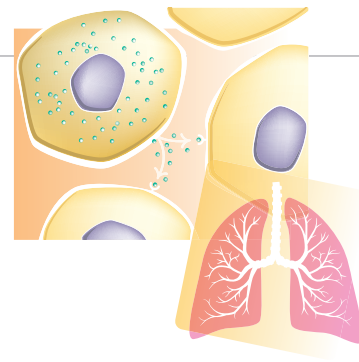


Unproven Stem Cell Treatments for Lung Disease— An Emerging Public Health Problem

What are stem cells and how can they potentially be used in medicine?

Stem cells are undifferentiated cells that have the ability to become specialized cells. They also are able to make more copies of themselves. There are different types of stem cells including those found in embryos (embryonic stem cells) and those produced in the laboratory by treating normal adult cells such as from the skin or muscle to become stem cells (induced pluripotent stem cells).



In addition, researchers are learning that every organ in the body has a small number of cells that serve as organ-specific stem cells that work to replace or repair damaged tissue. It is possible that each of these types of stem cells may one day be used to treat different human diseases. One example of successful use of stem cells is the use of bone marrow stem cells (hematopoietic stem cells) to treat certain types of leukemias and lymphomas.

However, there is much not yet known about all stem cell types and how they work. Much more research is needed to safely and effectively use these in people with other diseases. There are a number of areas of active research going on. One example is the research into finding a way to stimulate organ-specific stem cells in the body to repair diseased tissue. Another area of research involves isolating stem cells and stimulating them in the laboratory to become specialized cells for use in transplantation.

Are stem cell treatments an option for lung disease?

In theory, yes in the future. In many lung diseases, cells that make up the respiratory system are either lost or do not function properly. A stem cell treatment that restores lung cell function might be able to reverse or even cure some lung diseases. As of now, there are no proven stem cell treatments for any lung disease.

What is an unproven stem cell treatment?

Unproven stem cell treatments are those that have not yet been adequately or fully tested for safety and effectiveness (how well they work)³. The best way to test potential stem cell therapies is through clinical research trials that have to follow certain rules. These rules are set by national regulatory agencies such as the FDA (Food and Drug Administration) to make sure that the treatments are tested following proper scientific methods without any conflict of interest.

Who offers unproven stem cell treatments?

Unfortunately, there are hundreds of clinics and other groups offering unproven stem cell treatments in the U.S.² A frequent method that they use to treat lung disease involves removing cells from a person's fat or bone marrow and giving the cells back to the person through his or her bloodstream. These approaches have not been proven to work and are not FDA regulated or approved as accepted treatments for any type of lung disease. This means that the necessary clinical research trials to make sure that these treatments are safe and effective have not been done. Unfortunately, this does not prevent them from being offered despite unknown risk or benefit.

Do unproven stem cell treatments work for lung disease?

There have been promising studies in animal models of lung diseases. Yet, there is no reliable evidence that stem cell treatments are effective for any lung disease. To date, there have been some legitimate clinical trials, approved and regulated by the FDA or by appropriate regulatory agencies in other countries. These have been done for a number of lung diseases including COPD³, acute respiratory distress syndrome⁴, idiopathic pulmonary fibrosis, and pulmonary hypertension. These studies have used several different types of stem cells including mesenchymal stromal cells and endothelial progenitor cells. Initial results suggest that the stem cells used appear to be safe over a short term period. However, further follow-up is necessary to ensure long term safety. Importantly, none of these studies have shown any beneficial effect in any lung disease tested so far.

Could unproven stem cell treatments be harmful?

Yes, these treatments can be potentially harmful. Potential risks include cell embolism (stem cells clotting in the lungs) and the cells causing abnormal growth including tumors^{5,6}. In addition, a number of clinics are giving treatment in ways that do not meet normal standards of sterility (to prevent infection) and safety.

Are unproven stem cell treatments covered by insurance?

No, unproven stem cell treatments are not covered by insurance. Patients that choose to take such treatments have to cover all costs on their own (out-of-pocket) and will not get reimbursed by insurance. Many of the clinics that offer unproven stem cell therapies charge high prices for the treatments.

What do pulmonologists say about unproven stem cell treatments?

Pulmonologists (lung specialists) familiar with the issues of unproven stem cell therapies for lung diseases are opposed to this approach. However many lung specialists are also not yet familiar with the field. The American Thoracic Society (ATS) Stem Cell Working Group as well as other professional societies have developed educational resources for doctors as well as for patients and their families^{7,8}. All involved are strongly encouraged to read these resources to learn more about stem cells and their use. Patients and doctors should take time to learn all they can about the issues surrounding unproven stem cell therapies.

What do lung disease foundations and patient advocacy groups say about unproven stem cell treatments?

A growing number of national and international respiratory disease societies and patient advocacy groups have taken strong positions against unproven stem cell therapies. This is also true for the leading stem cell scientific societies who do not support use of unproven stem cell therapies at this time. All of these groups are trying to educate patients, families, caregivers, and health care professionals about the potential dangers of unproven stem cell treatments. In the U.S., these foundations include the Alpha-1 Foundation, American Lung Association (ALA), COPD Foundation, Cystic Fibrosis Foundation, Pulmonary Fibrosis Foundation, and the Pulmonary Hypertension Association. None of these groups believes there is enough known about stem cell therapies to use them in lung disease without more research.

I suffer from lung disease and I am interested in stem cell treatments. What should I do?

First, talk to your health care provider about current treatment options. These may include new medications that can slow down the progression of the disease. If they are unfamiliar with the stem cell field, refer them to the available educational resources that you are reading. You need to carefully read all you can as well. Particular points to consider and to discuss with your health care provider are: 1) whether there is any scientific evidence to support the proposed treatment approach for your lung disease and 2) whether the offered treatment has been studied in a legitimate clinical trial.

How can I find if a stem cell treatment for lung disease is part of a legitimate clinical trial?

The U.S. government compiles a list of all registered clinical trials in the U.S. and abroad, including clinical trials for stem cell treatments. This can be easily accessed on the website www.clinicaltrials.gov. You can use keywords such as “stem cells” and your lung disease diagnosis such as “chronic obstructive pulmonary disease”, “cystic fibrosis”, or “pulmonary fibrosis” to find clinical trials. However, you should be aware that some clinics offering unproven stem cell treatments register their treatments in the ClinicalTrials.gov database but have not gone through the proper approvals or inspections. The U.S. government is currently working to tighten the requirements for any potential new therapy or clinical trial to be legitimately listed on the database. Importantly, people who are research subjects **should not be charged for participation in clinical trials**. You should fully discuss any information you find on the [clinicaltrials.gov](http://www.clinicaltrials.gov) website with your health care provider.

Authors: Laertis Ikonou, PhD, Angela Panoskaltis-Mortari, PhD, D(ABMLI), Darcy E. Wagner, PhD, Robert J. Freishtat, MD, MPH, Daniel J. Weiss, MD, PhD on behalf of the American Thoracic Society Respiratory Cell and Molecular Biology Assembly Stem Cell Working Group

Reviewers: Marianna Sockrider MD, DrPH

References:

1. Srivastava, A., et al., Part 1: Defining unproven cellular therapies. *Cytotherapy*, 2016. 18(1): p. 117-9.
2. Turner, L. and P. Knoepfler, Selling Stem Cells in the USA: Assessing the Direct-to-Consumer Industry. *Cell Stem Cell*, 2016. 19(2): p. 154-157.
3. Weiss, D.J., et al., A Placebo-Controlled, Randomized Trial of Mesenchymal Stem Cells in COPD. *Chest*, 2013. 143(6): p. 1590-1598.
4. Wilson, J.G., et al., Mesenchymal stem (stromal) cells for treatment of ARDS: a phase 1 clinical trial. *Lancet Respiratory Medicine*, 2015. 3(1): p. 24-32.
5. Jung, J.W., et al., Familial Occurrence of Pulmonary Embolism after Intravenous, Adipose Tissue-Derived Stem Cell Therapy. *Yonsei Medical Journal*, 2013. 54(5): p. 1293-1296.
6. Berkowitz, A.L., et al., Glioproliferative Lesion of the Spinal Cord as a Complication of “Stem-Cell Tourism”. *New England Journal of Medicine*, 2016. 375(2): p. 196-198.
7. Statement on Unproven Stem Cell Interventions for Lung Diseases. 2016 [accessed 2016 December 28]; Available from: <http://www.thoracic.org/members/assemblies/assemblies/rcmb/working-groups/stem-cell/resources/statement-on-unproven-stem-cell-interventions-for-lung-diseases.pdf>.

8. Ikonou, L., et al., The Global Emergence of Unregulated Stem Cell Treatments for Respiratory Diseases—Professional Societies Need to Act. *Annals of the American Thoracic Society*, 2016. 18: p. 1205-1207.

Rx Action Steps

- ✓ If you have lung disease and wonder about stem cell therapy, talk to your health care provider.
- ✓ Take time to read and learn about what research has been done before starting any stem cell treatment as it likely is or remains unproven.
- ✓ Ask about the risks and costs of any treatment that you are considering.
- ✓ Support more clinical research in lung disease to test new treatments properly.

Resources:

Lung disease foundations and patient advocacy groups – Statements on unproven stem cell treatments

Alpha-1 Foundation:

<https://www.alpha1.org/Newly-Diagnosed/More-Alpha-1-Resources/News/ArtMID/5952/ArticleID/6589/Buyer-beware-Alphas-urged-to-avoid-companies-advertising-unproven-stem-cell-treatments-that-can-cost-you-a-fortune>

American Lung Association:

<http://www.lung.org/our-initiatives/research/about-our-research/stem-cell-therapy.html>

Cystic Fibrosis Foundation:

<https://www.cff.org/aboutCFFoundation/NewsEvents/2015NewsArchive/3-9-Stem-Cell-Therapies-and-Research-for-CF.cfm>

COPD Foundation:

<http://www.copdfoundation.org/Take-Action/Patient-Access/COPD-Foundation-Position-on-Stem-Cell-Therapy.aspx>

Pulmonary Fibrosis Foundation:

<http://www.pulmonaryfibrosis.org/our-role/news-media/viewannouncement/stem-cell-cell-based-therapies-for-pulmonary-fibrosis-beyond-the-context-of-clinical-trials>

Pulmonary Hypertension Association:

<http://www.phassociation.org/StemCellTherapy>

Canadian Stem Cell Foundation

<http://stemcellfoundation.ca/en/about-stem-cells/what-is-a-stem-cell/>

EuroStemCell—Resources for patients considering a stem cell treatment

<http://www.eurostemcell.org/considering-stem-cell-treatment-offer>

International Society for Cellular Therapy—Reference Guide on the Use of Unproven Cellular Therapies

<http://www.celltherapysociety.org/?page=PTF2015>

International Society for Stem Cell Research—Patient Resources

<http://www.closerlookatstemcells.org/patient-resources/>

International Society for Stem Cell Research—Q&A for stem cell treatments

<http://www.closerlookatstemcells.org/stem-cells-and-medicine/stem-cell-treatments-what-to-ask>

JAMA Patient Page—Stem Cell Treatments

<http://jamanetwork.com/journals/jama/fullarticle/2598269>

This information is a public service of the American Thoracic Society.

