

Regrowing the body



◀◀◀ -600 BC

In one of the first surgical textbooks, Indian surgeon Suśruta (**pictured**) discusses skin-graft techniques. The book details a method for repairing torn earlobes with skin from the cheek and includes the first written record of reconstruction of the nose from a flap of forehead skin.



1952

US scientists Robert Briggs and Thomas King report the first cloning using nuclear transfer. The researchers remove the nucleus from a frog egg and replace it with the nucleus from a frog-embryo cell. The egg develops

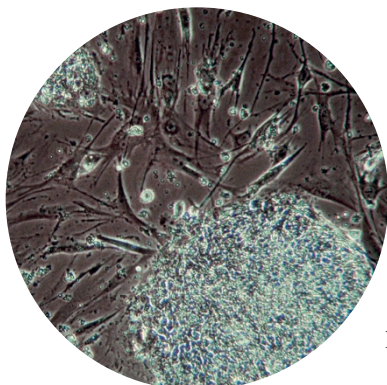
into a tadpole. The experiment shows that nuclei hold onto the organism's genome even after they have been transferred into a new cell body. Briggs's initial request for funds is dismissed by the US National Cancer Institute, which called nuclear transplantation a "hare-brained scheme".

1981

UK researchers Martin Evans and Matthew Kaufman are the first to isolate stem cells from mouse embryos. In the same year, US scientist Gail Martin discovers how to keep stem cells alive in a petri dish, enabling experimentation.

1997

A paper by Harvard Medical School researcher Joseph Vacanti and his team includes an image of what appears to be a human ear growing out of a mouse's back. The team hopes that its research will lead to lab-grown ears for people whose ears are damaged. But the image sparks a backlash from animal rights activists and people who find the image shocking.



1998

Two teams announce that they have isolated human embryonic stem cells (**pictured**). James Thomson at the University of Wisconsin–Madison and his colleagues derive cells from donated embryos originally intended for *in vitro* fertilization. And a team led by John Gearhart from Johns Hopkins University in Baltimore, Maryland, uses embryos from terminated pregnancies.

1740 AQUATIC DISCOVERY

Swiss naturalist Abraham Trembley, 'the father of biology', discovers that freshwater hydra can regenerate.

1901 HEREDITY MADE CLEAR

Thomas Hunt Morgan, a US scientist best known for his fruit-fly research on the role of chromosomes in inheritance, writes *Regeneration*. The book helps to bring order and clarity to a field rife with inconsistencies and confusing terminology.



1907 ENGINEERING ORIGINS

US biologist Ross Granville Harrison (**pictured**) discovers a technique for growing embryonic frog cells in the lab. His experiment, the first stem-cell experiment and the first successful method for culturing tissue, paves the way for tissue engineering.

1963 STEM-CELL PROOF

Canadian scientists James Till and Ernest McCulloch identify stem cells in mouse bone marrow that can self-renew and mature into platelets and red and white blood cells.

1981 REPLACEMENT SKIN

Biologist Eugene Bell and his colleagues report a method for repairing wounds with artificial skin made from an individual's own cells. Bell then founds Organogenesis, which in 1998 becomes the first company to receive US Food and Drug Administration approval for a medical product containing living cells.

CLOCKWISE FROM TOP LEFT: PARIS PIERCE/ALAMY; JOEL SARTORE/GETTY; EMBRYO PROJECT/MBL ARCHIVES/ARIZONA BOARD OF REGENTS; JEFF MILLER

For centuries, scientists have been captivated by the phenomenal feats of regeneration found in nature. Despite decades of research, attempts to replace or repair parts of the human body have met with only modest success. Fresh understanding of organ formation coupled with new technologies may help to unlock long-sought cures. By Cassandra Willyard

2001 OPPOSITE ACTS

US President George W. Bush prohibits federal funds being used to start new human embryonic cell lines or to conduct research on newly derived cell lines. The same year, the United Kingdom loosens restrictions on embryo research.

2006 BUILDING BODY PARTS

Anthony Atala, a surgeon at Wake Forest School of Medicine in Winston-Salem, North Carolina, successfully transplants lab-grown bladders into seven children and teenagers with congenital birth defects.

2009 ORDER OVERTURNED

US President Barack Obama lifts the ban on federal funding of new human embryonic stem cell lines.

2010 LARGE-SCALE SUCCESS

An individual with a spinal-cord injury becomes the first person to receive a therapy derived from embryonic stem cells. A large study the same year reports that stem cells harvested from patients' healthy cornea tissue can be grown in the lab and transplanted into the damaged corneas to restore eyesight.

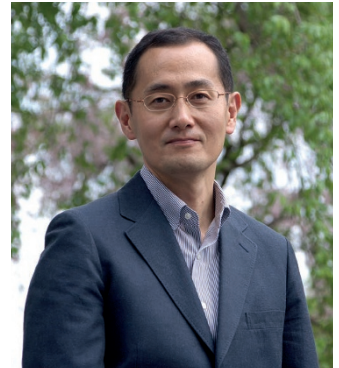


2015 FIRST TO MARKET

The Europe Commission approves the sale of Holoclar to treat people with severely damaged corneas. It is the first stem-cell therapy to reach the market.

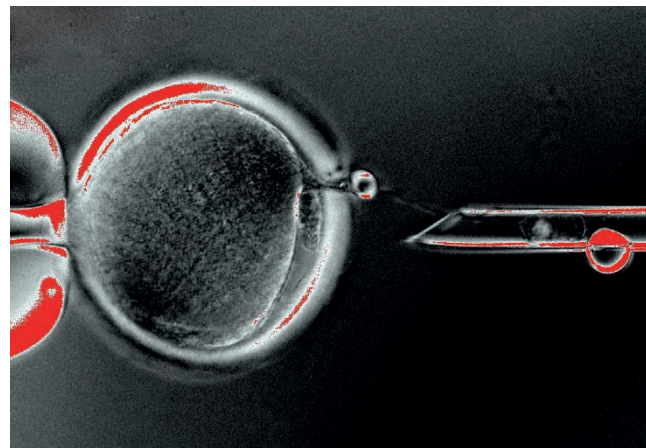
2006

Shinya Yamanaka (pictured) from Kyoto University in Japan coaxes adult mouse cells to return to an embryonic-like state by adding four transcription factors. These induced pluripotent stem (iPS) cells circumvent the ethical issues that surround embryonic stem cells. The year after, teams led by Yamanaka and James Thomson manage to reprogram adult human cells, and a group that includes more than 100 British medical charities writes a letter to *The Times* newspaper warning patients to be wary of stem-cell wonder cures.



2013

Shoukhrat Mitalipov at Oregon Health and Science University in Portland and his colleagues create the first human stem-cell lines by therapeutic cloning. The process involves somatic-cell nuclear transfer (pictured) — the same technique used to clone Dolly the sheep. First, researchers take the nucleus from a donor cell and inject it into an egg from which the nucleus has been removed. The researchers then coax the egg into dividing, harvest stem cells from the resulting embryo, and then culture those cells. Mitalipov's team used donor cells from a baby. The following year, two research



teams — one based in the United States and one in South Korea — report that they created human embryonic stem cells by cloning adult cells. This kind of therapeutic cloning could help researchers to develop genetically matched stem-cell therapies that are less likely to be rejected.

2014

A team of US and Japanese researchers reports that it can coax cells into an embryonic state by bathing the cells in acid, a technique called stimulus-triggered acquisition of pluripotency or STAP. The discovery promises an easy way to create patient-specific stem cells. But later that year, *Nature* retracts the two papers after it becomes clear that some of the data were falsified.

2016

Japanese scientists led by Katsuhiko Hayashi of Kyushu University in Fukuoka transform mouse skin cells into eggs by culturing them in clumps of fetal mouse ovary tissue. When fertilized and transplanted into a surrogate, these lab-grown eggs give rise to healthy, fertile pups.

CLOCKWISE FROM TOP: RIGHT: CIRAKI/KYOTO UNIV.; OHSU; TETRA IMAGES/GETTY