EuroStemCell

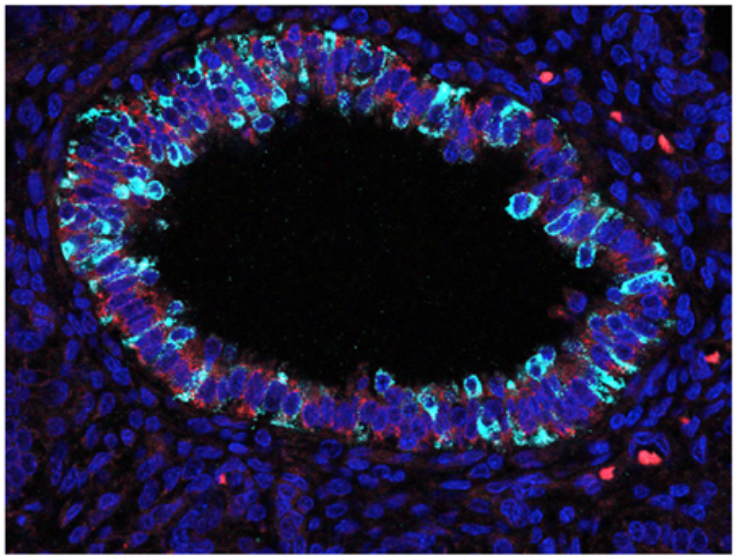
Last Updated: 13.08.2020

Lung stem cells in health, repair and disease

What do we know?

Many chronic lung diseases, such as COPD and fibrosis, are caused by changes in cells that make up the lung. Important cell populations in the lung are the stem cell populations. In healthy people the job of the lung stem cells is to maintain the normal lung structure. When they receive specific cues, stem cells function by dividing to replace old, or damaged, more specialist lung cells. In chronic lung diseases this process can go wrong leading to long-term breathing difficulties and ultimately death.

Pneumonia is another lung disease with a very high death rate, particularly among the elderly. Pneumonia is usually triggered by a lung infection and it can be caused by flu or COVID-19. Severe pneumonia is treated with mechanical ventilation which itself can cause lung damage. The lungs should be able to repair damage caused by ventilation by activating their stem cells to make new healthy lung tissue. However, when the damage is too severe the repair process cannot happen normally and fibrosis (when healthy cells are replaced by scar tissue) can occur.



Differentiating club and ciliated cells in the human embryonic airways

Image: Kyungtae Lim, Gurdon Institute, University of Cambridge

What are researchers investigating?

Most of the research focused on lung stem cells is performed in either mice or human tissue. We can isolate lung stem cells from donated human tissue and grow them into ‘organoid cultures’ which resemble mini-organs. This method allows researchers to alter the instructions received by the stem cells and observe what happens. Researchers can, for example, compare healthy stem cells with stem cells from patients. Organoid cultures can also be used as a drug screening model, and even serve as a basis for patient precision medicine. In that way stem cells may one day be used to cure lung diseases.

In a different type of research, modern genetic tools can be used for “correction” of disease-causing unhealthy genes. A good example of this is the correction of unhealthy versions of the CFTR gene in Cystic Fibrosis. So far these gene corrections have only been performed on cells growing in the laboratory, but scientists are actively working on ways to make the same changes in patient’s lungs.

What are the challenges?

Researchers can use human stem cells in organoid cultures, but a large challenge is that this is only a model and the cultures only recapitulate some aspects of human lung biology.

Much of the lung stem cell research that has been done so far has been performed in mice. Recent studies in cell profiling of both mice and human samples have revealed many new cell types that are present in the lungs. The function of all these different cell types is not known so far and using mice is an excellent way for researchers to study the functions of these new cell types in an intact lung. Mouse and human lungs are constructed in a very similar way, however, it has also become clearer that there are significant differences in cell populations between mouse lungs and human lungs. Another difference between mouse and human is how ageing occurs. This is important as many severe lung diseases mostly affect older people.

Researchers are increasingly trying to find animal models that more closely resemble humans. Pig physiology and anatomy resembles the human lung and body much better than that of mice.

For more information visit: **www.eurostemcell.org/lung**