1. No.
   2020G032

2. Title
   Study on the Relationship between Histone Loss-Induced Aging and Carcinogenesis Following Cigarette Sidestream Smoke Exposure

3. Period
   2020-2024

4. Summary
   Carbonyl compounds in cigarette sidestream smoke (CSS) could bind to histones, key nuclear proteins rich in basic amino acids. Decline of histone levels and DNA damage repair capacity with aging has been reported, suggesting that carbonyl-histone interactions may accelerate aging and carcinogenesis. This study examined histone levels and modifications, aging, and DNA damage repair after exposure to CSS and a carbonyl compound, formaldehyde (FA).

   Human skin fibroblasts (ASF-4-1) were exposed to CSS and FA for five days, followed by two-day incubation in fresh culture medium. Increased β-galactosidase activity, intracellular reactive oxygen species, and SASP induction indicated cellular senescence, accompanied by elevated H2AX levels and the phosphorylation. In these senescent cells, the repair of UV-induced DNA damage was impaired, suggesting an increased risk of carcinogenesis due to aging. H2AX knockdown (KD) with siRNA further enhanced these senescence markers upon exposure. These results indicate that aging induced by CSS containing carbonyl compounds inhibits DNA damage repair, which may lead to the increased risk of carcinogenesis, and that histone H2AX plays a protective role against CSS-induced cellular aging.