

## Molecular and cellular response of oral cavity cells to tobacco preparations

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We examined the effects of reference tobacco product preparations on cytotoxicity and DNA damage in human oral cavity cells. An oral carcinoma cell line (101A), normal gingival epithelial cells (HGEC), and gingival fibroblasts (HGF) were treated with total particulate matter from 3R4F cigarettes (TPM), 2S3 smokeless tobacco extracted with complete artificial saliva (ST/CAS), whole-smoke conditioned media (WS-CM) or nicotine alone (NIC). Cytotoxicity EC-50 values, as determined using sulforhodamine B assays, varied widely among the cell types and agents. When normalized to nicotine content, cytotoxicity for WS-CM and TPM was higher than that for ST/CAS at either low or high doses. Intriguingly, nonmalignant HGEC and HGF cells were more resistant to tobacco product exposure than the carcinoma cells. DNA damage in cells was assessed by alkaline Comet assays and immunofluorescence for the damage-specific protein  $\gamma$ -H2AX. Both methods showed that only TPM caused substantial DNA breaks in exposed cells whereas ST/CAS or NIC did not. Again, the malignant 101A cells were more susceptible to DNA damage than the normal HGEC and HGF cells. These preliminary studies demonstrate that combusted tobacco products (TPM, WS-CM) can cause substantial cytotoxicity and DNA damage in oral cavity cells, whereas non-combusted products (ST/CAS, NIC) exert no or only minimal DNA damage. The data will assist in evaluating genotoxic and other harmful effects of different types of tobacco products on oral cavity cells, and help to understand the involvement of combusted versus non-combusted tobacco products in the etiology of oral cancers.

### Biography

Wolfgang Zacharias completed his Ph.D in Biochemistry in 1980 at the University of Marburg, Germany, and performed postdoctoral studies at the University of Wisconsin at Madison, WI, USA. He is Professor in the Dept. of Medicine and the J. G. Brown Cancer Center, with a joint appointment in the Dept. of Pharmacology & Toxicology, University of Louisville, KY, USA. He has published more than 60 papers in peer-reviewed journals and has worked for over 10 years on molecular biological mechanisms relevant to oral cancer progression, including the effects of tobacco product components on oral cavity cells.

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