

Single transplantation of therapeutic macrophages improves rare lung disease in mice

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Hereditary pulmonary alveolar proteinosis (herPAP) is a rare disease characterized by the slow build-up of lipo-protein material in the lungs due to the failure of highly specialized cells called macrophages, which usually eat away this material from the pulmonary air-space. On August 9 in the journal *Stem Cell Reports*, researchers in Germany demonstrate that a single transplantation of murine macrophages derived from induced pluripotent stem cells (iPSC) into the lungs of mice suffering from herPAP can effectively treat this life-threatening disease.

"From previous studies, we know that pulmonary macrophage transplantation (PMT) works with bone marrow-derived [cells](#), so we wanted to see if a transplantation with iPSC-derived macrophages would show similar efficacy," says co-senior author Thomas Moritz, a hematologist at the Hannover Medical School. "We found that single transplantation of iPSC-derived macrophages directly into the lungs of herPAP mice profoundly ameliorates herPAP symptoms over the long term. Moreover, such PMT strategies also may be useful in related diseases."

Macrophages are immune cells found in every organ of the body that consume pathogens like bacteria or viruses. "In principle, they're kind of like Pac-Man," says Nico Lachmann, the corresponding senior co-author of the study. However, in herPAP [disease](#), the macrophages normally found in the air sacs of the lungs, the alveoli, are absent or non-

functional. Lachmann and Moritz then wanted to know if directly replacing the absent and non-functional lung macrophages with the iPSC-derived macrophages would have a therapeutic effect.

"Four months after transplantation we could see that the disease was markedly improved in herPAP mice that received the treatment," Moritz says. "And the transplanted iPSC-derived macrophages could function so efficiently because they exhibit great plasticity, which means that after transplantation, they differentiate and adapt to the murine lung environment, turning into the types of macrophages needed."

Moreover, Lachmann and Moritz observed that this plasticity allowed one [transplant](#) to be efficient enough to effectively treat the mice for at least six months representing roughly a third of a mouse's lifespan.

"This was a proof of concept study, but if the transplant to the [lung](#) worked to improve the conditions of [mice](#) with herPAP, we can expect that transplants to other organs—like the liver or brain—might work to improve the conditions of individuals with other similar diseases where macrophages are absent or non-functional," says Lachmann. "From here, our goal is to perfect this therapy in herPAP patients and then to translate the PMT concept into a long-term or short-term therapeutic approach for other diseases."

More information: *Stem Cell Reports*, Moritz et al.: "iPSC-derived macrophages effectively treat pulmonary alveolar proteinosis in Csf2rb-deficient mice" [www.cell.com/stem-cell-reports ... 2213-6711\(18\)30311-4](http://www.cell.com/stem-cell-reports/2213-6711(18)30311-4) , DOI: [10.1016/j.stemcr.2018.07.006](https://doi.org/10.1016/j.stemcr.2018.07.006)

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