

MEDIA RELEASE FOR IMMEDIATE RELEASE

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A STEP FORWARD IN MENDING DAMAGED LUNGS USING STEM CELLS

Researchers demonstrate that lung stem cells can help regenerate injured lungs in laboratory mice

Singapore – New research has discovered a means to partially repair damaged lungs. This holds promise for developing strategies to treat lung diseases that are incurable or not easily managed.

For the first time, researchers have demonstrated that they can grow lung stem cells¹ in large numbers in a petri dish. Upon injection into toxin-injured lungs, these lung stem cells were able to regenerate lung tissue in laboratory mice. The discovery, published in the journal Nature Methods. made was bv researchers from A*STAR's Genome Institute of Singapore (GIS) together with US collaborators from Stanford University, The Jackson Laboratory and Clarkson University.

The lungs can be impacted by diseases of great public health relevance, including cold and flu, viral infections, asthma,



(Image source: A*STAR's Genome Institute of Singapore. An image of the injured mouse lung partially regenerated by injected lung stem cells. All cells are labelled with blue (nuclei); the newly-regenerated lung tissue is labelled red; and a specific kind of lung cell (type II alveolar cells) is labelled green.

cystic fibrosis and idiopathic pulmonary fibrosis, amongst others. However, there is a dearth of regenerative therapies for lung diseases. The only treatment for end-stage lung diseases is the transplantation of a new lung, which are in short supply.

The lung is comprised of two sub-units: the airways (which carry air) and the alveoli (which allow gas exchange between inhaled air and the bloodstream). The researchers isolated lung stem cells with the ability to regenerate both airway and alveolar cells. They showed that a single lung stem cell placed in the petri dish could duplicate many

¹ Stem cells are cells capable of regenerating tissues. In brief, they can duplicate to make more of themselves ("self-renewal") and can turn into the more specialised cells within a tissue ("differentiation").

times, generating 100 billion billion, or 10²⁰ billion, new lung stem cells over the course of six months.

Upon injection into the toxin-injured lungs of laboratory mice, researchers discovered that the lung stem cells could regenerate new airway and alveolar lung tissue. This constitutes one of the first demonstrations that lung stem cells could be used to regenerate lung tissue. Dr Bing Lim, a Senior Group Leader at GIS and Dr Kyle Loh, the Siebel Investigator at Stanford University, share senior authorship of the study.

"Despite progress in treating other types of diseases, lung diseases are amongst the most fatal with few known cures. They place a heavy burden on society," said Dr Lim. "New regenerative therapies for lung diseases are sorely needed."

"Scientists have previously had little success in putting new lung cells into damaged lung to regenerate healthy lung tissue," explained Dr Loh. "This is a first step towards future lung regenerative therapies, and paves the way for future work that focuses on whether analogous stem cells can be found and cultivated from humans, which may open the way to eventually replenishing damaged lung tissue in the clinic."

The study was driven by first author Dr Massimo Nichane, formerly a postdoctoral researcher at the GIS, and presently a research scientist at Stanford University. Other GIS contributors included Dr Asif Javed, Ms Monisha Ganesan and Dr Lay Teng Ang.

"Singapore is a fertile environment for new ideas," said Dr Nichane. "My passion was to understand how the lung is constructed during embryonic development. Now our work with lung stem cells may allow us to 'reconstruct' the lung after injury. Our hope is that this new type of regenerative medicine may offer definitive treatments for otherwise incurable diseases."

Dr Tushar Desai, the Woods Family Faculty Scholar in Pediatric Translational Medicine and an Assistant Professor of Medicine at Stanford University, commented, "Nichane and colleagues have made an important step towards developing cellular therapy for lung diseases. They identified conditions enabling the long-term culture and expansion of embryonic lung progenitors at an early stage when they are still multipotent, and therefore capable of regenerating cells in airway and alveolar lung regions upon transplantation. This inherent flexibility makes the cells suitable for a broad range of potential therapeutic applications."

Executive Director of GIS, Prof Huck Hui Ng added, "This may well address one of the most important medical issues. Life expectancy and quality will improve significantly if a damaged lung can be repaired rather than having a patient wait for a replacement organ."

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Notes to Editor:

The research findings described in this media release can be found in the scientific journal *Nature Methods*, under the title, *"Isolation and 3D expansion of multipotent Sox9*+ *mouse lung progenitors*" by Massimo Nichane¹, Asif Javed², V Sivakamasundari³, Monisha Ganesan¹, Lay Teng Ang¹, Petra Kraus⁴, Thomas Lufkin⁴, Kyle M Loh^{5,7} & Bing Lim^{1,6,7}

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The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit <u>www.gis.a-star.edu.sg</u>

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As a Science and Technology Organisation, A*STAR bridges the gap between academia and industry. Our research creates economic growth and jobs for Singapore, and enhances lives by contributing to societal benefits such as improving outcomes in healthcare, urban living, and sustainability.

We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and Research Institutes, the wider research community and industry. A*STAR oversees 18 biomedical sciences and physical sciences and engineering research entities primarily located in Biopolis and Fusionopolis.

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