The role of sirtuin 3 in the differential pro-oxidant effects of (-)-epigallocatechin-3-gallate (EGCG) in oral cells

Abstract

Each year, over 640,000 new cases of oral cancer occur worldwide. The development of therapeutic and preventive strategies, including dietary approaches, is important for reducing oral cancer burden. (-)-Epigallocatechin-3-gallate (EGCG), the major polyphenol in green tea, has been reported to have both anticancer and cancer preventive effects. Previously, we found that EGCG induced mitochondrial dysfunction, oxidative stress and apoptosis in oral cancer cells but exerted antioxidant effects in normal oral cells. However, the mechanism by which EGCG causes these differential effects remains unclear. In this study, we will investigate the role of sirtuin 3 (SIRT3), an important mitochondrial redox balance regulator, in EGCG-induced differential pro-oxidant effects in oral cells. We will first determine if EGCG differentially regulates SIRT3 mRNA and protein levels, as well as, activity in oral cancer and normal cells. We will further determine if EGCG modulates the *SIRT3* gene expression by regulating the activity of the estrogen-related receptor alpha (transcription factor) and the peroxisome proliferator-activated receptor gamma coactivator 1 alpha (co-activator). To our knowledge, this study will be the first to identify how EGCG exerts differential pro-oxidant effects in oral cells by targeting SIRT3. The results will provide additional mechanistic information that can be further developed in animal studies.