Characterizing Genetic Mutations in Familial Lung Cancer: Insights & Implications

Carley Kronlage, Angelle Bencaz MSPH, and Diptasri Mandal PhD
LSUHSC Department of Genetics

Introduction

Background:

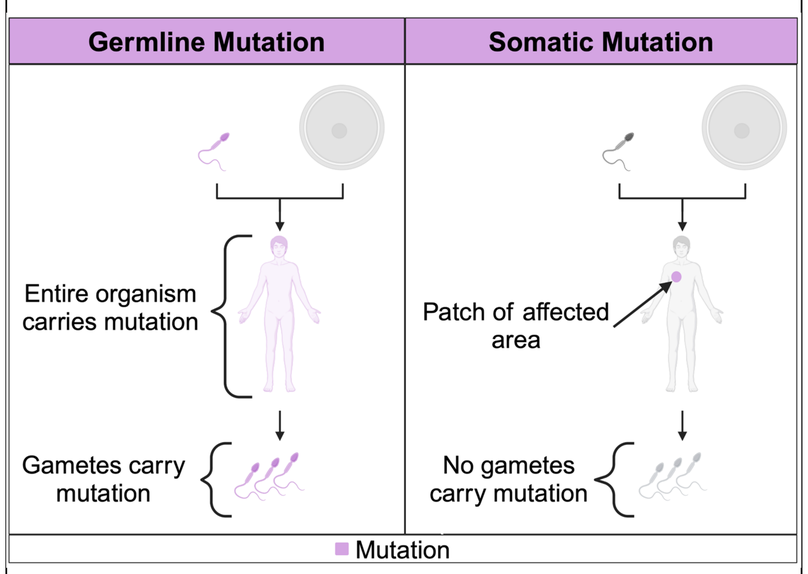
- Lung Cancer (LC) is the leading cause of cancer-related deaths worldwide
- First-degree relatives of LC patients have a 1.51 times higher risk of developing LC
- Less than 20% of smokers develop LC
  - ↪ suggests that genetics play a key role
- Difficult to pinpoint a list of specific genetic mutations that cause LC
  - ↪ Caused by a combination of both genetic and environmental risk factors
  - ↪ Multiple genes are responsible
- Identifying genetic mutations aids in determining the best treatment options
  - ↪ Precision Medicine (PM): specific drugs can target specific genetic mutations
  - ↪ PM can help LC patients avoid generalized harmful treatments like chemotherapy

Gaps:

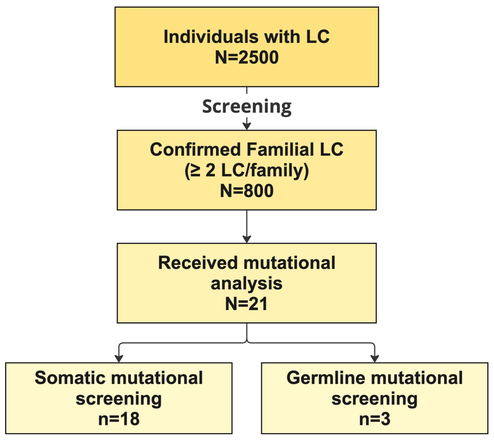
- Identified genetic mutations linked to LC susceptibility need further validation
- More research is required to confirm findings across different populations

Objective:

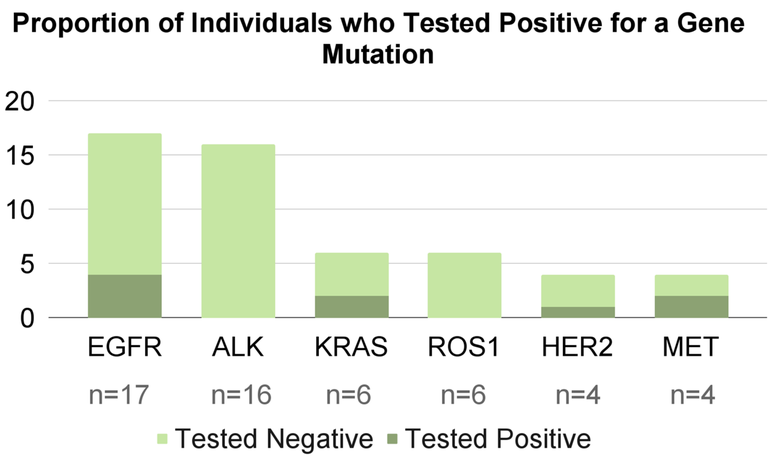
- Characterize genetic mutations in familial LC cases



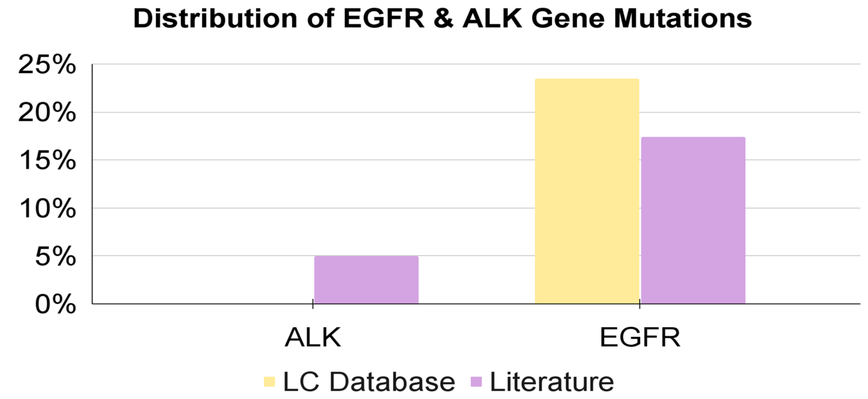
Methods



Results



Individuals	Mutation Type	Age of Diagnosis	Relatives with LC	Histology	Smoking History
# 1	EGFR	55	5	adenocarcinoma	S(ex)
# 2	EGFR	62	4	squamous cell	S(ex)
# 3	EGFR	51	5	adenocarcinoma	N
# 4	EGFR KRAS	62 65	9	adenocarcinoma adenocarcinoma	S(ex)
# 5	KRAS	75	2	adenocarcinoma	S(ex)
# 6	MET	87	2	adenosquamous carcinoma	N
# 7	MET	63	3	adenocarcinoma	S(ex)



Conclusions & Future Directions

Interpretations of Results

- Prevalence of the EGFR and ALK gene mutations amongst study participants varied by about 5% each from what they were reported to be in literature
- Those with EGFR mutation
  - ↳ Higher number of relatives with LC
  - ↳ Earlier age of onset
  - ↳ Different types of mutations were observed: exon 19 deletion, exon 20 insertion, and p.T790M mutation
- No participants tested positive for the ALK mutation despite being one of the most common genes tested for

Limitations

- No standard screening panels for mutational analysis
- Only included Caucasians
- Only 21 participants had mutational analysis

Future Directions

- How PM can be applied in the presence of multiple genetic mutations
- Whether somatic or germline mutations of a gene more commonly occur
- How the presence of certain gene mutations affects LC prognosis
- Average age of LC onset in patients with a germline mutation
- Common genetic mutations in never smokers
- How patients can posses certain germline mutations but never develop LC

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