

Breakout Session 6:

The NHBLI LungMAP Cloud Ecosystem: Connecting Diverse Digital and Lung Biology Resources

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The NHBLI LungMAP Cloud Ecosystem: Connecting Diverse Digital and Biology Resources

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Grand Challenges in Lung Biology



LungMAP
Molecular Atlas of Lung
Development Program



- Regeneration and repair
- Role of stem cells
- Developmental hierarchies
- Mechanisms of disease
- Genetics and infection

Addressing these questions challenges require:

- Team science approaches with diverse experts
- New tools and techniques to construct systems models
- Integrated atlas level initiatives

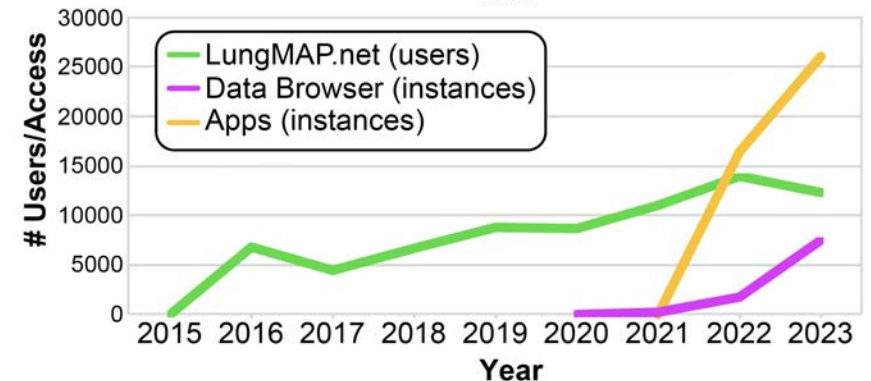
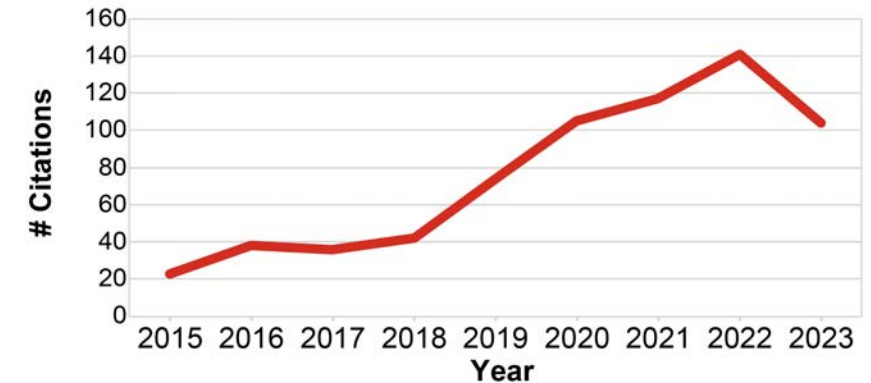
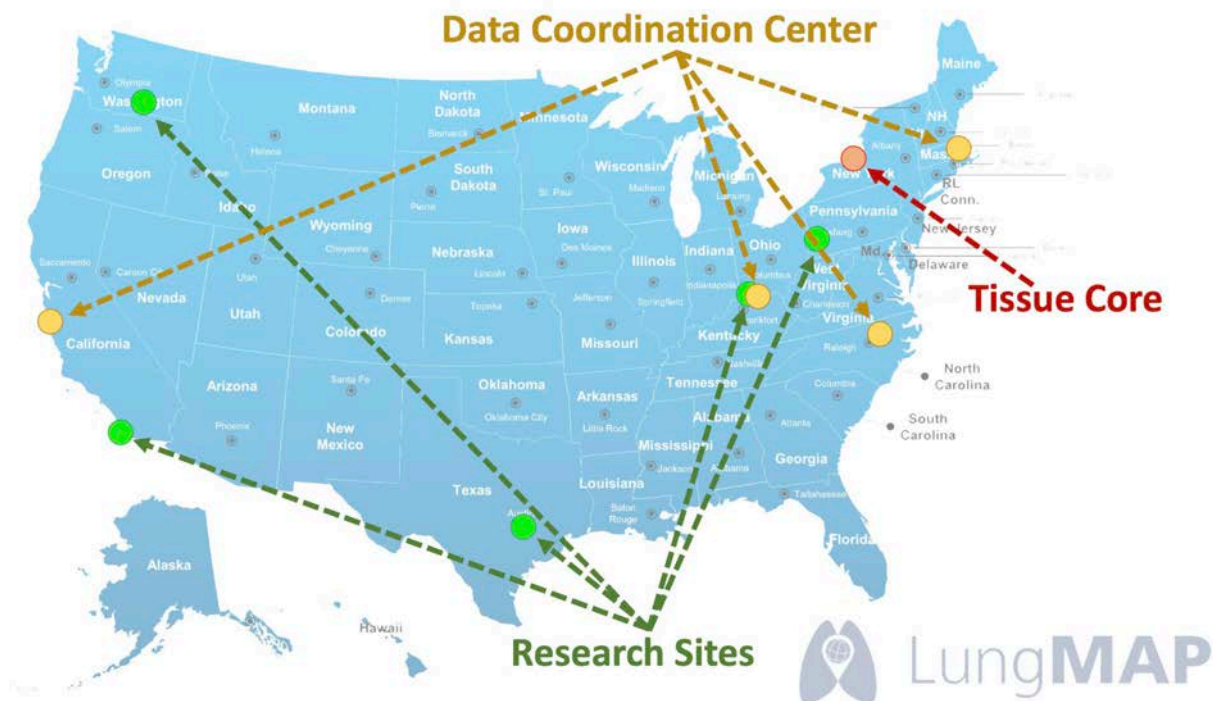
The LungMAP Consortium



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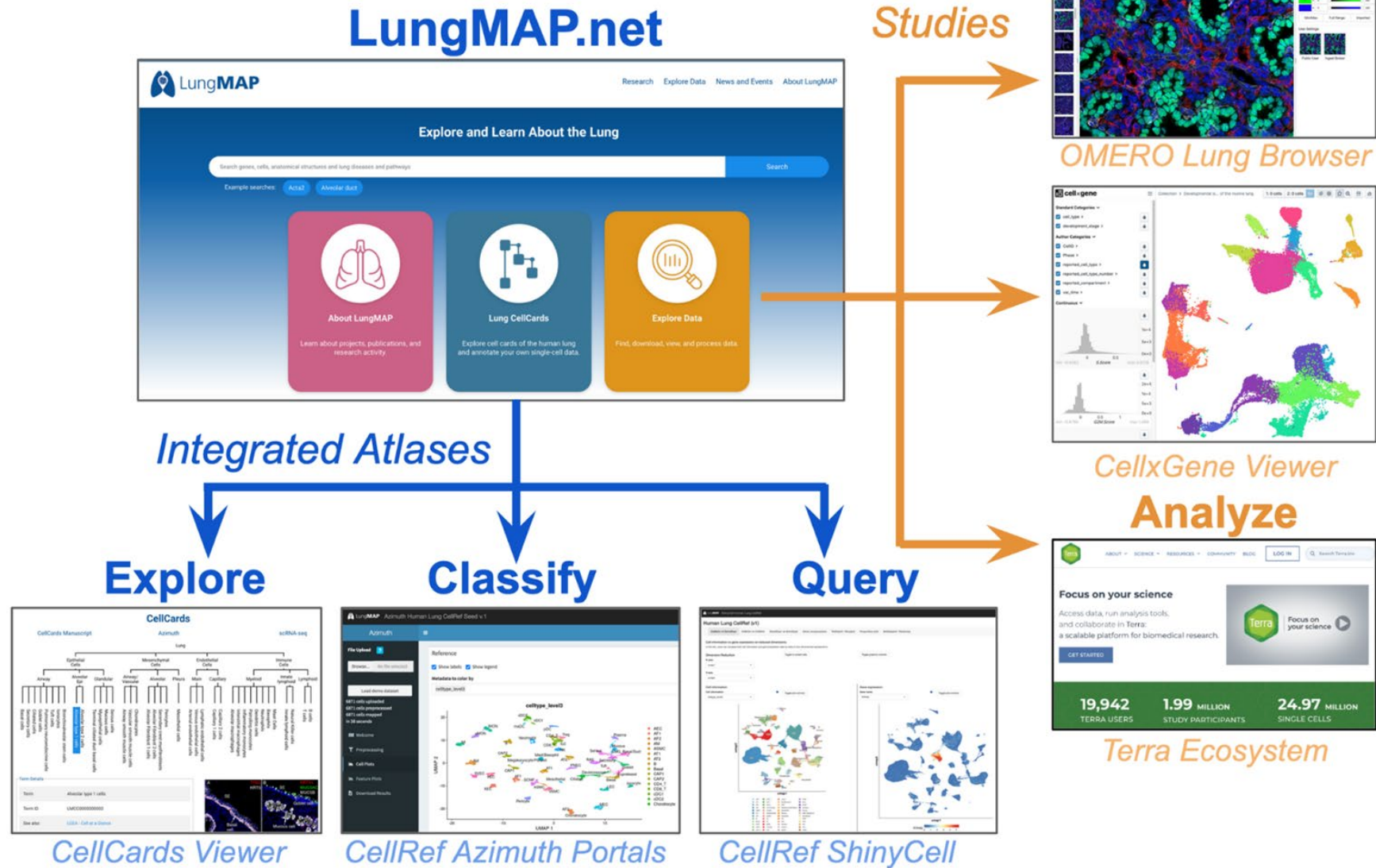


- NHBLI consortia spanning 6 research centers over the last 10 years
- Human Tissue Core at the University of Rochester (Gloria Pryhuber)
- Data Coordination Center: CCHMC, Broad, UCSC, RTI
- *Entering Phase 3 in 2023 to create accessible atlases of lung disease*



LungMAP Knowledgebase

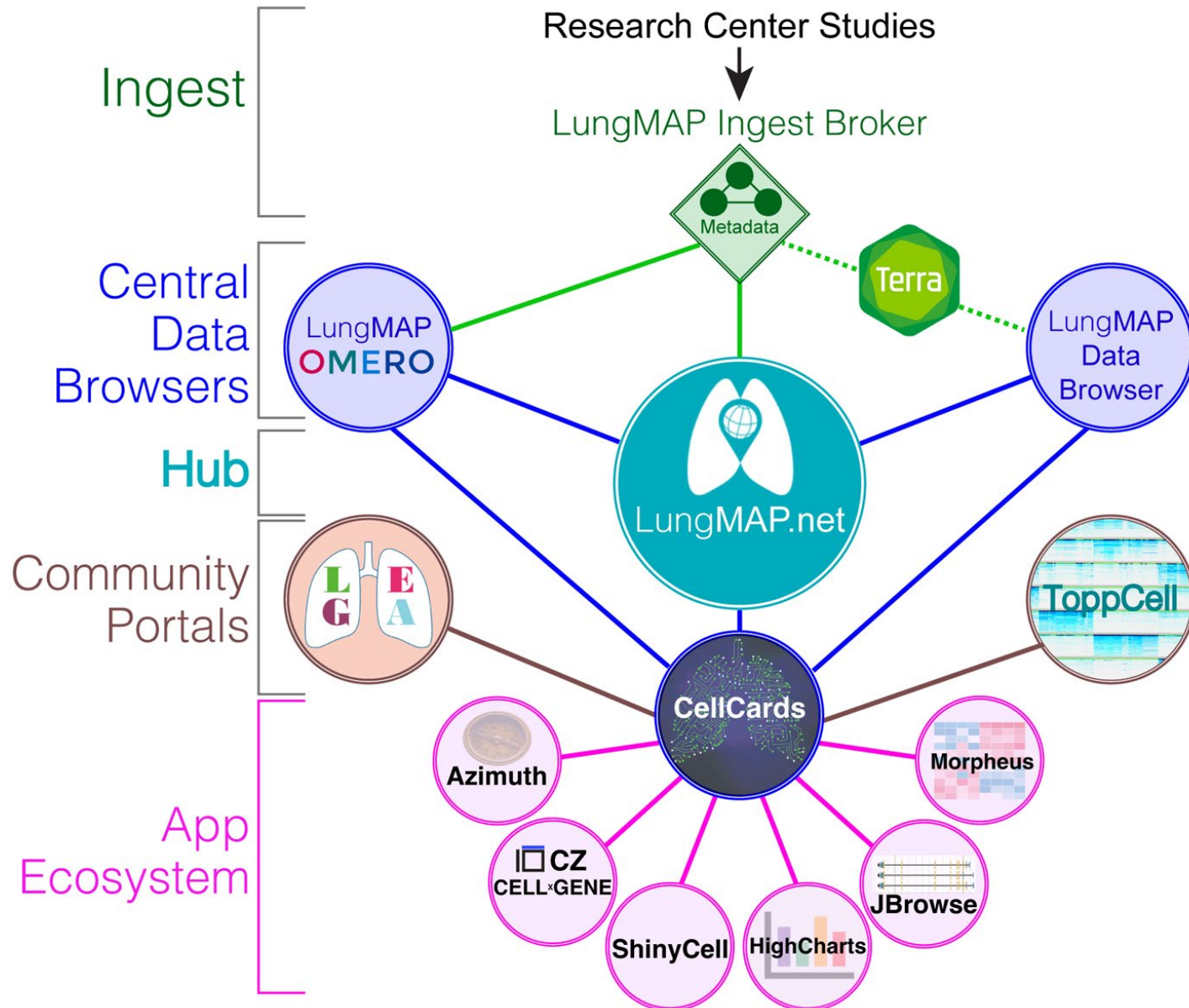
Gaddis et al. *Am J Respir Cell Mol Biol.* 2022



LungMAP.net Ecosystem



LungMAP
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- Redesigned website
- CellCards and App focused
- Driving towards maximal interactivity (within/between)
- Pushing data and analysis to the cloud.

What are the Products of LungMAP?



LungMAP
Molecular Atlas of Lung
Development Program



- **Insights:** New cell-states, regulatory models
- **Tissues:** Biopsies, whole lung
- **Data:** Omics, imaging
- **Protocols:** Experimental, analytical
- **Tools:** Organoids, omics, informatics

LungMAP Data Flow

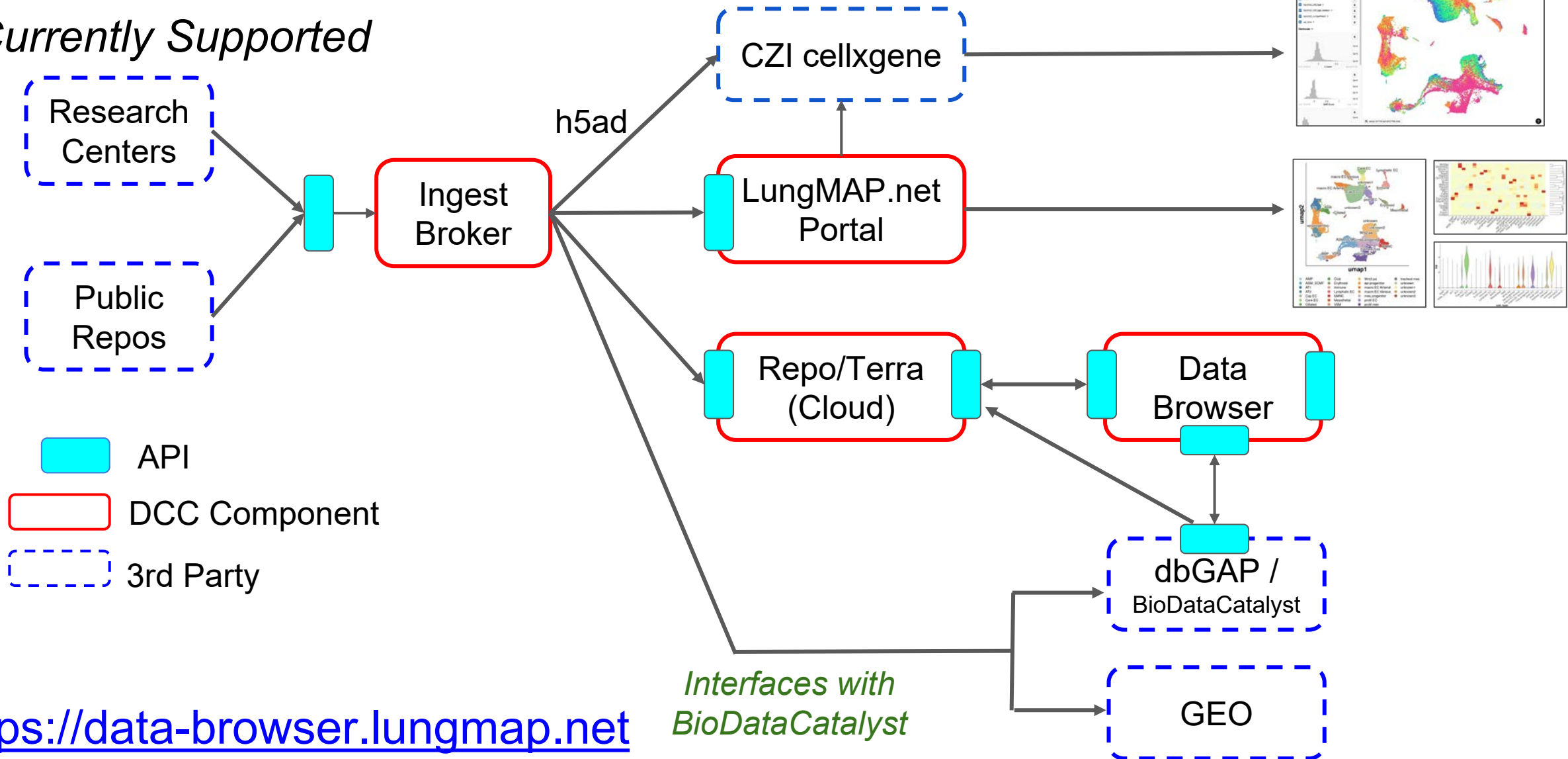


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Data Flow

Currently Supported



LungMAP.net Website



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lungmap.net

Update



Research Explore Data About LungMAP Resources

Explore and Learn About the Lung

Search genes, cells, anatomical structures and lung diseases and pathways

Search

Example searches:

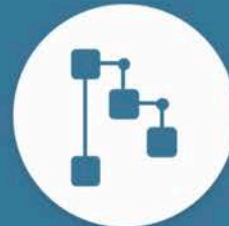
Acta2

Alveolar duct



About LungMAP

Learn about projects, publications, and research activity.



Lung CellCards

Explore cell cards of the human lung and annotate your own single-cell data.

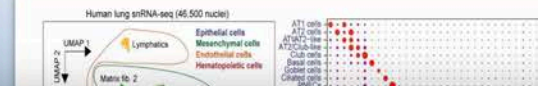


Explore Data

Find, download, view, and process data.

Highlights

Developmental Cell



https://lungmap.net/breath-search-page/?queries[]=Acta2&has_data=1



BRINDL Tissue Repository

The screenshot shows the BRINDL web interface. At the top, there's a navigation bar with "LungMAP BRINDL" and "Salomonis, N". Below that, there are tabs for "RC Requests", "HIVE Samples", and "Help". The main content area is titled "Donor: D001" and "Donor List". A search bar contains "D001". The "Participant" section is expanded, showing "INFORMATION" and "DEMOGRAPHICS".

DEMOGRAPHICS

Age/Gender	20 month old Female
Race	Black/AA
Weight	13 kg
Weight Percentile	92.9

DONOR INFORMATION

Health Status	No known lung disease
Cause of Death	Head Trauma
Lung Assessment on arrival	Very Good
Final Diagnoses	Path: Acute bronchopneumonia, moderate, focal bacteria

PATHOLOGIST REVIEW

Pathologist Impression	RLL: Acute bronchopneumonia, moderate, focal bacteria Patchy hemorrhage
	LLL: Normal growth and structure

On the right side, there's a "AVAILABLE TISSUE IN" section with a list of tissue samples like "Bronchus Left", "Bronchus Right", etc.

OMERO Image Viewer

The screenshot shows the OMERO Image Viewer interface. The main window displays a multi-channel fluorescence microscopy image of lung tissue. The image is composed of several channels: DAPI (blue), FITC (red), TRITC (green), and Cy5 (grey). A yellow circle highlights a specific region of interest in the image. The interface includes a top menu bar with "OMERO", "File", "ROIs", and "Help". Below the menu bar, there are navigation controls like zoom, pan, and fit. On the right side, there's a "Settings" panel with options for "Grayscale", "Histogram", and "Interpolate". Below that, there are color calibration sliders for each channel (DAPI, FITC, TRITC, Cy5) with min/max values. At the bottom right, there's a "User Settings" section with thumbnails for "Public User" and "root root".

Cross-Consortia Cell-Type Curation



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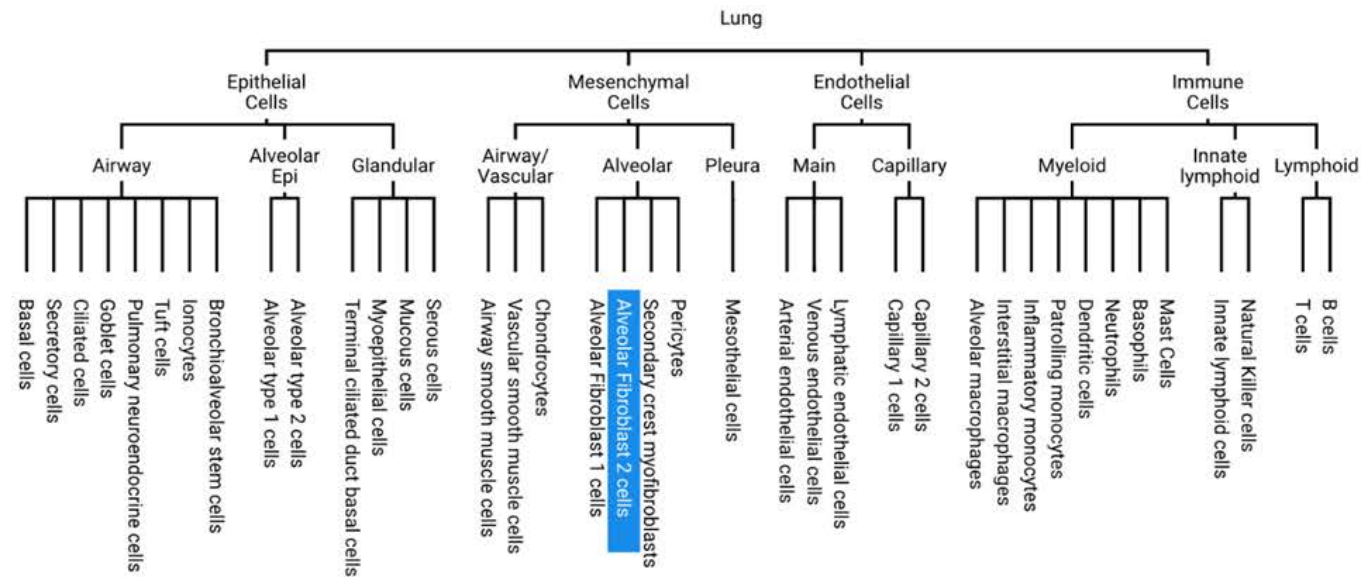
CellCards

CellCards Reference

CellRef scRNA-seq

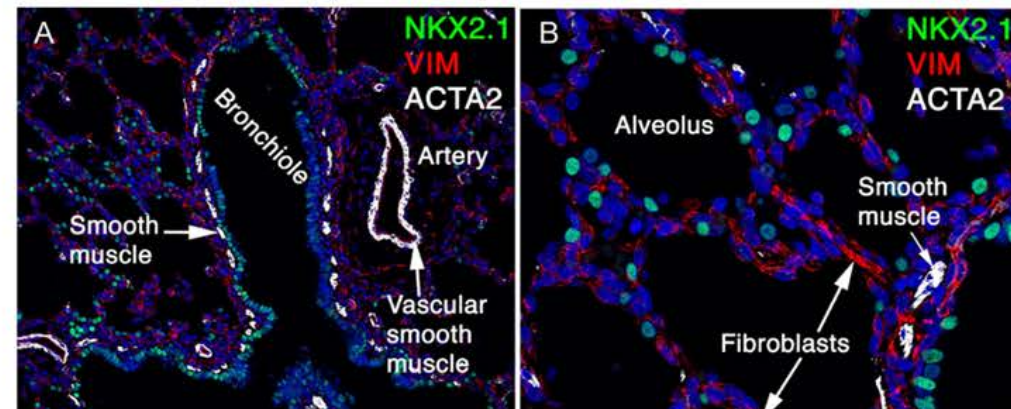
CellRef ATAC-seq

CellRef Azimuth



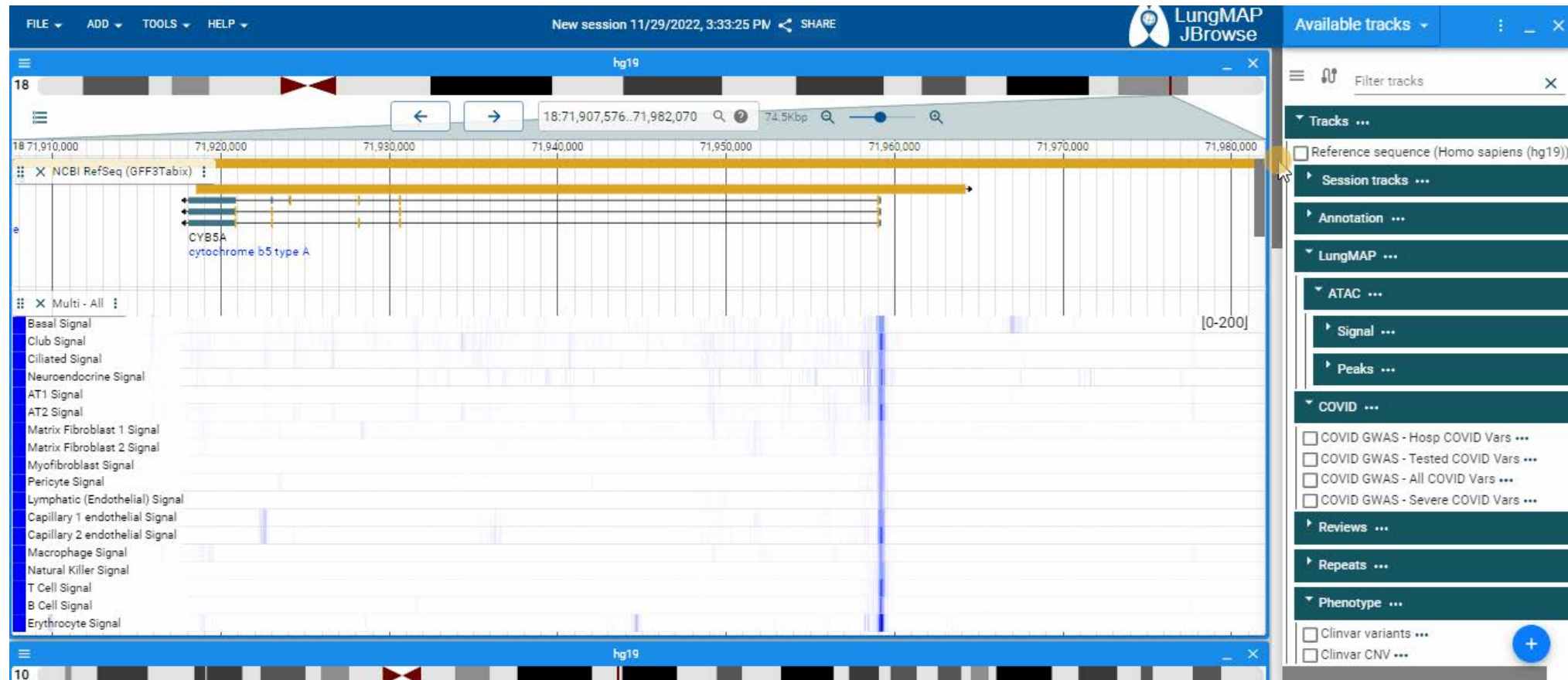
Term Details

Term	Alveolar Fibroblast 2 cells
Term ID	LMCC0000000026
See also	LGEA - Cell at a Glance
Related synonyms	Type-2 associated stromal cell (TASC)(Chung, et al., 2018) Type-2 associated stromal cell (TASC)(Chung, et al., 2018) Adventitial fibroblast (Travaglini, et al., 2020) Adventitial fibroblast (Travaglini, et al., 2020) Matrix fibroblast 2 MANC (Zepp, et al., 2017) (Park, et al., 2019) (Torday, et al., 2016) MANC (Zepp, et al., 2017) (Park, et al., 2019) (Torday, et al., 2016) Mesenchymal alveolar niche cell





- View pre-loaded, UCSC Track Hub, or bring-your-own-track
- View and compare multiple loci (including species*)



LungMAP App Ecosystem



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Human CellCards Multi-Study CellRef 1.0 Atlas

Minzhe Guo (CCHMC) | Jeremy Clair (PNNL) | Joshua N. Adkins (PNNL) | Gloria Pryhuber (HTC/URMC) | Ravi Misra (HTC/URMC) | Bruce Aronow (CCHMC) | Timothy L. Tickle (Broad) | Nathan Salomonis (CCHMC) | Xin Sun (UCSD) | Edward E. Morrisey (UPenn) | Jeffrey A. Whitsett (CCHMC) | Yan Xu (CCHMC)

How to explore data (tutorial)

Description

The "LungMAP Human Lung CellRef" atlas incorporates 48 well-defined lung cell types (CellCards) catalogued from diverse anatomic locations and stages of lung maturation. This atlas spans sc/snRNA-seq of 505,256 lung cells from 148 normal human lung samples from 104 donors from parenchyma, trachea, bronchi, bronchus SMG and small airway. This study includes 21 new lung samples. An accompanying R-shiny app (Azimuth) enables fast supervised annotation of user-provided single-cell RNA-Seq datasets (see below).

LungMAP ID: LMEX0000004396

Stages: Adult | Child | Adolescent

Technology: 10x Genomics

Organism: Human

Assay type: Single-cell RNA-seq

Reference: Guo, et al. (2022)

Exploratory Tools

Samples

Downloads



(Tutorial)



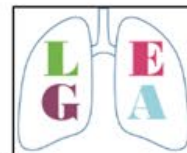
(Tutorial)



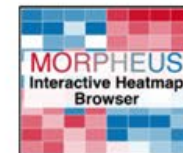
(Tutorial)



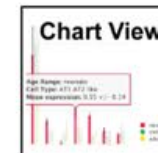
(Tutorial)



(Tutorial)



(Tutorial)



(Tutorial)



(Tutorial)

LungMAP App Ecosystem



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Visualize Data

Filter by:

Species ▾

Age Range ▾

Sample Type ▾

Researcher ▾

Technology ▾

Single-Cell RNA-seq (32)

RNA-seq (10)

mRNA (1)

microRNA (3)

Proteomics (10)

Metabolomics (1)

Lipidomics (4)

Methylation (5)

2D Imaging (3919 sets)

Search:

Dataset	Species	Stage	Cells	Explore
Human CellCards Multi-Study CellRef 1.0 Atlas	Homo sapiens	Adult Child Adolescent	505256	
Mouse CellCards Multi-Study CellRef 1.0 Atlas	Mus musculus	E16.5-E17.5 E17.5-E19.5 P0-P3 P4-P36	95658	
Single cell transcriptomic signatures of normal human newborn, child and adult lungs	Homo sapiens	Neonate Child Adult	46500	
Single cell transcriptomic profiling identifies molecular phenotypes of newborn human lung cells	Homo sapiens	Neonate	5499	
Systematic identification of 58 lung cell populations in bronchi and parenchyma from 3 normal lungs	Homo sapiens	Adult	65662	
A molecular single-cell lung atlas of lethal COVID-19	Homo sapiens	Adult	116314	
Single-cell RNA-seq reveals ectopic and aberrant lung-resident cell populations in idiopathic pulmonary fibrosis	Homo sapiens	Adult	312928	
Single-cell RNA-seq of 13 normal, LPS-exposed, or anti-inflammatory treated third trimester Rhesus macaque lungs	Macaca mulatta	Saccular	120042	

Interactive Visualization & Analysis



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LungMAP Apps

CELLxGENE Annotate Logo LungMAP_Hu..._g_CellRef.v1
cellxgene

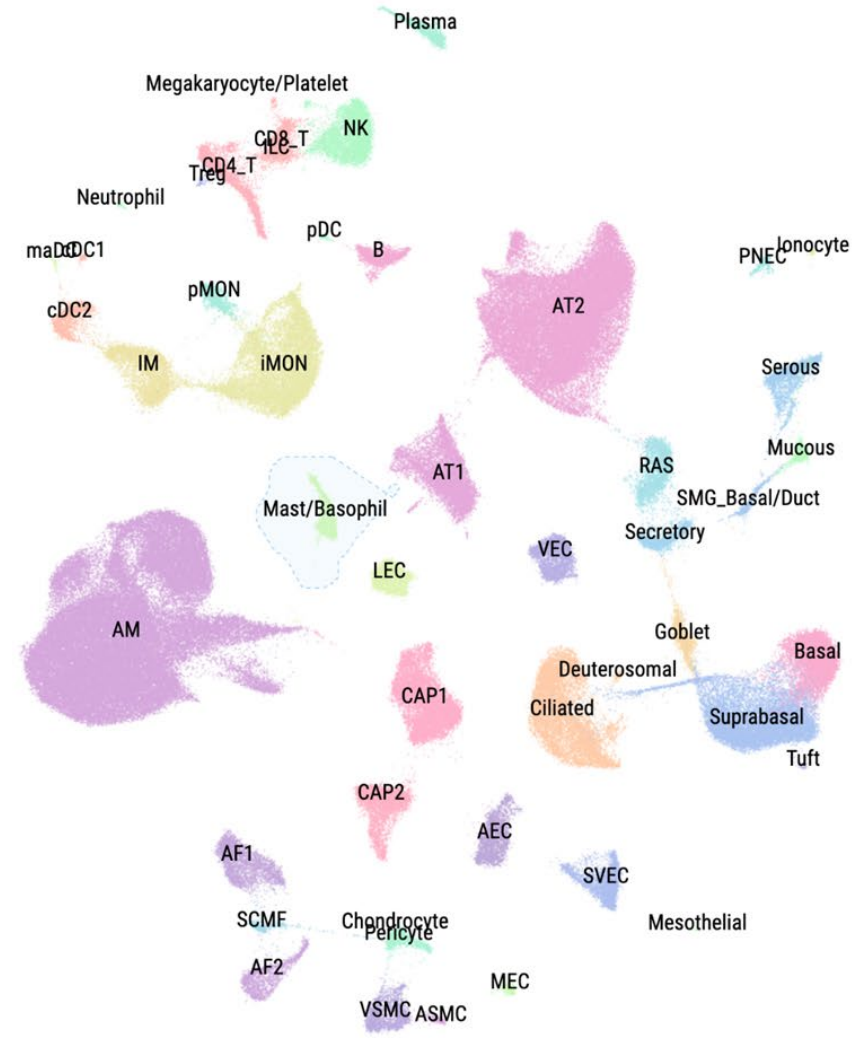
DataID >

Dataset >

DonorID >

<input type="checkbox"/> 001C		1041
<input type="checkbox"/> 002C		263
<input type="checkbox"/> 003C		2107
<input type="checkbox"/> 034C		226
<input type="checkbox"/> 065C		554
<input type="checkbox"/> 081C		265
<input checked="" type="checkbox"/> 084C		190
<input checked="" type="checkbox"/> 092C		2201
<input checked="" type="checkbox"/> 098C		5227
<input type="checkbox"/> 133C		4362
<input type="checkbox"/> 1372C		2239
<input type="checkbox"/> 137C		644
<input type="checkbox"/> 160C		1912
<input type="checkbox"/> 192C		1881
<input type="checkbox"/> 208C		907
<input type="checkbox"/> 218C		2679
<input type="checkbox"/> 222C		5612
<input type="checkbox"/> 226C		3842
<input type="checkbox"/> 244C		120
<input type="checkbox"/> 253C		679
<input type="checkbox"/> 296C		1450
<input type="checkbox"/> 388C		791

1: 977 cells 2: 1210 cells



Interactive Visualization & Analysis



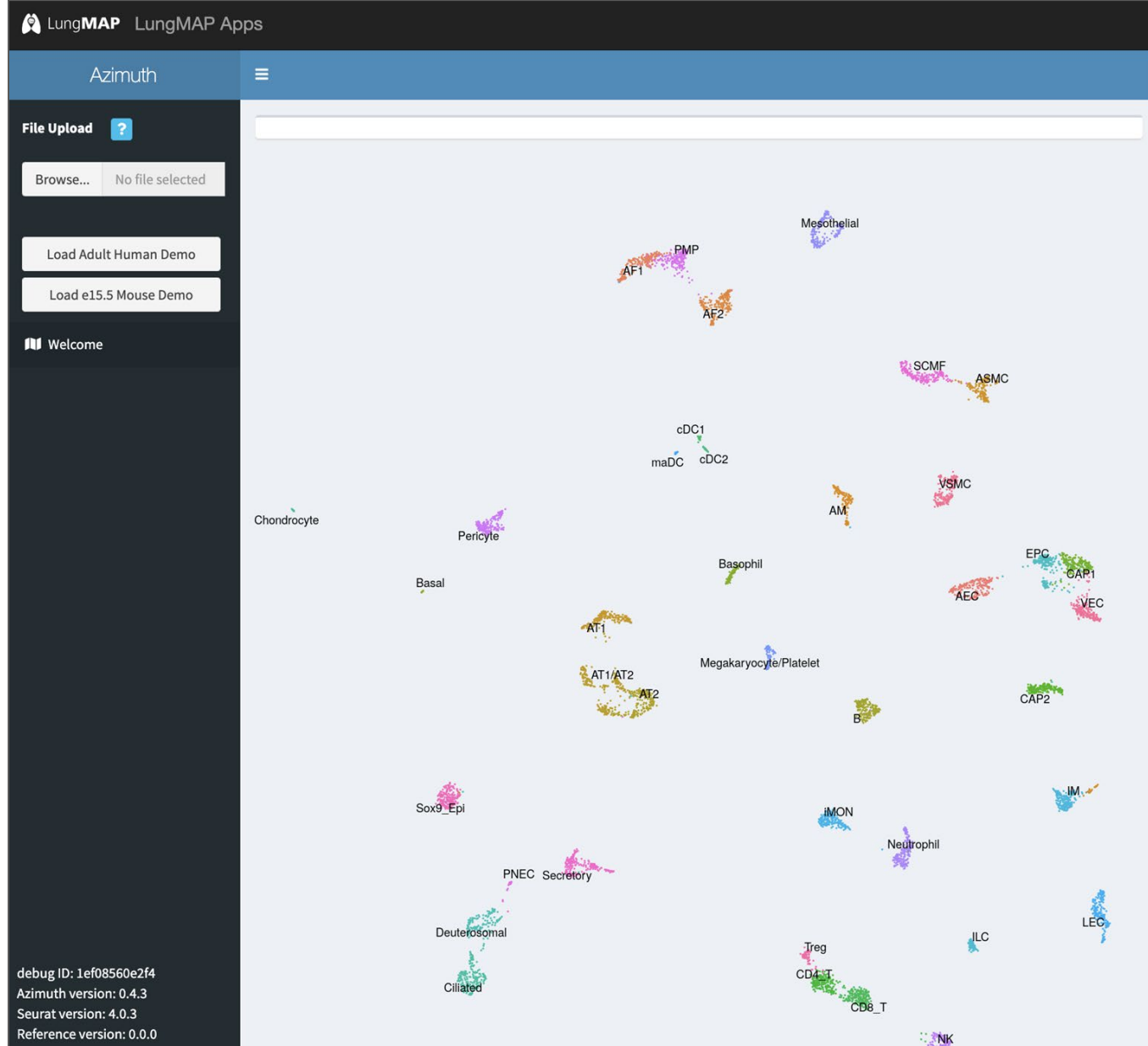
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Interactive Visualization & Analysis



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Interactive Visualization & Analysis



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LungMAP LungMAP Apps

Azimuth

File Upload ?

Browse... No file selected

Load Adult Human Demo

Load e15.5 Mouse Demo

8567 cells uploaded
8567 cells preprocessed
8567 cells mapped
in 38 seconds

Welcome

Preprocessing

Cell Plots

Feature Plots

Download Results

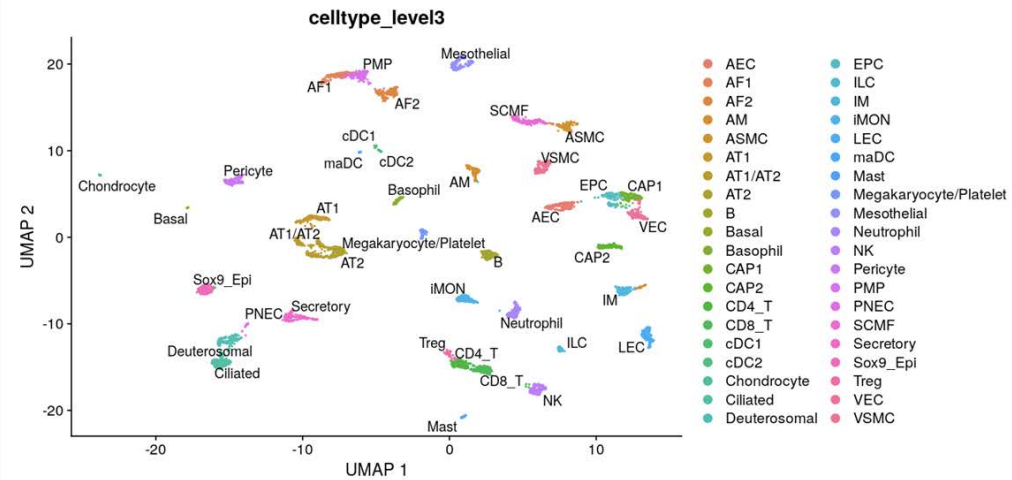
debug ID: 1ef08560e2f4
Azimuth version: 0.4.3
Seurat version: 4.0.3
Reference version: 0.0.0

Reference

Show labels Show legend

Metadata to color by

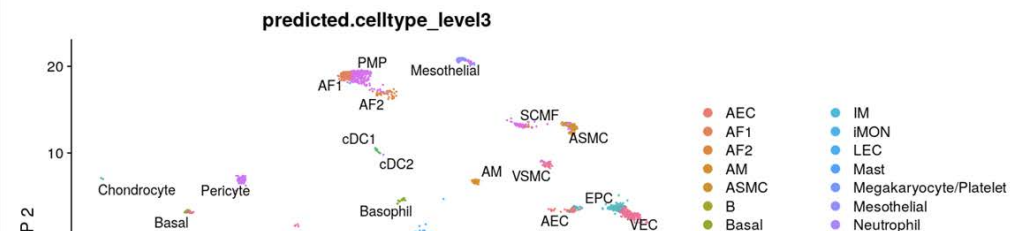
celltype_level3



Query

Metadata to color by

predicted.celltype_level3





#3 – LungMAP-HCA Data/Metadata Explorer

Explore Metadata APIs

Explore Data

Search all filters

Donor ▾

Tissue Type ▾

Specimen ▾

Method ▾

File ▾

556.0k Estimated Cells 206 Specimens 160 Donors 600 Files 1.57 TB File Size

Export Selected Data

Projects
Samples
Files

↑ Sample Id	Project Title	Species	Sample Type	Anatomical Entity	Organ Part	Model Organ	Selected Cell Types	Library Construction Method	Nucleic Acid Source	Paired End	Analysis Protocol	Age	Sex	Disease Status (Specimen)
(206)	(6)	(3)	(1)	(3)	(4)	(1)	(1)	(6)	(2)	(3)	(20)		(4)	(2)
022006ad-1...	Human Lung Reference Cell Atlas version 1.0	Hom...	specimens	Lung	Unspecified	–	Unspe...	10X 3' v2 sequencing	single cell	false	004d1c80-5b66-46f3-b01a-63757d4807ab, d818ffdf-fcdb-45f3-946a-fd725c32e6c3	29 y	male	normal
0257bc98-...	Genomic, epigenomic, and biophysical cues controlling the emergence of the lung alveolus	Mus ...	specimens	Lung	Unspecified	–	Unspe...	10X 3' v2 sequencing	single cell	Unspecified	1c145725-c287-45c8-b0d7-6b5ed78674fc, 823cb2ce-79ff-4737-82d8-c50c286ede54	Unspecified	female	normal
02a139f0-a...	Human Lung Reference Cell Atlas version 1.0	Hom...	specimens	Lung	Unspecified	–	Unspe...	10X 3' v2 sequencing	single cell	false	004d1c80-5b66-46f3-b01a-63757d4807ab, d818ffdf-fcdb-45f3-946a-fd725c32e6c3	33 y	male	normal
0458fcb6-f...	Human Lung Reference Cell Atlas version 1.0	Hom...	specimens	Lung	Unspecified	–	Unspe...	10X 3' v2 sequencing	single cell	false	004d1c80-5b66-46f3-b01a-63757d4807ab, d818ffdf-fcdb-45f3-946a-fd725c32e6c3	26 y	female	normal

Terra-powered Cloud Resources



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Open-access data repository facilitating integration with NHLBI ecosystem



HCA schema

Streamlined
integration



BioData
CATALYST

Cloud workspace for scalable analysis

The screenshot shows the Terra workspace interface. The top navigation bar includes 'WORKSPACES' and 'Dashboard'. The main content area is titled 'Explore LungMAP single-cell data' and contains a list of steps for using the workspace. A right-hand sidebar displays 'WORKSPACE INFORMATION' and 'CLOUD INFORMATION'.

ABOUT THE WORKSPACE

Explore LungMAP single-cell data

This tutorial workspace is a step-by-step guide to importing, accessing, and analyzing single-cell RNA sequencing data from the LungMAP [Data Browser](#) using community-supported single-cell analysis tools.

Using this workspace, you will:

1. Import 10x sequencing reads in FASTQ format from the LungMAP [Data Browser](#)
2. Use a Jupyter Notebook to create new data tables to organize data for downstream alignment and preprocessing with the Optimus workflow
3. Preprocess 10x FASTQs with the Optimus workflow
4. Convert the Optimus raw cell-by-gene matrix output to mtx format for downstream Seurat analysis
5. Import mtx files and visualize the count matrix in an example **Seurat** Jupyter Notebook

WORKSPACE INFORMATION

Last Updated	10/26/2022
Creation Date	10/18/2022
Workflow Submissions	2
Access Level	Reader

CLOUD INFORMATION

OWNERS

TAGS

Tutorials: <https://lungmap.net/resources-2/tutorials/>

- **Tutorial 5: Cloud-based omics data analysis with Terra**
- **Video 2: Exploring and Analyzing LungMAP Data in Terra**





- **Exponential Growth:** Dozens of new atlases & interfaces
- **Creating atlases in the cloud:** Public + consortia + user
- **Leveraging AI:** User facing language models and disease gene regulatory network models.
- **Cost management:** Balancing growth, community needs and cloud versus on prem compute.

Thank you!



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DCC Leadership



Bruce
Aronow



Nathan
Salomonis



Bing-Xing
Huo



Timothy
Tickle



Benedict
Patten



Eric
Bardes



Scott
Tabar



Joshua
Fortriede



Kevin
Burns



Liam
Dolan

DCC CCHMC



Surya Prasath



Michal
Kouril



Yan Xu



Jeff Whitsett



Benjamin
Crooks



Kang
Jin



Minzhe
Guo



Dan
Schnell

DCC Broad Institute



Nate
Calvanese



Kat
Thayer

ACC CCHMC



Stephanie
Loos



Chelsea
Yeary

DCC UCSC



Trevor
Heathorn



Hannes
Schmidt

RTI



Nathan
Gaddis

with assistance from CZI and the NIH Strides & dbGAP team