Interactions between Tobacco Smoke Constituents in Rodent Tumor Models
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Abstract:

Tobacco smoke is a complex mixture of chemicals, many of which are toxic and carcinogenic. How these chemicals interact to cause the human health effects of tobacco smoke and products is not well-understood. To decrease the toxicity and carcinogenicity of tobacco products and smoke, it is important to identify which of the many tobacco constituents to target for reduction. Lowering the levels of one type of chemical may not reduce the overall carcinogenic properties of the tobacco product if interactions amplify the effects of residual levels of the known human carcinogens. Given the complexity of the mixtures and the lack of information regarding how individual components of the mixtures act together to trigger cancer, we will explore the interactions between combinations of two chemicals that are likely to have synergistic tumorigenic effects. The goal of this project is to characterize the potential interactions between known human carcinogens (NNK, NNN, or BaP) and volatile components of tobacco smoke (acetaldehyde, acrolein, and formaldehyde) in established rodent tumor models as outlined in the following specific aims: Aim 1. Determine if acetaldehyde can influence the carcinogenic properties of NNN in a rat esophageal tumor model. Aim 2. Determine if inhaled aldehydes (formaldehyde, acetaldehyde, acrolein) can modulate the carcinogenic properties of NNK in the A/J mouse lung tumor model. Aim 3. Determine if inhaled aldehydes (formaldehyde, acetaldehyde, acrolein) can modulate the carcinogenic properties of BaP in the A/J mouse lung tumor model. In each aim, we will explore the influence of each aldehyde in combination with NNN, NNK, or BaP on tumor incidence, tumor multiplicity and tumor size to determine if reduction of both carcinogen and aldehyde is necessary to reduce harm, or if reductions in one group of constituents would suffice. Urinary metabolite and DNA adduct biomarkers will be measured to determine if the levels of these biomarkers are influenced by the co-exposure. These studies will provide important missing information about the ability of volatile compounds to influence the tumorigenic activity of established tobacco carcinogens