ADVANCING HAZARD ASSESSMENT STUDIES:

UTILIZING INHALATION ON-CHIP PLATFORM FOR TOBACCO PRODUCT EVALUATION

ALEXIS

IN COLLABORATION WITH

AlveoliX In-vitro models inspired by nature

VITROCELL SYSTEMS

RATIONALE

The inhalation of tobacco products, including traditional cigarettes, e-cigarettes, and emerging alternatives, significantly contributes to the progression of chronic lung diseases such as Chronic Obstructive Pulmonary Disease (COPD) and E-cigarette or Vaping-product Use-Associated Lung Injury (EVALI). These products release reactive chemicals that cause inflammation in lung tissue, particularly in the alveoli. Current animal models struggle to replicate the complexities of human lung exposure to these products, underscoring the need for advanced in vitro models. The Alexis smoke inhalation system offers a novel solution by simulating real-world inhalation on breathing cells, enabling more accurate studies of tobacco-related health impacts.

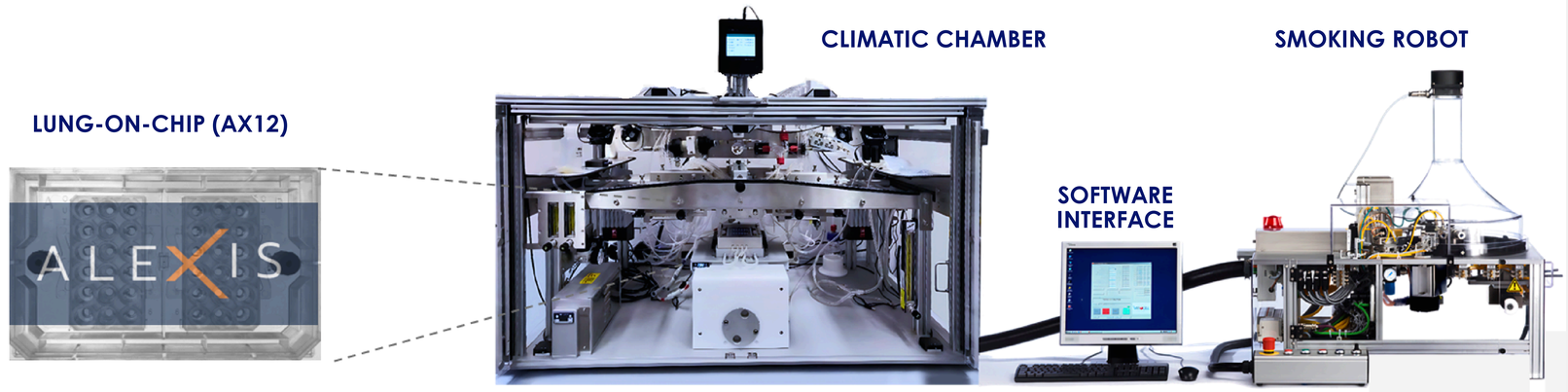
OBJECTIVE

The goal of this study is to evaluate the health risks of traditional and alternative tobacco products using the smoke inhalation system. By simulating both acute and chronic exposure, we aim to assess how different product formulations affect lung cells. Specifically, we seek to observe cytotoxicity and inflammatory responses, providing valuable data to support safer product development and regulatory decisions.

TECHNOLOGY

In this study, the Alexis Smoke inhalation platform was utilized to carry out comprehensive hazard assessments of a range of tobacco and alternative products. The system was integrated with complex co-culture bio-models of human lung cells, seeded in Lung-on-chip (AX12) developed by AlveoliX. Exposure regimens were carefully designed to simulate various smoking behaviors and inhalation patterns, representing different user experiences across traditional cigarettes, e-cigarettes, and vaping devices. Controlled doses of smoke and aerosolized vapors were applied, while real-time monitoring of cellular responses—including barrier integrity, reactive oxygen species (ROS) generation, and inflammatory signaling—was conducted.

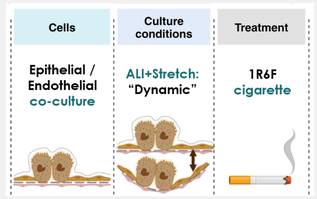
ALEXIS SMOKE ON-CHIP INHALATION PLATFORM



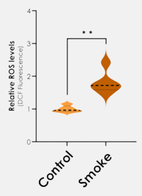
The Alexis Smoke Inhalation platfrom comprises of three key components: the software-controlled interface, the smoking robot, and the climatic chamber. Cigarettes are automatically loaded and ignited using an electric lighter. The lung-on-chip consumable, AX12, is used for exposure. The smoking robot delivers smoke to the dilution system, where it is mixed with dilution air and directed to the cells in the AX12 through "trumpet" inlets. After exposure, the smoke is exhausted through an exhaust tube, with continuous airflow ensuring no residual smoke remains.

RESULTS

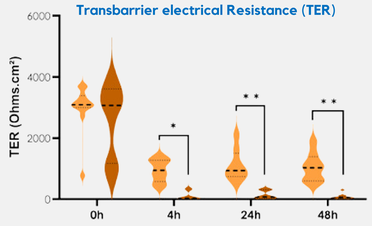
CIGARETTE SMOKE



Reactive Oxygen Species (ROS)

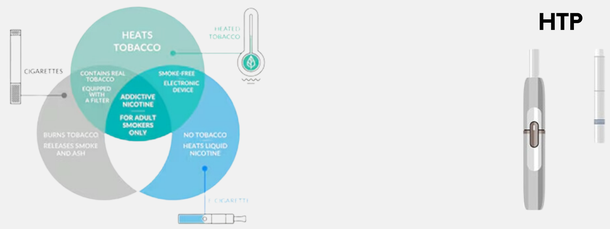


Cell barrier: Transbarrier electrical Resistance (TER)

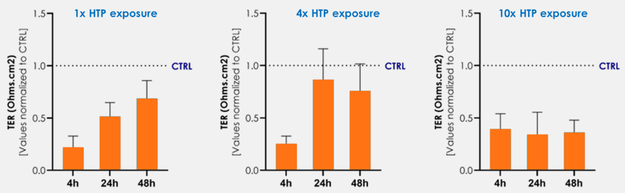


Human alveolar cells on the apical side and human endothelial cells on the basal side were exposed to whole cigarette smoke using the standard HCI smoking regimen using the Alexis smoke inhalation platform. A notable increase in ROS generation was observed at 48 hours post-exposure. Moreover, cell barrier integrity showed clear dysfunction starting at 4 hours and sustained until 48 hours, suggesting that the stress may have been acute, for any possible recovery mechanisms.

HEATED TOBACCO PRODUCT (HTP)



HTP



Apical epithelial and basal endothelial cells grown in a Lung-on-chip were exposed to HTP. After exposure to HTP on the chip, the barrier function of the cells, measured by TER, dropped after 4 hours. Interestingly, for lower exposures (1x and 4x), the cells were able to recover over time. However, at the highest concentration (10x), the cells could not regain their normal function.

CONCLUSION

Our findings emphasize the importance of replicating key physiological conditions for accurate in vitro lung models in smoke-associated studies. This approach not only advances understanding of tobacco-related diseases but also offers significant market potential for tobacco companies. By enabling precise toxicity studies and supporting the development of safer products, this platform can help companies meet regulatory demands and drive innovation, positioning them as leaders in the development of next-generation tobacco alternatives.

REFERENCES

Sengupta et al., Frontiers Toxicology, 2022 "A New Immortalized Human Alveolar Epithelial Cell Model to Study Lung Injury and Toxicity on a Breathing Lung-On-Chip System

Sengupta et al., Frontiers Pharmacology, 2023 "A multiplex inhalation platform to model in situ like aerosol delivery in a breathing lung-on-chip

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