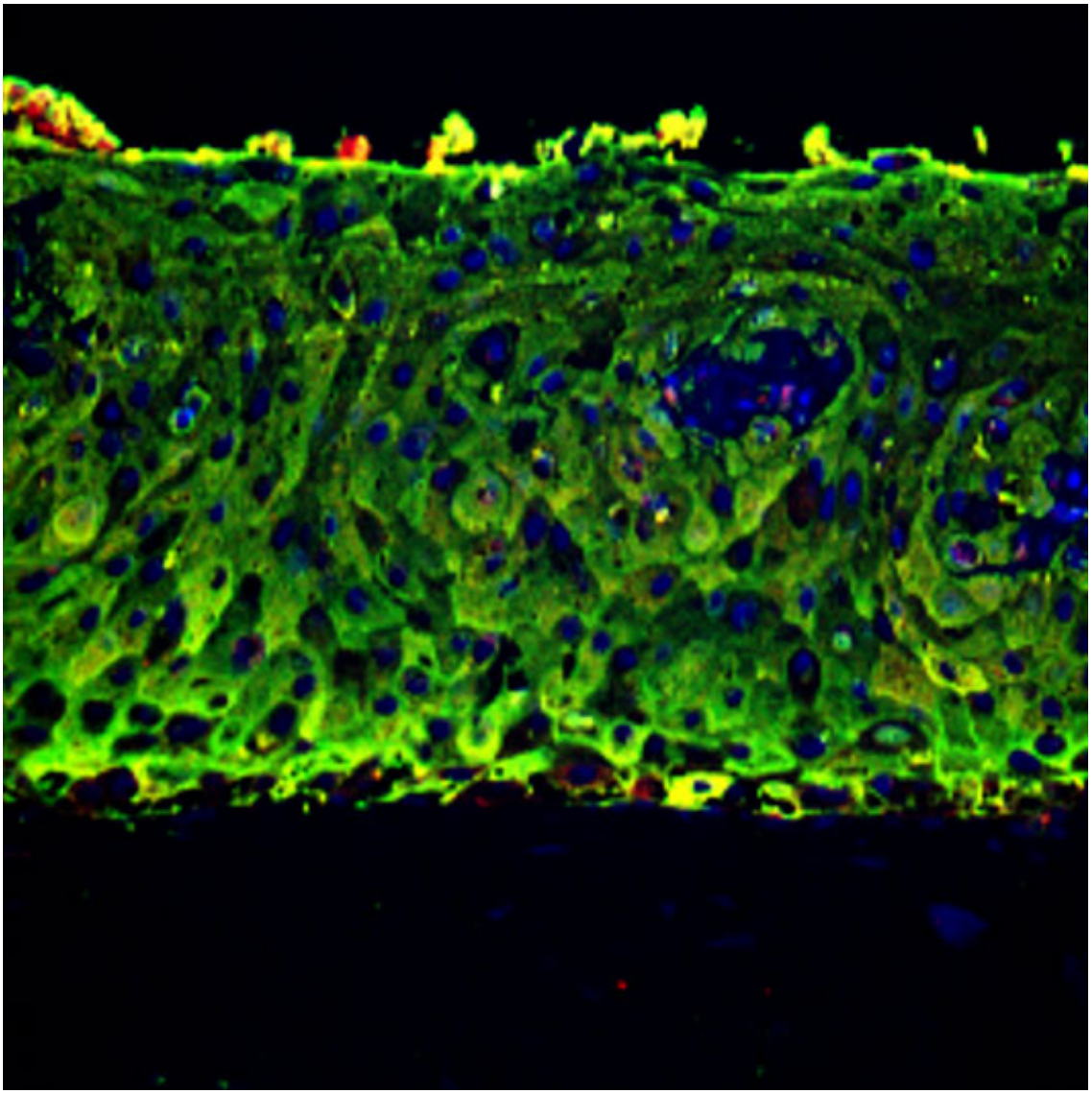
MedicalXpress

3-D skin made of stem cells treats backbone birth defect in rodents

June 6 2017



ISkin (three-dimensional cultured skin) derived from human iPSCs. Immunohistochemical analysis with antibodies to KERATIN 14 (KRT14), p63, cytokeratins (Pan-CK), involucrin, laminin 5, loricrin, KRT10, and filaggrin.

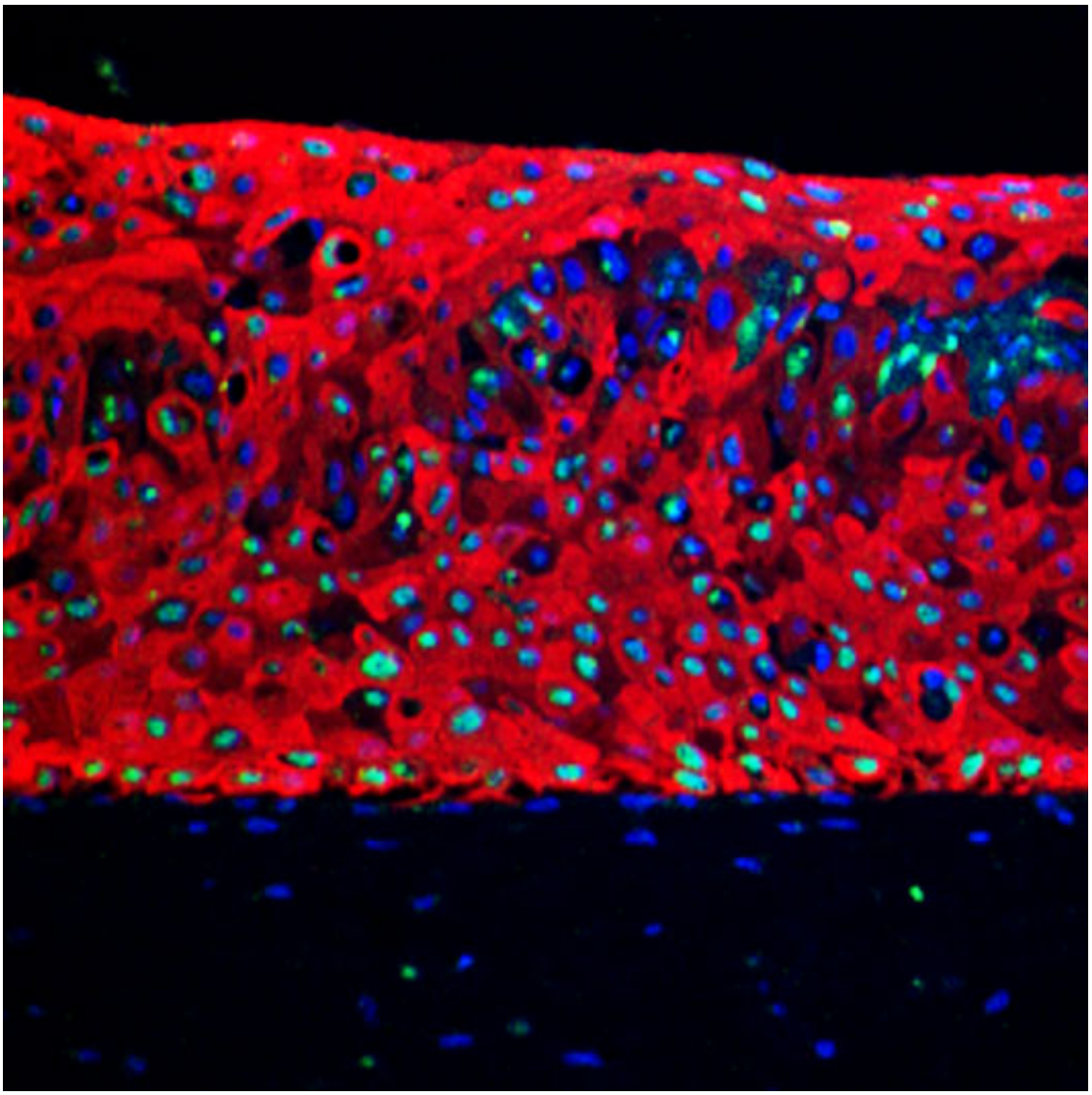
The multilayered epidermis expressed KRT14, involucrin, laminin 5, Pan-CK, loricrin, KRT10, and filaggrin in iSkin, indicating that iPSC-keratinocytes terminally differentiate in the skin equivalents. Scale bar is 100 μm. Credit: Kazuhiro Kajiwara.

Myelomeningocele is a severe congenital defect in which the backbone and spinal canal do not close before birth, putting those affected at risk of lifelong neurological problems. In a preclinical study published June 6th in *Stem Cell Reports*, researchers developed a stem cell-based therapy for generating skin grafts to cover myelomeningocele defects before birth. They first generated artificial skin from human induced pluripotent stem cells (iPSCs), and then successfully transplanted the skin grafts into rat fetuses with myelomeningocele.

"We provide preclinical proof of concept for a fetal therapy that could improve outcomes and prevent lifelong complications associated with myelomeningocele—one of the most severe birth defects," says senior study author Akihiro Umezawa of Japan's National Research Institute for Child Health and Development. "Since our fetal cell treatment is minimally invasive, it has the potential to become a much-needed novel treatment for myelomeningocele."

Myelomeningocele, which is the most serious and common form of spina bifida, is a neural tube defect in which the bones of the spine do not completely form. As a result, parts of the spinal cord and nerves come through the open part of the spine. A baby born with this disorder typically has an open area or a fluid-filled sac on the mid to lower back. Most children with this condition are at risk of brain damage because too much fluid builds up in their brains. They also often experience symptoms such as loss of bladder or bowel control, loss of feeling in the legs or feet, and paralysis of the legs.

Babies born with myelomeningocele usually undergo surgery to repair the defect within the first few days of life. Some highly specialized centers also offer intrauterine surgery to close the defect before the baby is born. Although prenatal surgery can improve later neurological outcomes compared with postnatal surgery, it is also associated with higher rates of preterm birth and other serious complications, underscoring the need for safe and effective fetal therapies.



ISkin (three-dimensional cultured skin) derived from human iPSCs. Immunohistochemical analysis with antibodies to KERATIN 14 (KRT14), p63,

cytokeratins (Pan-CK), involucrin, laminin 5, loricrin, KRT10, and filaggrin. The multilayered epidermis expressed KRT14, involucrin, laminin 5, Pan-CK, loricrin, KRT10, and filaggrin in iSkin, indicating that iPSC-keratinocytes terminally differentiate in the skin equivalents. Scale bar is 100 μm. Credit: Kazuhiro Kajiwara.

To address this problem, Umezawa and his team set out to develop a minimally invasive approach for generating and transplanting skin grafts that could cover large myelomeningocele defects earlier during pregnancy, potentially improving long-term outcomes while reducing surgical risks. In particular, they were interested in using iPSC technology, which involves genetically reprogramming patients' cells to an embryonic stem cell-like state and then converting these immature cells into specialized cell types found in different parts of the body. This approach avoids ethical concerns while offering the advantages of a potentially unlimited source of various cell types for transplantation, as well as minimal risk of graft rejection by the immune system.

In the new study, the researchers first generated human iPSCs from fetal cells taken from amniotic fluid from two pregnancies with severe fetal disease (Down syndrome and twin-twin3 transfusion syndrome). They then used a chemical cocktail in a novel protocol to turn the iPSCs into skin cells and treated these cells with additional compounds such as epidermal growth factor to promote their growth into multi-layered skin. In total, it took approximately 14 weeks from amniotic fluid preparation to 3D skin generation, which would allow for transplantation to be performed in humans during the therapeutic window of 28-29 weeks of gestation.

Next, the researchers transplanted the 3D skin grafts into 20 rat fetuses through a small incision in the uterine wall. The artificial skin partially

covered the myelomeningocele defects in eight of the newborn rats and completely covered the defects in four of the newborn rats, protecting the spinal cord from direct exposure to harmful chemicals in the external environment. Moreover, the engrafted 3D skin regenerated with the growth of the fetus and accelerated skin coverage throughout the pregnancy period. Notably, the transplanted skin cells did not lead to tumor formation, but the treatment significantly decreased birth weight and body length.

"We are encouraged by our results and believe that our fetal stem cell therapy has great potential to become a novel treatment for myelomeningocele," Umezawa says. "However, additional studies in larger animals are needed to demonstrate that our fetal stem cell therapy safely promotes long-term skin regeneration and neurological improvement."

More information: *Stem Cell Reports*, Kajiwara et al.: "Fetal therapy model of myelomeningocele with three-dimensional skin using amniotic fluid cell-derived induced pluripotent stem cells" www.cell.com/stem-cell-reports … 2213-6711(17)30220-5 , DOI: 10.1016/j.stemcr.2017.05.013

Provided by Cell Press

Citation: 3-D skin made of stem cells treats backbone birth defect in rodents (2017, June 6) retrieved 5 May 2024 from https://medicalxpress.com/news/2017-06-d-skin-stem-cells-backbone.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.