THE GRADUATE COLLEGE OF THE
UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER

ANNOUNCES THE FINAL EXAMINATION OF

Jimmy Manyanga

FOR THE DEFENSE OF THE DOCTOR OF PHILOSOPHY DEGREE
GRADUATE COLLEGE
Department of Cell Biology

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Electronic Cigarettes: Implications on Cancer Risk and Cisplatin Resistance in Oral Epithelial Cells

COMMITTEE IN CHARGE: Lurdes, Queimado, MD, PhD; Priyabrata, Mukherjee, PhD; H. Anne, Pereira, PhD: Susannah Rankin, PhD; James J. Tomasek, PhD

ABSTRACT: The increasing awareness of the danger of smoking has led to an increase in other smoking alternatives such as e-cigarettes, even among cancer patients. E-cigarettes have fewer chemicals and are proposed as a safer alternative. Are electronic cigarettes (e-cigarettes) safer than tobacco? Short-term e-cigarette studies are mostly limited and inconclusive. Long-term health effects are unknown. Our laboratory examined the impact of e-cigarettes on cancer risk and chemotherapy resistance in oral epithelial cell lines. Epithelial cell lines established from cancer and non-cancer tissues were exposed to e-cigarette aerosol extracts acutely, in the presence or absence of cisplatin, and chronically. Cells were evaluated for DNA damage, cellular reactive oxygen species (ROS), total antioxidant capacity (TAC), stemness, gene and protein expression, cell viability, cell death, and clonogenic survival. We observed that exposure to e-cigarette aerosol extracts increased DNA damage and cellular ROS while decreasing TAC and the expression of DNA repair enzymes. Exposure to e-cigarette extracts significantly increased the number of stem-like cells, spheroid formation, and protein levels of key stem cell regulators. Treatment with cisplatin in the presence of e-cigarette extracts resulted in a significant increase in cisplatin resistance, as measured by a reduction in cisplatin-induced cell death, and an increase in cell viability, IC50, clonogenic survival, and multidrug resistance protein expression compared to vehicle-control cells. We identified WNT1 as a potential facilitator for the observed changes after e-cigarette exposure. Taken together, our study shows that both short and long-term e-cigarette exposure can lead to genotoxicity, stemness, and cisplatin resistance in oral epithelial cells. Our findings have significant clinical implications as they suggest that like combustible tobacco, e-cigarette use might increase cancer risk and chemotherapy resistance. These results also emphasize the urgent need for further studies on the potential health effects associated with e-cigarette use and for evidence-based regulation of e-cigarettes.