**Lung Adenocarcinoma** is the most common form of lung cancer. The tumors initiate in epithelial cells in the outer part of the lung and then tumor growth spreads during metastasis causing fatigue, coughing, reoccurring respiratory infection and sometimes death1. EGFR is associated with lung adenocarcinoma, which is a transmembrane receptor that affects transcription factors and cell cycle progression. Growth factor signaling can change according to external stimuli and even diet2. In LADC, the receptor usually has a tendency to remain in its active dimerized form. For example, activating mutations in EGFR’s tyrosine kinase domain often result in epithelial transformations3; this cellular process encompasses both a change in proliferation and migration. However, kinase-independent survival and migratory functions involving palmitoylation of EGFR are an emerging area of study4. *It is still unclear how EGFR influences cell migration and proliferation in the lung epithelial.*

**My objective** is to determine the role that EGFR plays in migration and proliferation of epithelial cells in the lung. I **hypothesize** that specific tyrosine kinase mutations in EGFR will result in changes in epithelial cell proliferation, migration and protein palmitoylation (GO terms) in the lung. Mice **model organisms** are excellent models to study lung cancer because EGFR is conserved between humans. In addition, the receptor translocates to a variety of membranes within the cell, similar to humans5. Epidermal growth can also be observed on mouse skin6. The **long-term goal** of this study is to determine how tyrosine kinase-dependent versus independent EGFR function mediates cell proliferation and migration.

**Aim 1: Determine which part of the tyrosine kinase domain in EGFR *influences cell migration and proliferation.***

Approach:Ensemble and ClustalOmega will be used to align known homologs of the EGFR gene and I will identify unique Amino acids in the Tyrosine kinase domain that might be important for cell proliferation and cell adhesion in the lung. CRISPR/Cas9 plasmid delivery to mouse eggs will mutate the corresponding DNA segments in mouse eggs7, followed by DNA sequencing of wildtype and transfected mice. To measure cell the rate of proliferation and migration in the lung, I would use a cell counting kit and a wound healing (scratch) assay, respectively.

Rationale: Identifying the exact amino acid in EGFR, that leads to changes in the rate of proliferation and migration, will be important for understanding how EGFR signals normally in the lung to mediate cell.

Hypothesis:I hypothesize that mutation of tyrosine kinase specific residues, specifically in exon 19 and 20 will result in an increase in cell proliferation and adhesion.

**Aim 2: Determine how tyrosine-independent EGFR function *influences cell proliferation and migration.***

Approach:Reverse chemical genomic screening will quantify exogenous ligand to EGFR between wildtype and transfected mice. Samples will be subject to a variety of chemicals such as hydroxylamine that cleave cysteine- palmitoylation bonds8. Mutant epithelial and control sample tissues will be subjected to these chemicals. Once again, cultures will be measured for proliferation and cell migration by scratch assay and cell counting.

Rationale: Quantifying the effects of exogenous ligands on cell proliferation and migration between wild type and mutant mice will illustrate how prevalent tyrosine dependent function is for these phenotypes.

Hypothesis: I propose that chemical disruption of loss of function tyrosine kinase mutant cells will affect alternative mechanisms of increased cell proliferation and migration.

**Aim 3: Identify how EGFR function affects gene expression associated with epithelial transformation.**

Approach:I will perform a microarray on wildtype and transfected mice mouse cells treated with chemicals from the screen. Afterwards, Gene Ontology analysis using PANTHER can enrich gene expression with GO terms relating to cell growth patterns such as cell proliferation, migration and protein palmitoylation which are all implicated in epithelial transformations.

Rationale: Determining changes in proliferation, migration and protein palmitoylation related gene expression between cell samples will illustrate how EGFR binding mediates epithelial transformation.

Hypothesis: I hypothesize that mutant EGFR cell samples retains the ability to increase gene expression that can be affected by exogenous chemicals, through tyrosine kinase-independent mechanisms.

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