Areca nut extract up-regulates vimentin expression in oral cancer cells through the activation of ERK and COX-2 signalings

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Areca chewing is highly associated with the prevalence of oral carcinomas in Asians. Areca nut was approved a group I carcinogen by IARC in 2004. Vimentin is a mesenchymal intermediate filament that is also a marker for cells undergoing epithelial-mesenchymal transition (EMT). With 10 μg/ml subtoxic ANE treatment, OECM-1 oral carcinoma cells appeared the fibroblastoid cellular change, loss of membranous E-cadherin, and increase of vimentin and fibronectin, which were EMT-associated. ANE activated PI3K/AKT, ERK and NF-κB pathways in OECM-1 cells. The activation of the ERK but not PI3K/AKT activation was responsible for the COX-2 up-regulation and PGE2 production. Blockage of PI3K/AKT, ERK and COX-2 all attenuated the up-regulation of vimentin induced by ANE, while PGE2 treatment up-regulated vimentin expression. With curcumin treatment, ANE-induced NF-κB activation, and COX-2 and vimentin expression was attenuated, but the ERK pathways was affected. It might suggest the involvement of NF-κB activation for ANE-induced vimentin expression. The ERK activation and subsequent COX activation for vimentin up-regulation mediated by ANE treatment was also present in OC3 oral cancer cells. Our findings identified the signaling mechanisms for vimentin expression in areca-associated oral cancer cells, which might underlie the progression of oral carcinomas.