Cancer Bio Course

Session 3: From observation to experimentation. Cancer evolution and the role of the tumor microenvironment.

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Paper discussion

Article

Lung adenocarcinoma promotion by air pollutants

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Check for updates

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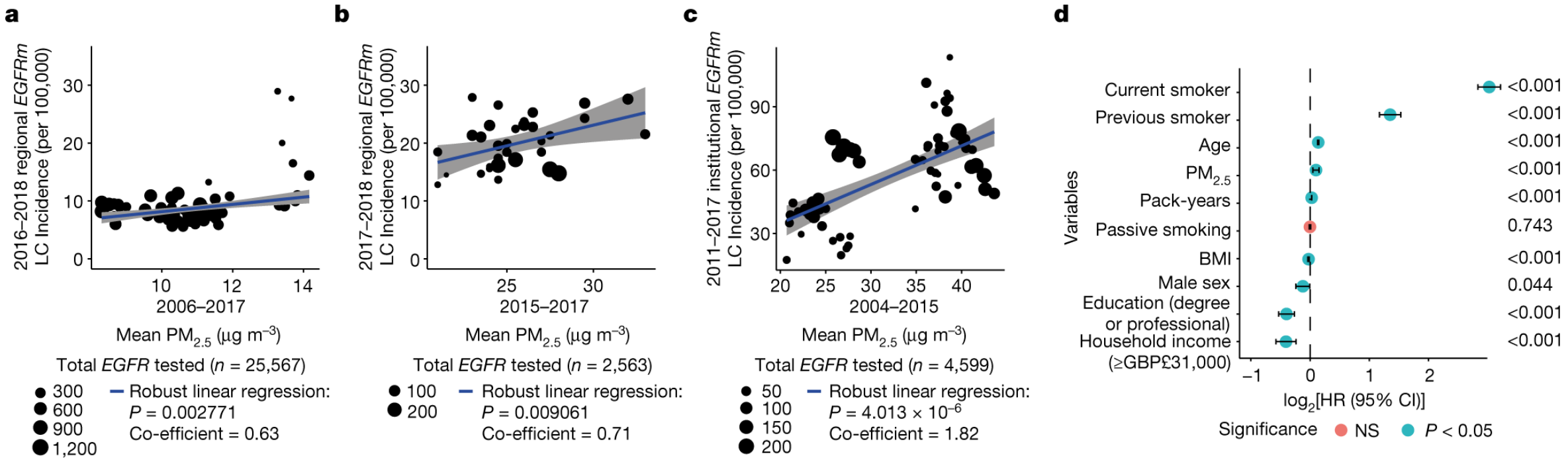
Paper discussion

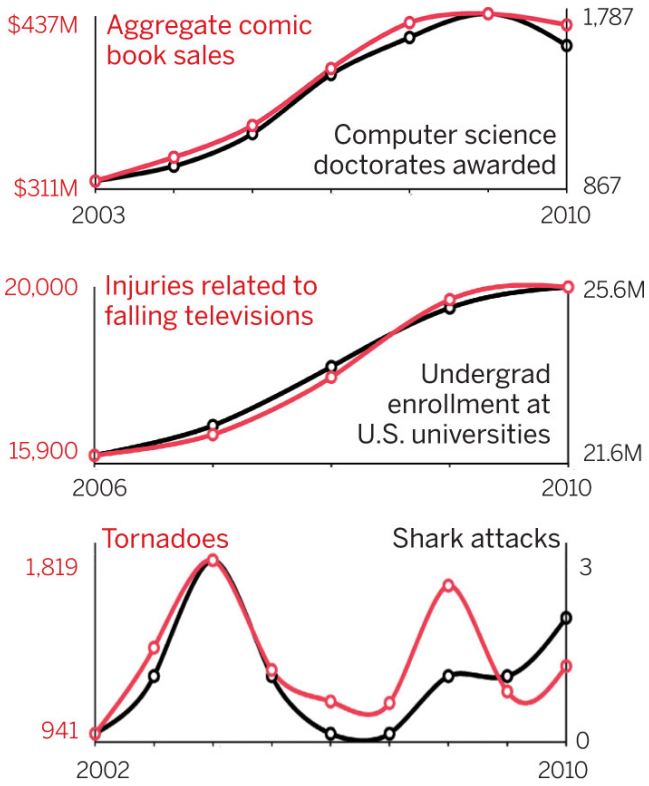
- **Explanation of the question under research** - *why did they decide to do this?*
- **Discussion figure by figure –** *is this paper not as good as authors think?:*
  - What is the point of each figure/panel?
  - Are there any missing experimental conditions?
  - Are results interpretable?
  - Do the results support the conclusions by the authors?
  - Would you have done anything differently?
  - Are there any missing experiments?
  - What are the limitations of the work?
  - What experiments could be done as a follow-up to the paper?

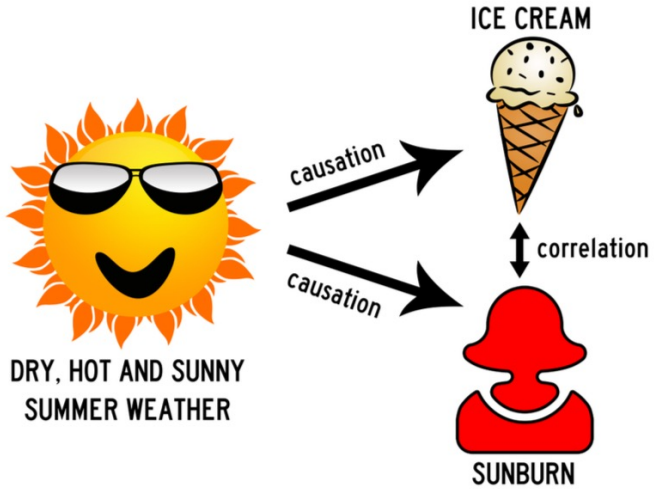
Fig. 1: Exploring the association between cancer and air pollution.

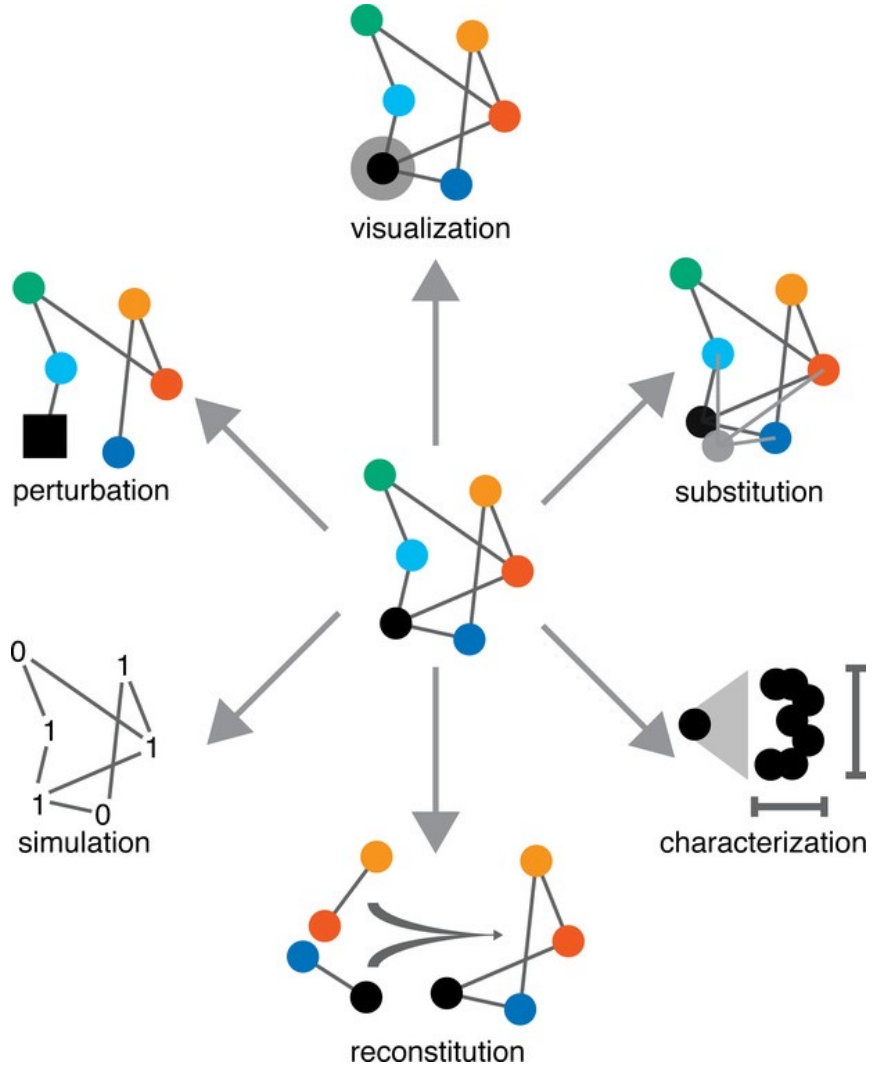


Basics about preclinical validation

Correlation versus causation



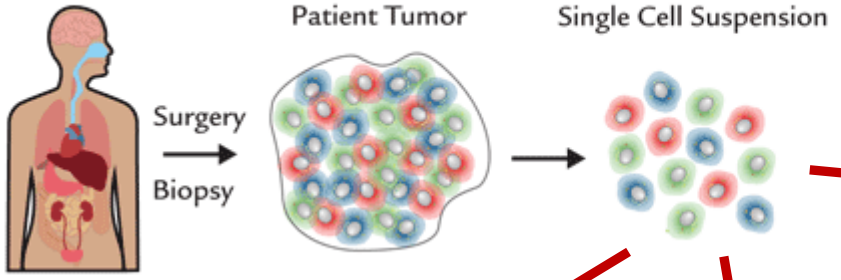




eLife 2020

Basics about preclinical validation

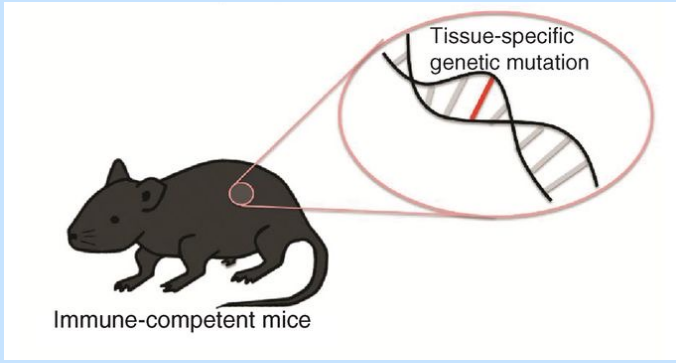
Preclinical models

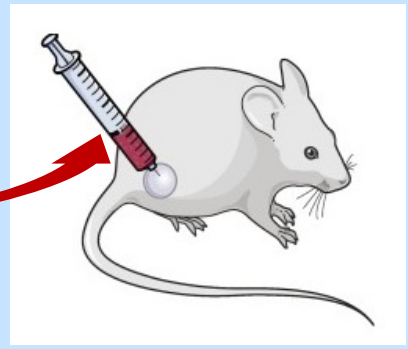


In vivo models

Patient-derived xenografts
(3D system)

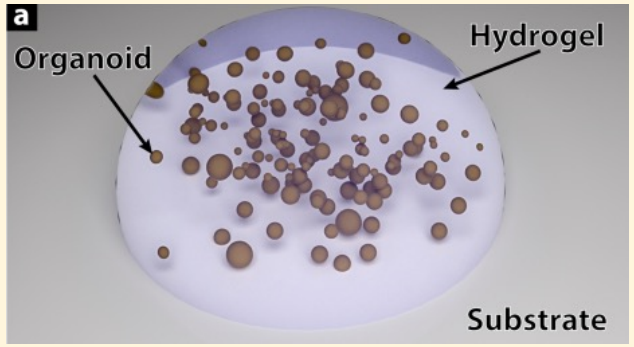
Genetically
engineered
mouse models
(GEMMs)





Cell line xenografts
(3D system)

Cell line (2D system)



Organoids (3D system)

In vitro models

Basics about preclinical validation

Some **pros** and **cons**

In vitro models

Cell lines

- Very easy to work with, quicker and cheaper
- Allow easy genetic manipulation
- Very simplified model, 2D, no tumor microenvironment (TME)

Organoids

- Relatively easy to work with, quick and cheap.
- Allow relatively easy genetic manipulation
- 3D system that reproduces fairly well the behavior of tumors
- Simplified model, no TME

In vivo models

Patient-derived xenografts (PDXs)

- Reproduce very well the behavior of tumors (specially in treatment response)
- As close as you can get to an actual human tumor
- No TME
- Expensive, time-consuming
- Very difficult genetic manipulation

GEMMs

- Can reproduce well the biology of human tumors
- TME
- Expensive and time-consuming
- **Not human!**

Cell line xenografts

- Allow easy genetic manipulation (cell line) and in vivo study (xenograft)
- No TME
- Derived from a very simplified model (cell line)

GEMM

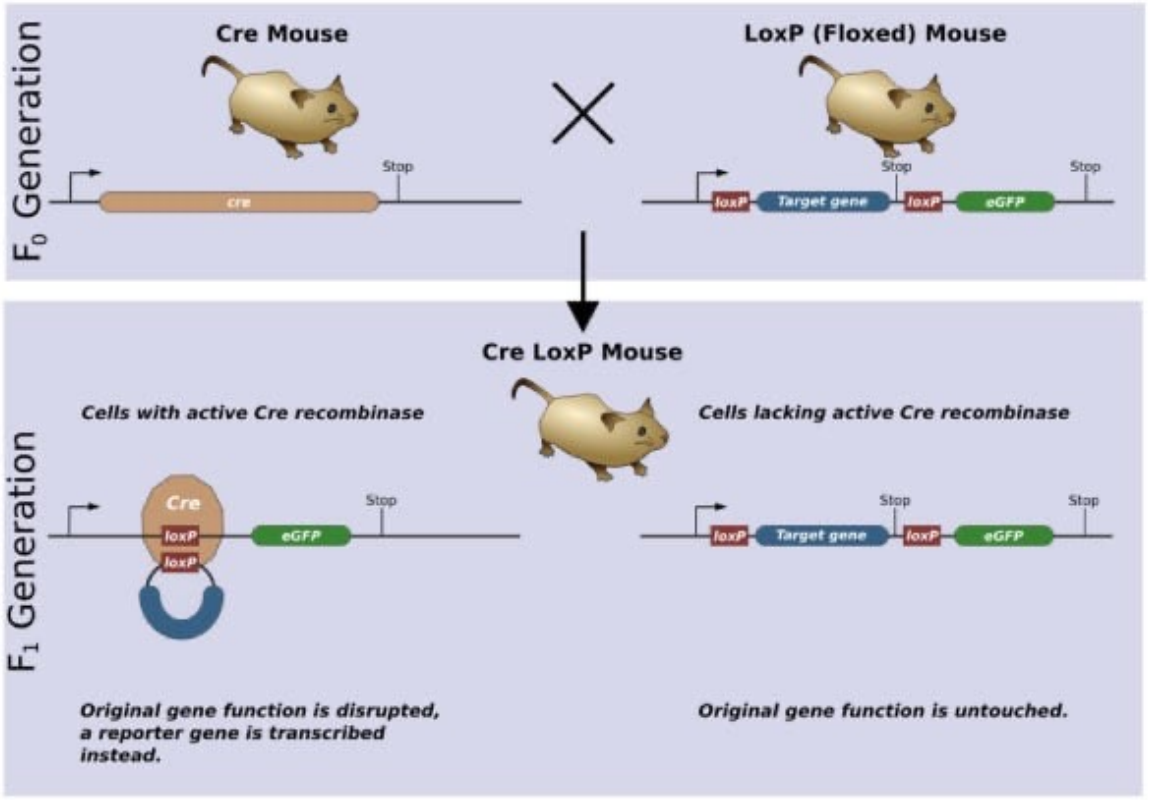


Figure 2: Cre-expressing and loxP-expressing mice are separately engineered, and then crossed to generate Cre-lox mice that express both Cre and a floxed gene segment. These mice can undergo recombination of the floxed gene segment to create knockouts or knockins. Image from Matthias Zepper.

GEMM control

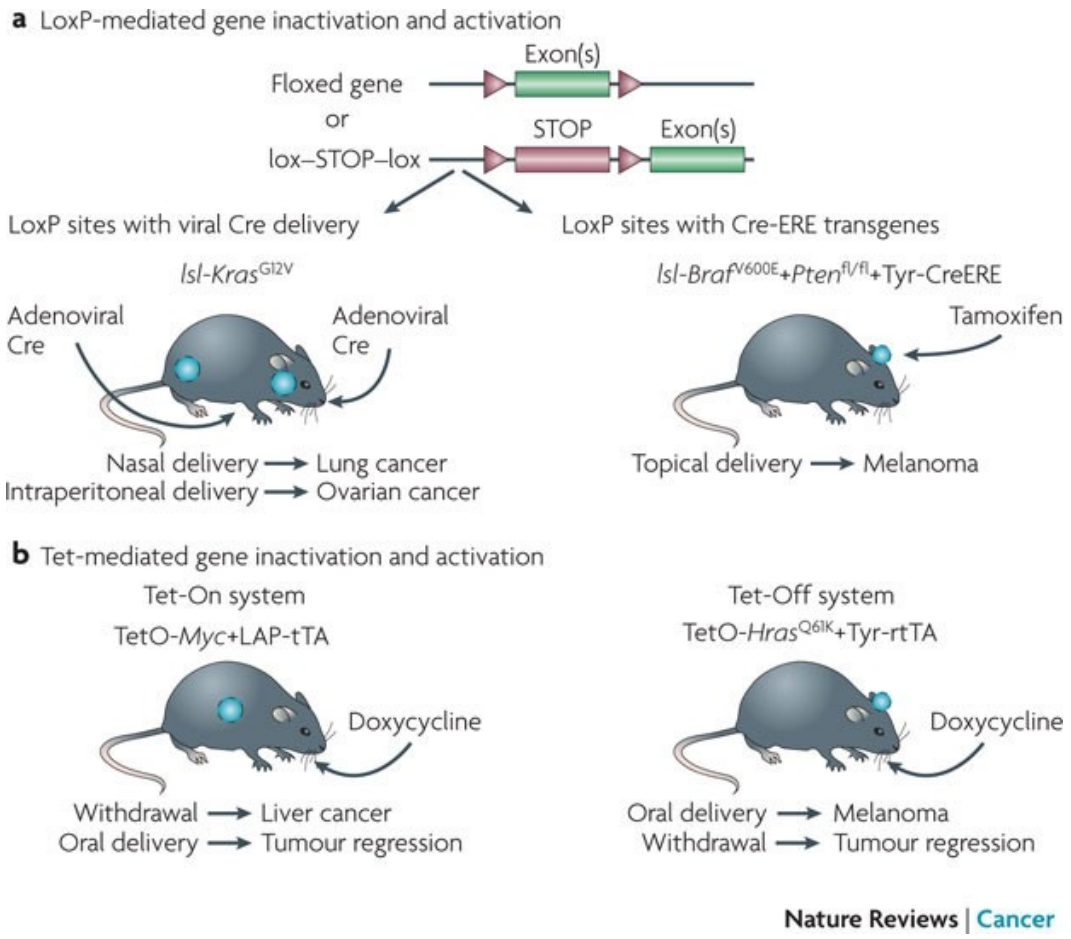


Fig. 2: PM promotes lung tumorigenesis.

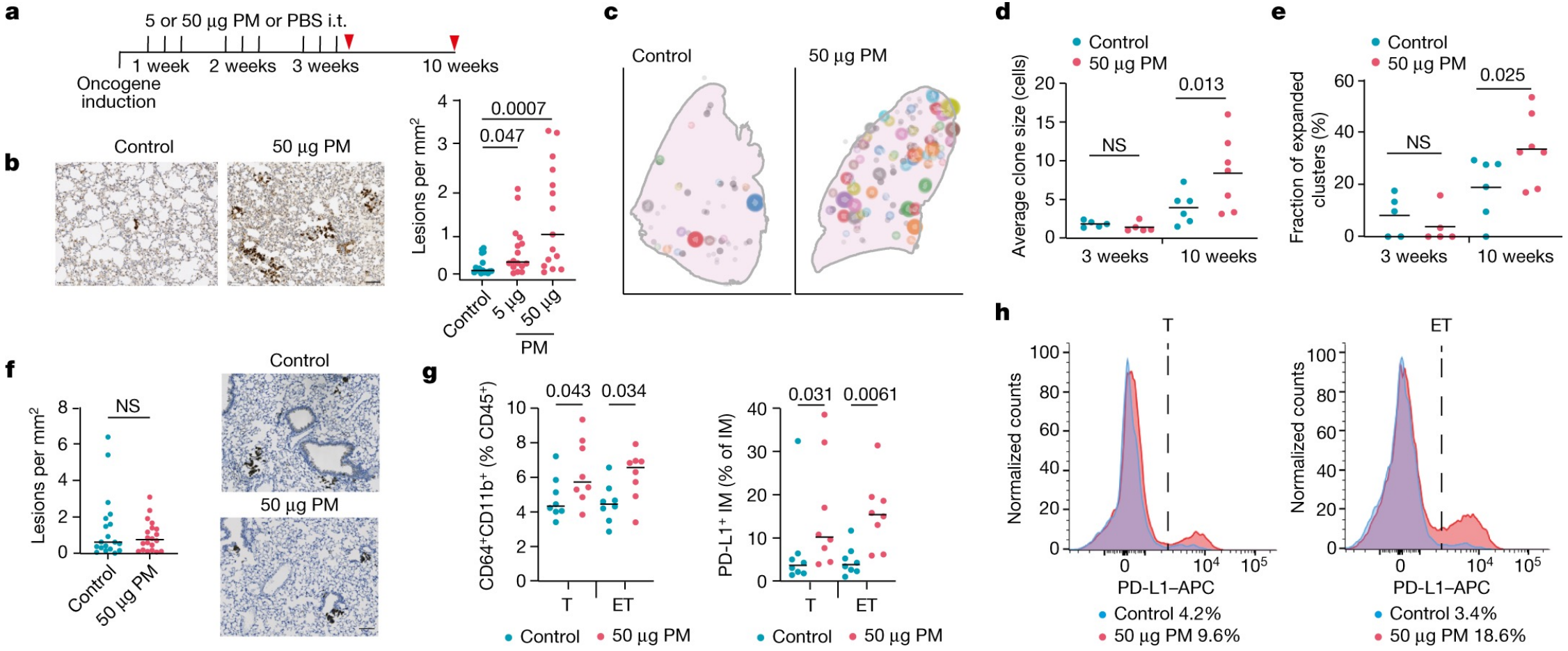
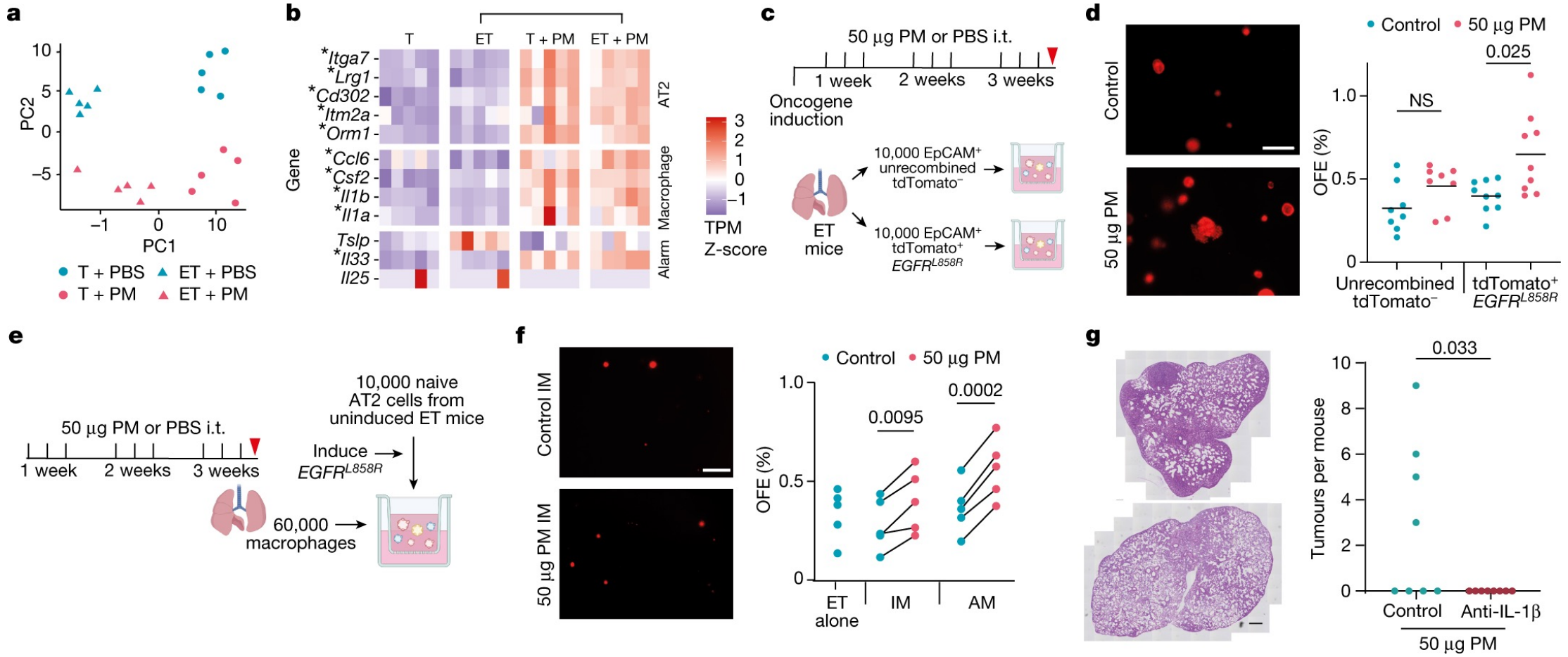
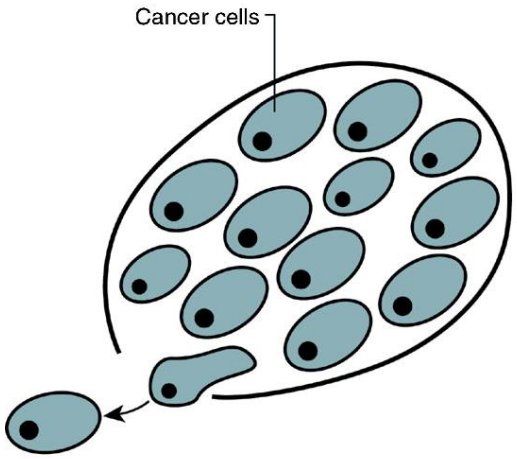


Fig. 3: Increased progenitor-like ability of EGFR mutant cells following PM exposure.

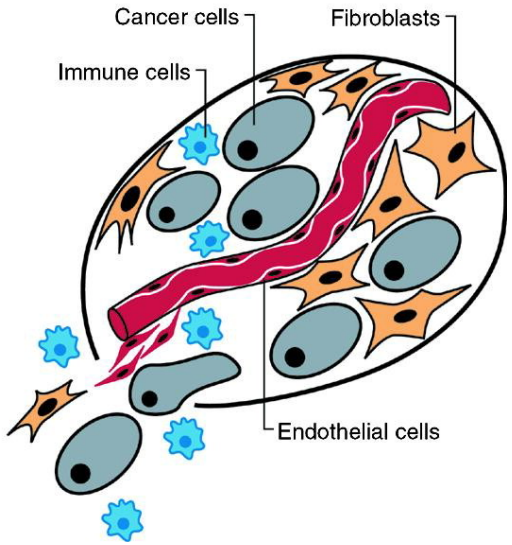


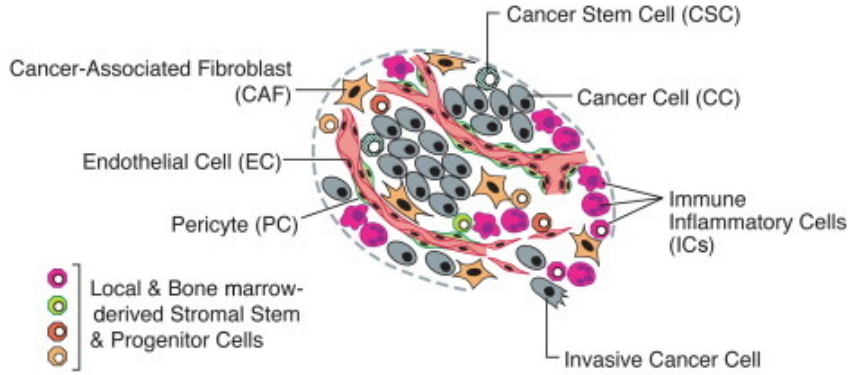
The importance of context

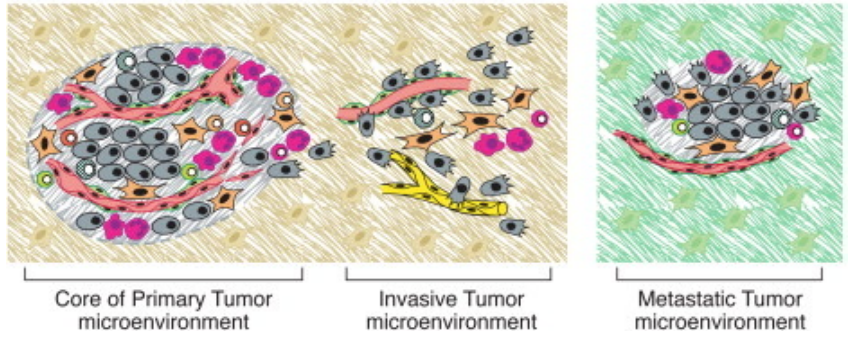
The Reductionist View



A Heterotypic Cell Biology







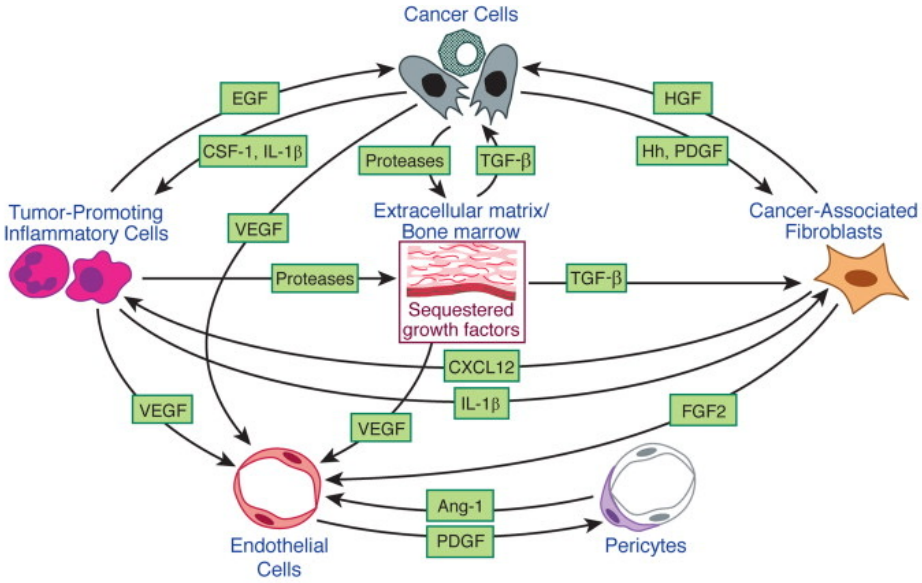
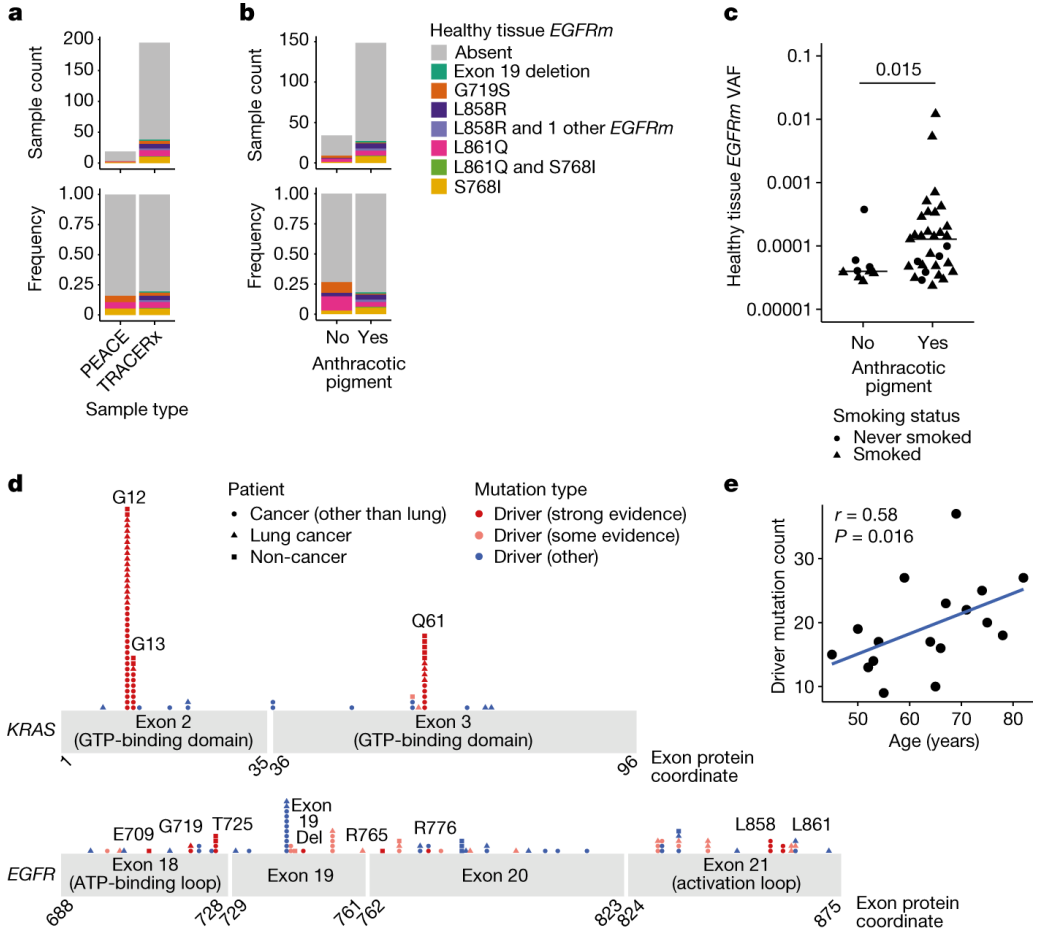
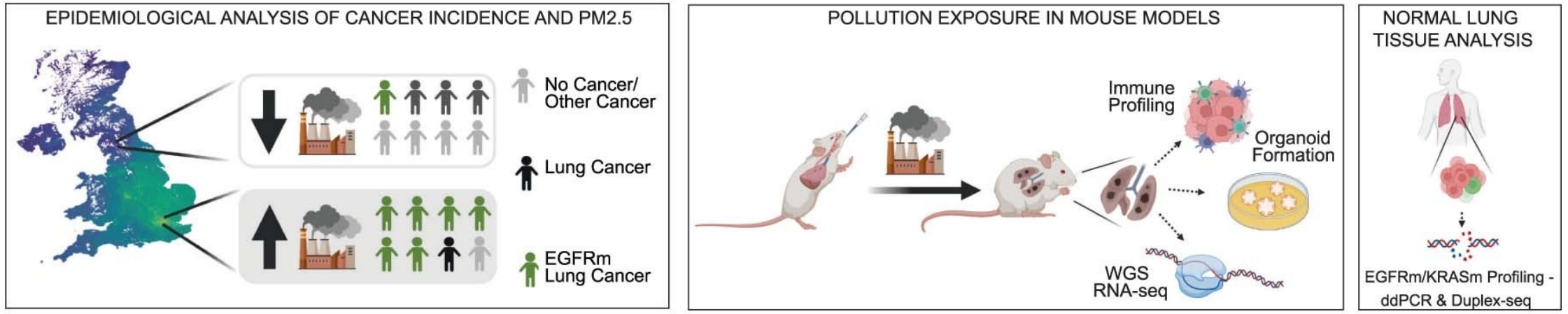


Fig. 4: Mutational landscapes of healthy lung tissue.



Study design, DNA analysis & epidemiology.

A



Thanks for your attention!

Any questions?

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