4. OBJECTIVES

Objectives of the present study include

1. Measure the expression of NRF2 in very early and late stage lung tumor biopsies using immunohistochemistry and correlate with disease status

   Expected outcome: Data generated from this objective helps to correlate the levels of Ki67 (a marker for proliferation) and p53 (a marker for apoptosis) with Nrf2 expression. This key information while establishing the correlation between Nrf2 expression, and Ki67 and p53, also shows whether the expressed Nrf2 is functionally active in tumor cells

2. Screen and select plant extracts that could inhibit A549 lung cancer cell line, which is known to express high levels of functionally active NRF2

   Expected outcome: Determination of the therapeutic efficacy of extracts (generated using solvents hexane, dichloromethane, alcohol and hydroalcohol) i.e., IC50 of Nrf2 expressing A549 cell line, VS IC50 of normal cell line FF244.1 (human fibroblast cell line). Results of this comparison helps to identify the plant extracts with good therapeutic efficacy for further studies

3. Determine the efficacy of selected plant extracts for modulating NRF2 and its downstream NQO1 and GST using a reporter assay and real time PCR and determine whether any changes do occur in cell proliferation, survival and apoptotic pathways

   Expected outcome: Results of this objective are expected to yield key information about the efficacy of selected plant extracts to (a) inhibit or enhance the Nrf2 expression/activity; and (b) induce apoptosis in cancer cells. This information’s critical to select appropriate plant extracts for further testing in animals

4. Measure the toxicity of selected plant extract in mice; and determine the efficacy for inhibiting EAC cells expressing high NRF2 in mice

   Expected outcome: Data from this objective yield information required for identifying extract(s) with good in vivo efficacy. The expected outcome is that extracts with good Nrf2 inhibitory effect, also inhibit the development of EAC cells in mice.