Chronic Obstructive Pulmonary Disease (COPD) may be a common disease in smokers is a common disease in smokers.

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**Conclusions:**
We show the existence of two fibroblast-derived gene expression programs modulating translational efficiencies of distinct pro-cancer secretomes in non-cancerous lung stroma that associate with lung cancer depending on lung status. Thus, this study exposes an unexplored role for translational control of stromal phenotypes and suggests that translation may be of importance for regulation of gene expression across multiple cell types in the tumor microenvironment.

**Introduction:**
- **Chronic Obstructive Pulmonary Disease (COPD)** is a common disease in smokers.
- COPD leads to increased risk of lung cancer independent of smoking.
- Primary lung cancers are associated with areas of worse regional emphysema.
- In mouse models, stromal fibroblasts are capable of initiating expression program(s) of secreted factors that favor tumor initiation.

**Hypothesis**
A comparison between gene expression in lung stroma from COPD subjects with or without lung cancer could reveal why COPD is a pre-malignant lesion for lung cancer.

**Results:**
The lung stroma proteome depends on FEV1 and lung cancer status.

The lung stroma proteome is largely modulated via changes in translational efficiency.

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**Two discrete pro-cancer stromal secretory programs distinctly associate with lung cancer depending on FEV1**

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**Two distinct cancer-associated gene-expression programs in lung stroma depending on FEV1**

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**Fibroblast subsets express factors from pro-cancer secretomes in both mild and severe COPD**

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**ET52 secretome**

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**Severe COPD**

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**ETS2 secretome**

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**No/mild COPD**

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**BMP1**

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**IL6**

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**Senescence secretome**

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**In both mild and severe COPD**

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**ET52 secretome**

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**Severe COPD**

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**ETS2 secretome**

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**No/mild COPD**

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**BMP1**

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**Senescence secretome**

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**In both mild and severe COPD**