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## RESEARCH TOPIC:

Selective epidermal growth factor receptor (EGFR), Kirsten rat sarcoma viral oncogene (KRAS) and the echinoderm microtubule associated protein-like 4 (EML4)-ALK mutation analysis in South Africans with non-small cell lung cancer.


### RESEARCH PROPOSAL ABSTRACT

Lung cancer remains to most common cause of cancer death. Globally “targeted” chemotherapy has become the norm in treatment of patients receiving both palliative and curative therapy for non-small cell lung cancer. The three most common mutations targeted are the epidermal growth factor receptor (EGFR) mutation, Kirsten rat sarcoma viral oncogene (KRAS) and the echinoderm microtubule associated protein-like 4 (EML4)-ALK mutation. There is currently no South African data on the frequency of these mutations in patients with lung cancer, nor is there any African data.

The aim of our study is to determine the frequency of and the clinical and pathological features associated with EGFR, KRAS and ALK mutations in South Africans with non-small cell lung cancer in order to contribute to the knowledge base of molecular mutations in African lung cancer patients.

The study will employ the quantitative research paradigm, because numeric variables will be identified and analysed in an objective manner. A cross-sectional correlational study design will be used. Study participants will be recruited from the Tygerberg Hospital Pulmonology Out-Patient Department by non-random purposive sampling of consecutive qualifying participants. This unit is representative of tertiary units in South Africa because of the high volume of lung cancer referrals from secondary and primary level facilities in the Western Cape region. Approximately 25 patients per month and 300 patients per year are diagnosed with primary lung carcinoma at the Tygerberg Academic Hospital Pulmonology Department.

With an estimated EGFR mutation prevalence of 10%, at least 300 patients with non-small cell lung cancer will have to be included in the study to satisfy the primary and secondary objectives. Inter-observer variation can occur during the cytological or histopathological evaluation of the samples, because different cytologists or pathologists may analyse the tissue slides and this can lead to inconsistent findings on the cytology or histology reports. We will limit this variation by using the final report from the pathologist as the conclusive diagnosis.

High-resolution melting curve analysis and sequencing is dependent on obtaining cytology or biopsy samples with adequate tumour cellularity, usually > 50% of the sample, for these tests to be performed. The analysis might thus not always be successful if samples with sparse cellularity are collected. Cytology and histology samples will thus first be evaluated by a cytologist or pathologist for a definitive diagnosis of lung cancer and to comment on the cellularity of the sample, prior to performing molecular analysis. The formalin that is routinely used for fixating biopsy material can inhibit PCR and sequencing reactions. This may lead to false negative tests for molecular mutations. By using a sensitive technique such as HRM on tissue with adequate cellularity, the number of false negative tests will be limited.