

# Cancer prevention by bovine lactoferrin and underlying mechanisms — a review of experimental and clinical studies

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**Abstract:** In experimental studies, bovine lactoferrin (bLF) has been found to significantly inhibit colon, esophagus, lung, and bladder carcinogenesis in rats when administered orally in the post-initiation stage. Furthermore, concomitant administration with carcinogens resulted in inhibition of colon carcinogenesis, possibly by suppression of phase I enzymes, such as cytochrome P450 1A2 (CYP1A2), which is preferentially induced by carcinogenic heterocyclic amines. Enhancement of the activities of their phase II counterparts, such as glutathione *S*-transferase might have also played a critical role in post-initiation suppression in a study of tongue carcinogenesis. Anti-metastatic effects were moreover detected when bLF was given intragastrically to mice bearing highly metastatic colon carcinoma 26 cells (Co 26Lu), with apparent enhancing influence on local and systemic immunity. Marked increase in the number of cytotoxic T and NK cells in the mucosal layer of the small intestine and peripheral blood cells was thus found, this in turn enhancing the production of Interleukin 18 (IL-18) and caspase-1 in the epithelial cells of the small intestine, with possible consequent induction of interferon (IFN)- $\gamma$  positive cells. Furthermore, bLF has been found to exert anti-hepatitis C virus (HCV) activity in a preliminary clinical trial in patients with chronic active hepatitis due to this virus, a main causative factor in hepatocellular carcinoma development in Japanese. More extensive clinical trials are now underway in the National Cancer Center Hospital and other institutes to further explore the preventive potential against colon carcinogenesis.

*Key words:* lactoferrin, chemoprevention, colon, carcinogenesis, metastasis.