobulin Production

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Concentrations of DSCG (M)

Fig. 1. Effect of DSCG on Ig production by B cell lines. IM-9 (A), GM-1056 (B), and AF-10 (C) were cultured with various concentrations of DSCG for 4 days, and Ig production was measured. Results are expressed as the mean $\pm$ 1 SD of the percent change of control from triplicate cultures. Control Ig production from IM-9, GM-1056 and AF-10 was 9.2 ± 1.0 ng/ml IgG, 28.0 ± 3.1 ng/ml IgA, and 44.2 ± 1.5 ng/ml IgE, respectively.

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Concentrations of DSCG (M)

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Concentrations of DSCG (M)

Fig. 2. Effect of DSCG on thymidine uptake and cell number by B cell lines. IM-9 (•), GM-1056 (O), and AF-10 (A) were cultured with various concentrations of DSCG for 4 days. Thymidine uptake (A) and cell number (B) were measured. Results are expressed as the mean $\pm$ 1 SD of the percent change of control from triplicate cultures. Control thymidine uptake (cpm) by IM-9, GM-1056, and AF-10 was $2,432 \pm 246$, $3,573 \pm 360$ and $1,364 \pm 179$, respectively.

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