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### **Repeated exposure to cigarette smoke increased gingival fibroblast proliferation, telomerase activity through the activation of cell cycle genes activity**

Mahmoud Rouabhi<sup>1</sup>, Witold Chmielewski<sup>1</sup>, Abdullah Alami<sup>1, 2</sup>, Eric Jacques<sup>1</sup> and Abdelhabib Semlali<sup>2</sup>

<sup>1</sup>Laval University, Canada

<sup>2</sup>King Saud University, Saudi Arabia

**Aim:** The aim of this study was to investigate the effect of repeated exposure to cigarette smoke condensate (CSC) on the survival, oncogenes profiling, telomere length and telomerase activity of primary human gingival fibroblasts.

**Methods:** Primary human gingival fibroblasts were exposed three times a day during 15 min to CSC at one of the following concentrations: 0, 2, 5 or 10%. The exposure periods were 10, 20 or 30 days. Cell proliferation was evaluated by mean of BrdU assay. Oncogenes and Tumor Suppressor Genes profiling was performed by using PCR Array. Protein telomerase detections were determined by protein telomerase assay. Telomere restriction fragment analysis was performed using the TeloTAGGG Telomere Length Assay Kit.

**Results:** Exposure to low concentration of CSC led to a significant increase in cell growth. Cell proliferation was starting from 10 days post exposure and maintained up to 20 days. Gene profiling demonstrated that CSC modulates the oncogenes pathway increasing CDK4, SRC JUND, NFKBIA and PIK/CA but decreasing other genes such as CASP8, RARA. Tumor suppressor genes pathway mostly showed repressed genes such as BRCA2, WWOX and BRCA1. When analyzing apoptosis genes pathway, multiple genes were repressed including BCL2, MCL1. Apoptotic gene activation is supported by the repression of those genes involved in cell cycling were we found decreased expression of TP53, CCND1 and BRCA2. The changes in gene expressions were confirmed by telomerase activity analyses showing significant ( $p < 0.01$ ) increase when the cells were exposed to CSC for 10 and 20 days. It is interesting to note that, greater the CSC concentration higher was the telomerase activity supporting the telomere length shortening following cell exposure to 10% CSC for ten days.

**Conclusion:** CSC increased fibroblast cell division through the modulation of different oncogenic genes. CSC also increases telomerase activity and a slight telomere length shortening. Overall, this study demonstrated that cigarette smoke deregulates cell cycle genes with potential cell mutation and cancer initiation/development.

#### **Biography**

Mahmoud Rouabhi is a full Professor at the Faculty of Dentistry of Laval University. He is a senior scientist in the field of immunology, cell biology, and tissue engineering. He got his PhD in France, followed by a Postdoctoral training for four years in Canada. His research interest includes studying the interaction between host & oral microorganisms, the role of local innate immunity, investigating the tobacco effect on the oral cavity, etc. He has more than 130 pair reviewed scientific publications. He is the editor/coeditor of three books. He published over 15 book chapters/review articles, and two patents.

[Mahmoud.Rouabhi@fmd.ulaval.ca](mailto:Mahmoud.Rouabhi@fmd.ulaval.ca)

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