

3rd International Conference on

Molecular Biology & Nucleic Acids

August 27-28, 2018 | Toronto, Canada

The potential protective role of urokinase plasminogen activator against oxidative induced DNA damage in periodontal ligament tissue

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There is a high concentration of urokinase plasminogen activator (uPA) in gingival cervical fluid and saliva. However, still not much is known about the physiological role and function of this serine protease in oral tissue. The aim of the present study was to investigate the effect of urokinase in DNA damage and repair process outcome after exposure to oxidative stress in fibroblasts derived from periodontal ligament (PDL) and to propose a new protective role for uPA in an oral cavity. To this aim, PDL fibroblasts were isolated from human wisdom teeth of healthy donors and were pre-incubated with urokinase or amiloride, a urokinase inhibitor, followed by exposure to the different concentrations of H₂O₂. After peroxide treatment, cells were re-incubated with urokinase. Cell viability and apoptosis were assessed by MTT and Annexin V/PI assay, respectively. The level of γ H2AX expression was studied as a sensitive marker of DNA damage using immune staining and flow cytometry. Alkaline comet assay was performed to detect DNA damage single and double-strand breaks. Our results showed that pre-incubation of the peroxide-treated cells with urokinase significantly increased cell viability and decreased cell apoptosis. Furthermore, there was a significant decreased in the expression of γ H2AX after peroxide treatment in cells incubated with urokinase. Oxidative stress-induced DNA damage breaks were reduced in urokinase-treated groups as measured by comet assay. However, inhibition of urokinase with amiloride, in turn, resulted in higher level of DNA damage breaks and increased apoptotic cells after exposure to peroxide. The present study suggested a new protective role for urokinase plasminogen activator against oxidative-induced DNA damages in oral tissue. As the oral cavity is constantly exposed to the oxidative agents, decreased in urokinase expression in saliva might be a marker for the subsequent development of the oral injury.

Biography

Her research is focused on evaluating the molecular basis of DNA damage and repair pathways. Of particular importance in her current research is assessing the role of urokinase plasminogen activator in DNA repairing pathways associated with oral disease. Another line of her research involves the study of genetic and epigenetic influences of environmental toxicants. She has a Ph.D. in molecular biology from Hannover Medical School, Germany. Her Ph.D. research project entitled "Urokinase plasminogen activator receptor in DNA damage repair mechanism and senescence". She has also completed two postdoctoral research associate jobs, one at the Max Planck Institute of Immunobiology and epigenetics and one at the toxicology department, the Institute of pharmaceutical science, Tehran University of medical sciences.

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