EGCG downregulates IL-1RI expression and suppresses IL-1-induced tumorigenic factors in human pancreatic adenocarcinoma cells.

Abstract:

Human pancreatic cancer is currently one of the fifth-leading causes of cancer-related mortality with a 5-year survival rate of less than 5%. Since pancreatic carcinoma is largely refractory to conventional therapies, there is a strong medical need for the development of novel and innovative therapeutic strategies. Increasing evidence suggests an association of carcinogenesis and chronic inflammation. Because IL-1 plays a crucial role in inflammation-associated carcinogenesis, we analyzed the biological effects of IL-1 and its modulation by the chemopreventive green tea polyphenol (−)-epigallocatechin-3-gallate (EGCG) in the human pancreatic adenocarcinoma cell line Colo357. Proinflammatory IL-6 and PGHS-2 as well as proangiogenic IL-8 and VEGF were induced by IL-1, whereas the secretion of invasion-promoting MMP-2 remained unaffected. IL-1 responsiveness and constitutive MMP-2 release in Colo357 were downregulated by EGCG in a dose- and time-dependent manner. Moreover, EGCG reduced cell viability via induction of apoptosis in Colo357. Since EGCG effects on cytokine production precede reduction in cell viability, we hypothesize that these findings are not only a result of cell death but also depend on alterations in the IL-1 signaling cascade. In this context, we found for the first time an
EGCG-induced downregulation of the IL-1RI expression possibly being caused by NF-κB inhibition and causative for its inhibitory action on the production of tumorigenic factors. Thus, our data might have future clinical implications with respect to the development of novel approaches as an adjuvant therapy in high-risk patients with human pancreatic carcinoma.