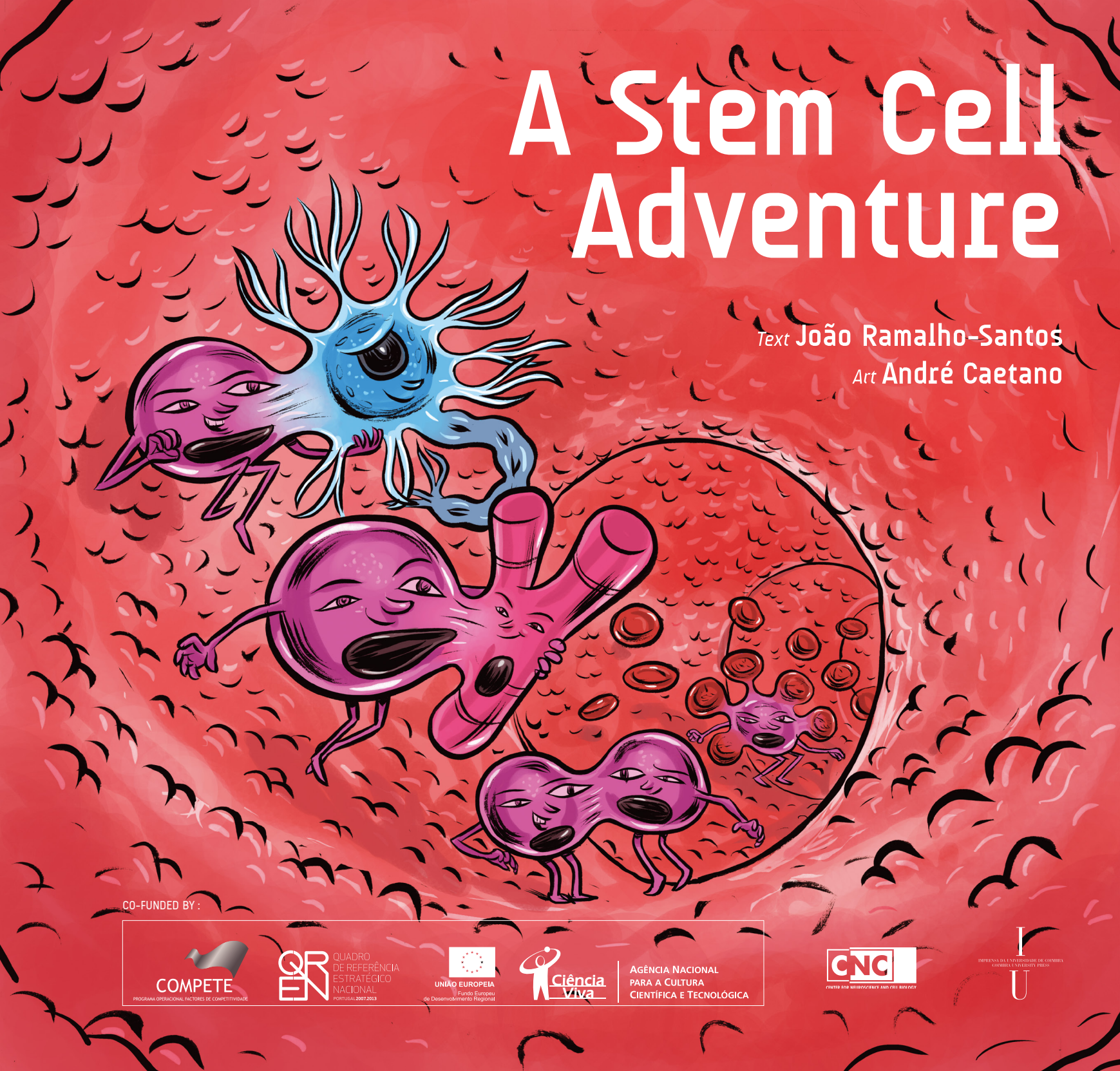
A Stem Cell Adventure

Text João Ramalho-Santos
Art André Caetano



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CNC
CENTER FOR NEUROSCIENCE AND CELL BIOLOGY

IMPRENSA DA UNIVERSIDADE DE COIMBRA
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This comic book is part of a science dissemination project, involving the media, developed by researchers of CNC - Center of Neuroscience and Cell Biology of the University of Coimbra, Portugal, funded by FEDER (Fundo Europeu de Desenvolvimento Regional), COMPETE - Programa Operacional Factores de Competitividade, and Ciência Viva – Agência Nacional para a Cultura Científica e Tecnológica. The science dissemination project, named " I want more and better cells! Stem cells: What are they? Where are they? For what can they be used?", focused on one of the major current topics in basic research and biomedicine - stem cells - and addressed questions that are commonly not fully understood by the public.

Team of Researchers: Cláudia Cavadas (coordinator), João Ramalho Santos, Inês Araújo, Lino Ferreira, Luís Pereira de Almeida, Teresa Girão;

Materials produced: during this project radio interviews and movies were produced, where each researcher explained one topic about stem cells; the movies were recorded at CNC laboratories and includes 2D and 3D animations (produced by the Television Web of the University of Coimbra); chronicles Illustrated with a cartoon done by Fernando Correia and published in the daily newspaper "Diario de Coimbra"; a "double book" - one side is composed by the illustrated chronicles and the other side is this comic book (Editor Imprensa da Universidade de Coimbra).

The materials and more information are available at http://www.cnbc.pt/outreach/outreachap_01.asp and https://sites.google.com/site/sciencedisseminationprojectcnc/

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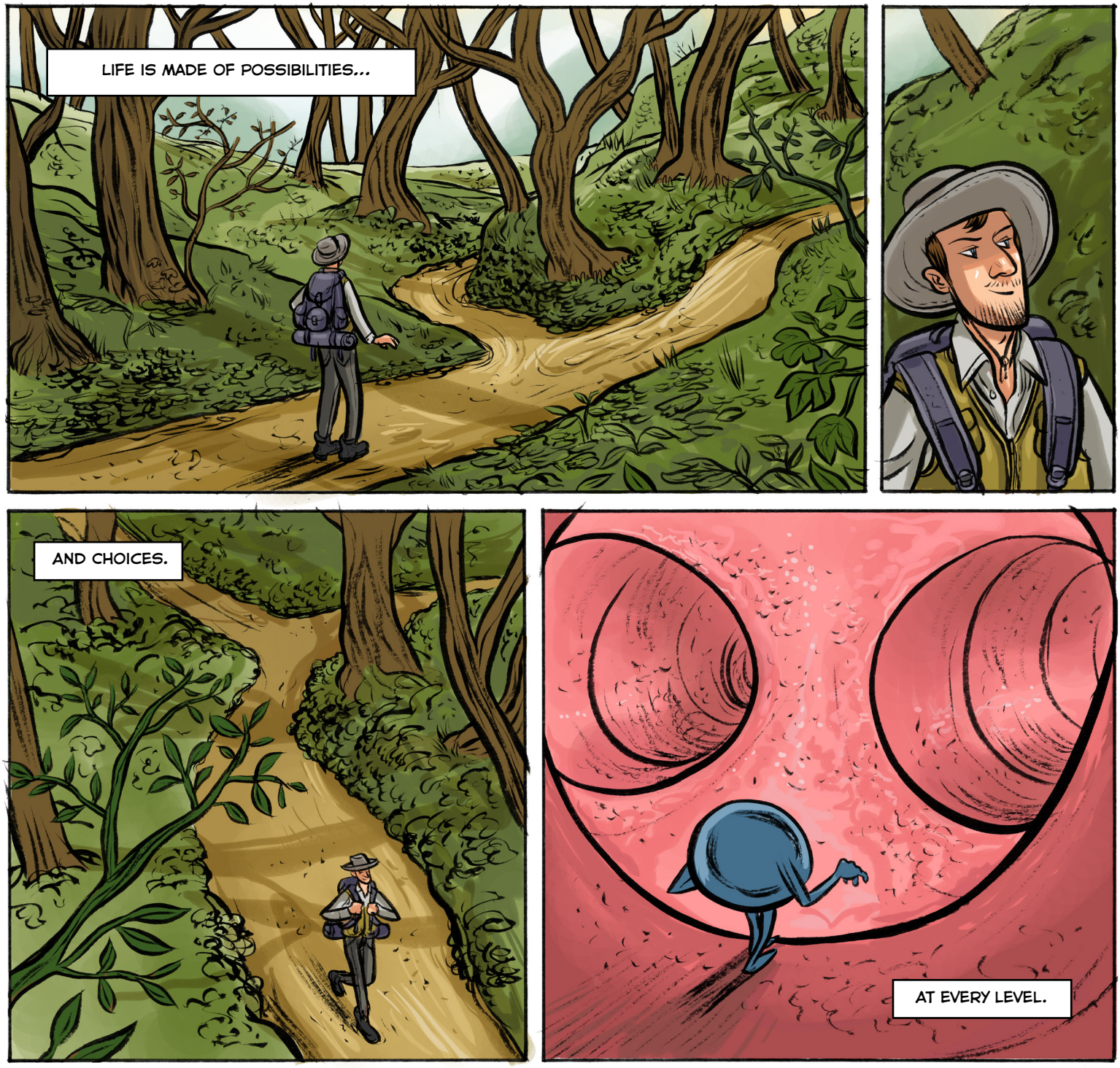
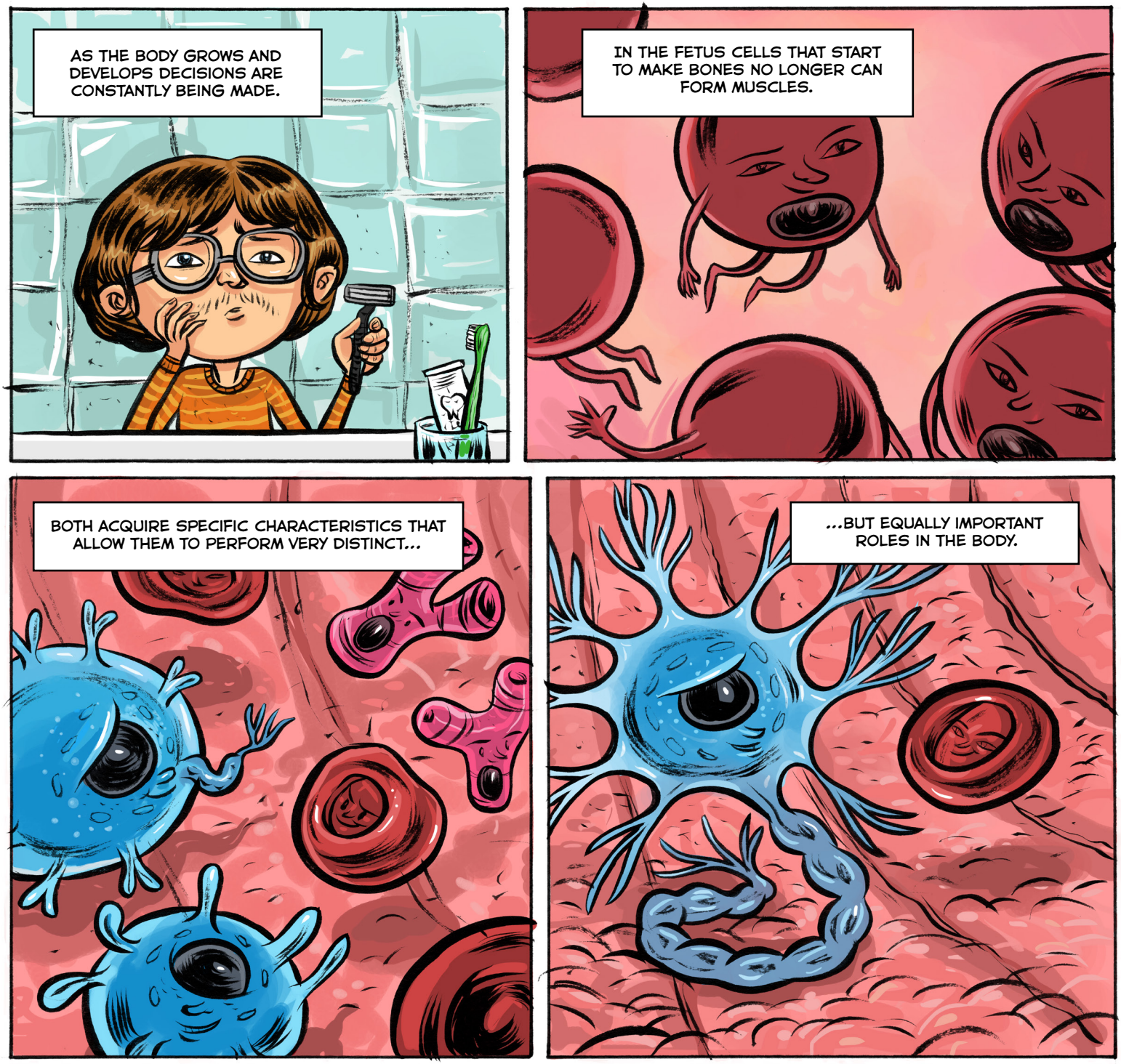
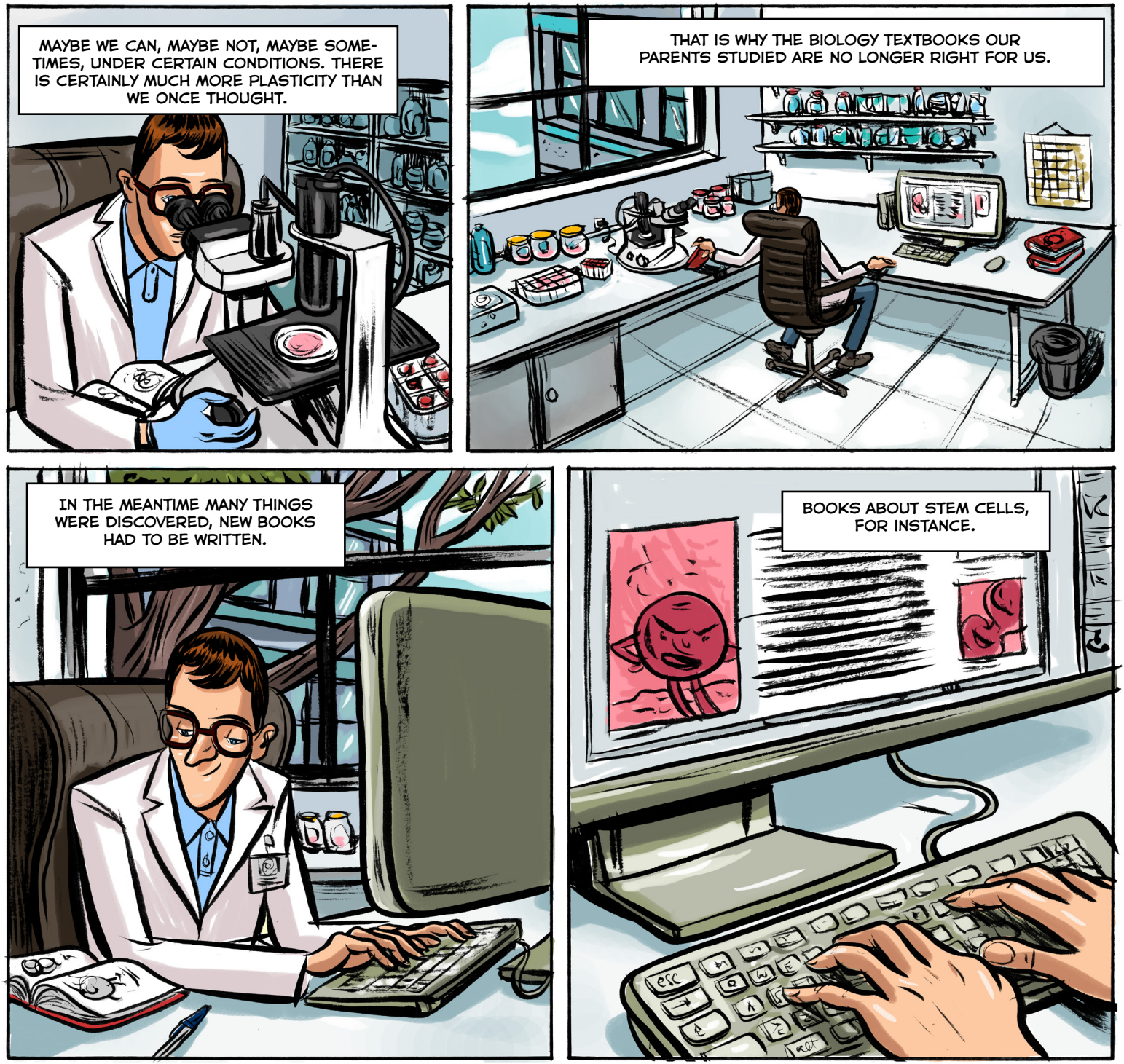
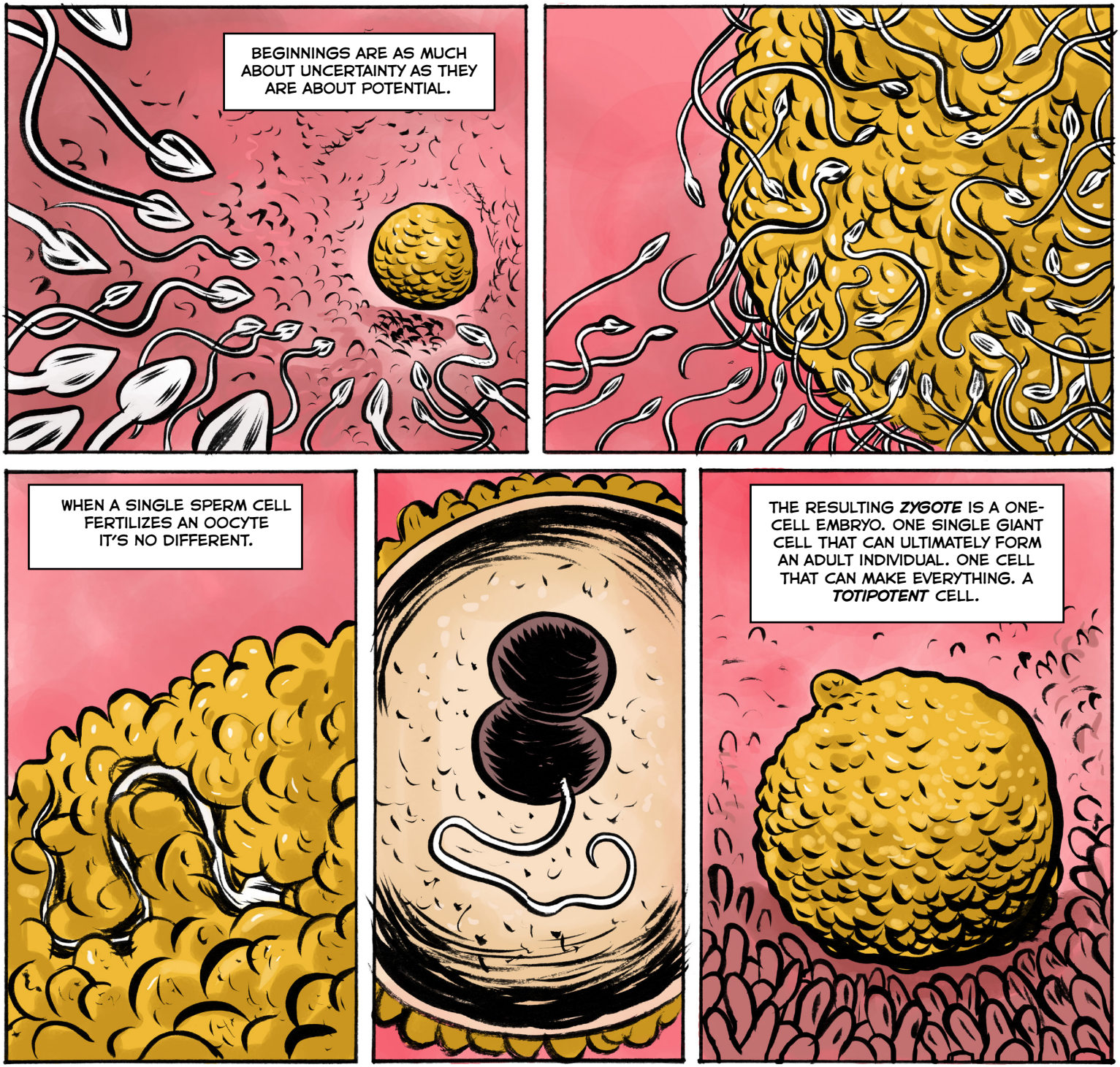
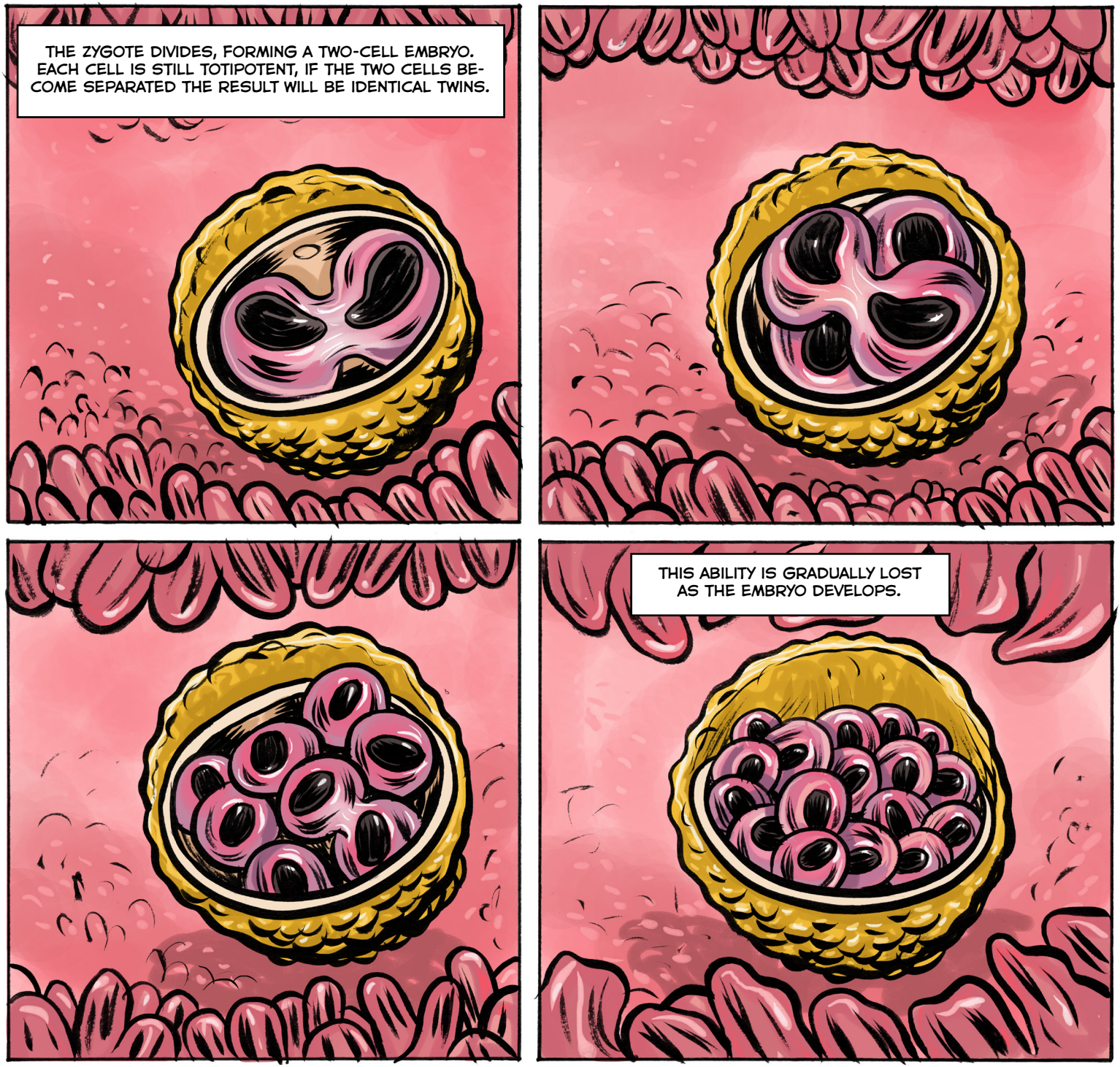

LIFE IS MADE OF POSSIBILITIES...
AND CHOICES.
AT EVERY LEVEL.


AS THE BODY GROWS AND DEVELOPS DECISIONS ARE CONSTANTLY BEING MADE.
IN THE FETUS CELLS THAT START TO MAKE BONES NO LONGER CAN FORM MUSCLES.
BOTH ACQUIRE SPECIFIC CHARACTERISTICS THAT ALLOW THEM TO PERFORM VERY DISTINCT...
...BUT EQUALLY IMPORTANT ROLES IN THE BODY.

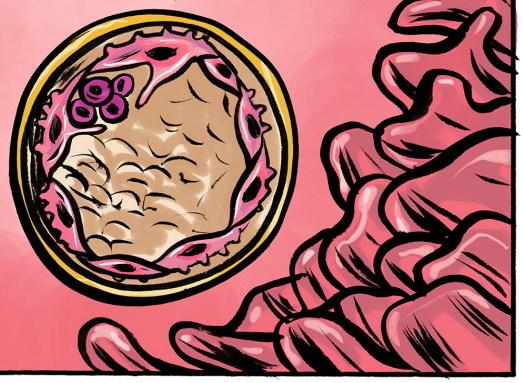

AS WE GROW OLDER WE MAKE ALL SORTS OF DECISIONS. WE CHOOSE TO STUDY SCIENCES, ARTS, TECHNOLOGIES.
WE PICK JOBS.
WE DECIDE TO BE FRIENDS, OR A BIT MORE.
WHETHER TO STAY OR TO LEAVE.
WE TRADE IN PLASTICITY FOR FULFILLMENT. WE CEASE TO BE POTENTIAL, AS WE BEGIN TO BE PRO-DUCTION. IT'S JUST THE WAY IT IS, WE'RE TOLD.
BUT HOW MANY OF THESE DECISIONS ARE TRULY FINAL? IS THERE ANY PLASTICITY LEFT IN OUR ADULT LIFE, IN OUR BODY, OUR CELLS?
CAN WE CHEAT FATE?


MAYBE WE CAN, MAYBE NOT, MAYBE SOMETIMES, UNDER CERTAIN CONDITIONS. THERE IS CERTAINLY MUCH MORE PLASTICITY THAN WE ONCE THOUGHT.
THAT IS WHY THE BIOLOGY TEXTBOOKS OUR PARENTS STUDIED ARE NO LONGER RIGHT FOR US.
IN THE MEANTIME MANY THINGS WERE DISCOVERED, NEW BOOKS HAD TO BE WRITTEN.
BOOKS ABOUT STEM CELLS, FOR INSTANCE.

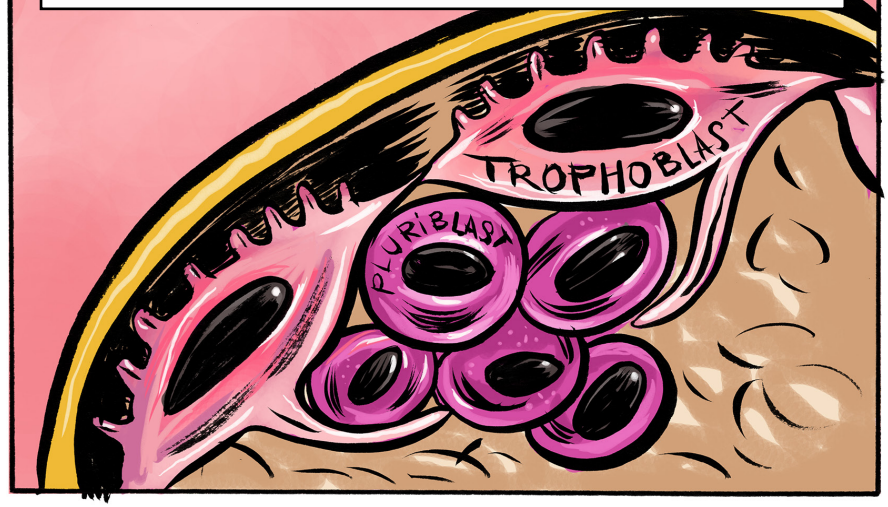

BEGINNINGS ARE AS MUCH ABOUT UNCERTAINTY AS THEY ARE ABOUT POTENTIAL.
WHEN A SINGLE SPERM CELL FERTILIZES AN OOCYTE IT'S NO DIFFERENT.
THE RESULTING ***ZYGOTE*** IS A ONE-CELL EMBRYO. ONE SINGLE GIANT CELL THAT CAN ULTIMATELY FORM AN ADULT INDIVIDUAL. ONE CELL THAT CAN MAKE EVERYTHING. A ***TOTIPOTENT*** CELL.


THE ZYGOTE DIVIDES, FORMING A TWO-CELL EMBRYO. EACH CELL IS STILL TOTIPOTENT, IF THE TWO CELLS BECOME SEPARATED THE RESULT WILL BE IDENTICAL TWINS.
THIS ABILITY IS GRADUALLY LOST AS THE EMBRYO DEVELOPS.

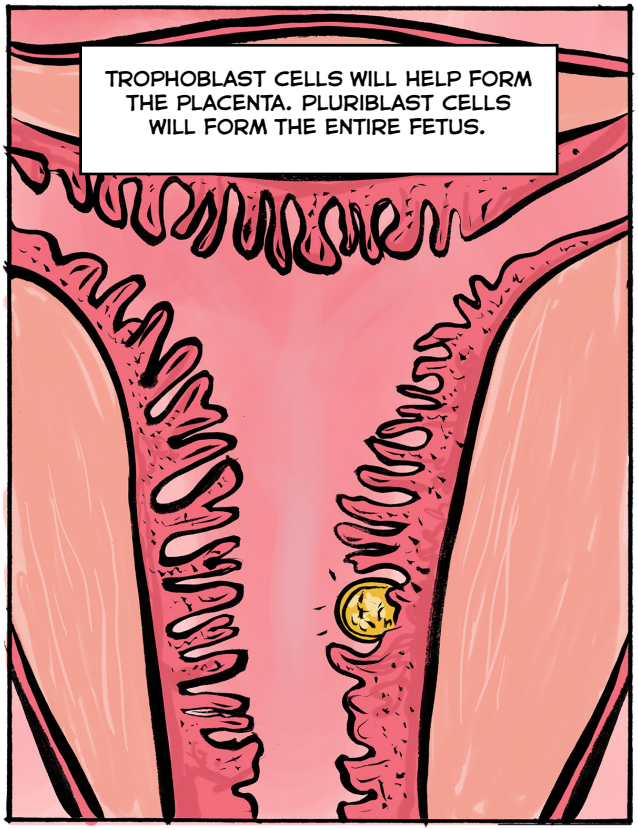
APPROXIMATELY FIVE DAYS AFTER FERTILIZATION, BEFORE IT IMPLANTS IN THE UTERUS, THE EMBRYO IS A MORE COMPLEX STRUCTURE, CALLED A ***BLASTOCYST.***



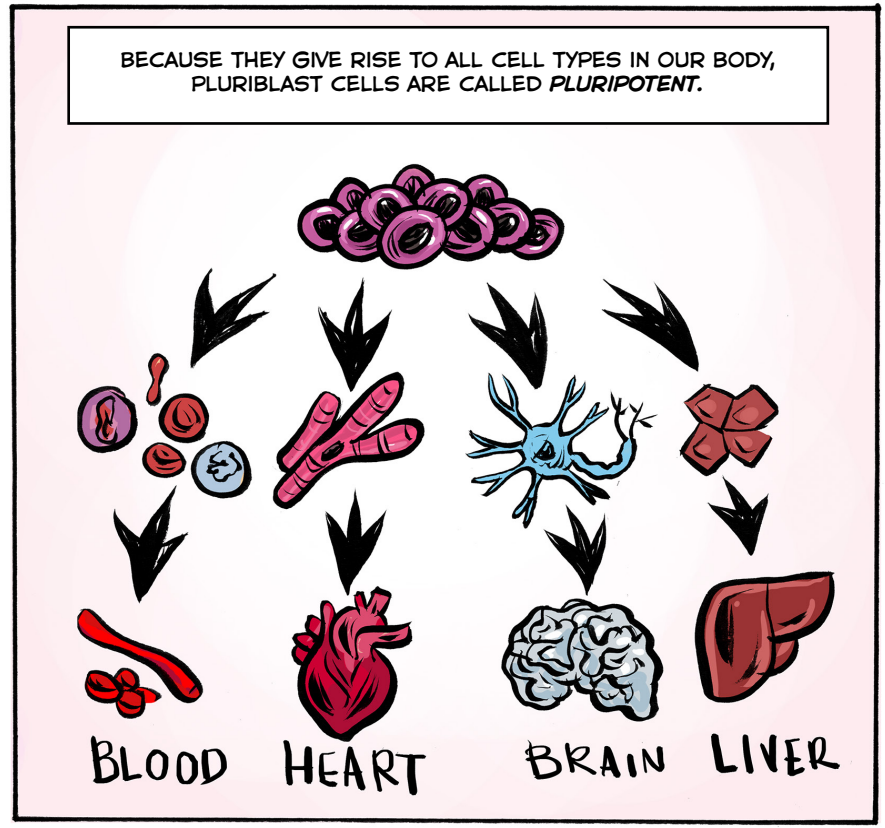
THE BLASTOCYST HAS TWO DIFFERENT TYPES OF CELLS: ***TROPHOBLAST*** CELLS AND ***PLURIBLAST*** (OR ***INNER CELL MASS***) CELLS.

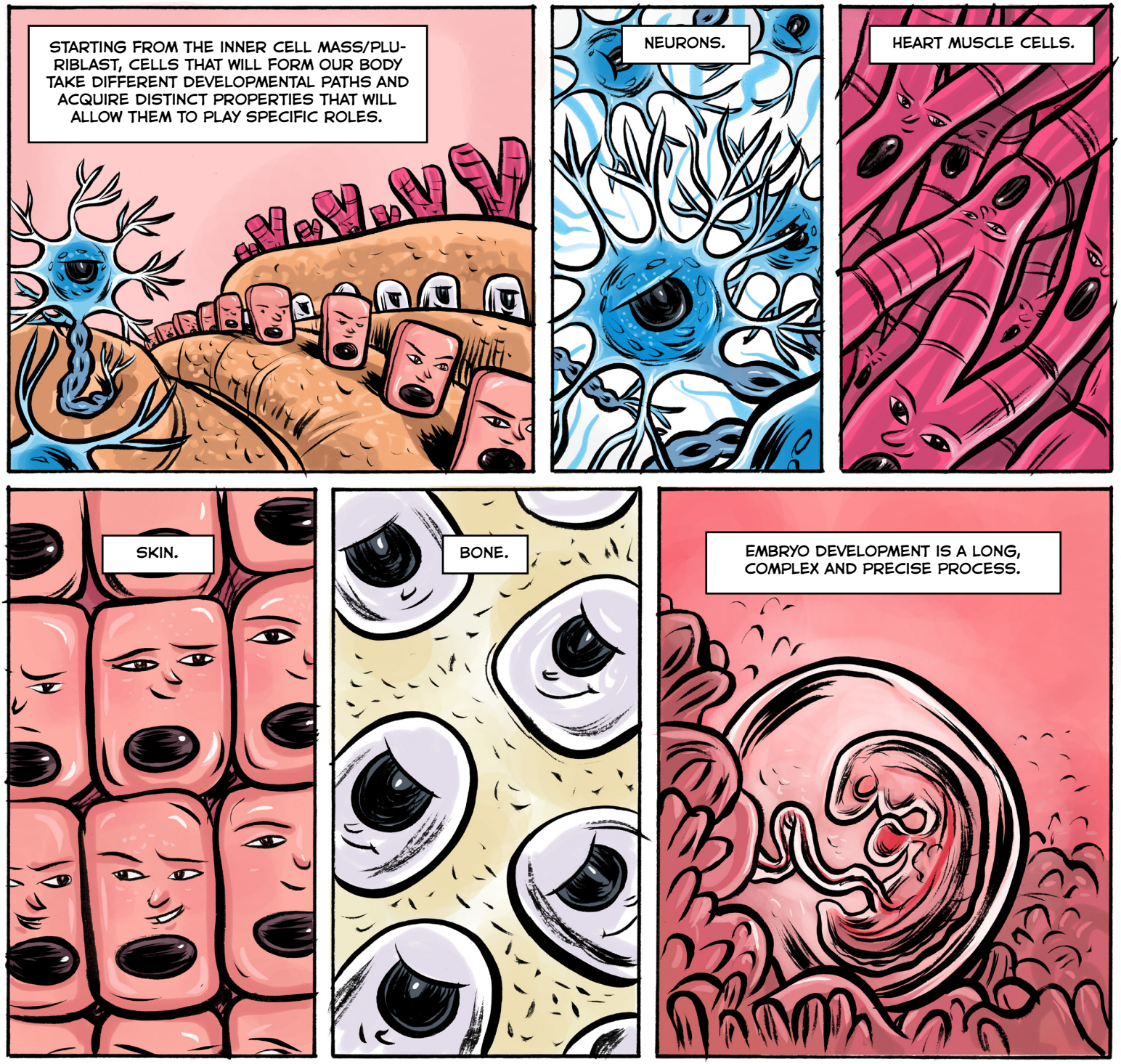


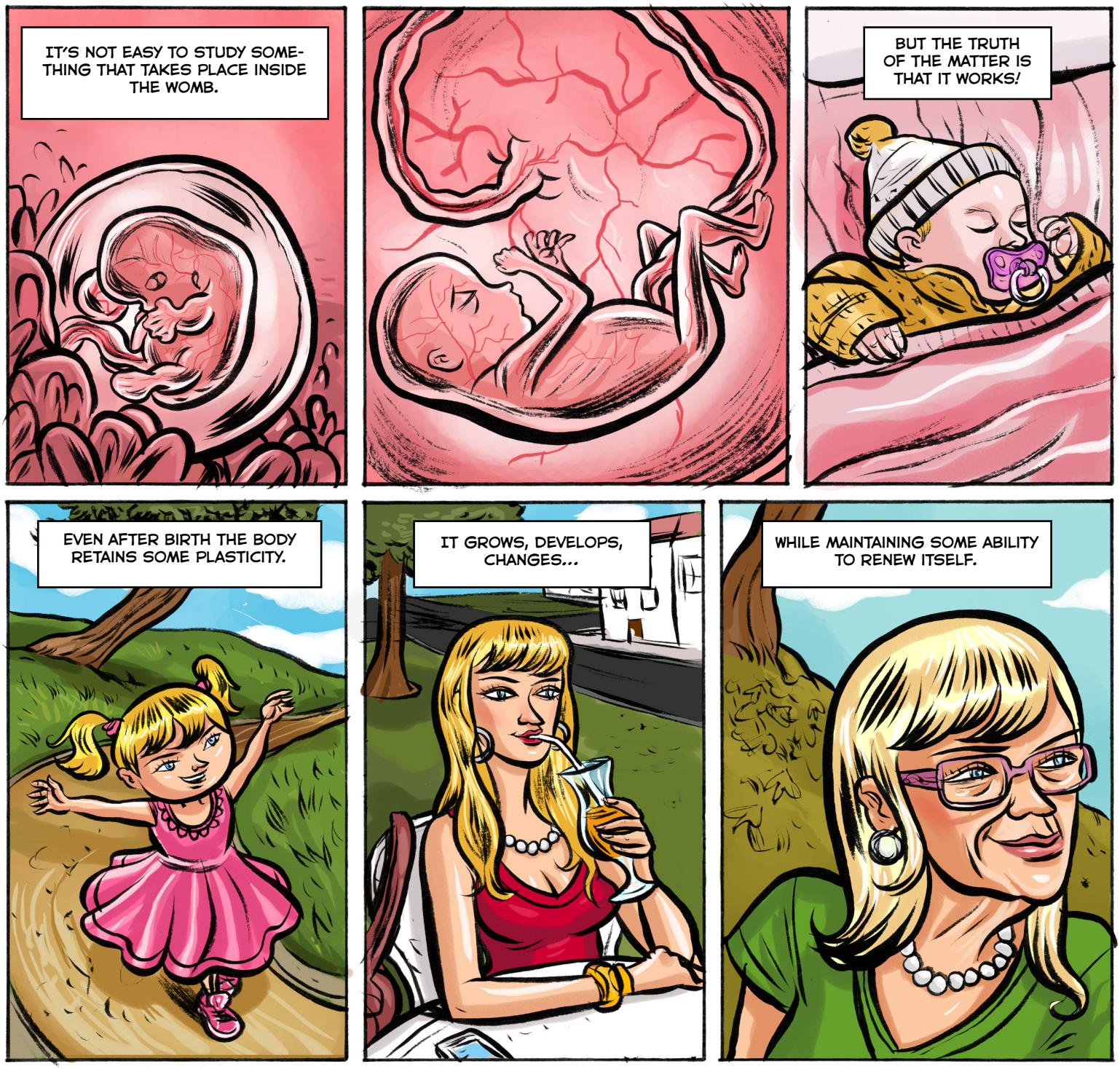
TROPHOBLAST CELLS WILL HELP FORM THE PLACENTA. PLURIBLAST CELLS WILL FORM THE ENTIRE FETUS.

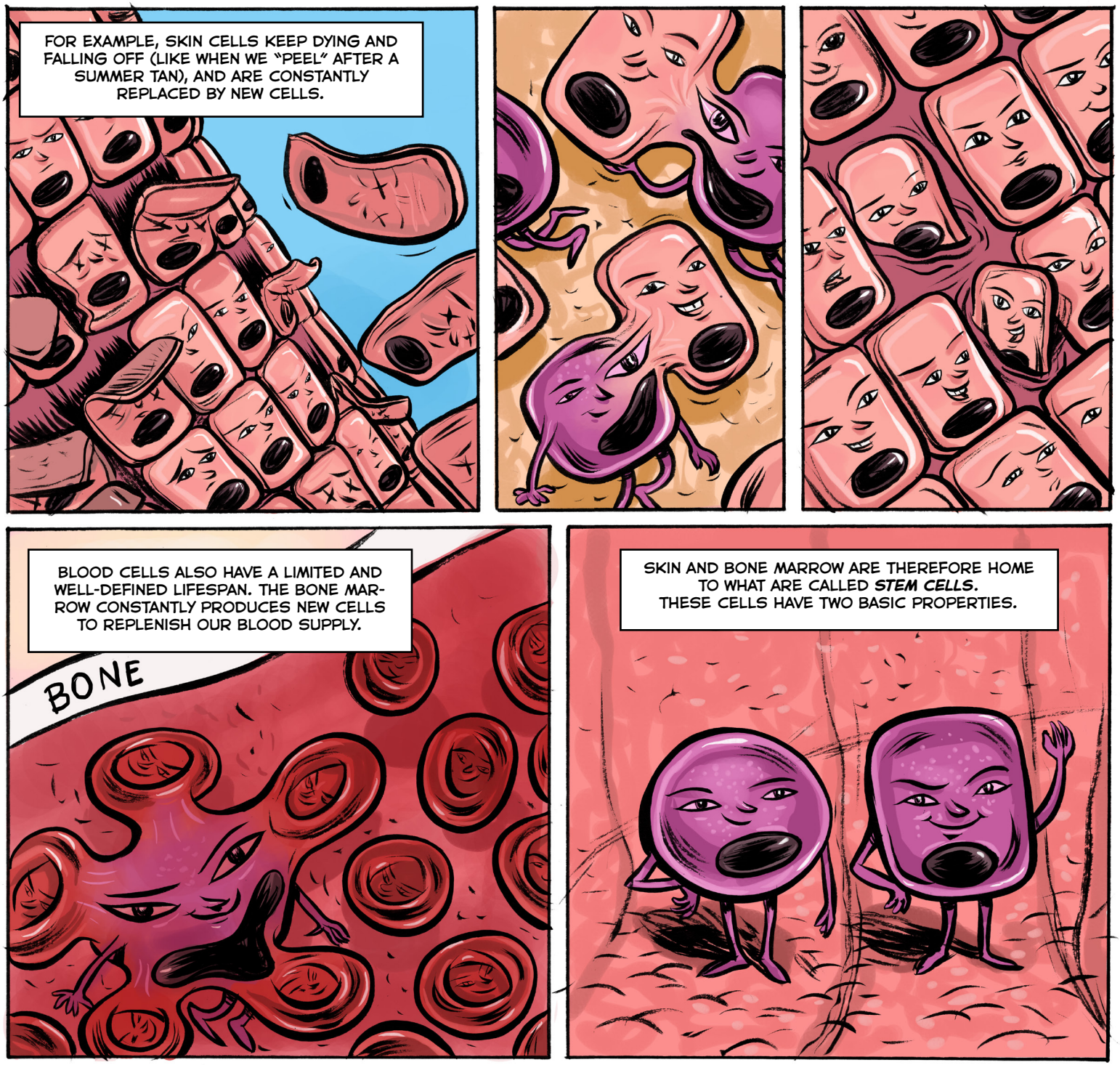


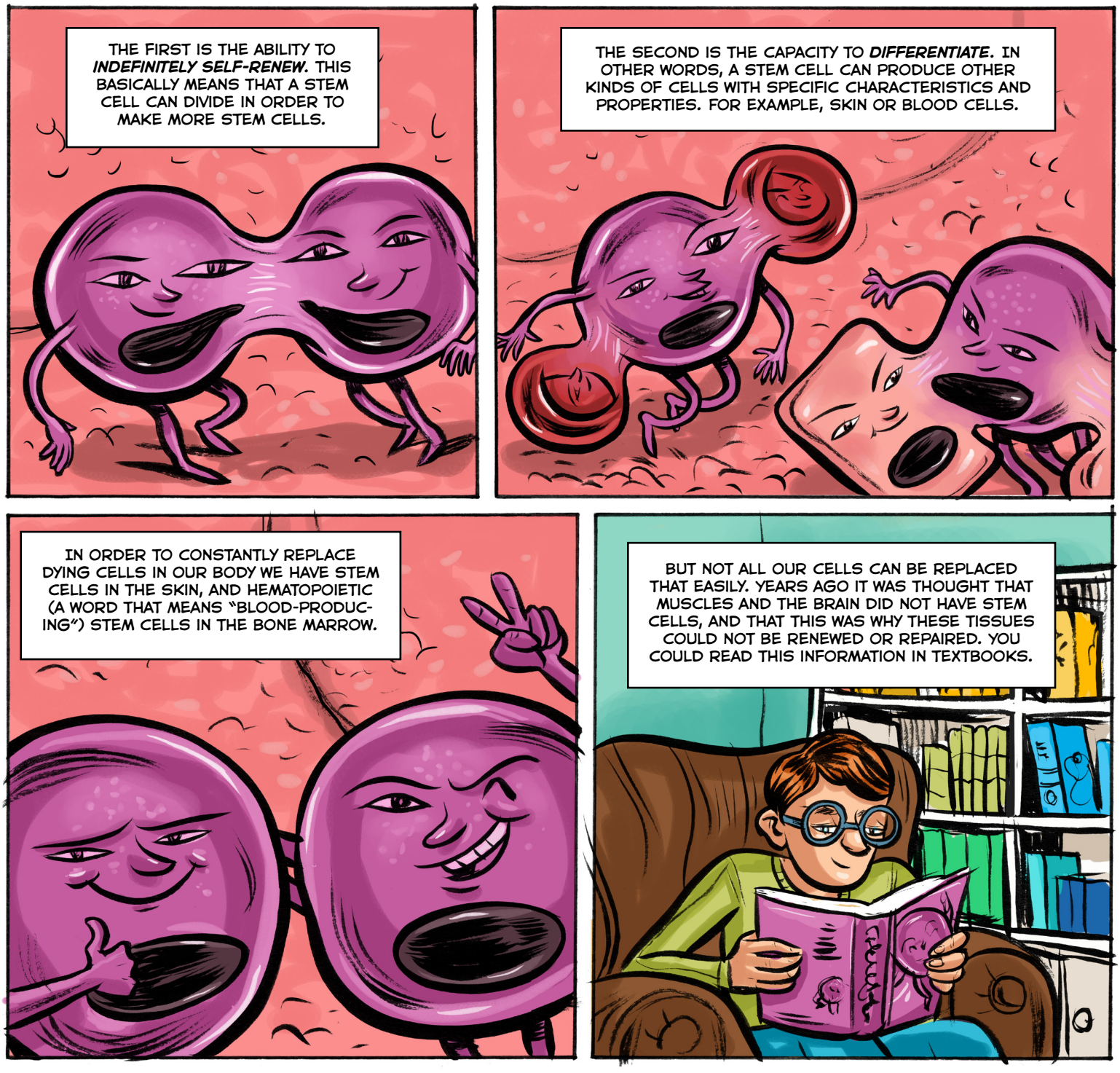
BECAUSE THEY GIVE RISE TO ALL CELL TYPES IN OUR BODY, PLURIBLAST CELLS ARE CALLED ***PLURIPOTENT.***

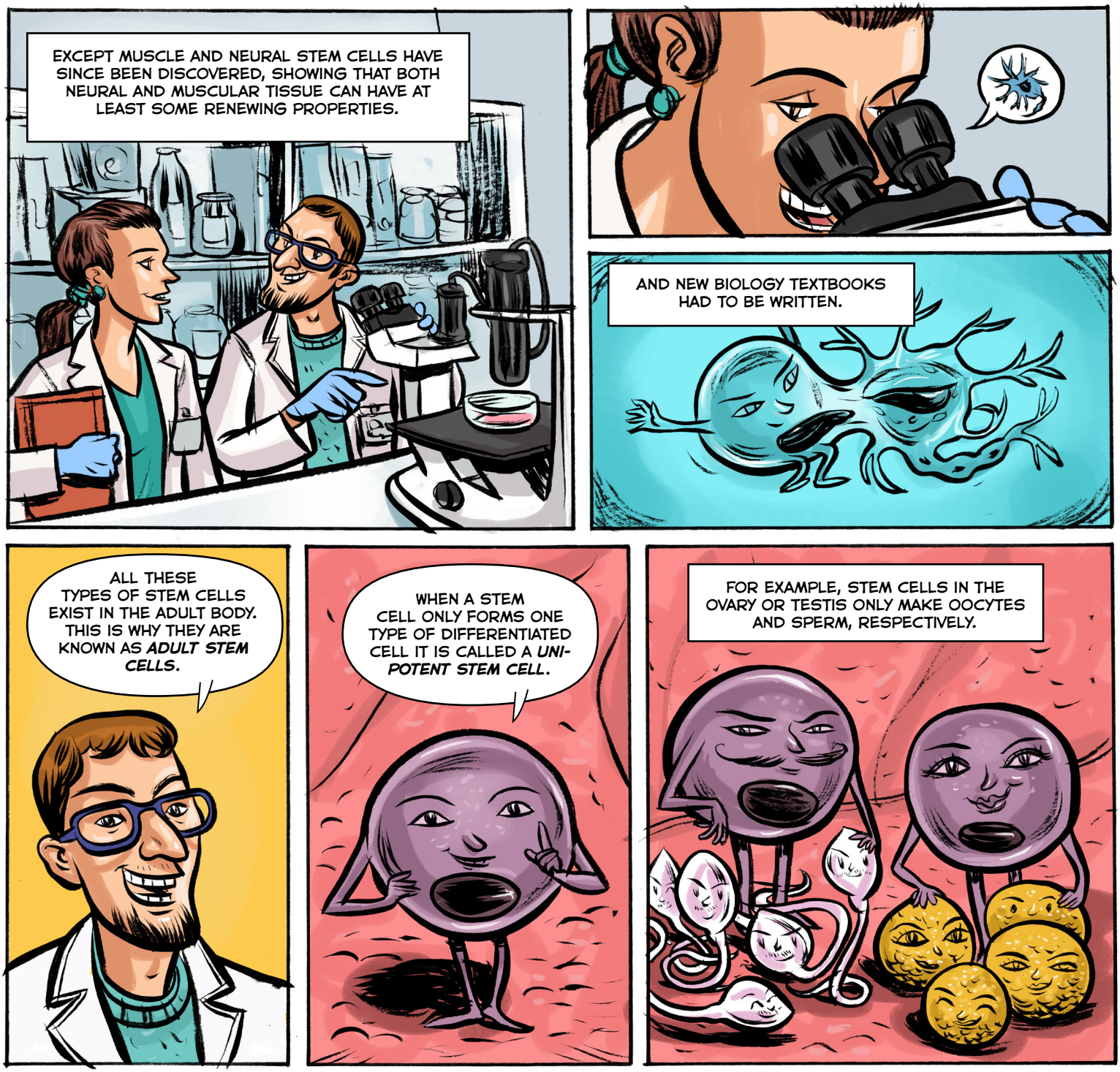


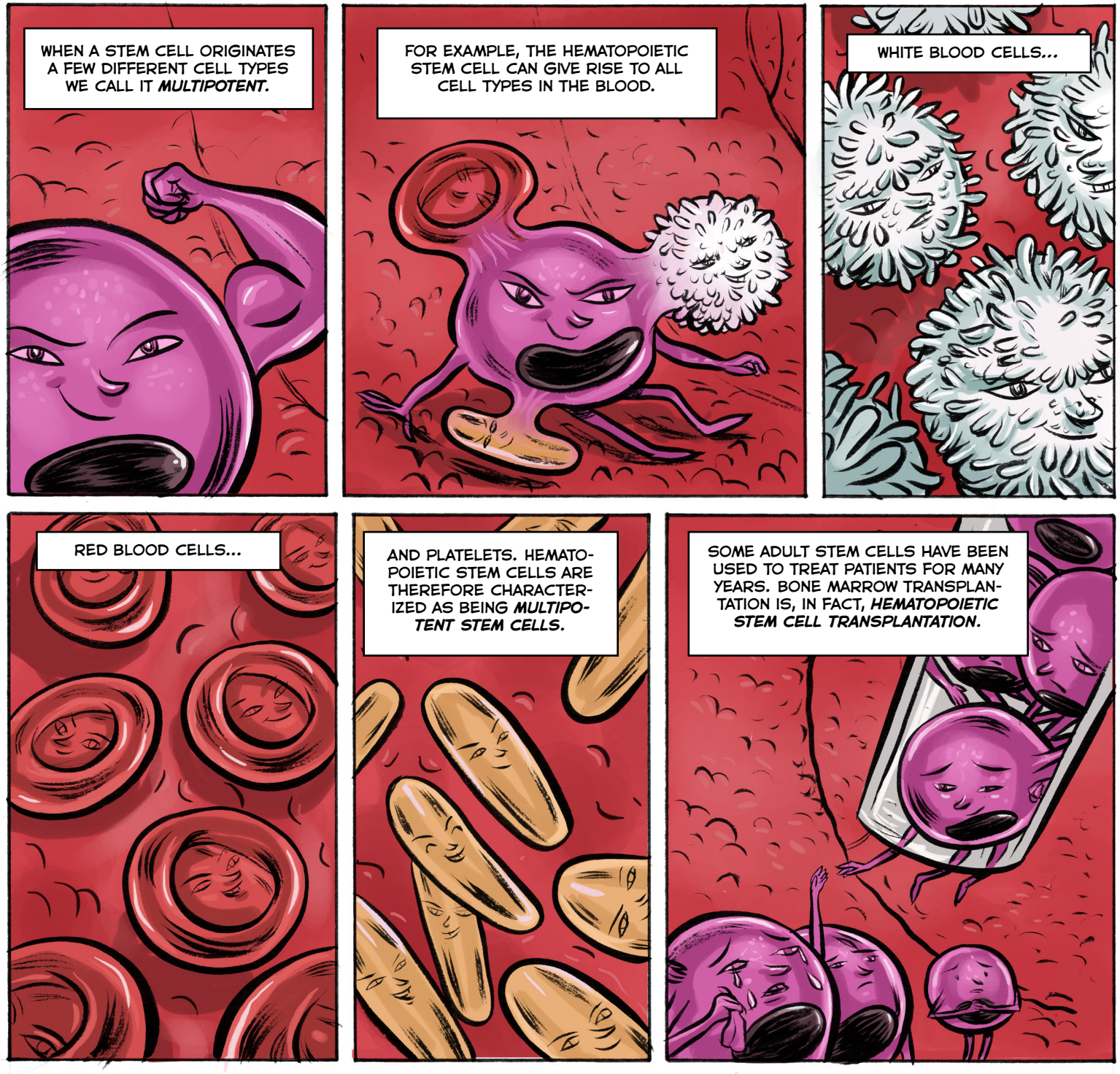

STARTING FROM THE INNER CELL MASS/PLURIBLAST, CELLS THAT WILL FORM OUR BODY TAKE DIFFERENT DEVELOPMENTAL PATHS AND ACQUIRE DISTINCT PROPERTIES THAT WILL ALLOW THEM TO PLAY SPECIFIC ROLES.
NEURONS.
HEART MUSCLE CELLS.
SKIN.
BONE.
EMBRYO DEVELOPMENT IS A LONG, COMPLEX AND PRECISE PROCESS.

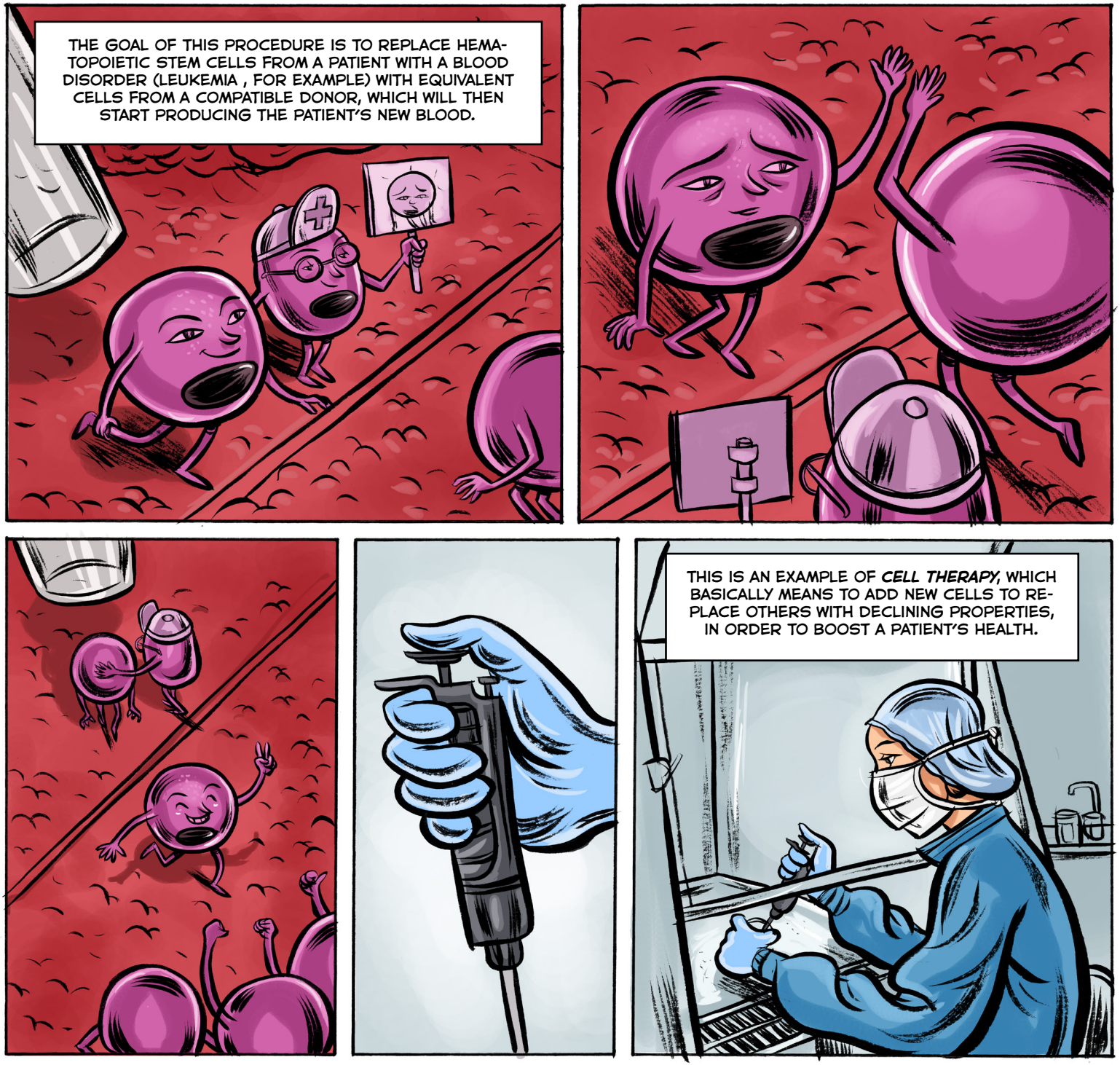

IT'S NOT EASY TO STUDY SOMETHING THAT TAKES PLACE INSIDE THE WOMB.
BUT THE TRUTH OF THE MATTER IS THAT IT WORKS!
EVEN AFTER BIRTH THE BODY RETAINS SOME PLASTICITY.
IT GROWS, DEVELOPS, CHANGES...
WHILE MAINTAINING SOME ABILITY TO RENEW ITSELF.

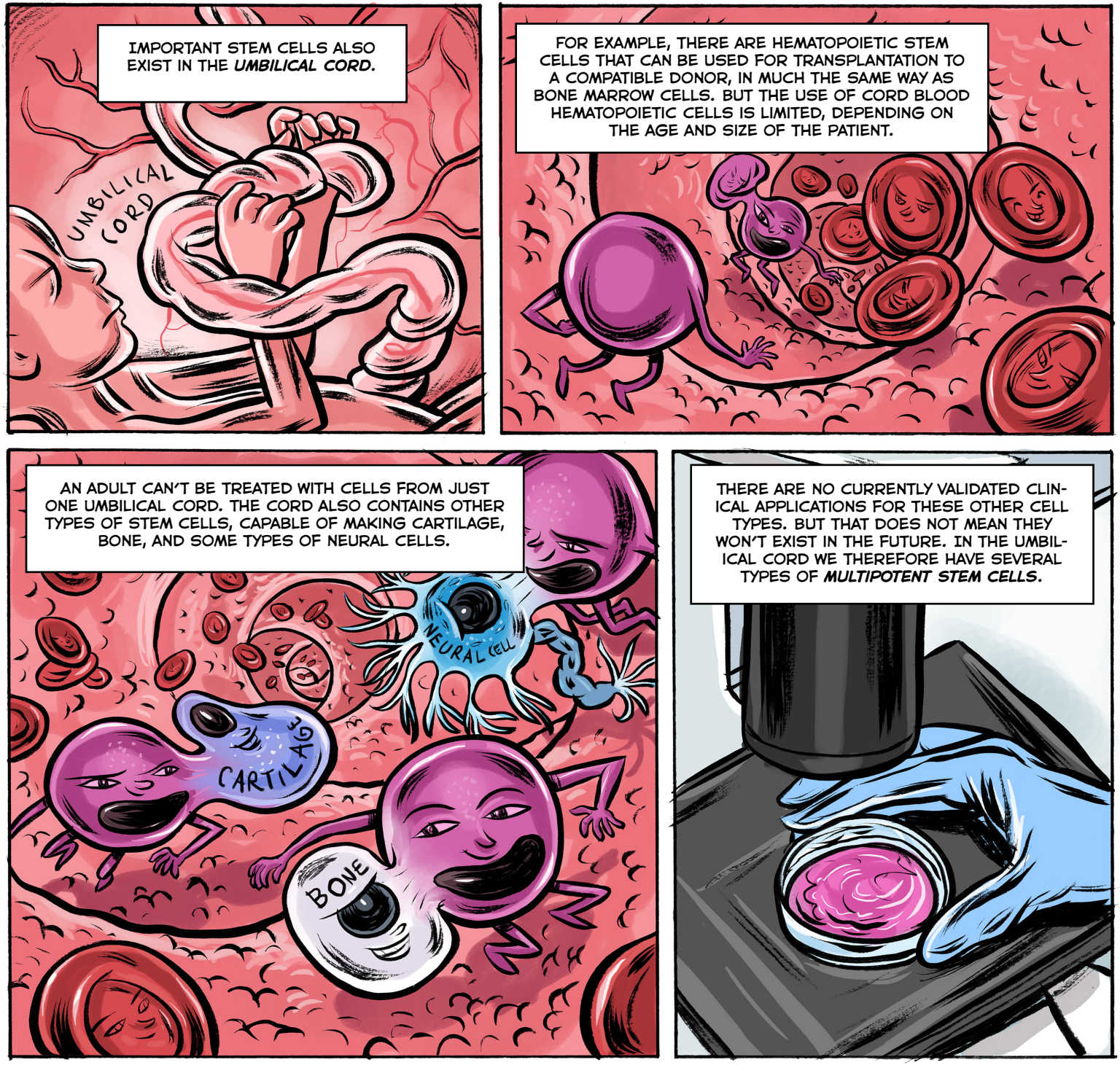

FOR EXAMPLE, SKIN CELLS KEEP DYING AND FALLING OFF (LIKE WHEN WE "PEEL" AFTER A SUMMER TAN), AND ARE CONSTANTLY REPLACED BY NEW CELLS.
BLOOD CELLS ALSO HAVE A LIMITED AND WELL-DEFINED LIFESPAN. THE BONE MARROW CONSTANTLY PRODUCES NEW CELLS TO REPLENISH OUR BLOOD SUPPLY.
BONE
SKIN AND BONE MARROW ARE THEREFORE HOME TO WHAT ARE CALLED ***STEM CELLS***. THESE CELLS HAVE TWO BASIC PROPERTIES.

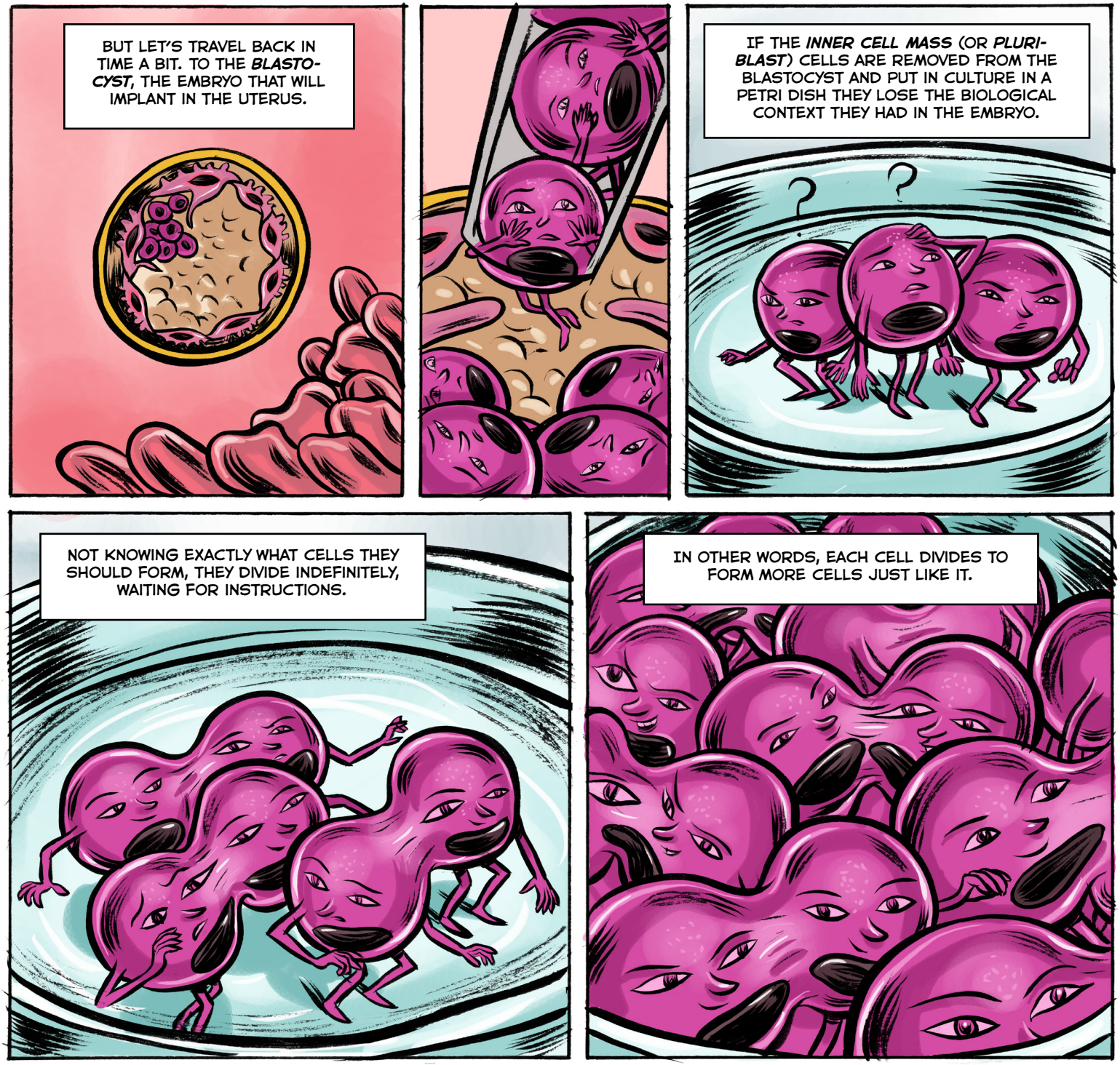

THE FIRST IS THE ABILITY TO ***INDEFINITELY SELF-RENEW.*** THIS BASICALLY MEANS THAT A STEM CELL CAN DIVIDE IN ORDER TO MAKE MORE STEM CELLS.
THE SECOND IS THE CAPACITY TO ***DIFFERENTIATE.*** IN OTHER WORDS, A STEM CELL CAN PRODUCE OTHER KINDS OF CELLS WITH SPECIFIC CHARACTERISTICS AND PROPERTIES. FOR EXAMPLE, SKIN OR BLOOD CELLS.
IN ORDER TO CONSTANTLY REPLACE DYING CELLS IN OUR BODY WE HAVE STEM CELLS IN THE SKIN, AND HEMATOPOIETIC (A WORD THAT MEANS "BLOOD-PRODUCING") STEM CELLS IN THE BONE MARROW.
BUT NOT ALL OUR CELLS CAN BE REPLACED THAT EASILY. YEARS AGO IT WAS THOUGHT THAT MUSCLES AND THE BRAIN DID NOT HAVE STEM CELLS, AND THAT THIS WAS WHY THESE TISSUES COULD NOT BE RENEWED OR REPAIRED. YOU COULD READ THIS INFORMATION IN TEXTBOOKS.


EXCEPT MUSCLE AND NEURAL STEM CELLS HAVE SINCE BEEN DISCOVERED, SHOWING THAT BOTH NEURAL AND MUSCULAR TISSUE CAN HAVE AT LEAST SOME RENEWING PROPERTIES.
AND NEW BIOLOGY TEXTBOOKS HAD TO BE WRITTEN.
ALL THESE TYPES OF STEM CELLS EXIST IN THE ADULT BODY. THIS IS WHY THEY ARE KNOWN AS ***ADULT STEM CELLS.***
WHEN A STEM CELL ONLY FORMS ONE TYPE OF DIFFERENTIATED CELL IT IS CALLED A ***UNI-POTENT STEM CELL.***
FOR EXAMPLE, STEM CELLS IN THE OVARY OR TESTIS ONLY MAKE OOCYTES AND SPERM, RESPECTIVELY.


WHEN A STEM CELL ORIGINATES A FEW DIFFERENT CELL TYPES WE CALL IT ***MULTIPOTENT.***
FOR EXAMPLE, THE HEMATOPOIETIC STEM CELL CAN GIVE RISE TO ALL CELL TYPES IN THE BLOOD.
WHITE BLOOD CELLS...
RED BLOOD CELLS...
AND PLATELETS. HEMATOPOIETIC STEM CELLS ARE THEREFORE CHARACTERIZED AS BEING ***MULTIPOTENT STEM CELLS.***
SOME ADULT STEM CELLS HAVE BEEN USED TO TREAT PATIENTS FOR MANY YEARS. BONE MARROW TRANSPLANTATION IS, IN FACT, ***HEMATOPOIETIC STEM CELL TRANSPLANTATION.***

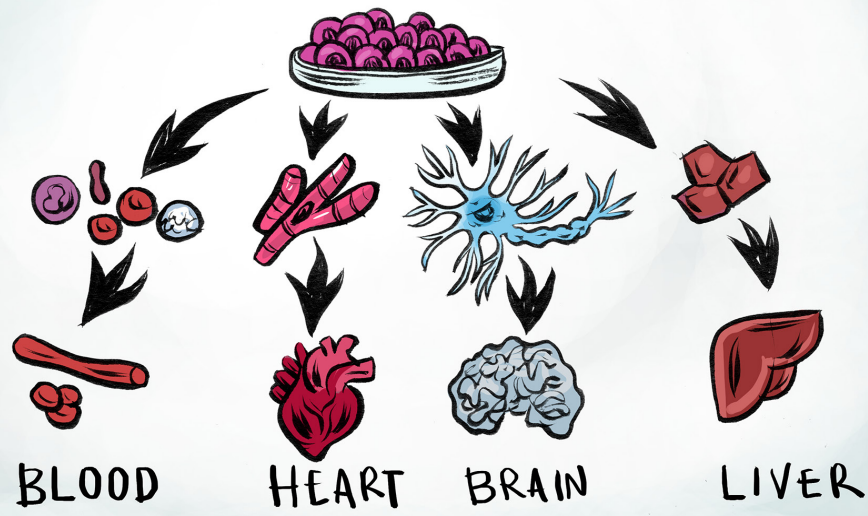

THE GOAL OF THIS PROCEDURE IS TO REPLACE HEMATOPOIETIC STEM CELLS FROM A PATIENT WITH A BLOOD DISORDER (LEUKEMIA , FOR EXAMPLE) WITH EQUIVALENT CELLS FROM A COMPATIBLE DONOR, WHICH WILL THEN START PRODUCING THE PATIENT'S NEW BLOOD.
THIS IS AN EXAMPLE OF *CELL THERAPY*, WHICH BASICALLY MEANS TO ADD NEW CELLS TO REPLACE OTHERS WITH DECLINING PROPERTIES, IN ORDER TO BOOST A PATIENT'S HEALTH.


IMPORTANT STEM CELLS ALSO EXIST IN THE *UMBILICAL CORD*.
UMBILICAL CORD
FOR EXAMPLE, THERE ARE HEMATOPOIETIC STEM CELLS THAT CAN BE USED FOR TRANSPLANTATION TO A COMPATIBLE DONOR, IN MUCH THE SAME WAY AS BONE MARROW CELLS. BUT THE USE OF CORD BLOOD HEMATOPOIETIC CELLS IS LIMITED, DEPENDING ON THE AGE AND SIZE OF THE PATIENT.
AN ADULT CAN'T BE TREATED WITH CELLS FROM JUST ONE UMBILICAL CORD. THE CORD ALSO CONTAINS OTHER TYPES OF STEM CELLS, CAPABLE OF MAKING CARTILAGE, BONE, AND SOME TYPES OF NEURAL CELLS.
NEURAL CELL
CARTILAGE
BONE
THERE ARE NO CURRENTLY VALIDATED CLINICAL APPLICATIONS FOR THESE OTHER CELL TYPES. BUT THAT DOES NOT MEAN THEY WON'T EXIST IN THE FUTURE. IN THE UMBILICAL CORD WE THEREFORE HAVE SEVERAL TYPES OF *MULTIPOTENT STEM CELLS*.


BUT LET'S TRAVEL BACK IN TIME A BIT. TO THE BLASTOCYST, THE EMBRYO THAT WILL IMPLANT IN THE UTERUS.
IF THE INNER CELL MASS (OR PLURIBLAST) CELLS ARE REMOVED FROM THE BLASTOCYST AND PUT IN CULTURE IN A PETRI DISH THEY LOSE THE BIOLOGICAL CONTEXT THEY HAD IN THE EMBRYO.
NOT KNOWING EXACTLY WHAT CELLS THEY SHOULD FORM, THEY DIVIDE INDEFINITELY, WAITING FOR INSTRUCTIONS.
IN OTHER WORDS, EACH CELL DIVIDES TO FORM MORE CELLS JUST LIKE IT.

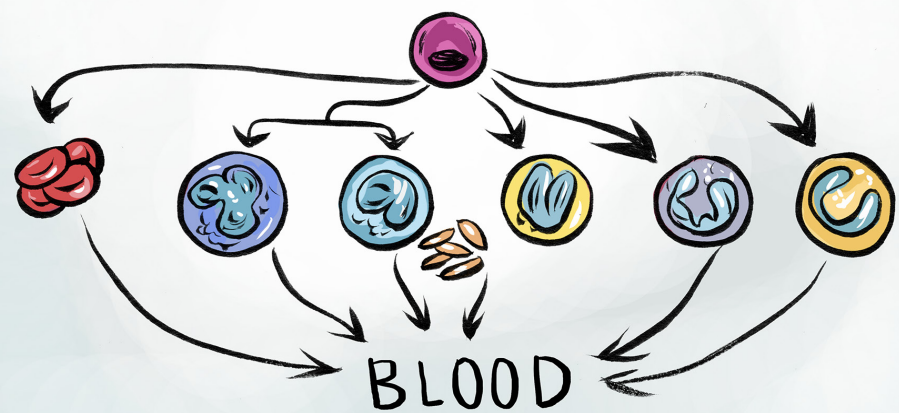
AS STEM CELLS FOUND IN THE ADULT BODY, THESE CELLS REMOVED FROM THE EMBRYO HAVE THE SAME ***SELF-RENEWAL*** PROPERTY.

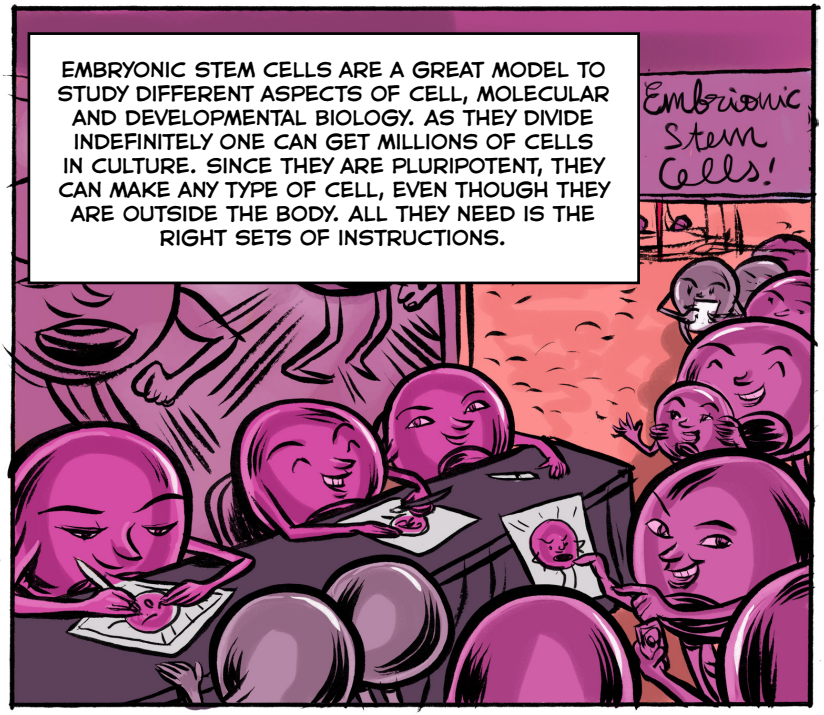
FURTHERMORE, THEY CAN ***DIFFERENTIATE*** INTO ***ALL*** THE DIFFERENT CELL TYPES IN THE BODY, WHICH IS WHAT WOULD HAVE HAPPENED HAD THEY REMAINED AS PART OF THE BLASTOCYST. THEREFORE, THESE ARE ***PLURIPOTENT STEM CELLS.***

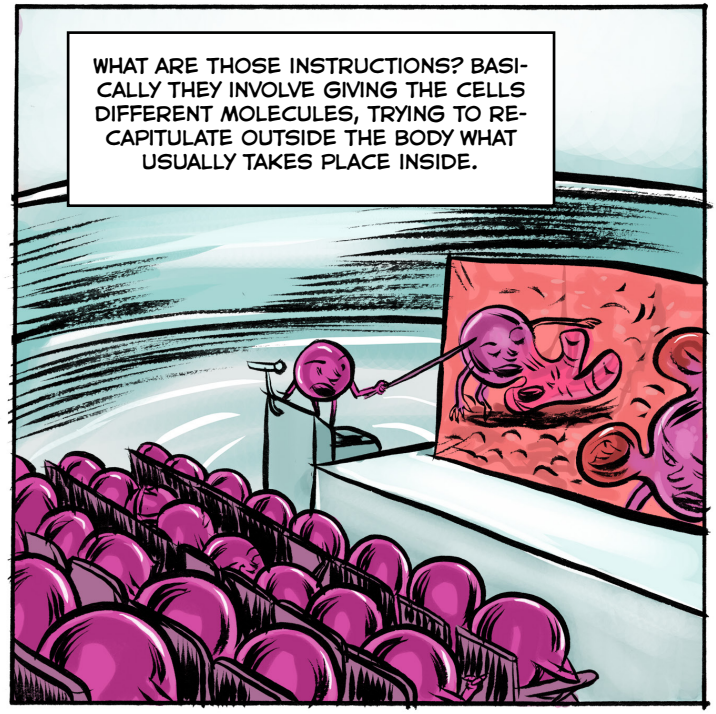


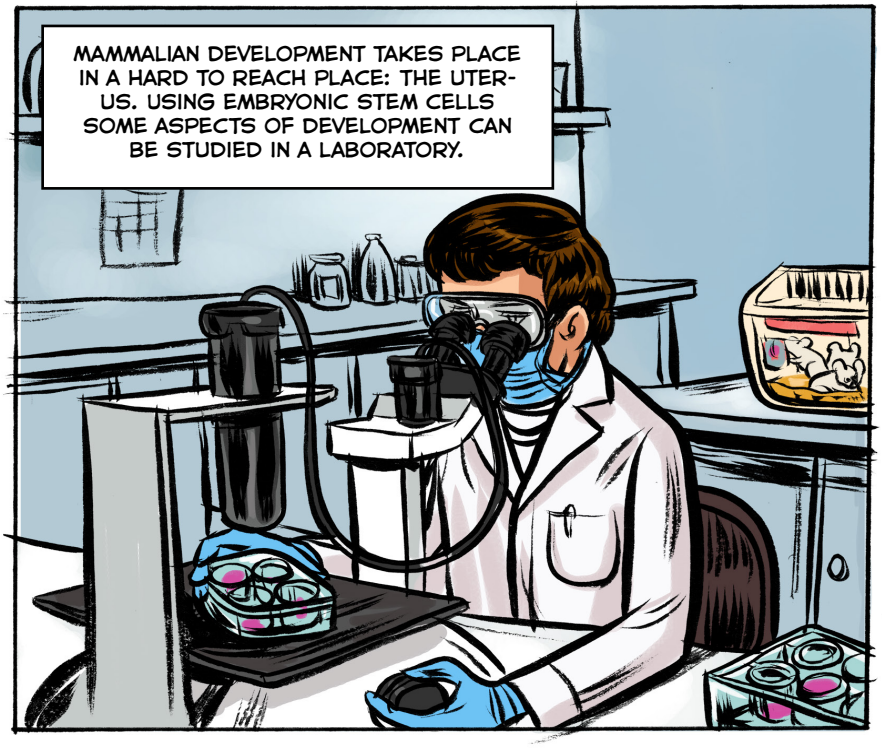
AS THEY ORIGINATED FROM EMBRYOS THEY ARE ALSO WIDELY KNOWN AS ***EMBRYONIC STEM CELLS.***

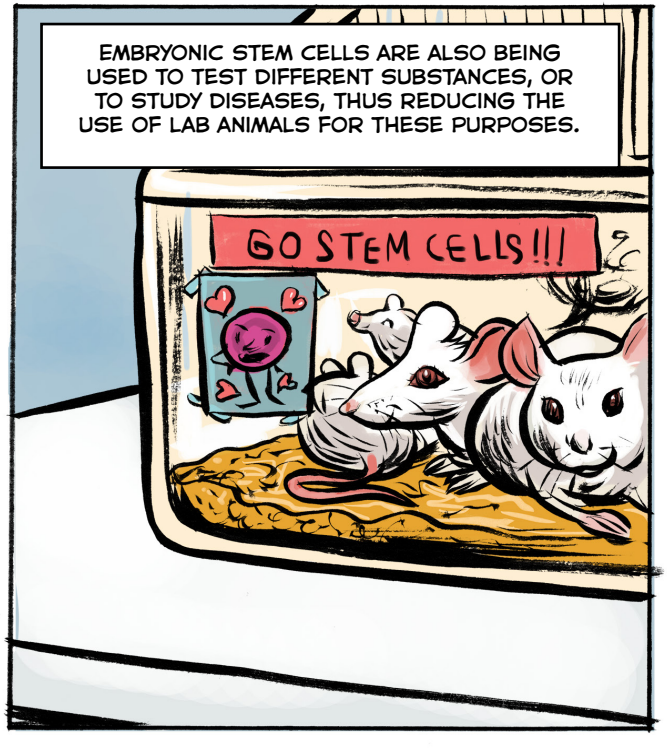
ON THE OTHER HAND, STEM CELLS IN THE ADULT BODY OR UMBILICAL CORD CAN ONLY FORM ***SOME*** TYPES OF FUNCTIONAL CELLS, DEPENDING ON WHERE THEY ARE, BUT NOT ***ALL*** CELLS TYPES. THAT'S WHY THEY ARE CALLED ***MULTIPOTENT.***

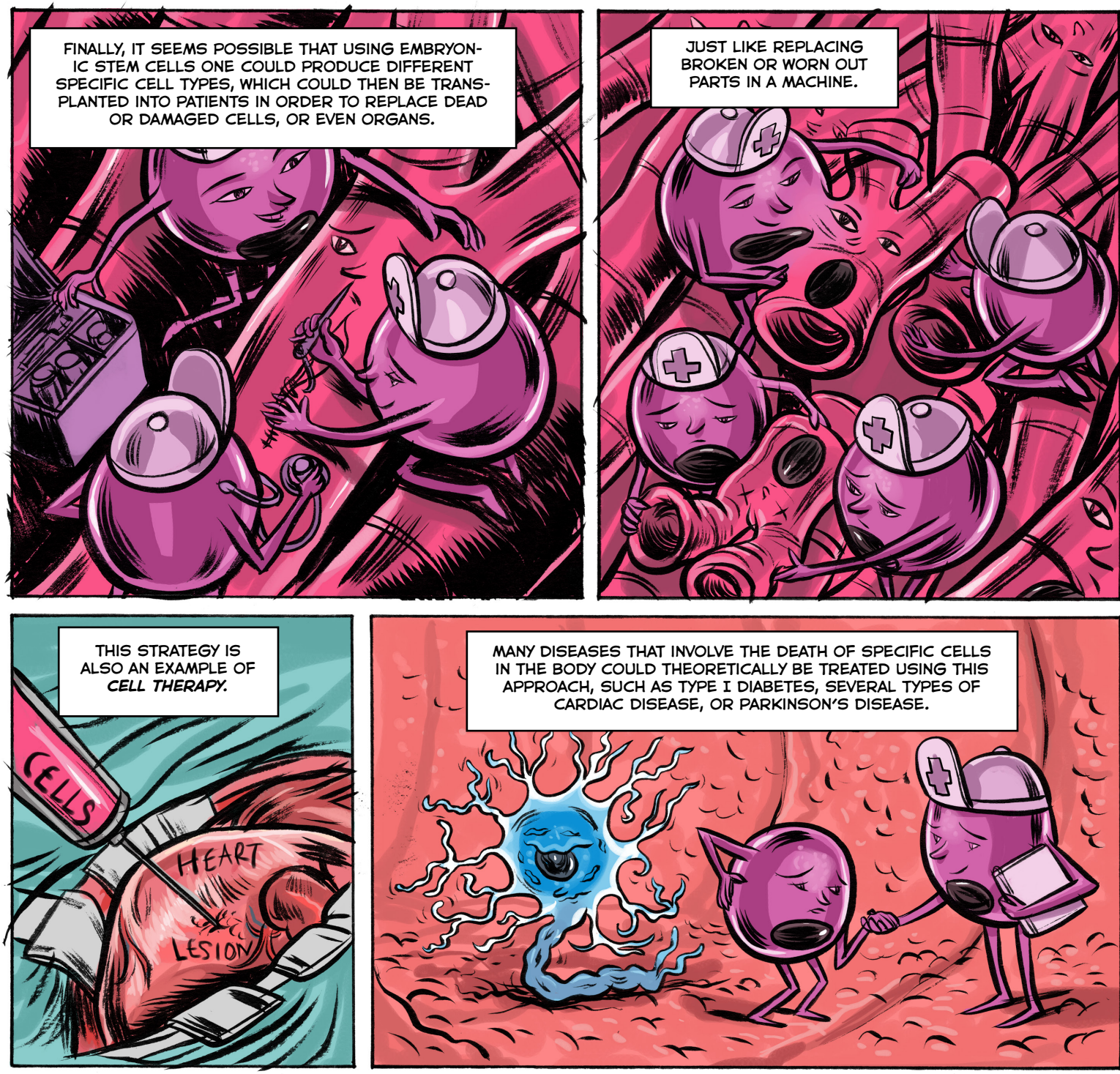


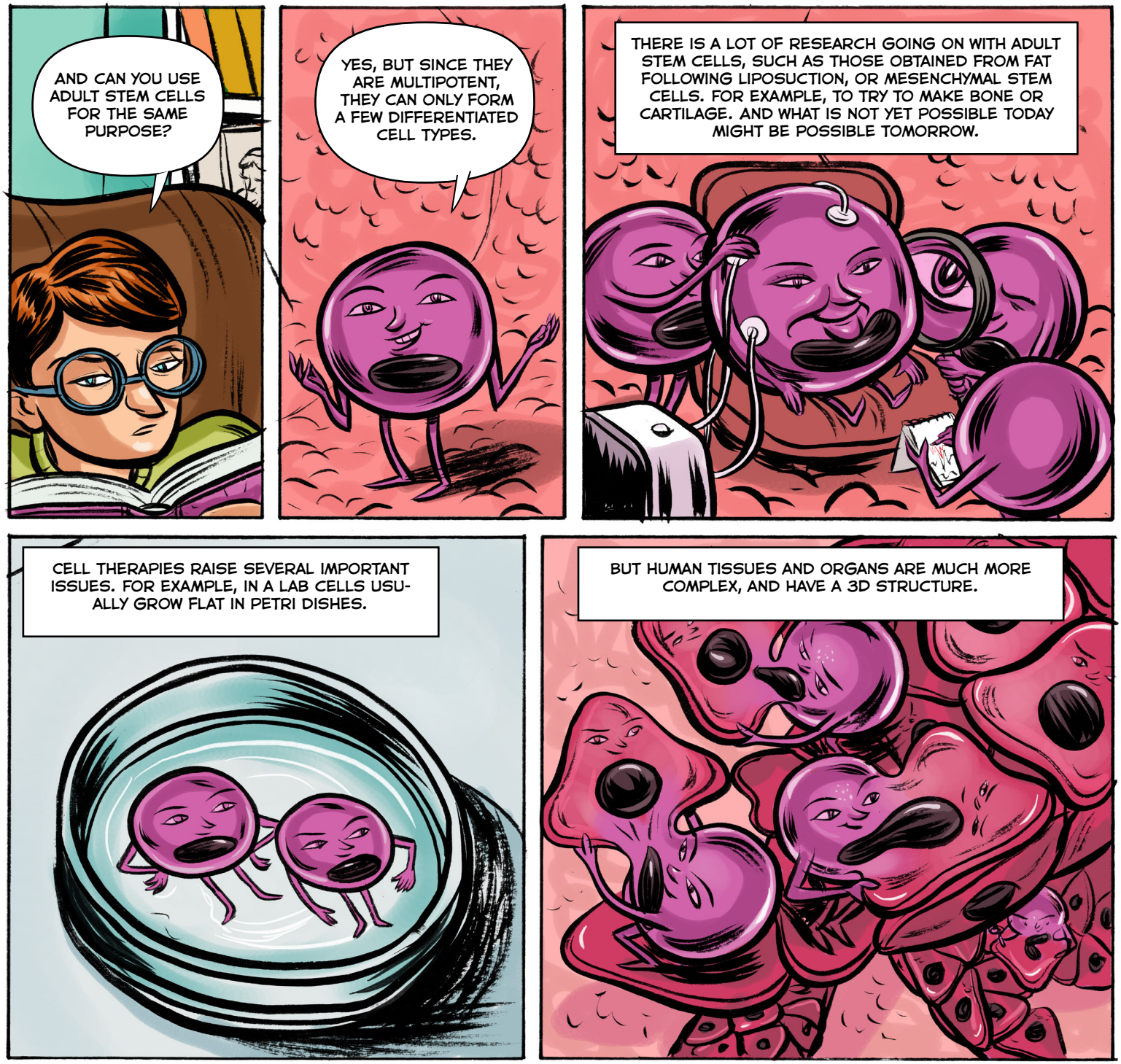

EMBRYONIC STEM CELLS ARE A GREAT MODEL TO STUDY DIFFERENT ASPECTS OF CELL, MOLECULAR AND DEVELOPMENTAL BIOLOGY. AS THEY DIVIDE INDEFINITELY ONE CAN GET MILLIONS OF CELLS IN CULTURE. SINCE THEY ARE PLURIPOTENT, THEY CAN MAKE ANY TYPE OF CELL, EVEN THOUGH THEY ARE OUTSIDE THE BODY. ALL THEY NEED IS THE RIGHT SETS OF INSTRUCTIONS.
Embryonic Stem Cells!

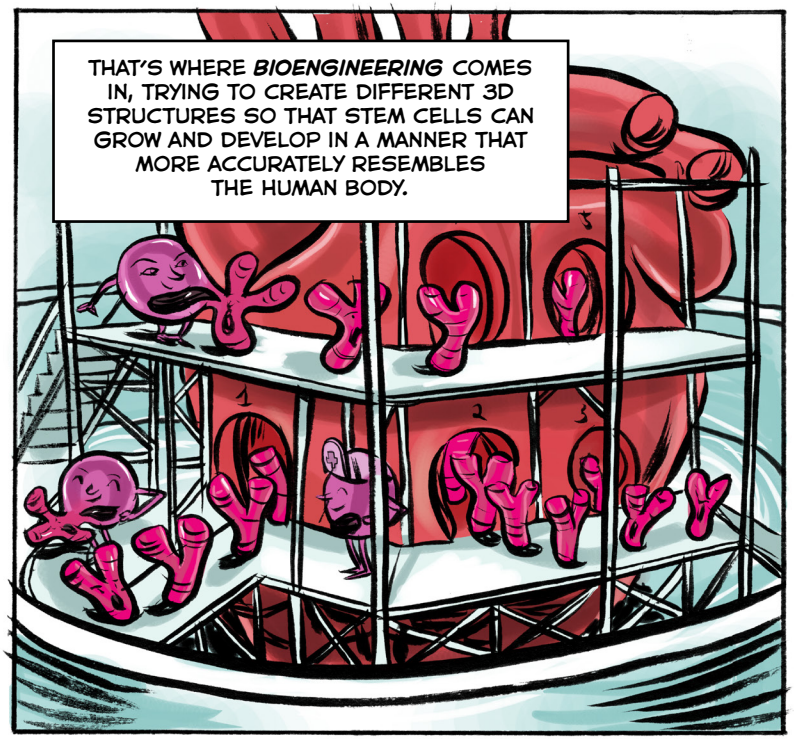

WHAT ARE THOSE INSTRUCTIONS? BASICALLY THEY INVOLVE GIVING THE CELLS DIFFERENT MOLECULES, TRYING TO RECAPITULATE OUTSIDE THE BODY WHAT USUALLY TAKES PLACE INSIDE.


MAMMALIAN DEVELOPMENT TAKES PLACE IN A HARD TO REACH PLACE: THE UTERUS. USING EMBRYONIC STEM CELLS SOME ASPECTS OF DEVELOPMENT CAN BE STUDIED IN A LABORATORY.

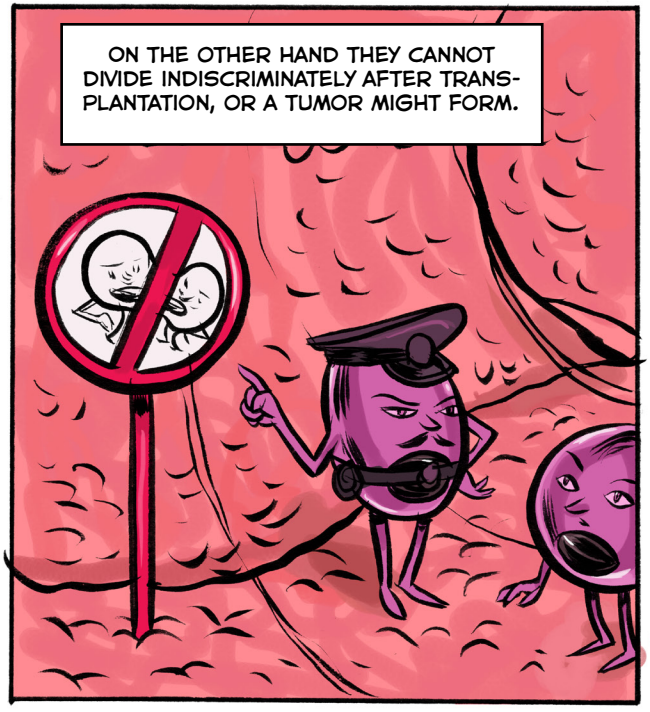

EMBRYONIC STEM CELLS ARE ALSO BEING USED TO TEST DIFFERENT SUBSTANCES, OR TO STUDY DISEASES, THUS REDUCING THE USE OF LAB ANIMALS FOR THESE PURPOSES.
GO STEM CELLS!!!

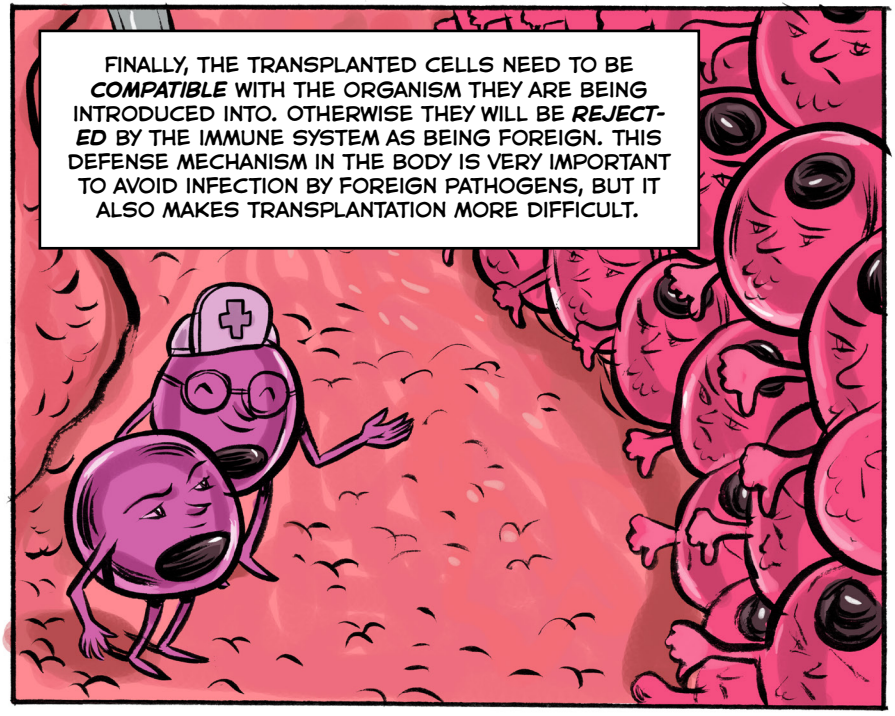

FINALLY, IT SEEMS POSSIBLE THAT USING EMBRYONIC STEM CELLS ONE COULD PRODUCE DIFFERENT SPECIFIC CELL TYPES, WHICH COULD THEN BE TRANSPLANTED INTO PATIENTS IN ORDER TO REPLACE DEAD OR DAMAGED CELLS, OR EVEN ORGANS.
JUST LIKE REPLACING BROKEN OR WORN OUT PARTS IN A MACHINE.
THIS STRATEGY IS ALSO AN EXAMPLE OF *CELL THERAPY.*
CELLS
HEART
LESION
MANY DISEASES THAT INVOLVE THE DEATH OF SPECIFIC CELLS IN THE BODY COULD THEORETICALLY BE TREATED USING THIS APPROACH, SUCH AS TYPE I DIABETES, SEVERAL TYPES OF CARDIAC DISEASE, OR PARKINSON'S DISEASE.

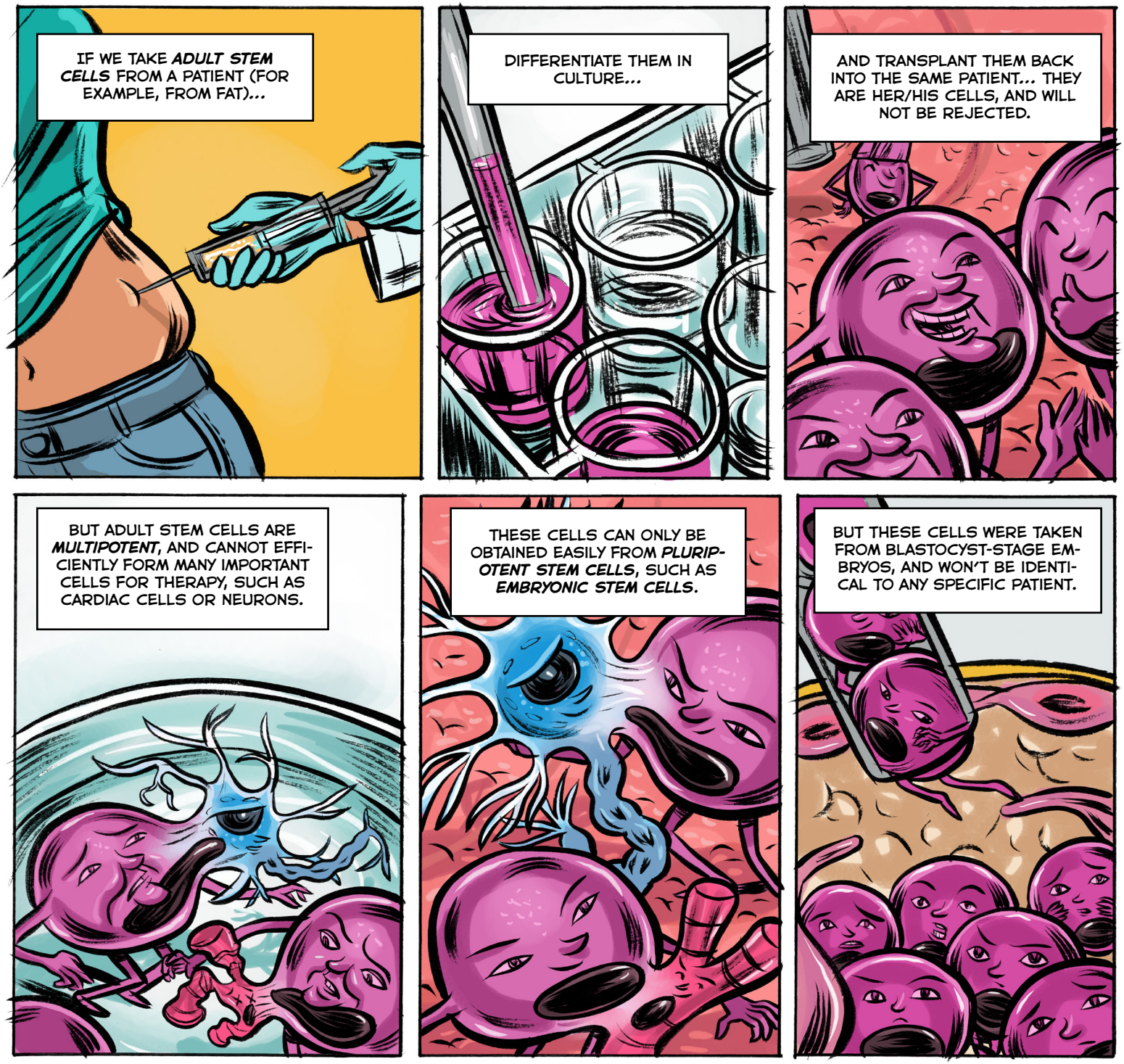

AND CAN YOU USE ADULT STEM CELLS FOR THE SAME PURPOSE?
YES, BUT SINCE THEY ARE MULTIPOTENT, THEY CAN ONLY FORM A FEW DIFFERENTIATED CELL TYPES.
THERE IS A LOT OF RESEARCH GOING ON WITH ADULT STEM CELLS, SUCH AS THOSE OBTAINED FROM FAT FOLLOWING LIPOSUCTION, OR MESENCHYMAL STEM CELLS. FOR EXAMPLE, TO TRY TO MAKE BONE OR CARTILAGE. AND WHAT IS NOT YET POSSIBLE TODAY MIGHT BE POSSIBLE TOMORROW.
CELL THERAPIES RAISE SEVERAL IMPORTANT ISSUES. FOR EXAMPLE, IN A LAB CELLS USUALLY GROW FLAT IN PETRI DISHES.
BUT HUMAN TISSUES AND ORGANS ARE MUCH MORE COMPLEX, AND HAVE A 3D STRUCTURE.

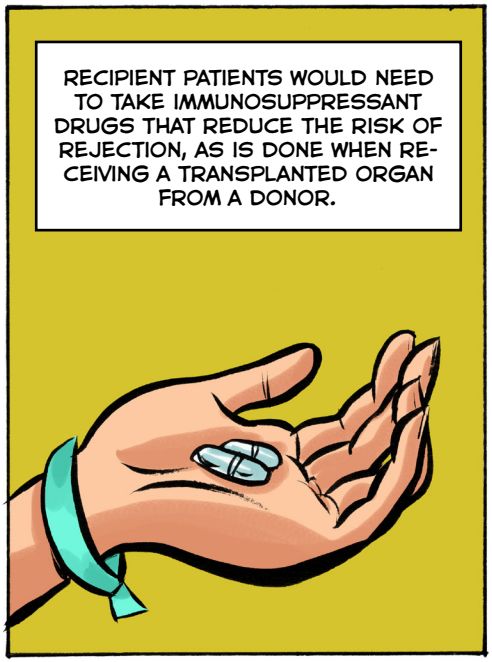

THAT'S WHERE ***BIOENGINEERING*** COMES IN, TRYING TO CREATE DIFFERENT 3D STRUCTURES SO THAT STEM CELLS CAN GROW AND DEVELOP IN A MANNER THAT MORE ACCURATELY RESEMBLES THE HUMAN BODY.


OF COURSE IT'S NOT ENOUGH TO JUST MAKE A SPECIFIC CELL TYPE FROM A STEM CELL. THE CELLS THAT ARE GOING TO BE TRANSPLANTED MUST FIT IN PERFECTLY WITH OTHER CELLS IN THE BODY, AND WORK WITH THEM AS A WHOLE.

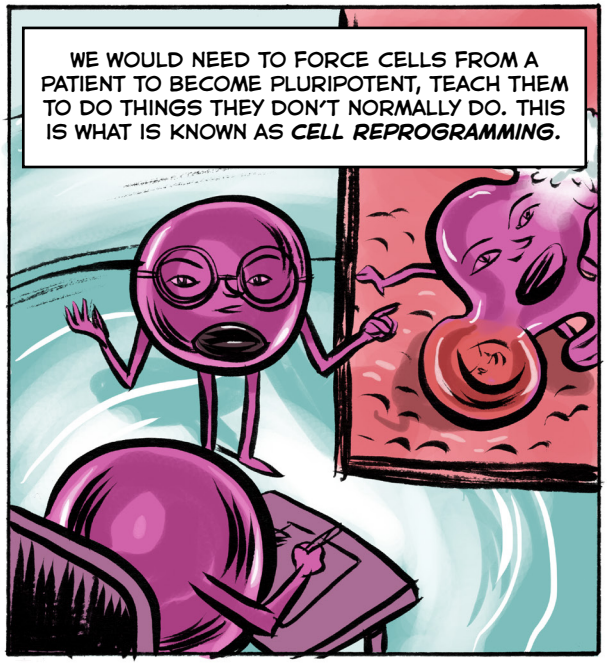

ON THE OTHER HAND THEY CANNOT DIVIDE INDISCRIMINATELY AFTER TRANSPLANTATION, OR A TUMOR MIGHT FORM.

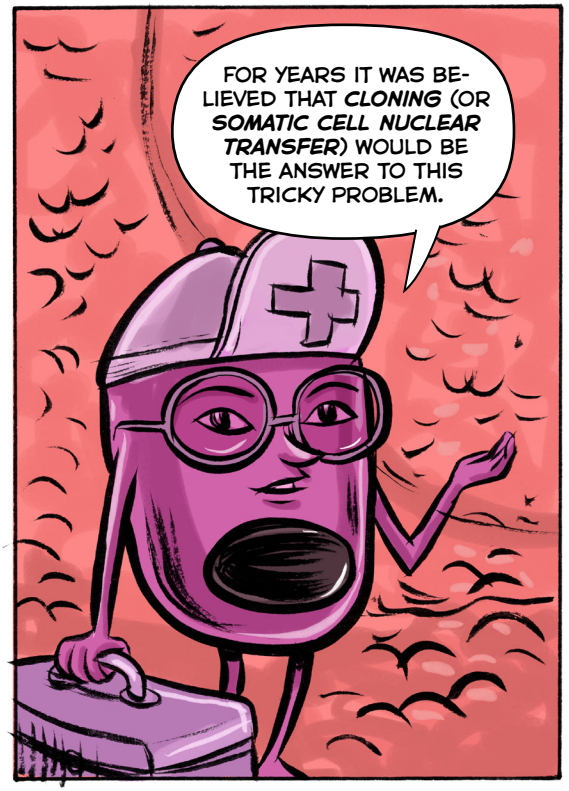

FINALLY, THE TRANSPLANTED CELLS NEED TO BE ***COMPATIBLE*** WITH THE ORGANISM THEY ARE BEING INTRODUCED INTO. OTHERWISE THEY WILL BE ***REJECTED*** BY THE IMMUNE SYSTEM AS BEING FOREIGN. THIS DEFENSE MECHANISM IN THE BODY IS VERY IMPORTANT TO AVOID INFECTION BY FOREIGN PATHOGENS, BUT IT ALSO MAKES TRANSPLANTATION MORE DIFFICULT.

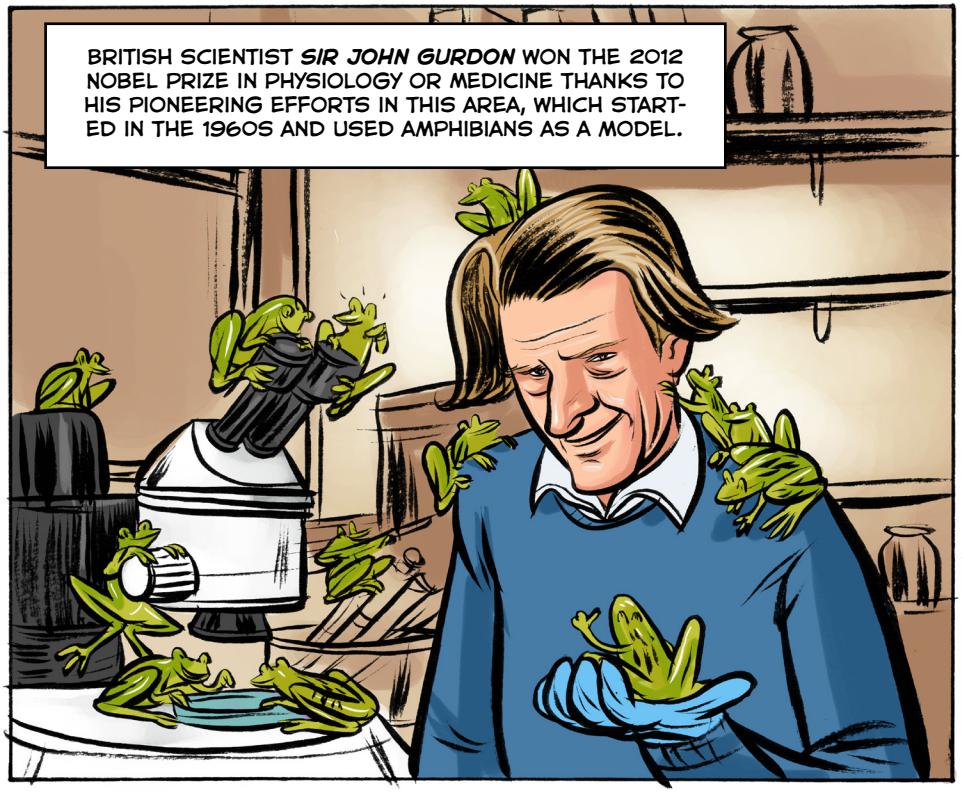

IF WE TAKE ADULT STEM CELLS FROM A PATIENT (FOR EXAMPLE, FROM FAT)...
DIFFERENTIATE THEM IN CULTURE...
AND TRANSPLANT THEM BACK INTO THE SAME PATIENT... THEY ARE HER/HIS CELLS, AND WILL NOT BE REJECTED.
BUT ADULT STEM CELLS ARE MULTIPOTENT, AND CANNOT EFFICIENTLY FORM MANY IMPORTANT CELLS FOR THERAPY, SUCH AS CARDIAC CELLS OR NEURONS.
THESE CELLS CAN ONLY BE OBTAINED EASILY FROM PLURIPOTENT STEM CELLS, SUCH AS EMBRYONIC STEM CELLS.
BUT THESE CELLS WERE TAKEN FROM BLASTOCYST-STAGE EMBRYOS, AND WON'T BE IDENTICAL TO ANY SPECIFIC PATIENT.

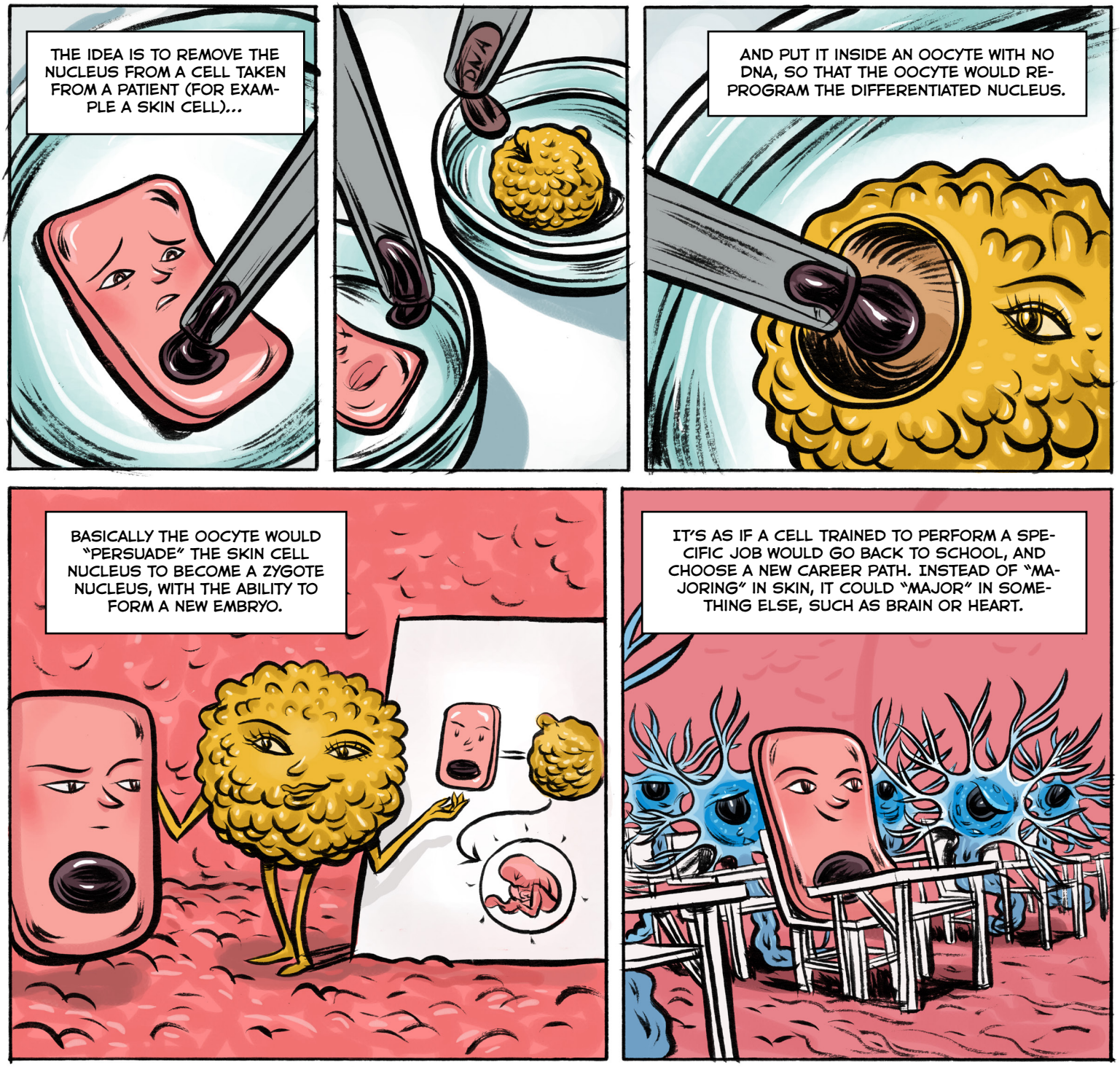

RECIPIENT PATIENTS WOULD NEED TO TAKE IMMUNOSUPPRESSANT DRUGS THAT REDUCE THE RISK OF REJECTION, AS IS DONE WHEN RECEIVING A TRANSPLANTED ORGAN FROM A DONOR.

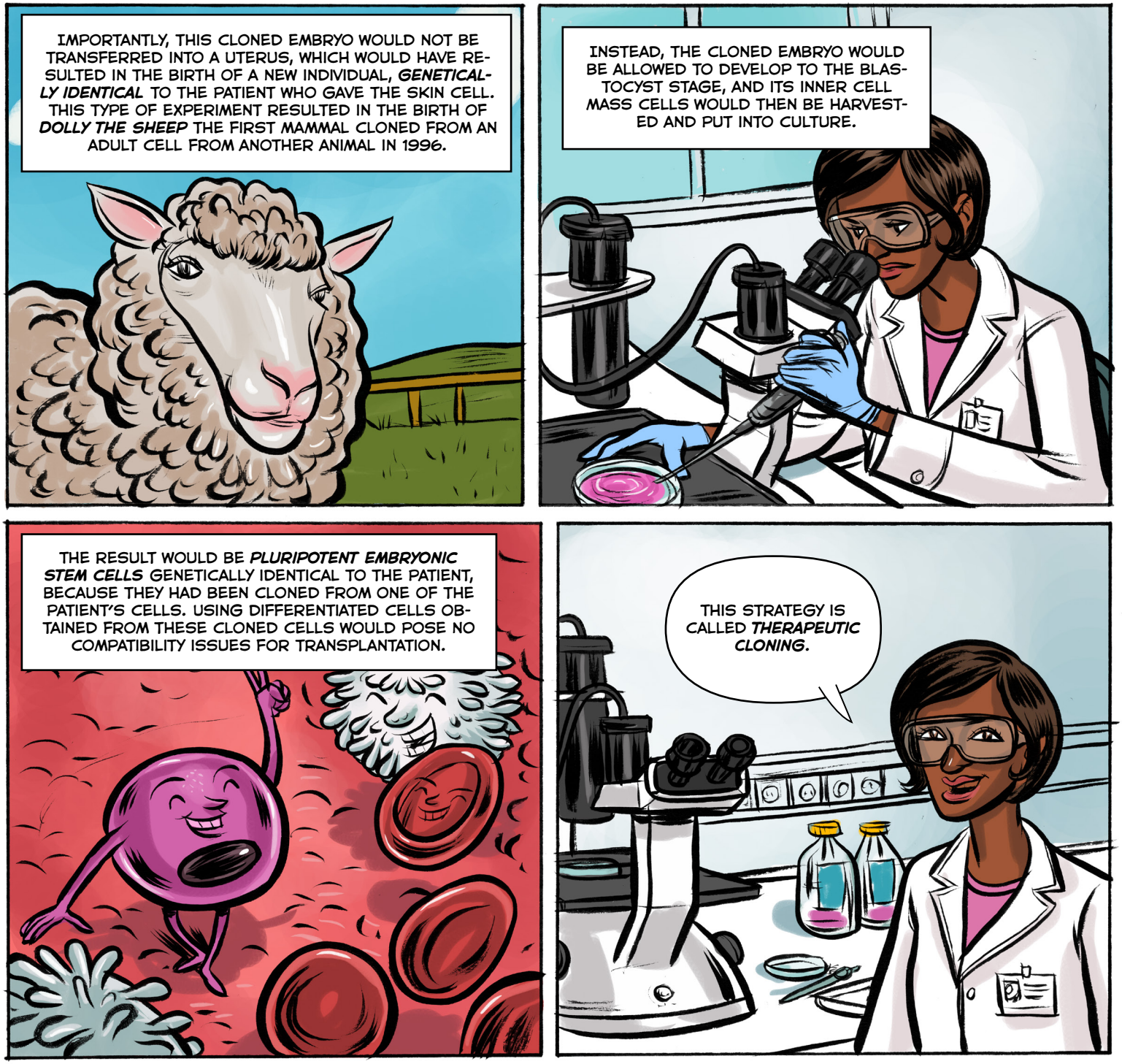

SO HOW CAN WE MAKE PLURIPOTENT STEM CELLS THAT ARE FULLY COMPATIBLE WITH ONE SPECIFIC PATIENT?

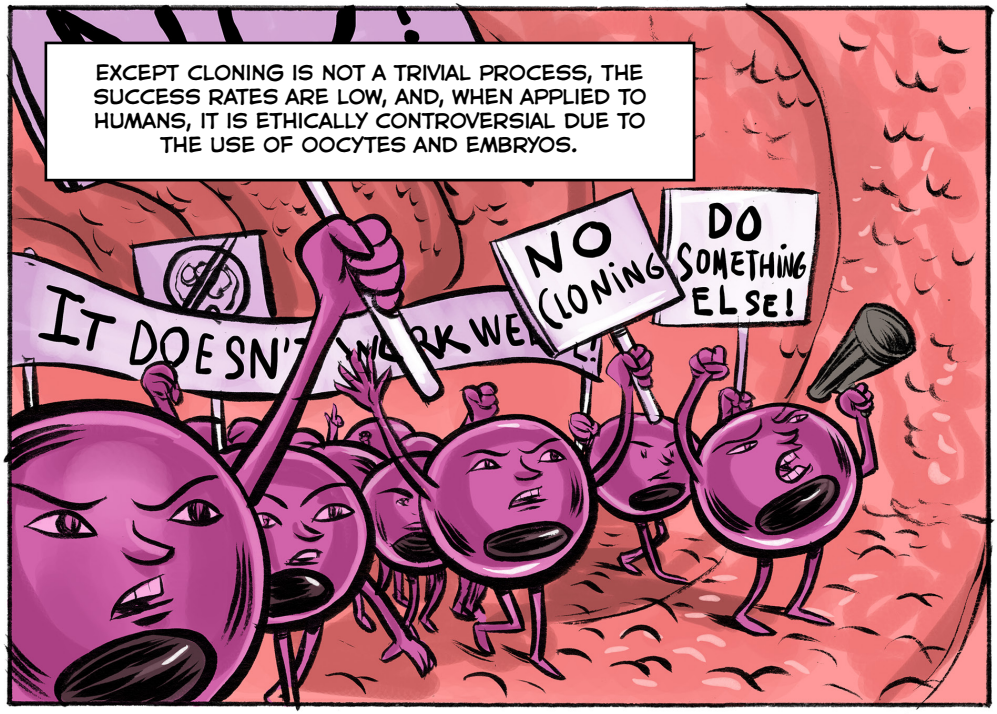

WE WOULD NEED TO FORCE CELLS FROM A PATIENT TO BECOME PLURIPOTENT, TEACH THEM TO DO THINGS THEY DON'T NORMALLY DO. THIS IS WHAT IS KNOWN AS ***CELL REPROGRAMMING.***


FOR YEARS IT WAS BELIEVED THAT ***CLONING*** (OR ***SOMATIC CELL NUCLEAR TRANSFER***) WOULD BE THE ANSWER TO THIS TRICKY PROBLEM.


BRITISH SCIENTIST ***SIR JOHN GURDON*** WON THE 2012 NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE THANKS TO HIS PIONEERING EFFORTS IN THIS AREA, WHICH STARTED IN THE 1960S AND USED AMPHIBIANS AS A MODEL.

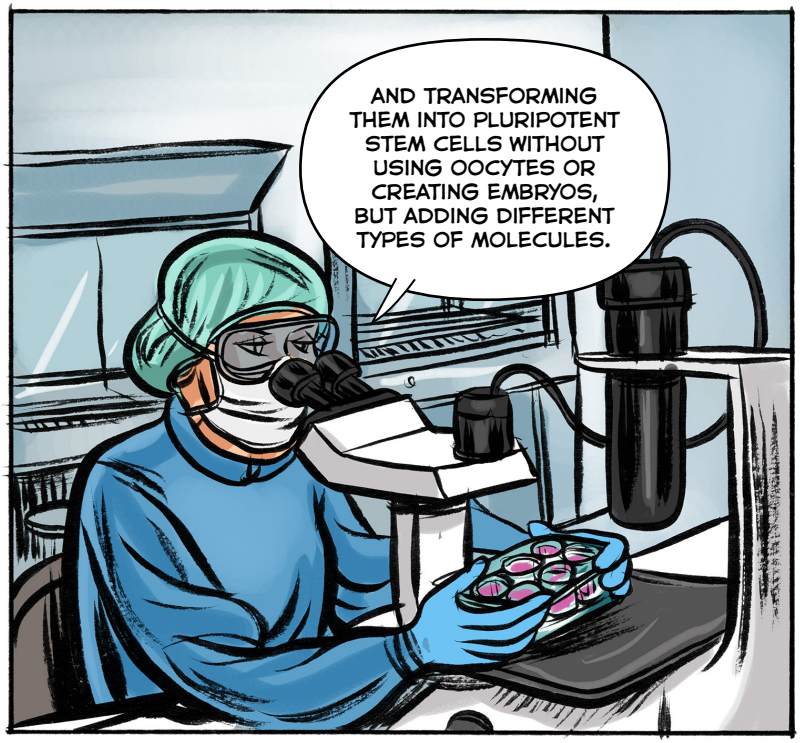

THE IDEA IS TO REMOVE THE NUCLEUS FROM A CELL TAKEN FROM A PATIENT (FOR EXAMPLE A SKIN CELL)...
DNA
AND PUT IT INSIDE AN OOCYTE WITH NO DNA, SO THAT THE OOCYTE WOULD REPROGRAM THE DIFFERENTIATED NUCLEUS.
BASICALLY THE OOCYTE WOULD "PERSUADE" THE SKIN CELL NUCLEUS TO BECOME A ZYGOTE NUCLEUS, WITH THE ABILITY TO FORM A NEW EMBRYO.
IT'S AS IF A CELL TRAINED TO PERFORM A SPECIFIC JOB WOULD GO BACK TO SCHOOL, AND CHOOSE A NEW CAREER PATH. INSTEAD OF "MAJORING" IN SKIN, IT COULD "MAJOR" IN SOMETHING ELSE, SUCH AS BRAIN OR HEART.

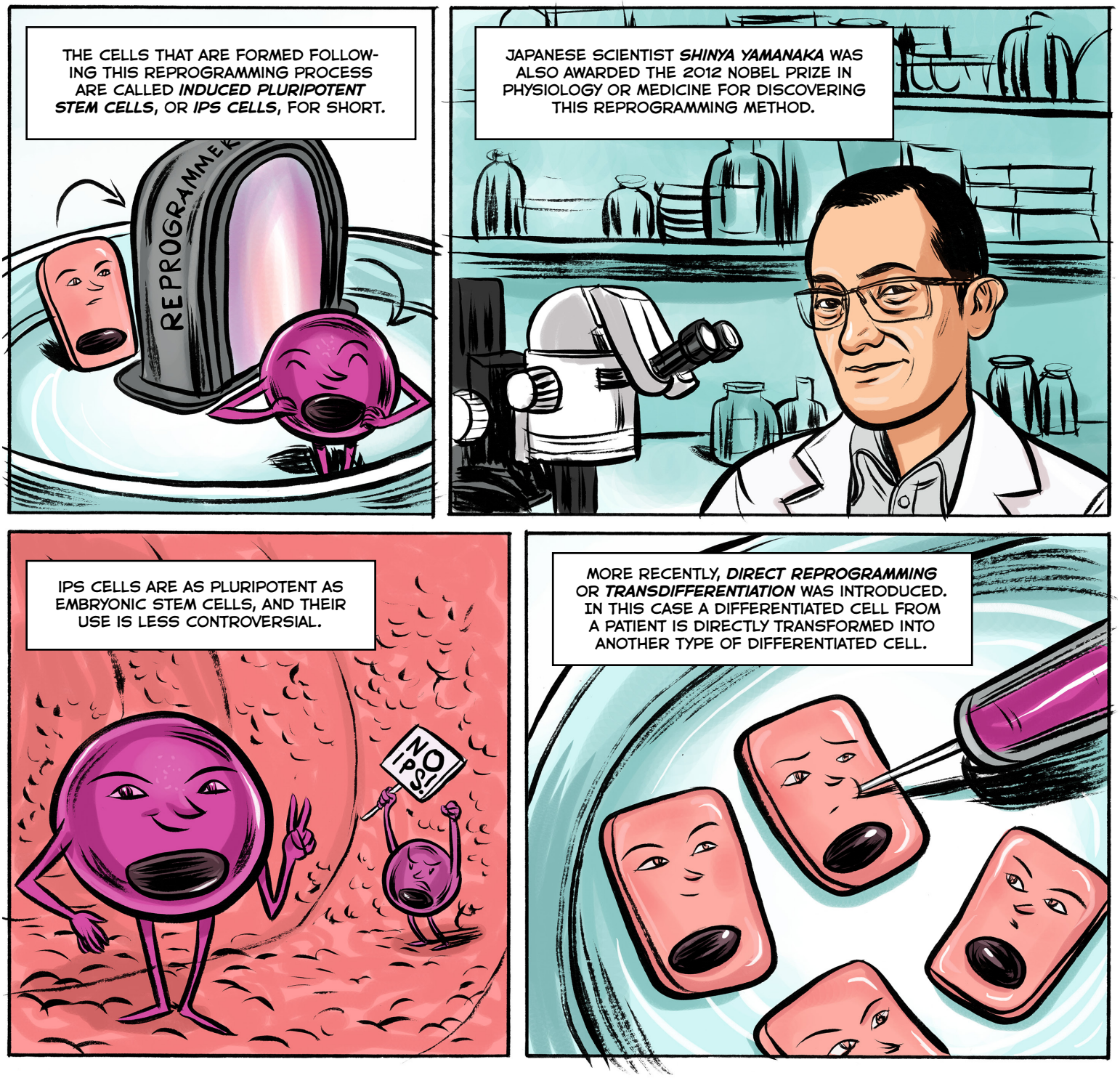

IMPORTANTLY, THIS CLONED EMBRYO WOULD NOT BE TRANSFERRED INTO A UTERUS, WHICH WOULD HAVE RESULTED IN THE BIRTH OF A NEW INDIVIDUAL, GENETICALLY IDENTICAL TO THE PATIENT WHO GAVE THE SKIN CELL. THIS TYPE OF EXPERIMENT RESULTED IN THE BIRTH OF DOLLY THE SHEEP THE FIRST MAMMAL CLONED FROM AN ADULT CELL FROM ANOTHER ANIMAL IN 1996.
INSTEAD, THE CLONED EMBRYO WOULD BE ALLOWED TO DEVELOP TO THE BLASTOCYST STAGE, AND ITS INNER CELL MASS CELLS WOULD THEN BE HARVESTED AND PUT INTO CULTURE.
THE RESULT WOULD BE PLURIPOTENT EMBRYONIC STEM CELLS GENETICALLY IDENTICAL TO THE PATIENT, BECAUSE THEY HAD BEEN CLONED FROM ONE OF THE PATIENT'S CELLS. USING DIFFERENTIATED CELLS OBTAINED FROM THESE CLONED CELLS WOULD POSE NO COMPATIBILITY ISSUES FOR TRANSPLANTATION.
THIS STRATEGY IS CALLED THERAPEUTIC CLONING.

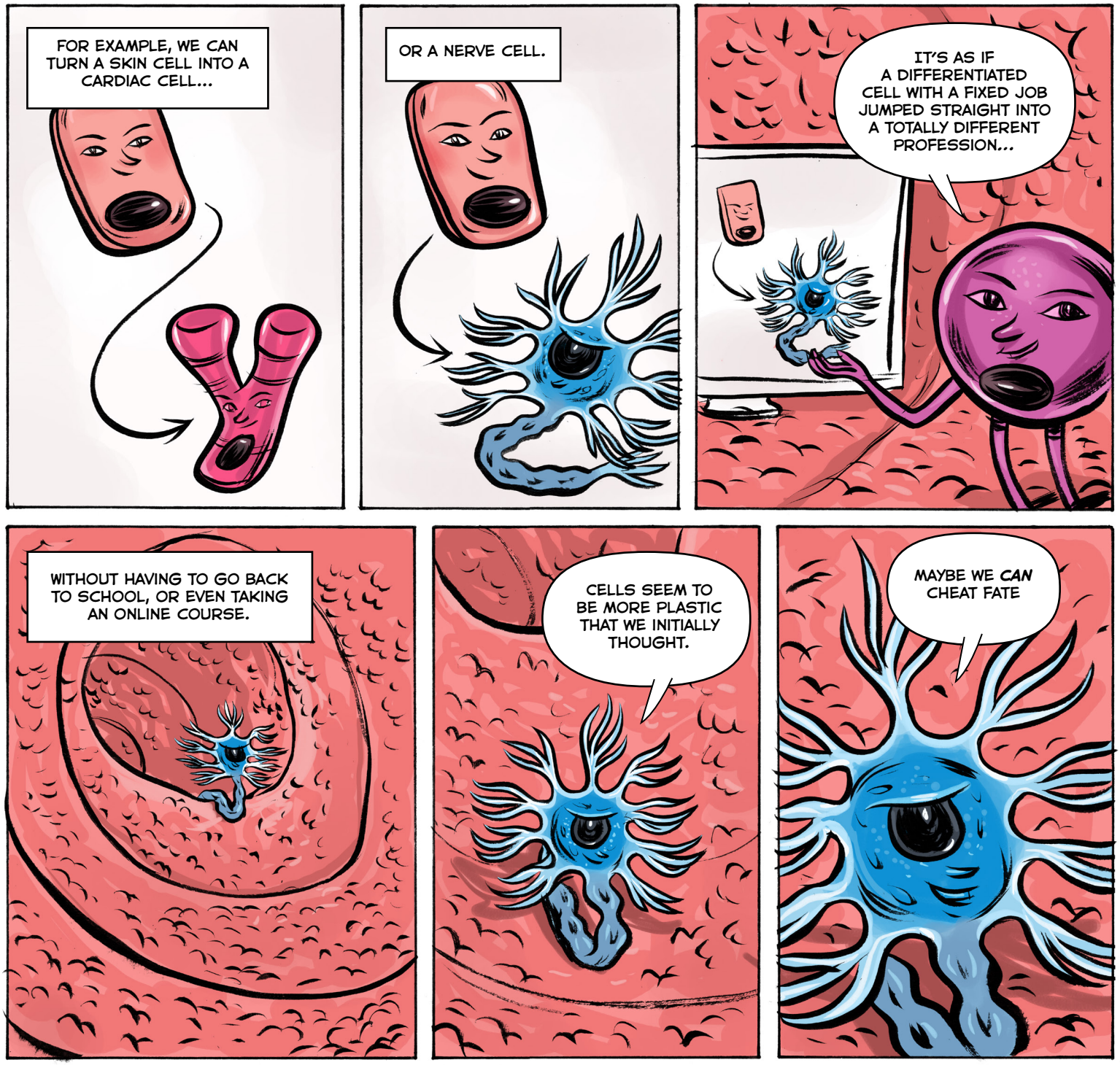

EXCEPT CLONING IS NOT A TRIVIAL PROCESS, THE SUCCESS RATES ARE LOW, AND, WHEN APPLIED TO HUMANS, IT IS ETHICALLY CONTROVERSIAL DUE TO THE USE OF OOCYTES AND EMBRYOS.
NO CLONING
DO SOMETHING ELSE!

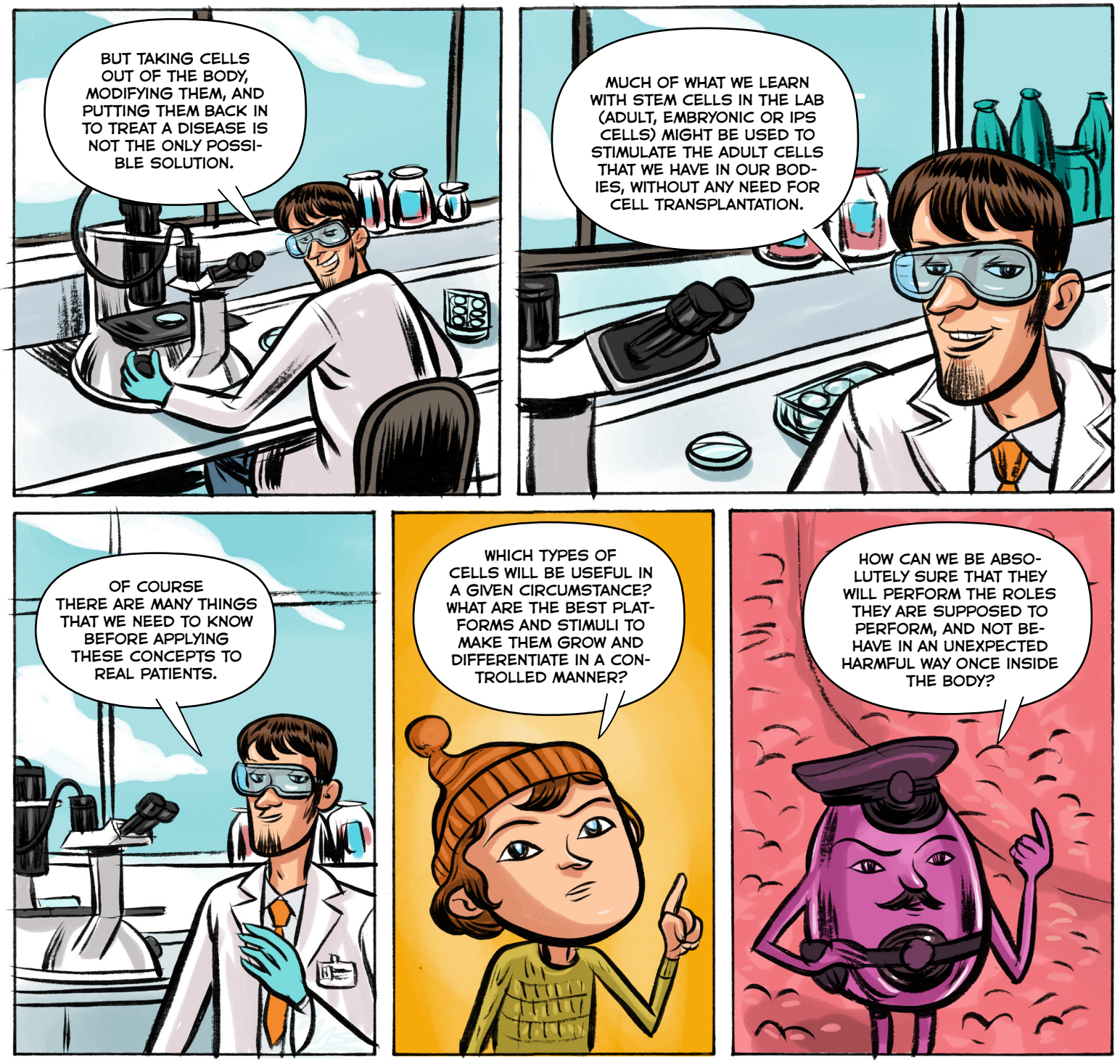

IN THE 21ST CENTURY A NEW STRATEGY FOR CELL REPROGRAMMING WAS CREATED.


IT IMPLIED TAKING CELLS FROM A PATIENT (BLOOD OR SKIN CELLS, FOR EXAMPLE)...


AND TRANSFORMING THEM INTO PLURIPOTENT STEM CELLS WITHOUT USING OOCYTES OR CREATING EMBRYOS, BUT ADDING DIFFERENT TYPES OF MOLECULES.

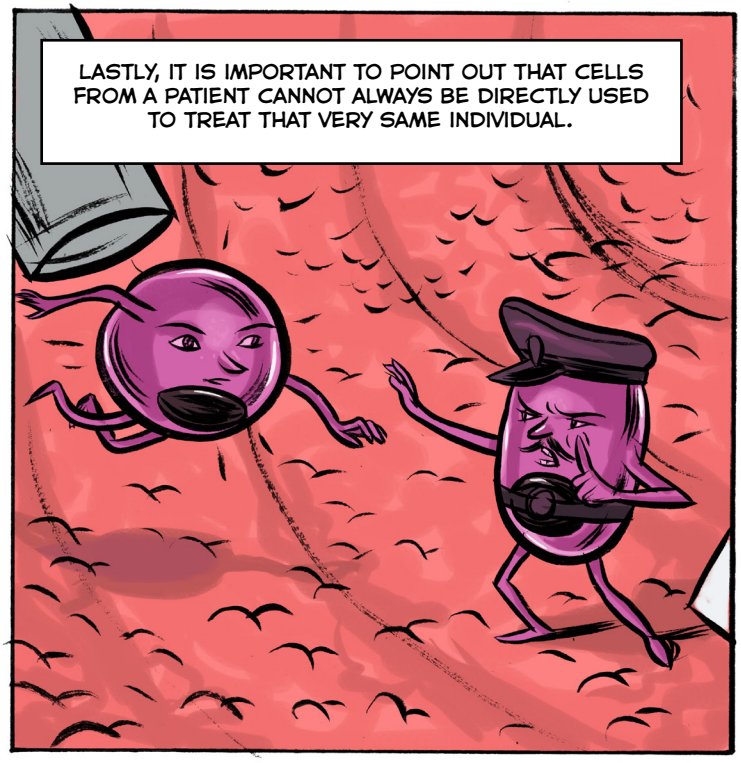

THE CELLS THAT ARE FORMED FOLLOWING THIS REPROGRAMMING PROCESS ARE CALLED *INDUCED PLURIPOTENT STEM CELLS*, OR *IPS CELLS*, FOR SHORT.
REPROGRAMMER
JAPANESE SCIENTIST *SHINYA YAMANAKA* WAS ALSO AWARDED THE 2012 NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE FOR DISCOVERING THIS REPROGRAMMING METHOD.
IPS CELLS ARE AS PLURIPOTENT AS EMBRYONIC STEM CELLS, AND THEIR USE IS LESS CONTROVERSIAL.
NO iPS!
MORE RECENTLY, *DIRECT REPROGRAMMING* OR *TRANSDIFFERENTIATION* WAS INTRODUCED. IN THIS CASE A DIFFERENTIATED CELL FROM A PATIENT IS DIRECTLY TRANSFORMED INTO ANOTHER TYPE OF DIFFERENTIATED CELL.

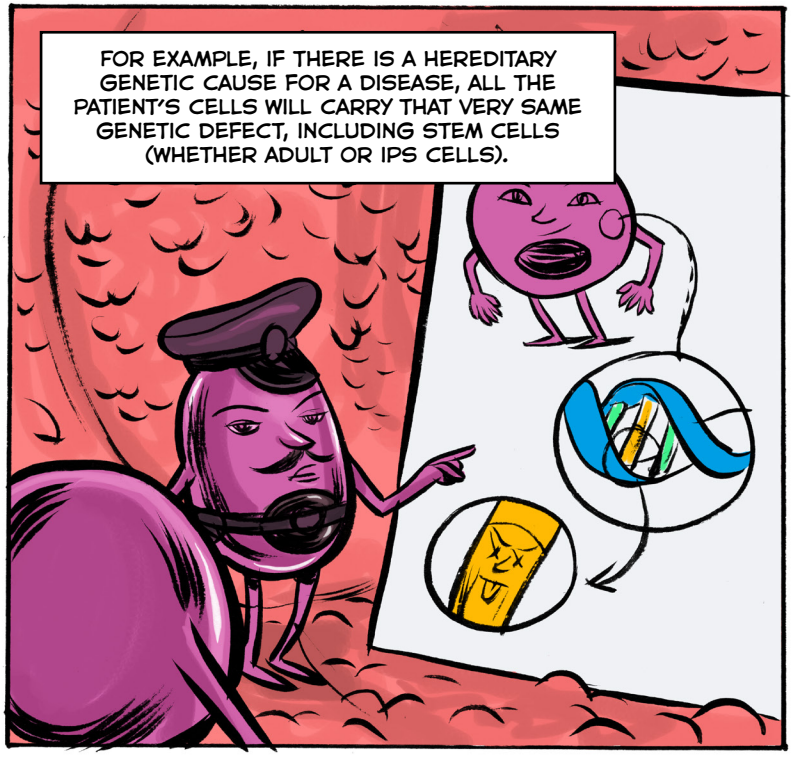

FOR EXAMPLE, WE CAN TURN A SKIN CELL INTO A CARDIAC CELL...
OR A NERVE CELL.
IT'S AS IF A DIFFERENTIATED CELL WITH A FIXED JOB JUMPED STRAIGHT INTO A TOTALLY DIFFERENT PROFESSION...
WITHOUT HAVING TO GO BACK TO SCHOOL, OR EVEN TAKING AN ONLINE COURSE.
CELLS SEEM TO BE MORE PLASTIC THAT WE INITIALLY THOUGHT.
MAYBE WE *CAN* CHEAT FATE

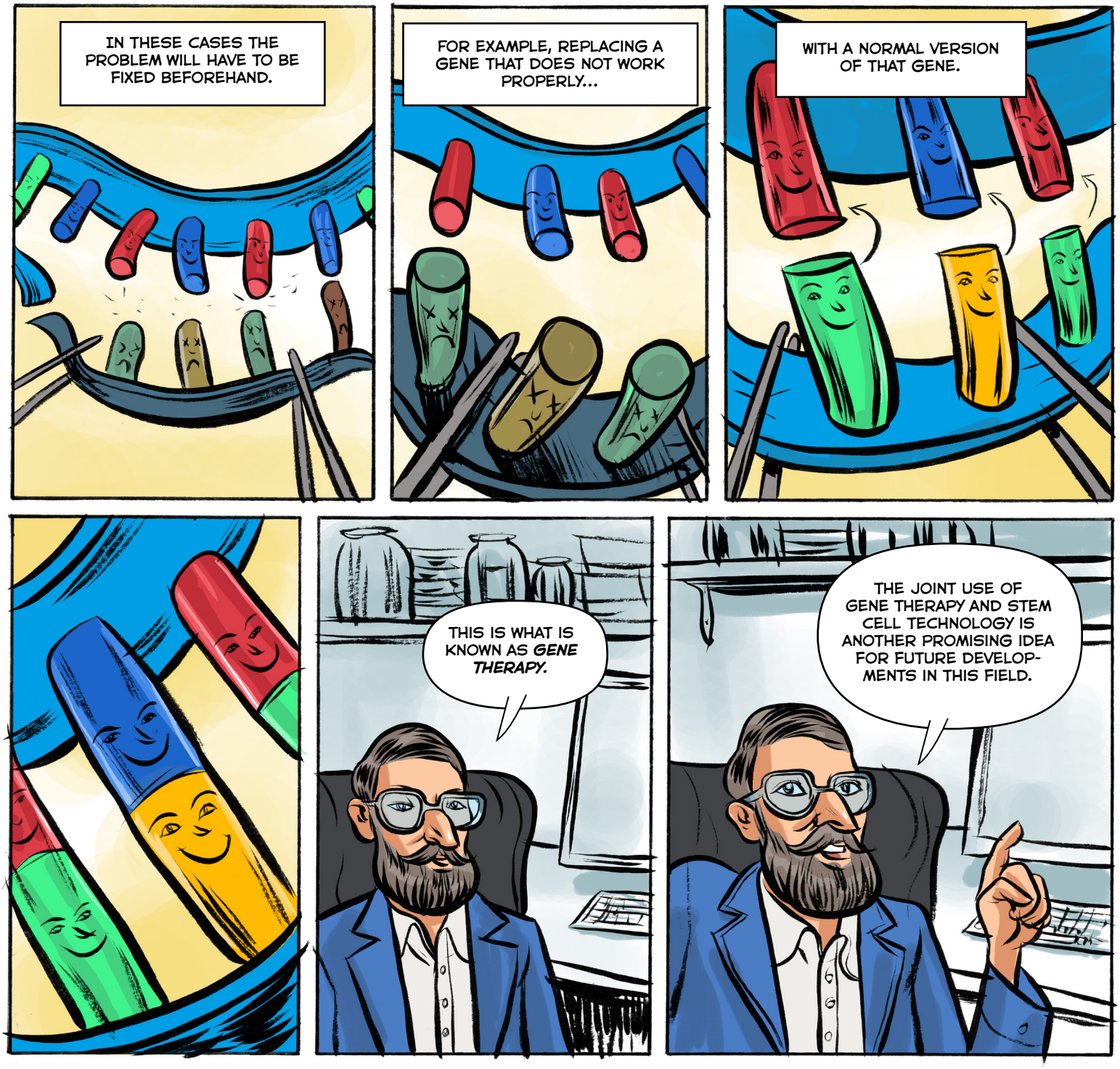

BUT TAKING CELLS OUT OF THE BODY, MODIFYING THEM, AND PUTTING THEM BACK IN TO TREAT A DISEASE IS NOT THE ONLY POSSIBLE SOLUTION.
MUCH OF WHAT WE LEARN WITH STEM CELLS IN THE LAB (ADULT, EMBRYONIC OR IPS CELLS) MIGHT BE USED TO STIMULATE THE ADULT CELLS THAT WE HAVE IN OUR BODIES, WITHOUT ANY NEED FOR CELL TRANSPLANTATION.
OF COURSE THERE ARE MANY THINGS THAT WE NEED TO KNOW BEFORE APPLYING THESE CONCEPTS TO REAL PATIENTS.
WHICH TYPES OF CELLS WILL BE USEFUL IN A GIVEN CIRCUMSTANCE? WHAT ARE THE BEST PLATFORMS AND STIMULI TO MAKE THEM GROW AND DIFFERENTIATE IN A CONTROLLED MANNER?
HOW CAN WE BE ABSOLUTELY SURE THAT THEY WILL PERFORM THE ROLES THEY ARE SUPPOSED TO PERFORM, AND NOT BEHAVE IN AN UNEXPECTED HARMFUL WAY ONCE INSIDE THE BODY?

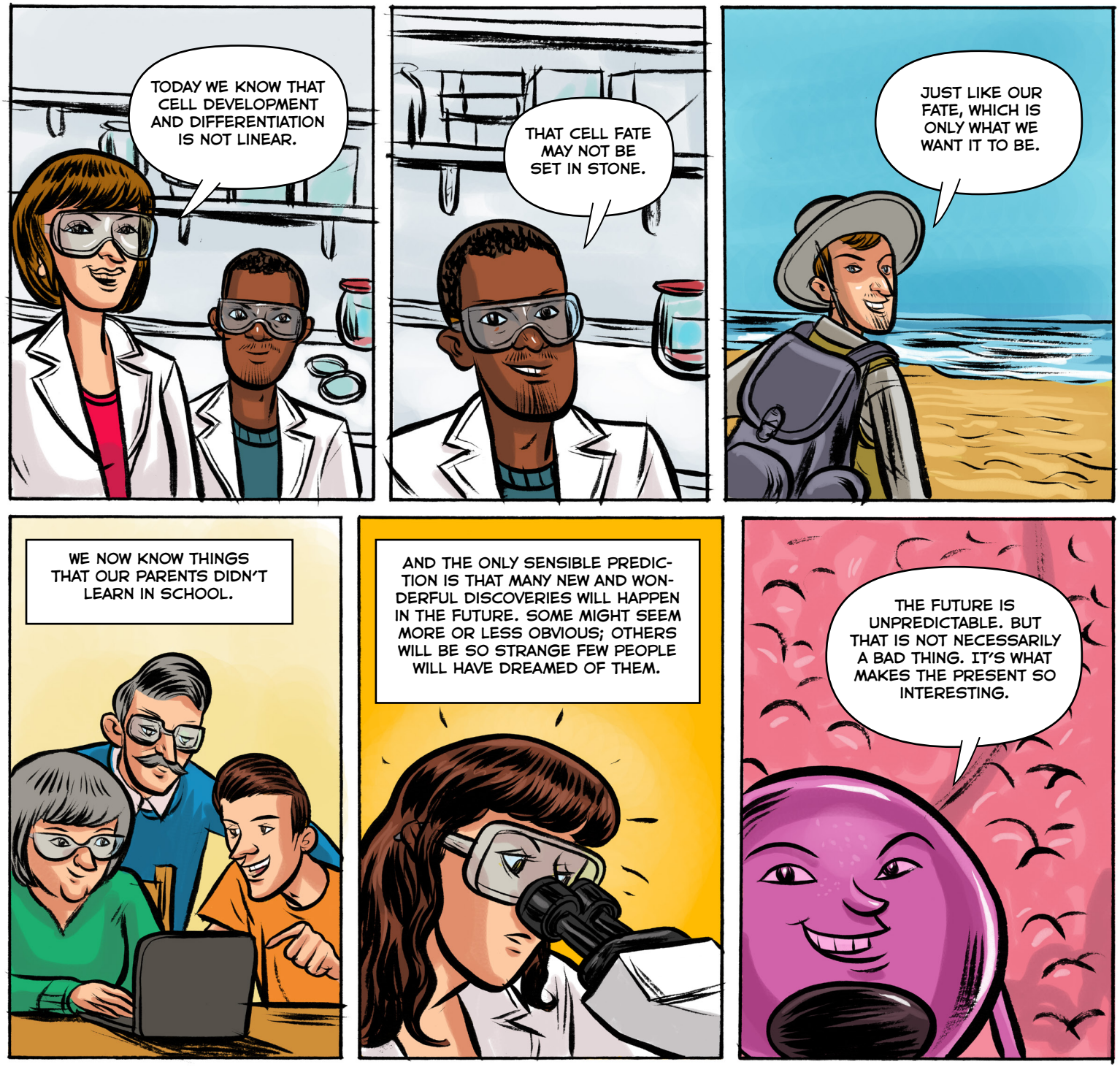

A POSITIVE RESULT OBTAINED WITH CELLS IN A LAB, OR EVEN WITH MODEL TEST ANIMALS, DOES NOT MEAN THAT WE CAN QUICKLY PERFORM THE SAME PROCEDURES IN HUMAN BEINGS.


TO ENSURE SAFETY AND THE BEST POSSIBILITY OF SUCCESS IN HUMANS MANY PRELIMINARY TESTS MUST BE CARRIED OUT.


LASTLY, IT IS IMPORTANT TO POINT OUT THAT CELLS FROM A PATIENT CANNOT ALWAYS BE DIRECTLY USED TO TREAT THAT VERY SAME INDIVIDUAL.


FOR EXAMPLE, IF THERE IS A HEREDITARY GENETIC CAUSE FOR A DISEASE, ALL THE PATIENT'S CELLS WILL CARRY THAT VERY SAME GENETIC DEFECT, INCLUDING STEM CELLS (WHETHER ADULT OR IPS CELLS).


IN THESE CASES THE PROBLEM WILL HAVE TO BE FIXED BEFOREHAND.
FOR EXAMPLE, REPLACING A GENE THAT DOES NOT WORK PROPERLY...
WITH A NORMAL VERSION OF THAT GENE.
THIS IS WHAT IS KNOWN AS *GENE THERAPY.*
THE JOINT USE OF GENE THERAPY AND STEM CELL TECHNOLOGY IS ANOTHER PROMISING IDEA FOR FUTURE DEVELOPMENTS IN THIS FIELD.


TODAY WE KNOW THAT CELL DEVELOPMENT AND DIFFERENTIATION IS NOT LINEAR.
THAT CELL FATE MAY NOT BE SET IN STONE.
JUST LIKE OUR FATE, WHICH IS ONLY WHAT WE WANT IT TO BE.
WE NOW KNOW THINGS THAT OUR PARENTS DIDN'T LEARN IN SCHOOL.
AND THE ONLY SENSIBLE PREDICTION IS THAT MANY NEW AND WONDERFUL DISCOVERIES WILL HAPPEN IN THE FUTURE. SOME MIGHT SEEM MORE OR LESS OBVIOUS; OTHERS WILL BE SO STRANGE FEW PEOPLE WILL HAVE DREAMED OF THEM.
THE FUTURE IS UNPREDICTABLE. BUT THAT IS NOT NECESSARILY A BAD THING. IT'S WHAT MAKES THE PRESENT SO INTERESTING.

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Is **Principal Investigator** and **President of the Center for Neuroscience and Cell Biology**, and Associate Professor at the Department of Life Sciences, University of Coimbra, Portugal. He has been a visiting researcher at the Oregon Health & Sciences University, University of Pittsburgh, and the University of California San Francisco. He carries out research in reproductive and stem cell biology, has over 100 publications, and serves as an editor for the journals Human Reproduction and Reproduction. His interest in fiction has led to the publication of a novel (Portland, Portugal; 2007), stories about science in the site LabLit.com, and several contributions to the Nature Futures science fiction section of the journal Nature. One of his stories was selected for the Nature Futures 2 Anthology (2014). He is a part owner of the Comic Book Store **Dr Kartoon** in Coimbra, and previously co-authored three comic books, and three books about comics.

André Caetano
Is an independent **illustrator** and **Graphic designer**. In 2001 attended the Escola Universitária de Artes de Coimbra, studying Communication Design, graduating in 2006. Working since September 2008, has illustrated and designed for clients like Porto Editora, Edições Asa, Grupo de Teatro O Celeiro, and many more. The picture book Sem Palavras, written by Eugénio Roda and published by Porto Editora was selected to be one "100 books for the future", an exhibition in Bologna Children's Books Fair, in 2012, when Portugal was the invited country. For the work developed in the comic book "A Stem Cell Adventure", he's awarded for Colorist of the Year. and is nominated for Letterer, and Artist of the Year, in the Prémios Profissionais de BD of 2014 (Professional comic book Awards).. He also has been invited to go to schools, libraries and book related events,. Also has been invited to talk at the Master in illustration, of ESAP Guimarães.

You can follow his work at:
http://www.andrecaetano.com