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Triphlorethol-A Activates Heme Oxygenase-1 in Lung Fibroblast Cells via Up-Regulation of NF-E2 Related Factor 2

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Recently, we reported that triphlorethol-A, a phlorotannin found in *Ecklonia cava* (brown alga), showed cytoprotective activity against oxidative stress through activation of antioxidant enzymes. In this work, we assessed the ability of triphlorethol-A to up-regulate heme oxygenase-1 (HO-1) expression via activation of NF-E2 related factor 2 (Nrf2) in V79-4 lung fibroblast cells. Nrf2 is a transcription factor involved in the cellular protection against oxidative stress through antioxidant response element (ARE)-directed induction of several phase 2 detoxifying and antioxidant enzyme such as HO-1. Here, we report that triphlorethol-A induces HO-1 expression via the ARE-mediated transcriptional activation of Nrf2. Moreover, V79-4 cells treated with triphlorethol-A exhibited activation of extracellular signal regulated protein kinase (ERK). U0126, a specific inhibitor of ERK kinase, attenuated triphlorethol-A induced HO-1 expression. Taken together, these data suggest that triphlorethol-A augments cellular antioxidant defense capacity through induction of HO-1 via Nrf2-ARE signaling, thereby protecting V79-4 cells from oxidative stress.