

## How insulin shapes lung development in a new human stem cell organoid model

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### Organisation

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**Country** Belgium

**Geographical Area** Brussels Region

### Partners and collaborations

Université Libre de Bruxelles (ULB), Université Libre de Bruxelles (ULB)

## SCOPE OF THE METHOD

<b>The Method relates to</b>	Human health
<b>The Method is situated in</b>	Basic Research, Translational - Applied Research
<b>Type of method</b>	In vitro - Ex vivo
<b>Specify the type of cells/tissues/organs</b>	Human embryonic stem cells derived lung organoids

## DESCRIPTION

### Method keywords

lung organoids  
insulin  
lung development  
airways organoids  
alveolar organoids  
3D in vitro model  
glucose metabolism  
idiopathic pulmonary fibrosis  
human embryonic stem cell derived organoid model

### Scientific area keywords

lung airways organoids  
lung alveolar organoids  
hESC-derived organoids

lung diseases  
insulin metabolic pathways  
diabetes and idiopathic pulmonary fibrosis

### **Method description**

Respiratory diseases are one of the leading causes of mortality. Despite the efforts to understand lung development, physiology, and pathology, this field remains in its early stages. *In vitro* models can replicate lung physiology to comprehend development, function, and pathology. Lung organoids (LOs) are 3D models that emulate the diverse developmental stages of the lung and its 3D architecture and functional characteristics. We adopted an organoid model derived from hESCs with transient overexpression of the lung/thyroid transcription factor NKX2.1. Insulin plays a role in LO generation, and airway, alveolar, and mesenchymal cell types were identified. Transcriptomic analysis reveals insulin's role in enhancing lung progenitors' differentiation, glycolysis, and PI3K pathway activation. Insulin's indispensability throughout lung development is evident, as its removal at different stages disrupts LO generation and maturation. The protocol adopted is under the International Patent (WO/2023/099526). Our research emphasizes insulin's pivotal role in transforming NKX2.1 endodermal cells into LOs and aims to unveil the intricate dynamics behind it. Finally, this method has been applied to model idiopathic pulmonary fibrosis (IPF). IPF is a chronic lung condition associated with alterations in glucose metabolism and characterized by fibrosis accumulation in alveolar cells, leading to breathing difficulties.

### **Lab equipment**

- cell culture equipment;
- molecular biology lab equipment;
- microscopy facilities, including electron microscopy;
- sequencing facilities.

### **Method status**

Still in development

## **PROS, CONS & FUTURE POTENTIAL**

### **Advantages**

- cellular diversity,
- functional model,
- development model,
- physiological and disease model,
- regeneration studies,
- easy to culture,
- high material availability,
- easy to genetically modify.

### **Challenges**

- absence of human body's microenvironment,
- lab differences in between protocols,
- variability from batch-to-batch experiment.

### **Future & Other applications**

- lung organoids on a chip,
- pollution effect on lung development,

- lung development studies,
- lung physiology and pathology studies.

## REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

### References

- 1) Romitti, M. et al. Transplantable human thyroid organoids generated from embryonic stem cells to rescue hypothyroidism. Nat. Commun. 13, 7057 (2022);
- 2) Goulburn, A. L. et al. A targeted NKX2.1 human embryonic stem cell reporter line enables identification of human basal forebrain derivatives. Stem Cells Dayt. Ohio 29, 462–473 (2011);
- 3) Longmire, T. A., Ikonomidou, L. & Kotton, D. N. Mouse ESC Differentiation to Nkx2.1+ Lung and Thyroid Progenitors. Bio-Protoc. 2, e295 (2012);
- 4) Serra, M. et al. Pluripotent stem cell differentiation reveals distinct developmental pathways regulating lung- versus thyroid-lineage specification. Dev. Camb. Engl. 144, 3879–3893 (2017).

### Links

[The following protocol is adapted from this paper](#)  
[PhD position is funded by the Belgian Kids' Fund \(HUDERF\)](#)

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