

## 科学研究費助成事業 研究成果報告書

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研究種目：基盤研究(B) (一般)

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研究課題名(和文) 異種-脱細胞化組織骨格の再細胞化による、再生気管、再生肺の移植研究

研究課題名(英文) Transplantation studies of tissue engineered trachea and lung regenerated from recellularized xenogeneic-decellularized scaffold

研究代表者

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交付決定額(研究期間全体)：(直接経費) 12,600,000円

研究成果の概要(和文)：本研究では、主に2つの成果が得られた。動物由来の脱細胞化肺組織骨格では、ヒトに超急性拒絶反応を引き起こす  $\alpha$ -gal 抗原は減少し、さらにこの組織骨格をヒト細胞で再細胞化するとほぼ消失したため、ヒトに使用しても免疫反応は少ないことが示唆された。異種脱細胞化組織骨格を持つ再生臓器を移植した場合、従来以下の免疫抑制でコントロール可能なことが示唆された。脱細胞化組織骨格に血管内皮細胞と脂肪由来幹細胞を同時に播種すると、脂肪由来幹細胞はペリサイトに分化して、移植後の肺出血を抑制し、血管の成熟に有効であった。一方でモルモット-ラット間で異種組織骨格の肺移植を行うことは、手技上極めて困難であった。

研究成果の学術的意義や社会的意義

この研究の最終形態は、同種や異種の脱細胞化組織骨格を土台とした、自己の再生肺の創出である。臨床応用できるようになれば、現在の移植医療で不足する臓器を一気に解消でき、また、理論的には免疫抑制剤も不要になるため、移植再生医療の革新的な治療法になると考えられる。気管においては、この技術によって、自己の細胞を持つ気管や気管支を、より安価でより簡便に作成可能となる。この手法による再生研究は米国で先行しているが、今後の臓器再生の主流になることも予想される。また細胞接着や幹細胞技術の様々な研究分野に関連しており、この研究を進めること自体が、臓器再生について深い知見を得ることに繋がると考える。

研究成果の概要(英文)：We have two major achievements in the present study. In the animal decellularized lung scaffold,  $\alpha$ -gal epitope, which induce hyper acute reaction in human, was decreased. In addition,  $\alpha$ -gal epitope disappeared after the recellularization with human cells. The result suggest transplantation of engineered lung using xeno-decellularized scaffold will cause little immunoreaction in the human body. After the endothelial cell and adipose derived stromal cell (ASC) seeding in the decellularized scaffold, ASC differentiate into pericyte and suppress hemorrhage after the engineered lung transplantation. ASC might play role for vascular maturation. The other hand, xenotransplantation between rat and guinea pig was technically quite difficult.

研究分野：組織工学 臓器工学

キーワード：肺再生 気管再生 脱細胞化 臓器移植 異種移植 組織骨格 移植免疫

0. 背景

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1. 目的

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2. 方法

2.1. 動物

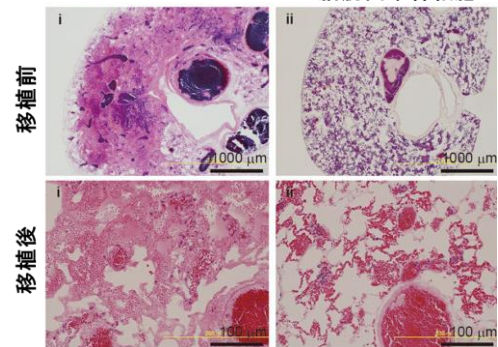
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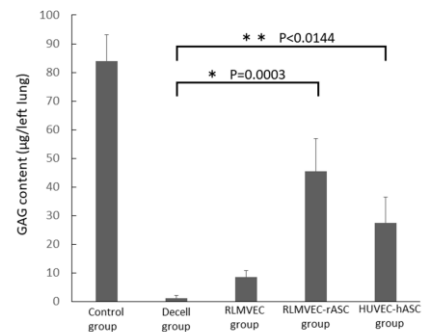
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2.3. 評価

2.3.1. 組織学

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Western blot

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(1)  $\text{NaOH}$  based non-detergent decellularizing solution for rat lung. Sengyoku H, Tsuchiya T, Obata T, Doi R, Hashimoto Y, Ishii M, Sakai H, Matsuo N, Taniguchi D, Suematsu T, Lawn M, Matsumoto K, Miyazaki T, Nagayasu T. Organogenesis. 2018 Jun 11:1-13. doi: 10.1080/15476278.2018.1462432 (1w )

(2)  $\text{NaOH}$  based non-detergent decellularizing solution for rat lung. Sengyoku H, Tsuchiya T, Obata T, Doi R, Hashimoto Y, Ishii M, Sakai H, Matsuo N, Taniguchi D, Suematsu T, Lawn M, Matsumoto K, Miyazaki T, Nagayasu T. Organogenesis. 2018 Jun 11:1-13. doi: 10.1080/15476278.2018.1462432 (1w )

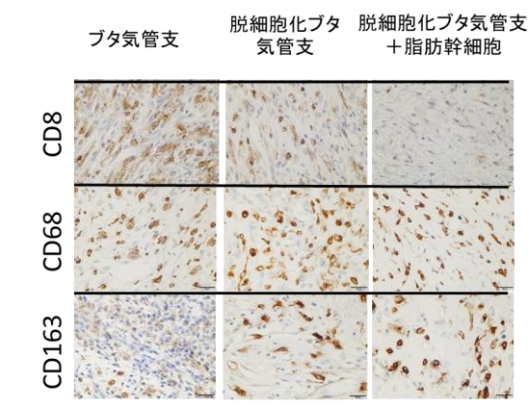
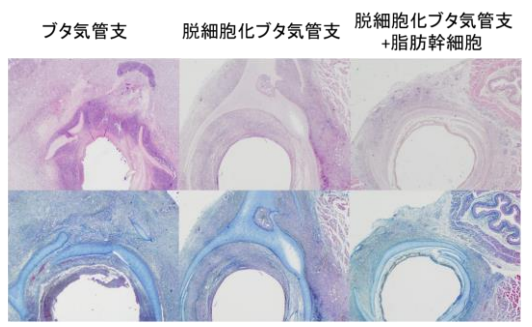
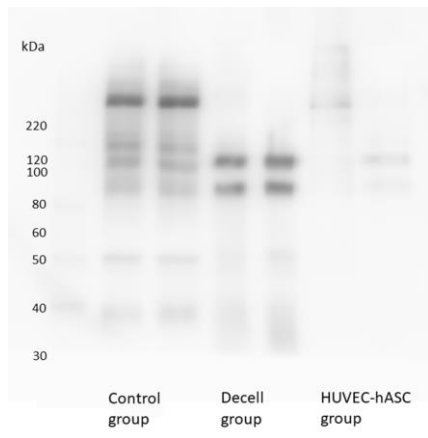
(3)  $\text{NaOH}$  based non-detergent decellularizing solution for rat lung. Sengyoku H, Tsuchiya T, Obata T, Doi R, Hashimoto Y, Ishii M, Sakai H, Matsuo N, Taniguchi D, Suematsu T, Lawn M, Matsumoto K, Miyazaki T, Nagayasu T. Organogenesis. 2018 Jun 11:1-13. doi: 10.1080/15476278.2018.1462432 (1w )

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IHC staining for  $\alpha$ -gal, b, and mbK8.

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w Tomoshi Tsuchiya, Ryoichiro Doi, Hironosuke Watanabe, Go Hatachi, Keitaro Matsumoto, Takuro Miyazaki, Koichi Tomoshige, Takeshi Nagayasu Ig " 33 G 2017 ° 1 v 28 ¥ ( )

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