

CORRESPONDENCE/REBUTTAL

Comment on Inhibitory Effect of (–)-Epigallocatechin 3-Gallate, a Polyphenol of Green Tea, on Neutrophil Chemotaxis in Vitro and in Vivo

Sir: In a recent report by Takano et al., (–)-epigallocatechin 3-gallate (EGCG), a major component of green tea catechin, was shown to inhibit the neutrophil infiltration to the sites of inflammation (1). This inhibitory effect was neither dependent on the cytotoxicity of EGCG nor affected by the type of chemoattractants. Although a clear dose-dependent inhibition was confirmed, the mechanisms regulating this inhibition were not clarified. In our recent paper, we demonstrated the suppressive effect of EGCG on the migration of CD11b(+)CD8(+) T cells, which was dependent on the direct binding of EGCG to the cell surface CD11b, and the consequent inhibition of the binding to its specific ligands (2). The same mechanism should also be involved in the suppression of neutrophil infiltration reported by Takano et al.

CD11b is a member of α -chain integrin and forms a complex with β 2-integrin as Mac-1. CD11b is expressed on neutrophils, monocytes, NK cells, and a subset of CD8(+) T cells. It plays a central role in mediating the migration of neutrophils from peripheral blood to sites of inflammation. CD11b contributes to firm leukocyte adhesion, not only to the endothelium via the intercellular adhesion molecule 1 (ICAM-1) but also to the underlying subendothelium and interstitial extracellular matrix by binding diverse kinds of ligands.

In our study, we demonstrated that EGCG strongly bound to the cell surface CD11b and competitively inhibited the specific-antibody binding to CD11b expressed on T cells, neutrophils, and monocytes. Furthermore, binding of EGCG to CD11b on CD11b(+) T cells resulted in a significant decrease in the ability of these cells to bind ICAM-1. The migration of T cells was

also inhibited, regardless of the type of chemoattractant tested. This suppressive effect of EGCG on the CD11b function needed only a few minutes to develop, which is also consistent with the findings of Takano et al., where the effective inhibition of neutrophils chemotaxis could be achieved by 20 min of exposure to EGCG.

In summary, our findings on the effect of EGCG on CD11b(+) T cells strongly corroborate the report by Takano et al. Further investigation of the mechanism of EGCG-induced suppression could be achieved if extracellular matrix proteins other than the ligands of CD11b, such as fibronectin, are used to coat the membrane in migration assays.

LITERATURE CITED

- (1) Takano, K.; Nakaima, K.; Nitta, M.; Shibata, F.; Nakagawa, H. Inhibitory effect of (–)-epigallocatechin 3-gallate, a polyphenol of green tea, on neutrophil chemotaxis in vitro and in vivo. *J. Agric. Food Chem.* **2004**, *52*, 4571–4576.
- (2) Kawai, K.; Tsuno, N. H.; Kitayama, J.; Okaji, Y.; Yazawa, K.; Asakage, M.; Hori, N.; Watanabe, T.; Takahashi, K.; Nagawa, H. Epigallocatechin gallate attenuates adhesion and migration of CD8+ T cells by binding to CD11b. *J. Allergy Clin. Immunol.* **2004**, *113*, 1211–1217.

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