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Noble Strategy for Culturing Lung Cancer Organoid with High Cancer Cell Purity in All Stages of Lung Cancer

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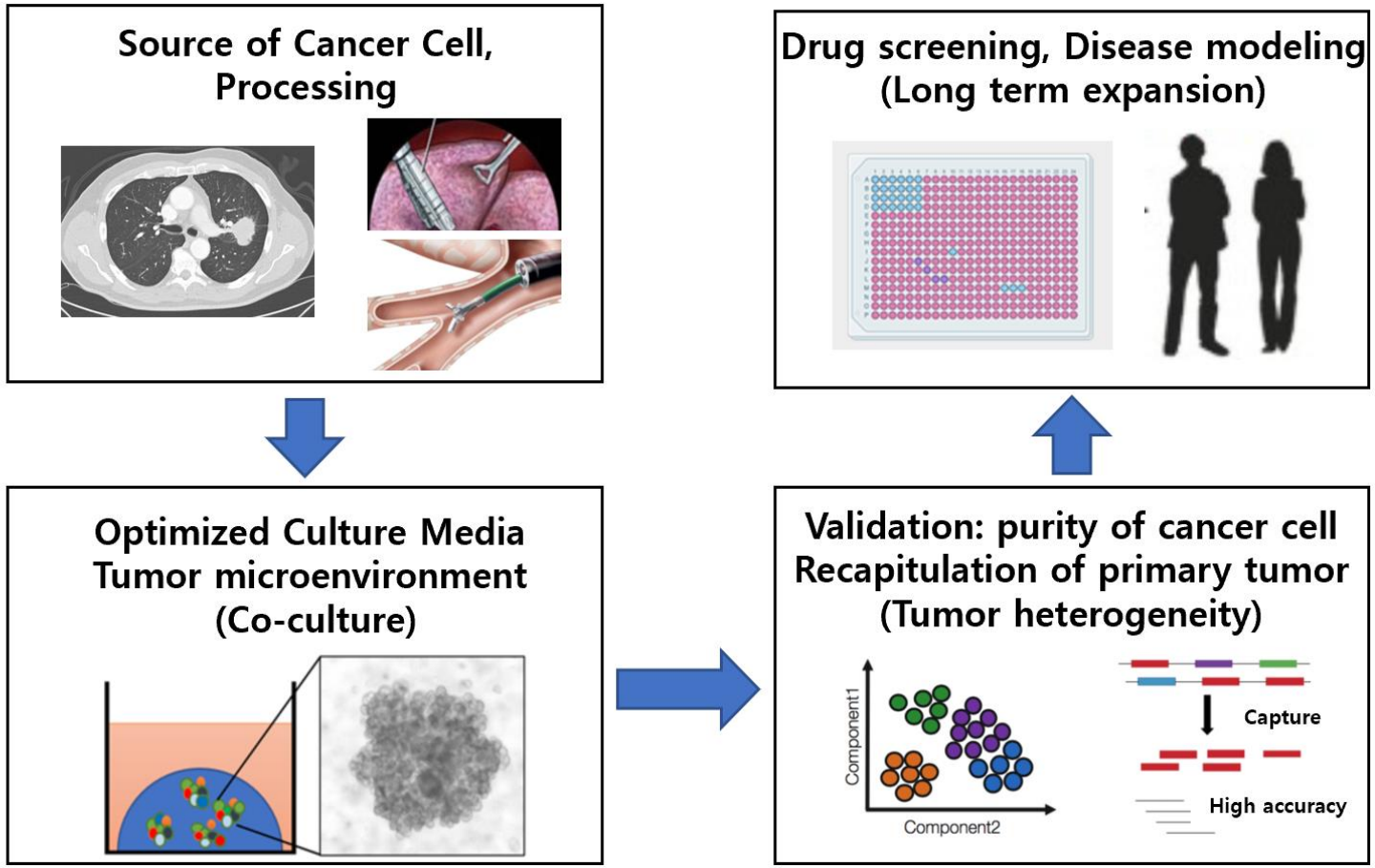
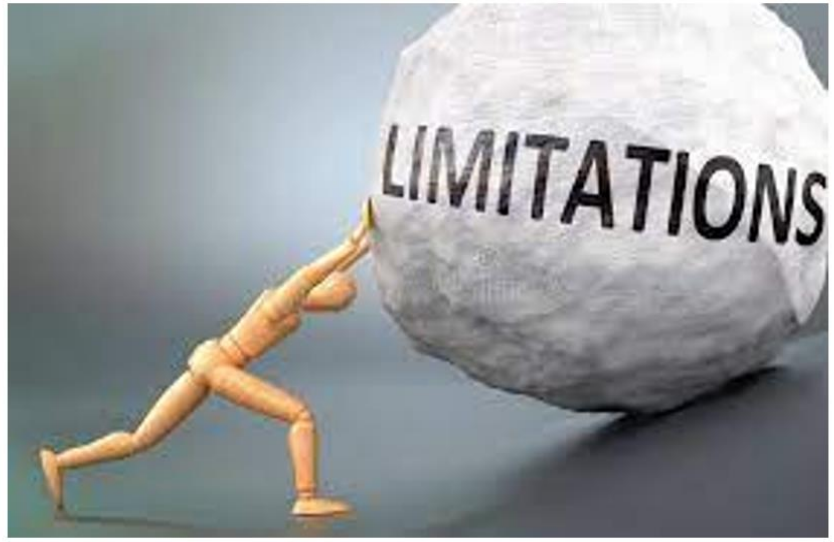
Background and Aim

Lung cancer organoids derived from surgical specimen have many limitations





Limitations of lung cancer organoid

Surgical specimen)
- Organoid from only early lung cancer
- Low purity of cancer cells in late passage

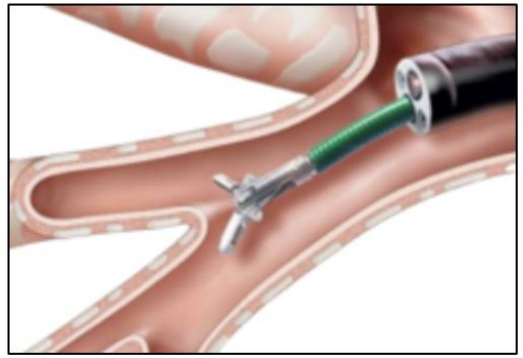
Biopsy specimen)
- Very low success rate of organoid culture

Background and Aim

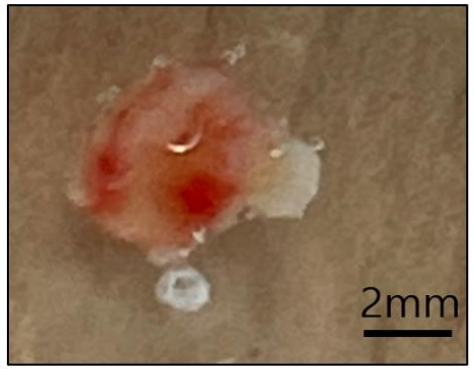
To overcome the limitations, lung cancer organoids were derived from small biopsy (cryo-biopsy) specimens of all stages of lung cancer

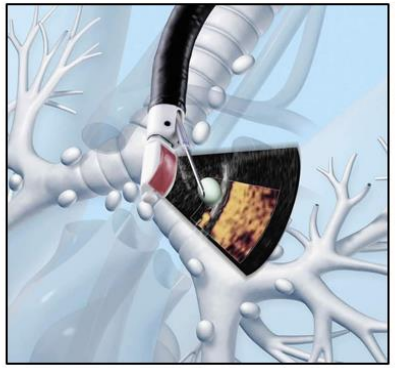
(Percutaneous needle biopsy)

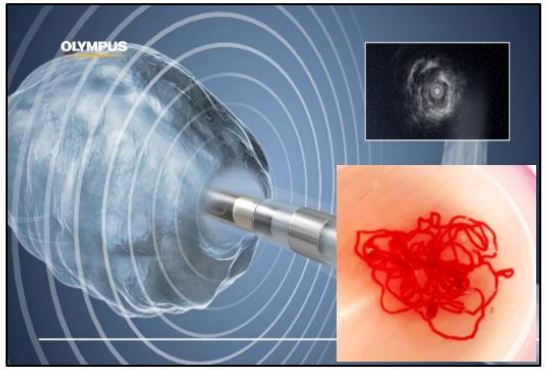
(Bronchoscopic biopsy)



(Linear, Radial EBUS)



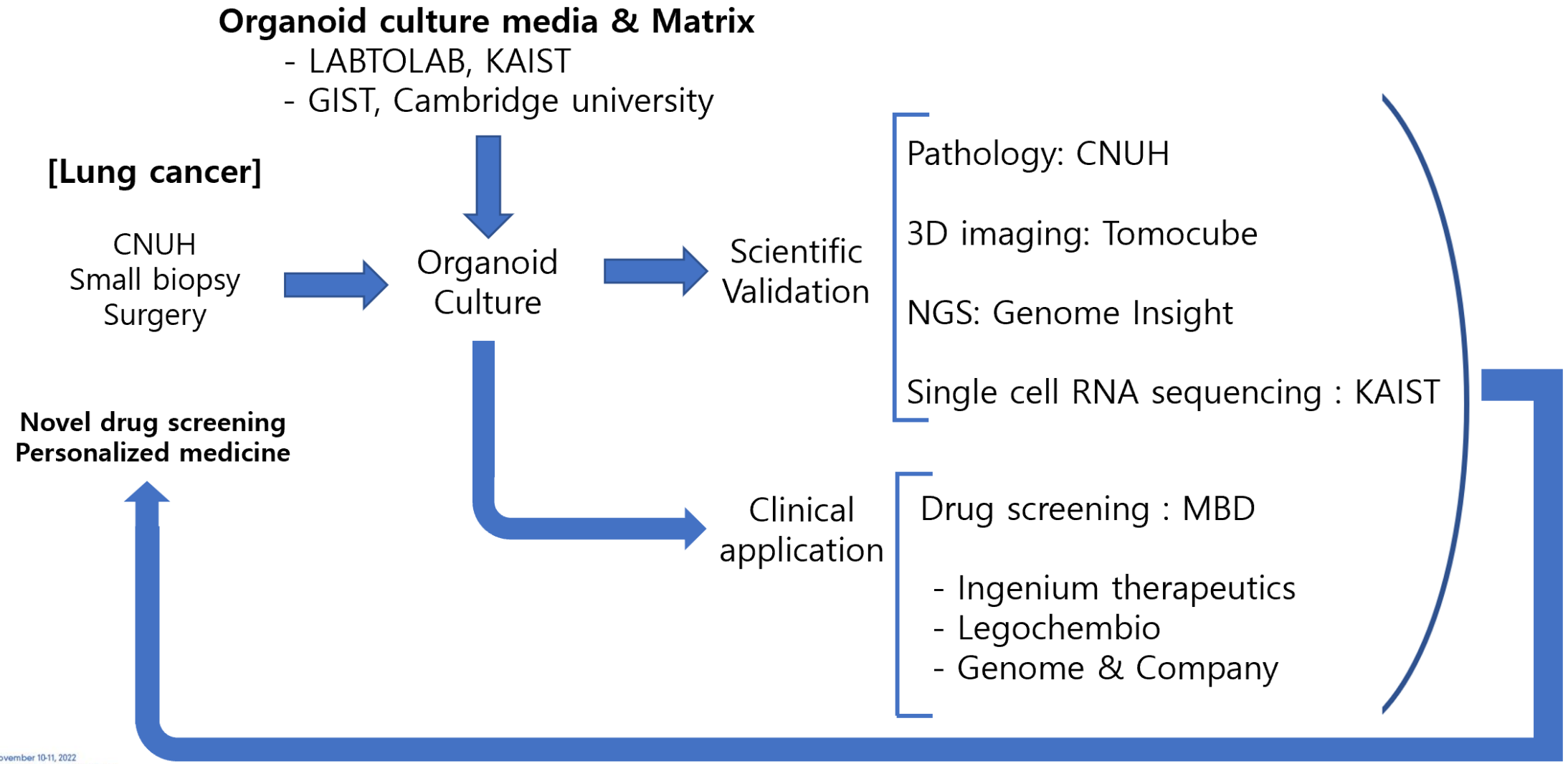




Cryo-biopsy

Methods

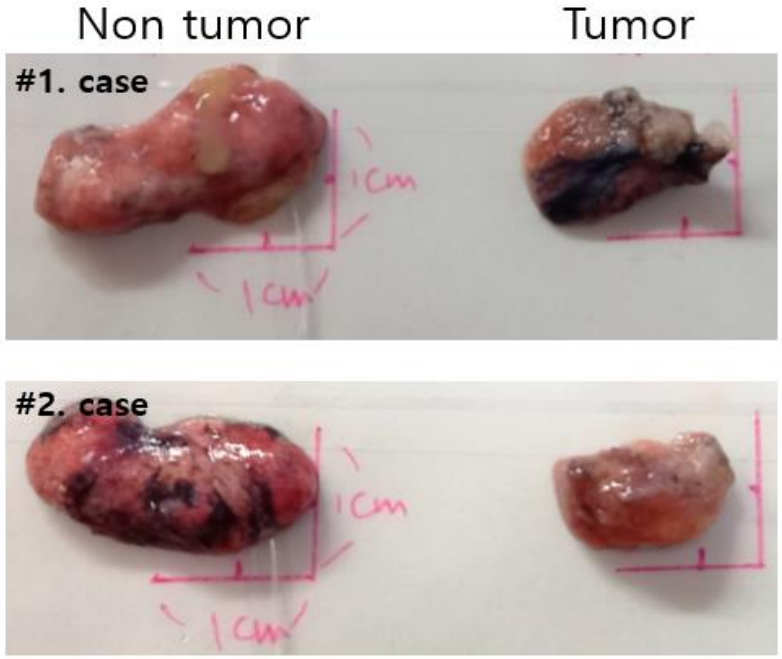
Scientific validation and clinical application of lung cancer organoids



Results

1. Normal lung cells overgrow after several passages in lung cancer organoid from surgical specimen

A



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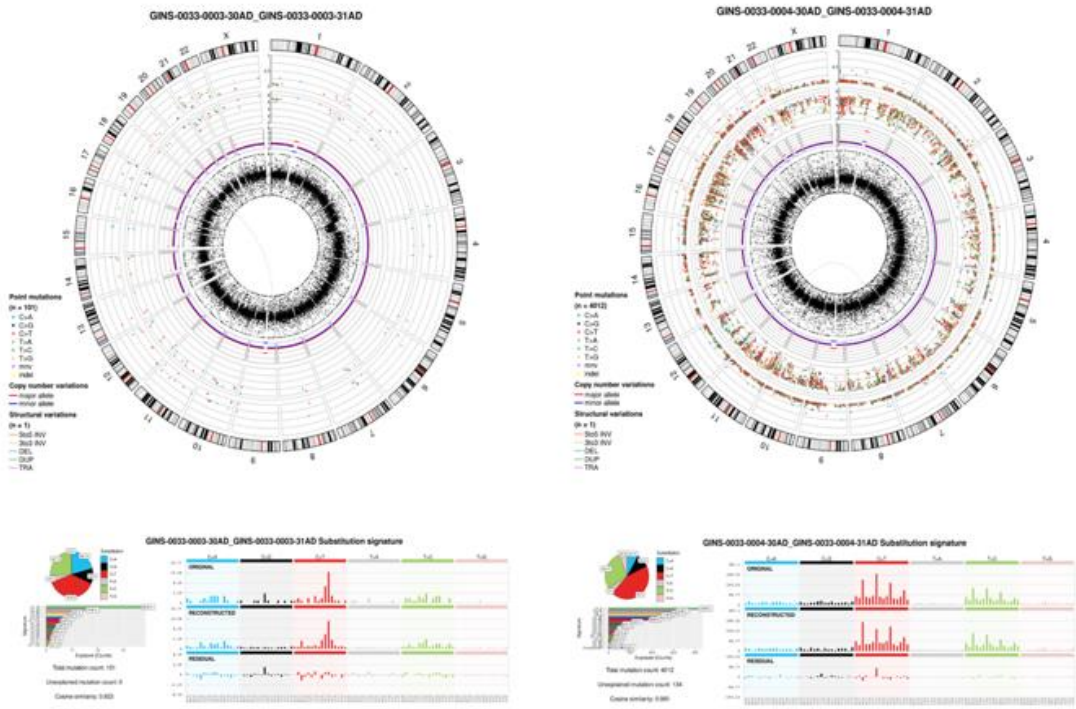
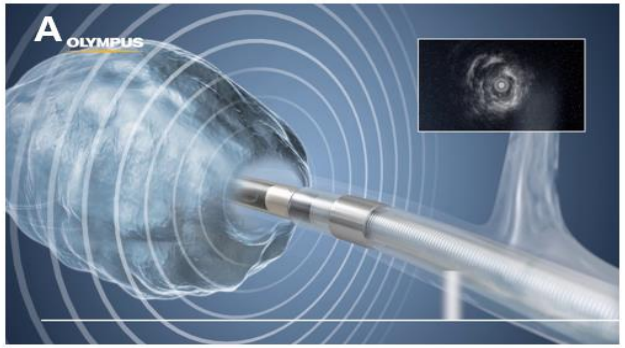


(A) Representative pictures of surgical specimen from lung cancer patients. We made organoids from both non-tumor specimen and tumor specimen. Then we compared the NGS data from normal lung organoids and lung cancer organoid from tumor specimen.

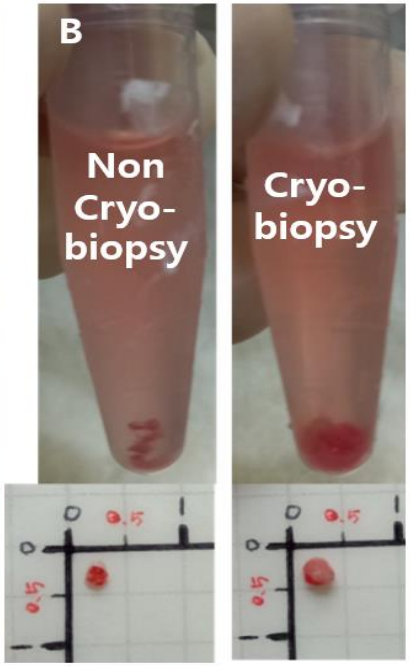
(B) NSG data showed that normal cells overgrew after several passages in lung cancer organoid. There were quiescent copy number profile and less than 4% variant allele frequency.

Results

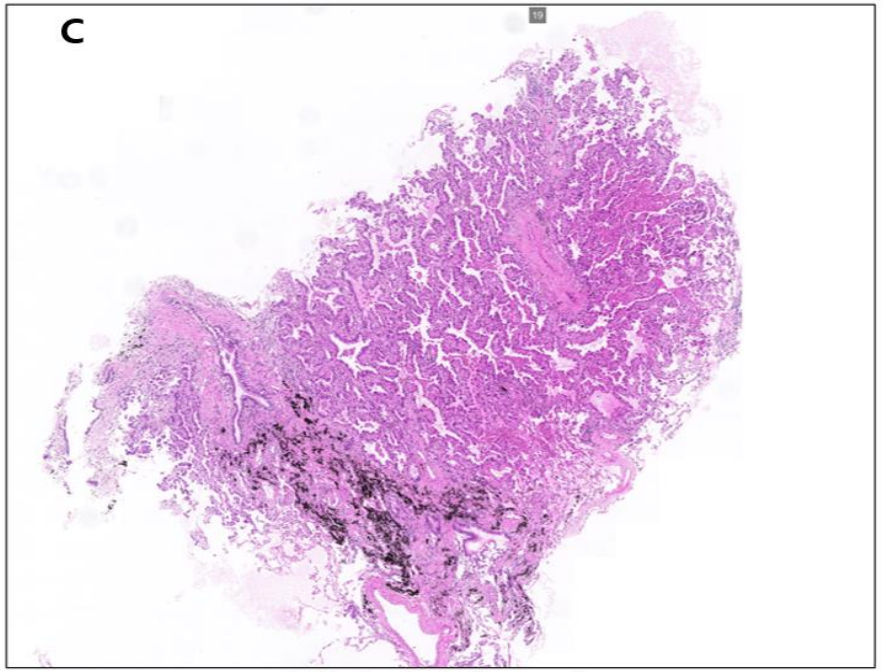
2. Radial endobronchial ultrasonography(EBUS) guided cryobiopsy acquired the small biopsy tissues for lung cancer organoid



Radial endobronchial ultrasonography- Cryobiopsy



Biopsy samples



H&E staining of small biopsy tissue

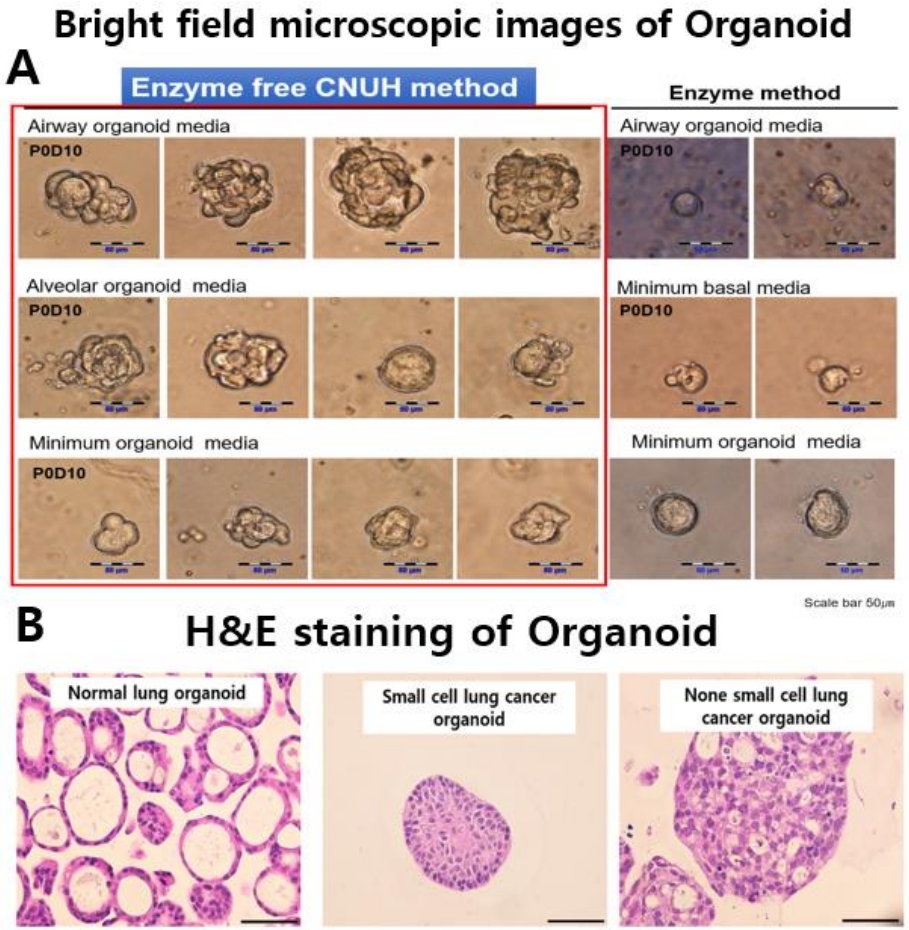
(A) Radial EBUS guided cryobiopsy can acquire lung cancer tissues from not only central lesions but also peripheral lung lesions with few complications.

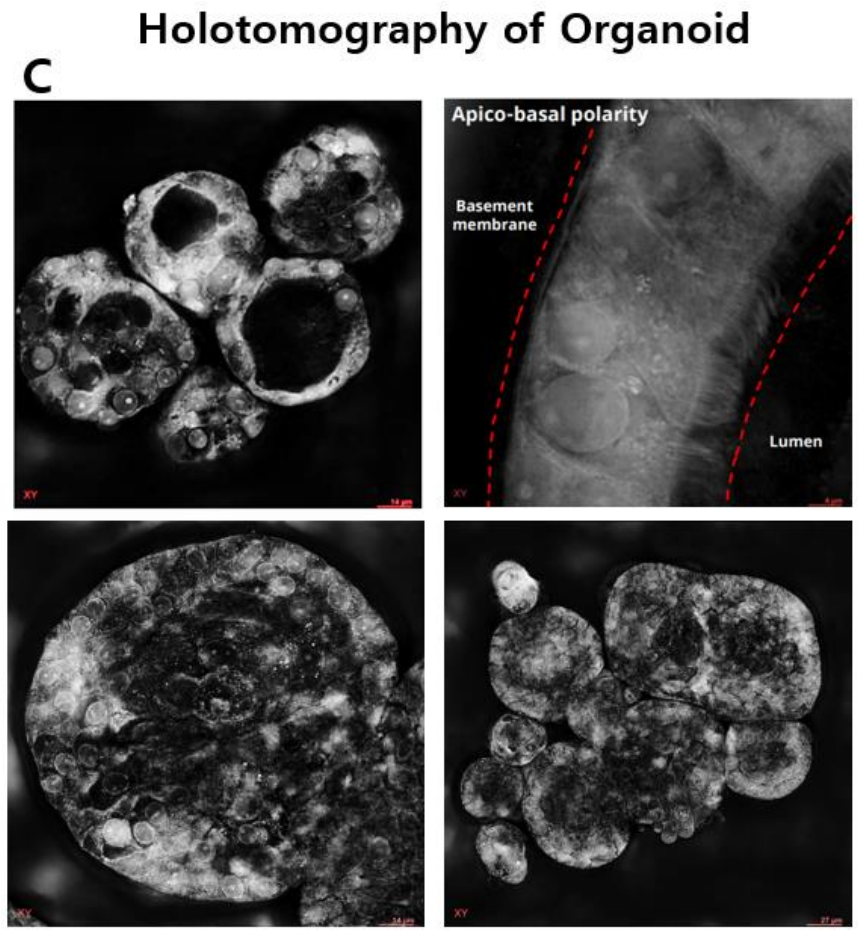
(B) Cryobiopsy can get much bigger cancer tissues compared to conventional non cryo-biopsy.

(C) The representative picture of H&E staining of cryo-biopsy tissue from lung cancer patients. This slide shows high purity of cancer cell. This finding suggests cryobiopsy tissues with high purity can guarantee the high purity of lung cancer cells in lung cancer organoid and prevent the overgrowth of normal lung cells.

Results

3. Successful culture of lung cancer organoids derived from cryo-biopsy samples of lung cancer





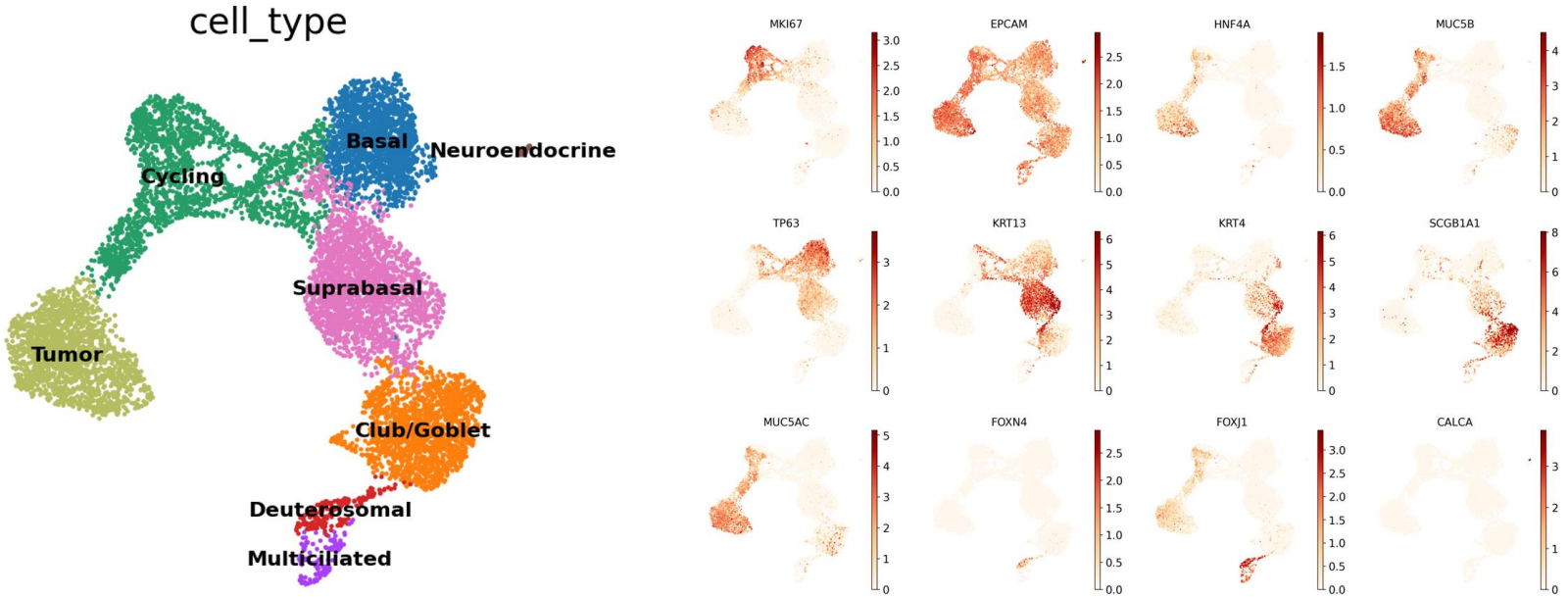
(A) Lung cancer organoids grow more rapidly and bigger with CNUH protocol (only mechanical dissection and strainers without enzyme digestion) compared to conventional enzyme methods
(B) H&E staining shows typical morphology of normal lung organoid and lung cancer organoid.
(C) Holotomography demonstrates that the normal lung organoid and lung cancer organoid are composed of various cells, and it reveals the apical-basal polarity and cilia.

Results

4. High cancer cell purity in lung cancer organoid from Cryo-biopsy tissues.

A

Single cell RNA sequencing of lung cancer organoid



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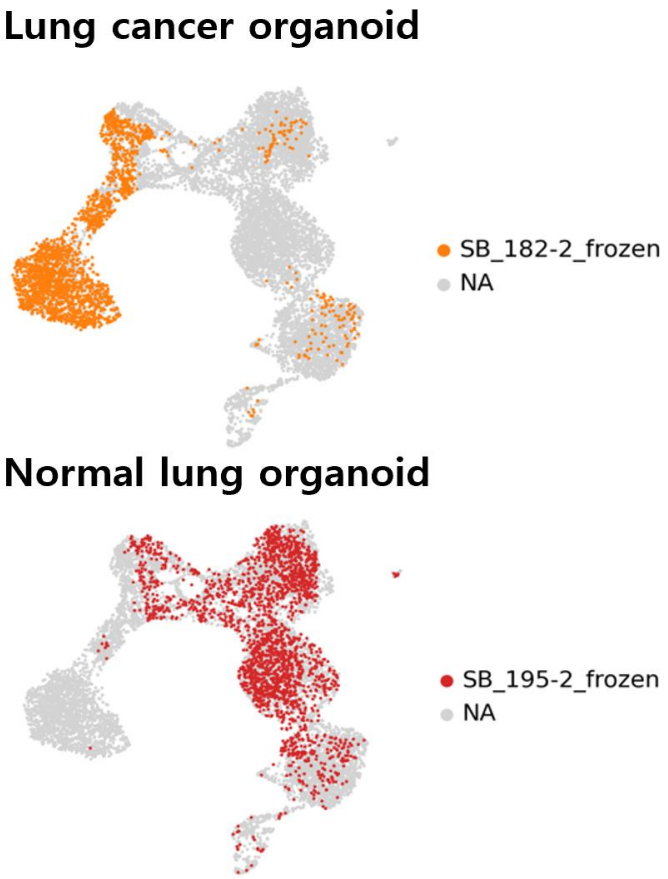


(A) Single cell RNA sequencing showed normal lung organoid and lung cancer organoid have many different cell populations
(B) Lung cancer organoids were mostly composed of tumor cells and cycling cells, and there were few normal cells in early passages. Normal lung organoid have several normal lung cell populations.

Conclusion

Cryobiopsy is a Noble Strategy for Culturing Lung Cancer Organoid with High Cancer Cell Purity in All Stages of Lung Cancer

Non small cell lung cancer

Stage 1 (29.7%)	Stage 2 (8.4%)	Stage 3 (18.2%)	Stage 4 (43.7%)
Operable			

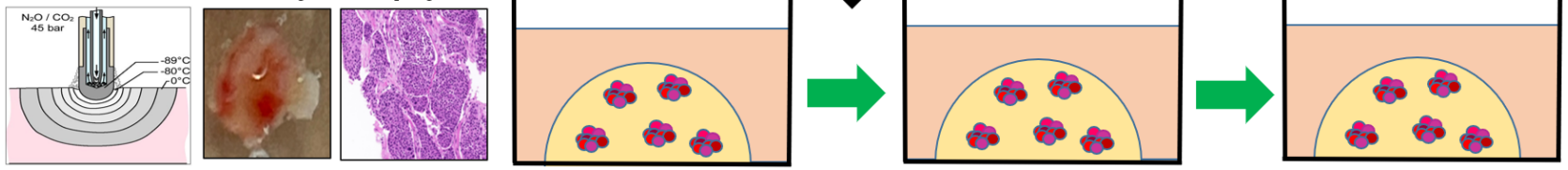
Small cell lung cancer

Limited (29.7%)	Extensive (70.3%)
Op.	

Non-surgical biopsy (primary lesions)	
Mediastinal Lymph node	Metastatic lesion, malignant pleural effusion
Lung cancer recurrence, progression (re-biopsy)	

Non-surgical biopsy	
Lymph node	Metastasis, effusion
Re-biopsy	

Lung cancer tissues derived from Cryo-biopsy



(High purity lung cancer organoid)

Lung cancer organoids derived from cryobiopsy tissue can overcome the shortcomings of present lung cancer organoids. We expect that this method will be a breakthrough strategy of clinical application of lung cancer organoid