Smoking and smoking cessation

Intermittent Hypoxia and cigarette smoke - The Effect on Nrf2 nuclear localization in HaCaT keratinocytes

K. Avezov[1,2], D. Aizenbud[1,3], *A. Z. Reznick[3], L. Lavie[2]
[1]Rambam Health Care Campus, Orthodontic and Craniofacial Department (Haifa, Israel, Israel)
[2]Technion - Israel Institute of Technology, Lloyd Rigler Sleep Apnea Research Laboratory, Department of Anatomy and Cell Biology, Rappaport Faculty of Medicine (Haifa, Israel, Israel)
[3]Technion - Israel Institute of Technology, Department of Anatomy and Cell Biology, Rappaport Faculty of Medicine (Haifa, Israel, Israel)

The transcription factor Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) is known to be activated and translocated to the nucleus under oxidative stress (OS), in order to promote cellular antioxidant response systems. Oral cavity tissues are a unique environment constantly exposed to internal and external hazards and OS inducers. One such known OS inducer is cigarette smoke (CS). Cycles of hypoxia/reoxygenation related to obstructive sleep apnea, termed intermittent hypoxia (IH), also promote oxidative stress. Very little is known about the regulation of antioxidant defenses including the Nrf2 pathway in the oral environment. In a pilot study, the role of Nrf2 nuclear localization in HaCaT keratinocytes was examined under CS and IH, to possibly identify a common pathways of antioxidant responses in the oral cavity.

HaCaT cells, representing oral keratinocytes, were exposed to 10 IH-cycles (5-20% oxygen) during 4-hours using the BioSpherix OxyCycler-C42 system. Control cells were maintained in normoxic conditions for the same duration. In parallel experiments, HaCaT cells were exposed to whole phase CS for 3 hours using a unique smoking simulator apparatus that mimics the exposure in smokers. Nrf2 nuclear localization was observed using confocal microscopy. Cellular OS was established by DCF (2,7-dichlorodihydrofluorescein) assay.

Nrf2 specific nuclear fluorescence was increased by 4-fold following CS exposure and by 2.5-fold after IH cycles, as compared to control cell cultures. Nuclear size and shape remained similar in all experiments.

Further research is warranted to evaluate Nrf2 as a common mechanism of antioxidant response in HaCaT cells, following exposure to various OS inducers.