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

The Method relates to	Human health
The Method is situated in	Basic Research, Translational - Applied Research
Type of method	In vitro - Ex vivo
Specify the type of cells/tissues/organs	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., Ikonomou, 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

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