Regenerative intermediates could be culprits in lung scarring

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Video Abstract

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Abstract

Our lungs use very fine tissues to exchange oxygen and carbon dioxide between the air and our blood. About 95% of this tissue is made up of a single kind of cell, called type-1 pneumocytes, or AT1 cells. Because they're so delicate and thin, these cells are vulnerable to damage by pollutants, viruses, and bacteria. Fortunately, lung tissues also have specialized stem cells called AT2 cells that can replace damaged AT1 cells. But exactly how these cube-shaped AT2 cells generate large, flat AT1 cells has remained something of a mystery. To study this problem, the Tata lab in Cell Biology at Duke University has created "mini lungs" inside Petri dishes. They found that inside these "organoids", the blocky stem cells enter an intermediate state on their way to generating the thin AT1 cells. The stem cells stretch considerably while passing through this transitional state, making them vulnerable to DNA damage. Cells normally pass through that transition within days. But under certain conditions, stem cells can become locked in the transition state, leading to lung scarring. Once the researchers knew what to look for, they found increasing numbers of transitional cells in scarred human lungs. This kind of damage can be seen when any number of harmful factors take hold of the lung, including toxins and infectious diseases, like COVID-19. Though more research is needed, the researchers believe that this intermediate state of stem cells is key to healing from COVID-19 to prevent scarring.