iGEM Abstract: Antioxidant-Based Genetic Circuit Prevention of Benzo(a)pyrene

doi: 10.35493/medu.48.34

AUTHORS:
RASHA IMTIAZ[1], AMIRA JAFRI[2], & MAYA KAMATH[3]
[1] Bachelor of Engineering (Chemical and Biomedical Engineering Co-op), Class of 2028, McMaster University
[2] Bachelor of Science (Honours Molecular Biology and Genetics), Class of 2027, McMaster University
[3] Bachelor of Science (Honours Molecular Biology and Genetics Research Specialization Co-op), Class of 2028, McMaster University

ARTIST:
ISRA CHOWDHURY [4]
[4] Bachelor of Science (Honours Life Sciences Co-op), Class of 2026, McMaster University

INTRODUCTION

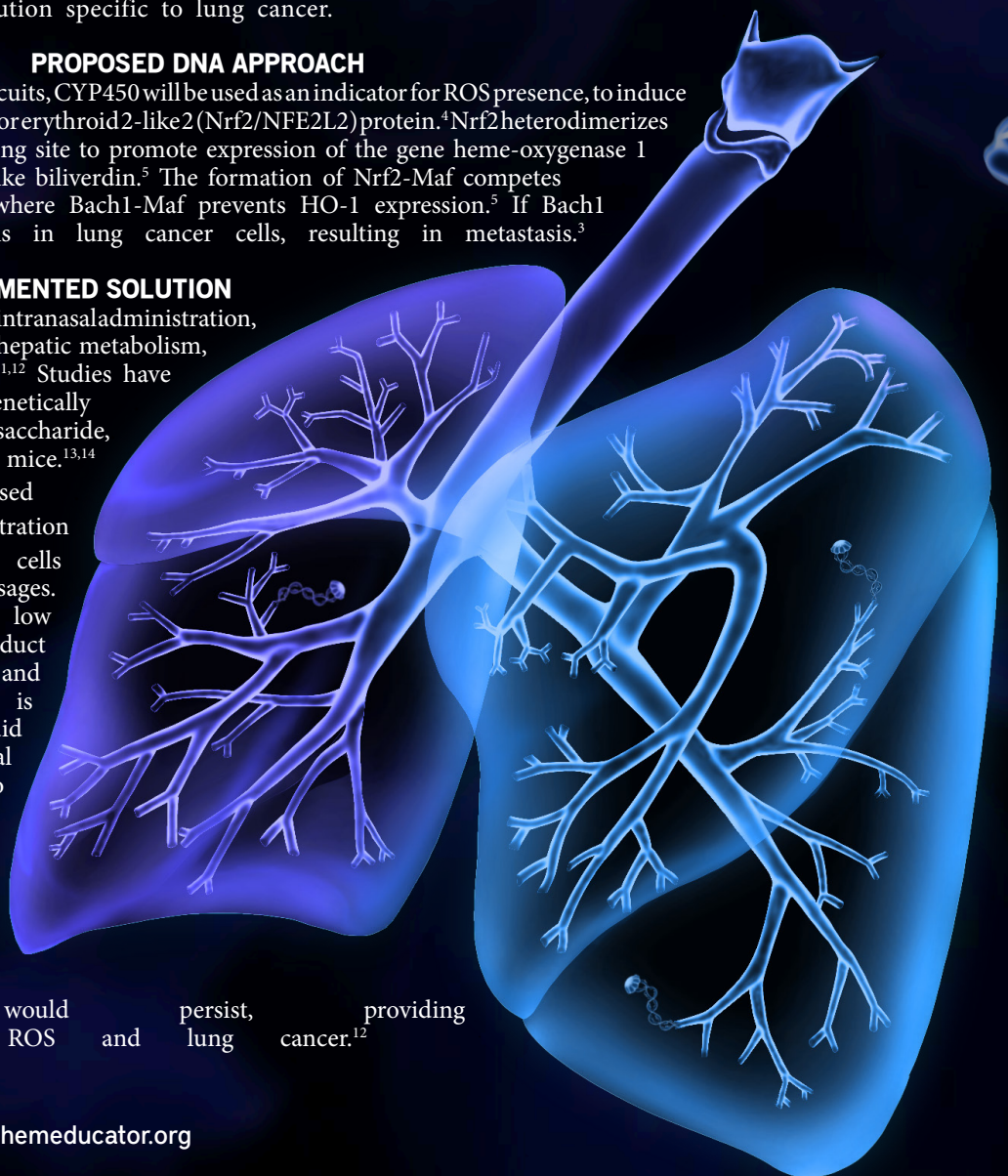
A novel prevention strategy is proposed to offset the effects of benzo(a)pyrene (BaP), a byproduct significantly produced by the Hamilton metal industry, increasing lung cancer risk. BaP is involved in a pathway which activates gene expression of cytochrome P450 (CYP450), a major reactive oxygenated species (ROS) generator associated with lung cancer.[1,2] Current antioxidant-based prevention is diet-based, which lacks specificity, and may promote metastasis if not controlled.[3] Therefore, we aim to genetically engineer a targeted and cost-effective Nrf2-antioxidant-based solution specific to lung cancer.

PROPOSED DNA APPROACH

Using genetic circuits, CYP450 will be used as an indicator for ROS presence, to induce the translation of Nuclear factor erythroid 2-like 2 (Nrf2/NFE2L2) protein.[4] Nrf2 heterodimerizes with Maf protein at the ARE binding site to promote expression of the gene heme-oxygenase 1 (HO-1), which activates antioxidants like biliverdin.[5] The formation of Nrf2-Maf competes with Bach1-Maf heterodimerization, where Bach1-Maf prevents HO-1 expression.[5] If Bach1 is active, it can increase glycolysis in lung cancer cells, resulting in metastasis.[3]

FEASIBILITY OF THE IMPLEMENTED SOLUTION

To target the lungs, the proposed method is intranasal administration, which is non-invasive, direct, bypasses hepatic metabolism, self administerable, and cost-effective.[11,12] Studies have successfully intranasally administered genetically engineered E.coli, with removed lipopolysaccharide, to target alveolar epithelial cells in mice.[13,14] Trials will take place in BaP-exposed mice to ensure intranasal administration is specific to target lung cancer cells and to determine safe human dosages. Efficacy will be measured with low 8-hydroxyguanine, a ROS attack by-product found in saliva, allowing for non-invasive and cost-effective extraction.[14] The saliva is analyzed using high-performance liquid chromatography with electrochemical detection.[15,16] The solution employs two genetic circuits, adding complexity, but amplifies the existing Nrf2 metabolic pathways to lower costs, improving accessibility, and avoiding the need for additional foreign mechanisms in the body. Post-successful medication, the the E. coli would persist, providing long-term protection against ROS and lung cancer.[12]



References can be found on our website: themeducator.org

LANGS COMMUNITY HEALTH CENTRE

Langs Community Health Centre is an accredited, non-profit organization funded by the MOH that provides primary health care. We employ an interdisciplinary team of physicians, nurse practitioners, nurses, social workers, dietitians and health promoters. CHCs are unique as they offer a salaried model for physicians with full benefits.

As part of our team, you would provide primary health care with the support of a range of health promotion, illness prevention and community development programs and services. For more information about practicing at Langs, contact us today!

OUR VALUES Integrity · Respect · Accountability · Innovation · Excellence

WWW.LANGS.ORG 519-653-1470 INFO@LANGS.ORG 1145 CONCESSION RD CAMBRIDGE, ON