

Bone Marrow Stem Cells May Prevent Chronic Lung Disease

December 1 2009

(PhysOrg.com) -- Researchers at Children's Hospital Boston have discovered a possible way to protect the fragile lungs of premature babies by using stem cells harvested from bone marrow. In experiments on laboratory mice, they found that bone marrow stromal cells (BMSCs), a type of stem cell with the potential to form lung cells, were able to reduce inflammation in lung tissue. Inflammation is the key factor that leads to chronic lung disease in premature babies. Surprisingly, even the fluid in which the cells were grown was able to protect the lungs - in fact, better than the stem cells themselves.

Findings were published in the December 1 issue of [American Journal of Respiratory and Critical Care Medicine](#).

Doctors often place premature babies on ventilators to deliver oxygen and expand their underdeveloped lungs. However, the high oxygen concentration and mechanical force of the ventilator often cause inflammation and prevent proper lung growth. Long-term complications of chronic lung disease can include increased risk of asthma and impaired neurological development.

"Chronic lung disease is a condition with life-long consequences," says senior investigator Stella Kourembanas, MD, Chief of Children's Division of Newborn Medicine. "It's very important that neonatologists prevent the disease or minimize its severity."

Doctors have had limited success in preventing chronic lung disease with

anti-inflammatory drugs or alternative ventilation devices, but such treatments have had side effects and have not been effective enough. Based on past research, Kourembanas and her colleagues saw BMSCs as a possible treatment to prevent chronic lung disease because they have the potential to become different cell types, including lung cells. Because BMSCs can be taken from the patients themselves, they would pose no risk of immune-rejection.

The research team exposed newborn mice to high concentrations of oxygen to create a model for early chronic lung disease. (The lungs of mice at birth are at the same stage of development as the human premature infant at 24 to 28 weeks gestation, making the mouse a suitable model for studying the human disease.) The team then obtained BMSCs from adult mice and injected them into the bloodstream of the newborn mice. From the bloodstream, the cells found their way to the lungs. Results showed that mice receiving BMSCs had partial protection from injury; the lungs' blood vessels were better maintained and inflammation was reduced.

Intriguingly, some of these benefits were present even though the lungs retained very few of the transplanted cells. This observation suggested that direct physical tissue repair may not be how the BMSCs protected the lungs.

"How do BMSCs work? Do they go in and repair the lung tissue, or do they release factors that act in a paracrine manner and stimulate the cells to heal themselves?" asks Kourembanas. (Paracrine factors are chemical messengers that a cell secretes to communicate with a neighboring cell.)

To test the latter idea, the team collected BMSC conditioned media -- the media in which the stem cells were grown during culture. Injecting this media into the bloodstream of newborn mice not only maintained healthy blood vessels and reduced inflammation, but also ensured proper

growth of the lungs' alveoli (the small air sacs of the lungs where gas exchange takes place), something BMSCs themselves had limited capability to do. The experiment supports the idea that BMSC conditioned media contains therapeutic paracrine factors, which Kourembanas believes may impact the way scientists approach stem cell medicine for other diseases.

"Being able to use the media is far easier and more efficacious than using the stem cells themselves," Kourembanas says. If scientists find effective paracrine factors in other types of stem cells, such as neural stem cells from the brain, using conditioned media could be less costly and easier to handle than the actual cells, she speculates.

Analysis of BMSC conditioned media's various proteins revealed two likely paracrine factors secreted in high abundance that may confer beneficial effects on chronic lung disease: osteopontin (Opn) and macrophage colony stimulating factor 1 (Csf1). Past studies characterize Opn as a regulator of inflammation, while Csf1 controls the growth and behavior of various immune system cells. Kourembanas thinks these proteins likely work with each other or together with other proteins, rather than any one protein being the lone factor.

To translate these results into a future therapy for children or adults with lung or cardiovascular disease, further studies must determine exactly how these proteins protect the lungs, and whether they can reverse disease, not just prevent it. Kourembanas would also like to test BMSC conditioned media in other animal models of lung injury, and to try deriving conditioned media from human umbilical cord [stem cells](#), which can be obtained from premature babies in a far less invasive manner than BMSCs.

More information: [ajrccm.atsjournals.org/cgi/con ...
abstract/180/11/1122](http://ajrccm.atsjournals.org/cgi/con...abstract/180/11/1122)

Provided by Children's Hospital Boston ([news](#) : [web](#))

Citation: Bone Marrow Stem Cells May Prevent Chronic Lung Disease (2009, December 1)
retrieved 10 April 2024 from
<https://medicalxpress.com/news/2009-12-bone-marrow-stem-cells-chronic.html>

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