EGCG, A GREEN TEA POLYPHENOL, INDUCES DIFFERENTIATION OF NORMAL HUMAN EPIDERMAL KERATINOCYTES.

Sivaprakasam Balasubramanian[1], Michael T. Sturniolo[1] and Richard L. Eckert[1]
1: Department of Physiology and Biophysics, Case Western Reserve University School of Medicine, 2109 Adelbert Road, Cleveland, Ohio 44106-4970, USA.

Epigallocatechin-3-gallate (EGCG) is an important chemopreventive agent derived from green tea. We recently reported that EGCG treatment enhances keratinocyte differentiation as evidenced by increased human involucrin promoter activity and gene expression and reduced cell viability (Balasubramanian *et al*., J. Biol. Chem., 277, 828-836, 2002). However, induction of keratinocyte differentiation markers is not casually associated with reduced cell survival. Thus, we sought to identify the mechanism responsible for the EGCG-dependent reduction in keratinocyte viability. In the present study we show that EGCG treatment does not increase apoptosis-associated caspase (caspase-3, -8, -9) activity or alter the ratio of Bcl2/Bax. Moreover, treatment with the pan-caspase inhibitor, Z-VAD-FMK, does not reverse the EGCG-associated reduction in cell viability. Instead, reduced cell viability is associated with activation of type I transglutaminase. This is evidenced by direct assay, and by the ability of EGCG to stimulate covalent incorporation of fluorescein cadaverine substrate into cross linked intracellular structures. EGCG treatment markedly increases the expression of procaspase-14, a marker of keratinocyte differentiation. Our results suggest EGCG promotes differentiation-associated changes in human epidermal keratinocytes.