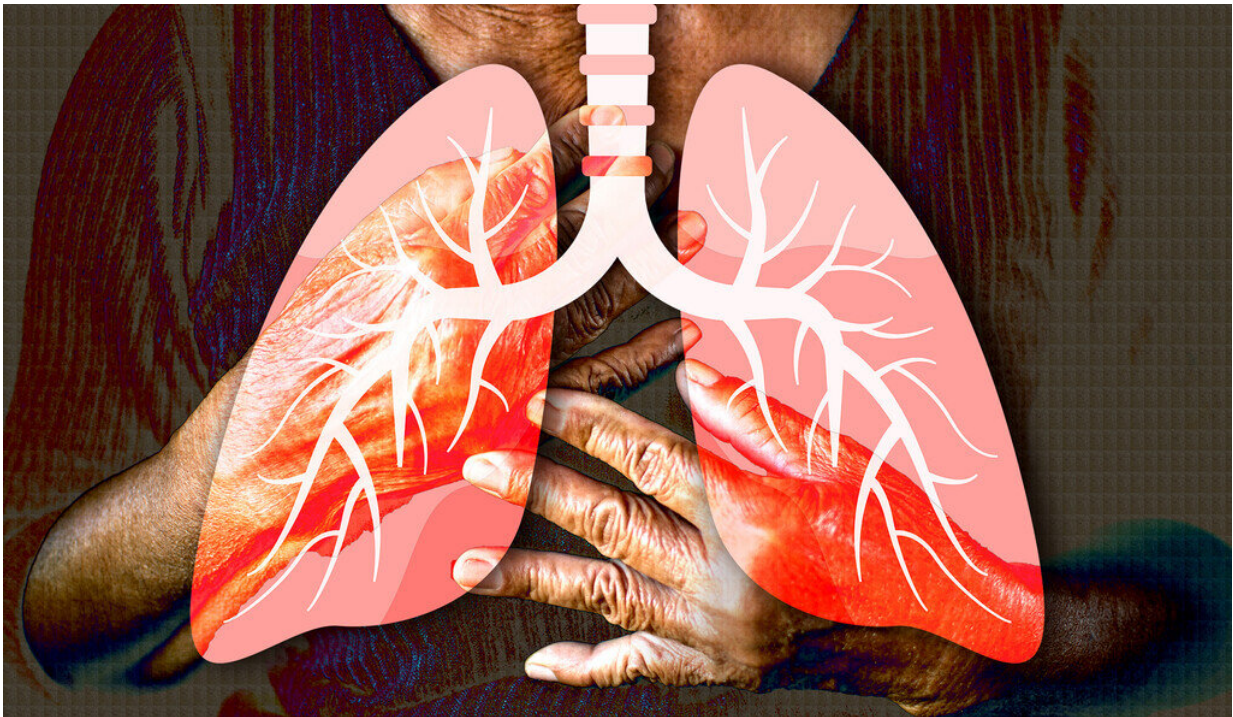# Researchers create cellular blueprint of healthy lungs

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Credit: Michael S. Helfenbein

The primary function of the lung is to facilitate transfer of oxygen to the blood stream. Crucial to this lifegiving task are endothelial cells, which line blood vessels permeating the lung and through which gas exchange occurs.

Malfunction of these cells is implicated in a range of different diseases, including COPD ([chronic obstructive pulmonary disease](#)), [pulmonary fibrosis](#), and pulmonary hypertension. And the COVID-19 pandemic has raised important questions about these cells: Why are some endothelium cells, particularly in the elderly, more susceptible to injury from the disease?

"The assumption has been that all pulmonary [endothelial cells](#) were relatively the same," said Naftali Kaminski, the Boehringer Ingelheim Pharmaceuticals Inc. Professor of Medicine (Pulmonary) and chief of Yale's Section of Pulmonary, Critical Care, and Sleep Medicine.

In a new study, Kaminski's team and a multinational team of investigators and the Human Cell Atlas project, an international initiative to describe all cells in the human body, examined the diverse characteristics of these relatively understudied cells.

In analysis of healthy lung tissues in 15,000 endothelial cells obtained from 73 individuals, they established a reference map of endothelial cells in the lung which will help researchers identify specific abnormalities that occur in a host of lung diseases, including COVID-19.

The results were published in the journal *Circulation*.

"If you want to return to normal, you need to know what normal is," Kaminski said.

For the study, the team integrated single-cell RNA sequencing data generated by several groups of collaborators and applied machine learning methods that enabled them to assess activity of tens of thousands of genes within each endothelial cell. They were also able to analyze the interactions and communications between these cells and other cells in the lung.

"It is like the Hubble telescope of biology," said Yale's Jonas Schupp, the first author on the paper and a postdoctoral fellow in Kaminski's lab. "We were able to identify cell types that were indistinguishable before, as well as augment the understanding of discoveries made by others."

In addition to identifying markers of endothelial cells and their function in capillaries, arteries, veins, and lymphatic system, the researchers also provided detailed descriptions of two novel endothelial cell populations.

The paper is accompanied by a highly interactive data mining and dissemination portal that will allow scientists to explore the data without being experts in data analysis.

"We hope that the availability of our data will accelerate the development of endothelial cell specific therapies in lung disease," Kaminski said.

More information: Jonas C. Schupp et al, Integrated Single Cell Atlas of Endothelial Cells of the Human Lung, *Circulation* (2021). DOI: 10.1161/CIRCULATIONAHA.120.052318

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