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Learning Activity 2: Teaching Notes for Sources of Stem Cells: IVF, PGD Clones, Cybrids, SHEEFs, Menstrual Blood, Cord Blood, Ovaries, Fetuses, and Fat

Eggs & Blood: Gifts & Commodities Module

by Katayoun Chamany Updated July 2018

In this activity students move through the 7E model of learning proposed by Arthur Eisenkraft (Engage, Elicit, Explore, Explain, Elaborate, Evaluate, Extrapolate) by *exploring* secondary literature, infographics, and animations and *explaining* what they have learned about the biological, ethical, legal, and social dimensions of stem cell sources associated with embryos, fetal tissue, and adult tissue. The learning resources invite students to consider advantages and disadvantages associated with each stem cell source with regard to procurement processes and scientific and therapeutic potential. This activity is designed to encourage students to *explore* the material on their own and *explain* what they have learned through *visual narratives* that combine images and text. This approach to teaching and learning is constructivist because the narratives reveal what is most important to students and can then serve as reasoning tools in discussing policies for regulating stem cell resources. As students construct their knowledge they become more self-aware of their own learning. With respect to Blooms Taxonomy, students acquire and remember content knowledge, connect specifics to broader concepts, and synthesize mental models of the information at hand.

Students' visual narratives should not be a replica of the infographics or animations that are assigned but, rather, highlight the biological, ethical, legal, and social issues most important to them and/or a specific community. Using a set of questions provided in the assignment, each student, or group of students, generate(s) *a personalized* visual narrative. Because the activity draws on personal interest, each group or student will respond to the questions differently, highlighting those aspects that are most relevant and meaningful to them. By viewing all narratives, students can see the diversity of responses even within their own class environment. The activity can serve as segue to lectures on basic cell biology topics as cell signaling, cell differentiation, cloning, and embryogenesis, and can also be used in seminar courses to explore the relationship between science and other academic disciplines and activist movements.

Because different kinds of resources, the activity can be customized for a variety of courses. In courses where primary scientific research articles can be read, the **Research** or **Scientific Research** articles can be assigned, and in courses where scientific background is limited perhaps only the abstract, introduction, or discussion of these articles can be assigned alongside secondary resources such as video, infographics, news, blogs etc.

STUDENT LEARNING OUTCOMES:

- Gain awareness of the ethical, legal, and social issues tied to various stem cell sources that are isolated or derived using eggs, menstrual blood, cord blood, fetuses, and fat.
- Compare the ethical issues associated with procurement processes for each stem cell type. Is the source contentious? How easily can cells be retrieved; are they numerous or a minority population? How invasive is the process? Are there any health risks associated with the procurement process? Are there any other scientific manipulations of the source material? Is any money exchanged? Are the processes legal, and are regulations in place?

- Compare the scientific and therapeutic potential of stem cells derived from different kinds of embryonic sources with respect to the qualitative and quantitative dimension of genetic content. Does a diploid nuclear genome exist and, if so, is there both paternal and maternal contribution? Do sperm reprogramming factors play a role in the generation of this stem cell type? Are there animal components present? Which of these sources of stem cells offer the most flexibility and for what purposes?
- Compare the scientific and therapeutic potential of stem cells derived from embryos with those derived from fetus and adult tissue. Which source proves more immunocompatible? Which source has a wider range of possible cell fates? Which source has less potential for the development of unwanted outcomes such as tumor formation?
- Describe how advances in stem cell research can both challenge and confirm stereotypical views on the role of females in society and tissues and cells associated with female bodies or reproduction (cord, placenta, fetal, menstrual, breast).
- Distinguish between different sectors, public and private, and identify ways in which they are interdependent.
- Recognize the influence that advances in basic science, law, business, human rights, and medicine can have on one another.

FORMAT:
A version of this activity has been used in a non-majors stem cell course designed for liberal arts and design students at The New School and in a Science, Technology, and Society course offered at Vassar College in which students were asked to address the source of stem cells that can arise from IVF combined with PGD. Examples of their work appear in the assessment section of these teaching notes.

An adaptation of this activity was administered in a more traditional developmental biology course at San Francisco State University, and students were broken into groups and asked to present on each stem cell type to the class via a ppt slide show that also included a timeline.

The assignment can involve small group work where each group of students is responsible for reporting out the findings via a visual narrative of the techniques involved in procuring a particular stem cell source. The articles and video clips are explored outside of class; students develop their narratives on their own, and develop a collective narrative with their peers once they assemble in groups in class.

Alternatively, each student can submit a visual narrative for a specific source and the instructor can use examples to teach through common misconceptions or highlight interesting connections to the ethical, legal, and social dimensions. In courses with more space to cover the material, the different sources can be addressed in different class sessions. In this latter format, each student, or group of students, is responsible for crafting a visual narrative for each source over the course of many class sessions.

Instructors should be aware that some topics have a heavy reading load (IVF, Cord Blood, PGD, and Parthenotes/Clones/Cybrids) while others have much less. Additionally, the bold faced text preceding each article indicates the reference type. The primary research articles highlight the translation of basic science to the clinic and use many scientific acronyms common to genetics, immunology, and stem cell research and thus, more appropriate for students with some background in biology. The translational medicine pieces intentionally address disease or disability most commonly in need of cell replacement and include: neurodegenerative disease (fetal); cardiac disease (menstrual blood); spinal cord injury (adipose); and sickle cell anemia (cord blood). Instructors can choose and assign accordingly. More articles for each topic can be found in the Refworks link at *Stem Cells Across the Curriculum*

FURTHER LEARNING: Instructors and students would benefit from following this engagement activity with Learning Activity 3 (elaborate, evaluate, extrapolate) or assigning the Primer associated with this module. A collection of Discussion Questions**,** Timelines**,** PPT slide sets**,** Essential Resources**,** and Infographics tracing the trajectory of technologies and policies are also available in this module.

IMPORTANT CONSIDERATIONS:

1. The IVF industry in the US is neither regulated by the government nor FDA approved.
2. In IVF, all embryos are graded based on criteria that are fast evolving. In the past, the symmetry and number of cells at specific time points proved to be important, however, with the development of the time-lapse closed system incubation and microscopy (Embryoscope), the timing of cell divisions during the first three to five days of embryogenesis *in vitro* proves most important in predicting a successful implantation and, thus, pregnancy (Cruz, M. et al., 2012).
3. New York is the only state that compensates for egg provision specifically for creating embryos for stem cell research over and beyond medical bill reimbursement, and though the California Congress passed a bill to pay providers in 2013, Governor Gerry Brown vetoed the bill.
4. In PGD, genetic testing prior to embryo transfer can involve testing oocytes, embryos at the 3-day/8-cell stage, or embryos at the 5-day/150-cell blastocyst stage. Most commonly the latter is used. For some, the genetic testing of oocytes alleviates moral issues connected to the destruction of potential life. Because oocytes are not yet fertilized, any oocytes that are found to have genetic anomalies are excluded from IVF, thus, avoiding any embryos undergoing negative genetic selection and possible destruction. The testing of embryos at the blastocyst stage means that only trophoblast cells are being tested and not those of the developing embryo; it is known that in many animals the developing embryo throws off chromosomally aberrant cells to the trophoblast, so this testing may result in false positives for chromosomal abnormalities leading to extranumerary embryos that could be used for stem cell research (Kalousek, D. et al 1983). Relatively few studies have analyzed the presence of this phenomenon in human development, and some research suggests this does not occur in humans (Derhaag, J. et al. 2003)
5. Parthenogenesis is not used for reproductive purposes in mammals, but can be artificially stimulated in a lab environment creating early stage embryos for research.
6. In somatic cell nuclear cloning (SCNT) many more eggs are needed as human cloning efficiency is low; however, the most recent cloning success appears to have increased efficient drastically, using only 20 eggs from two providers (Tachibana et al., 2013).
7. In cybrid technology the nuclear genome and the mitochondrial genome are from different species.
8. Ninety-seven percent of cord blood in US hospitals is discarded, and of the small percentage banked, most is banked privately, meaning only family members can access this stem cell source. In addition, the diversity of cord blood is very low, with those of mixed race having less than 25% chance of a match in some national regions.
9. Adult stem cell sources are heterogeneous in nature making FDA approval challenging.
10. Fetal tissue can be used directly in transplants to address neurodegenerative diseases in adults.
11. Synthetic MSCs and SHEEFs present alternatives to sourcing cells from embryos or adult tissues. These sources were proposed and in the case of synMSCs used to treat disease in 2017. In the same year, some have called for more accurate representation of MSCs, not as stem cells, but medicinal signaling cells, since their action appears to be trophic, acting on cells *in vivo.*

Visual Narrative Construction

All students will need to engage with graphic representations of information, whether graphs, maps, or diagrams. However, instructors should not assume that students always know how to interpret or use these appropriately. Making their own versions helps to develop a more sophisticated understanding of the relationship between symbolic representations and what is being described. Instructors may want to explore pedagogical resources that demonstrate how the use of visual narrative or graphical summaries can improve student retention of content knowledge. For instance, *Cell Stem Cell* has graphical abstracts listed on their website and data visualization is on the rise more generally. Verbal encouragement for the utility of diagrams and visual narratives and practice in class has been shown to support students' motivation to use these learning tools spontaneously. Visual narratives can also serve as formative assessments of student learning in two ways; by highlighting what aspects of the topic are relevant to students, and where alternative conceptions or misconceptions in student understanding exists. A short bibliography is provided below that reviews strategies and tools to promote this kind of activity. The resources provided by Dan Roam can be shared with students; there are Youtube tutorials and cheat sheets like his CODEX. The last reference is research based article that serves well for assessment.

Ainsworth, S. et al. Aug 2011. Drawing to learn. *Science.* 333 (6046): 1096-97. Link Response by Manalo and Ueseka Link

Chamany, K. et al. 2013. Using Preimplantation Genetic Diagnosis to Teach the Biological, Ethical, and Social Dimensions of Stem Cell Research in an Undergraduate Curriculum-Biology, Bodies, and Beliefs. 12th International Conference on Preimplantation Genetic Diagnosis. POSTER. Istanbul, Turkey. May 8-11. *See ResearchGate.*

Dietz, K. 2012. Storied Infographics: Why do they Fail? *In* Why Data and Infographics Help. E Marketing 101 Serving a Need. Link

Quillin, K. & Thomas, S. 2014. Drawing-to-learn: A framework for using drawings to promote model-based reasoning in biology. *CBE- Life Sciences Education.* 14 (1):es2. Link

Ridley, P. and A. Rogers. 2010. Drawing to Learn in the Arts and Humanities. Centre for Learning and Teaching University of Brighton. Link

Uesaka, Y. et al. 2010. The effects of perception of efficacy and diagram construction skills and students' spontaneous use of diagrams when solving math word problems. Lectures Notes in Computer Science. *In* Diagrammatic Representation and Inference. 6170: 197-211. Link

Picturing to Learn. Contains a database of student samples.

Roam, D. The Visual Codex cheat sheet and the Back of the Napkin for Visual Narrative/ Visual Grammar

Arneson, J. and Offerdahl, E. 2018. Visual literacy in Bloom. Using Bloom's Taxonomy to support Visual Learning Skills. *LSE*. 17 (1): Link (7 pages)

Common Alternative Conceptions of Emerging Biotechnologies

Because many students are familiar with assisted reproductive technologies (ARTs) the activity also elicits alternative conceptions or understandings of the people, policies, and practices associated with ART. For instance, students often believe that embryos are implanted into the uterus after in vitro fertilization (IVF) rather than transferred. Others are not aware that oocytes are matured in the body and surgically removed for IVF. Most are unaware of the incidence of health risks associated with ovarian hyperstimulation, factors that might place one at higher health risk of OHSS, and that the stimulation protocol is associated with a technique that is neither FDA approved, nor regulated. Similarly, most have little to no understanding of positive and negative selection of traits via preimplantation genetic diagnosis (PGD) of embryos created via IVF with the intent of giving birth to saviour siblings that are disease free and immunologically matched to the sibling living with disease and/or disability. As this is a fast-moving field, most are also not aware of the existence of adult stem cells in breast tissue, fat tissue, and menstrual blood.

Examples of Visual Narrative Scope
The level of discussion and the complexity of questions generated during the visual narrative development will vary depending on academic background and interest. For instance, students in biology courses could view Tilly's work described in the video by Dolgin and apply the scientific method referring to FACs analysis for the identification of ovarian stem cells. In addition, science students could be asked to place this in the context of tissue markets highlighting the ethical, social, and economic dimensions. This same resource can be useful as a "baiting" technique for students with no biology foundation to create narratives that highlight the "billions" of eggs that could be generated from just a few women while considering the characteristics of such women, such as their place of origin, age, ethnicity, and socioeconomic class.

ASSESSMENT: A rubric can be constructed based on the goals of the course and shared with students beforehand. For instance, for PGD, instructors may want to add criteria regarding the temporal and spatial aspects of removing oocytes, fertilizing them in vitro, genetic testing, and addressing the negative and positive selection criteria and how this plays into uses of the extranumerary embryos in the context of stem cell research. A more generalized example is provided below:

Aspect	**Struggling**	**Developing**	**Mastering**
Source of cells	Not clear; ambiguous; no ethical address	Only indicated with text; ethics is indicated	Clear from either text or image; clarifies ethical issues
Process of Procurement	Cursory address; no temporal or spatial imagery, or what resources needed (egg, sperm, etc), nor any address of decisions points	Some attention to sequence of steps and resources needed and temporal and spatial aspects; indicates some decision points	Clearly indicates specific steps, resources needed, their location, and their timing in appropriate sequence; highlights the number of choices/ decisions regarding the creation of by- products or excess and related ethical issues
Laws and Regulation	Does not address policy	Some address of policy	Using text and image indicates where regulation if any takes place and its impact on the process and the product
Biology Characteristics	Not clear if cells must be modified in any way	Addresses the status of the DNA and cellular potential	Indicates with text and image whether genetic content and cell potential is manipulated and why
Scientific Potential	Not clear how this source and technique could advance science	Some attention to the source providing a resource for scientific investigation	Addresses why source is useful for scientific inquiry (reprogramming, differentiation)
Therapeutic Potential	Does not indicate how useful the products would be for transplant or drug development, or immunocompatibility range	Provides one potential use of the product in biomedicine and its ethical perspectives; addresses some immunocompatibilty issues	Clearly illustrates how product will move from various spaces to a clinical setting, and how it will be developed and administered and related ethical issues (access, informed consent, clinical trial etc); indicates whether source is universally immunocompatible or indicates needed interventions to address this issue.

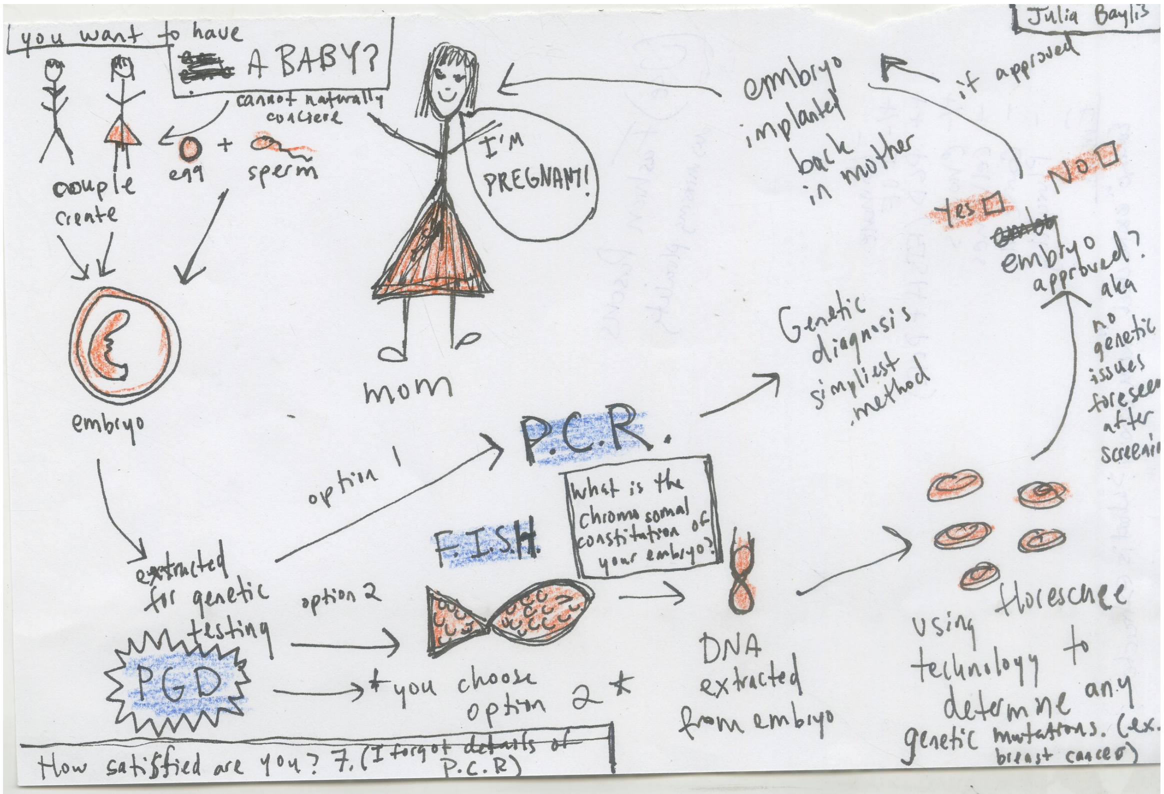
Banking and Access	No address	Some address of either banking, compensation, harms, and participant pool	Addresses banking, compensation, harms, and participant pool
Public or Private	Does not indicate whether the procurement and/or the products are coming or ending up in one sector of the other	Indicates either procurement or products location in the private or public sectors	Using text and images highlights the location of procurement, manipulation, and product storage with respect to private and public sector and access issues.
Social Views	Does not address the social views of using this source	Addresses at least one social view of using this source	Using text and images highlights a range of social views regarding the use of this source including feminist, religious, or social justice perspectives
Self Reflection	Did not reflect on the quality of their work or areas in need of improvement	Reflects on the quality of their work but is not specific about areas in need of improvement	Reflects on the quality of their work and is specific about areas in need of improvement

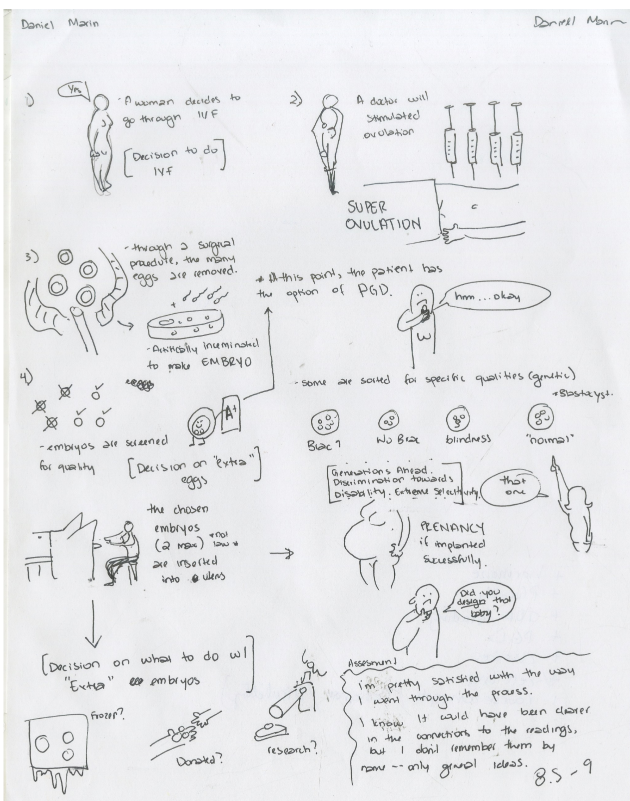
Sample of Student Work for PGD-related sources below and a larger draft of sketch notes for a visual narrative comparing all sources. Permission to showcase student work with names was secured.

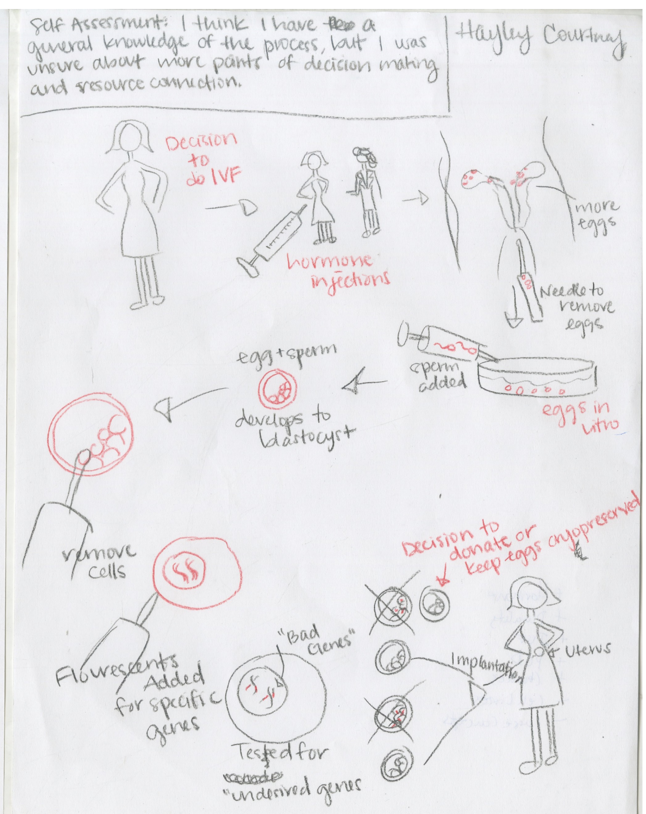
Non-science majors registered for a university lecture course focused on stem cell research were given 15 minutes to draft a visual narrative of the IVF/ PGD process using these prompts

- Include the source, manipulations, and technologies involved in performing PGD
- Highlight the key points at which decisions are made
- Indicate where course concepts, ideas, resources, and/or case studies map to the visual narrative
- Reflect on the quality of your work and areas in need of improvement

As can be seen in the examples below, some students did not indicate which cells of the embryos are tested and at what time, nor did they address the extranumerary embryos' possible fates (those that tested for disease susceptibility and those that did not), while others did this creatively using imagery for gifting, selling, and banking (freezing). One common misconception, which students glean from the literature, is the use of the verb "implantation" when in actuality the embryo is simply transferred to the uterus, and the process of implantation may or may not follow. What is telling about even this small sample, is that each student has identified unique aspects of the process of procuring stem cells using embryos created in the reproductive sector and subjected to PGD (hormone administration, decision making about embryo fate, genetic testing and designer babies).


Julia Baylis
you want to have A BABY?
cannot naturally conceive
couple create
egg + sperm
I'M PREGNANT!
mom
embryo
embryo implanted back in mother
if approved
Yes ☐ No ☐
embryo approved? aka no genetic issues foreseen after screening
Genetic diagnosis simpliest method
P.C.R.
option 1
extracted for genetic testing
option 2
F.I.S.H.
What is the chromosomal constitution of your embryo?
PGD
you choose option 2
DNA extracted from embryo
using floresence technology to determine any genetic mutations. (ex. breast cancer)
How satisfied are you? 7. (I forgot details of P.C.R)


Daniel Marin
1)
Yes
- A woman decides to go through IVF
[Decision to do IVF]
2)
A doctor will stimulated ovulation
SUPER OVULATION
3)
- through a surgical procedure, the many eggs are removed.
- Artificially inceminated to make EMBRYO
* At this point, the patient has the option of PGD.
hmm... okay
4)
- embryos are screened for quality
[Decision on "extra" eggs]
A+
- some are sorted for specific qualities (genetic)
*Blastocyst.
"normal"
blindness
Generations Ahead. Discrimination towards Disability. Extreme Selectivity.
that one
the chosen embryos (2 max) *not law* are inserted into uterus
PRENANCY if implanted successfully.
Did you design that baby?
[Decision on what to do w/ "Extra" embryos]
Frozen?
Donated?
research?
Assesment
I'm pretty satisfied with the way I went through the process. I know it could have been clearer in the connections to the readings, but I don't remember them by name -- only general ideas.
8.5 - 9


Self Assessment: I think I have a general knowledge of the process, but I was unsure about more parts of decision making and resource connection.
Hayley Courtney
Decision to do IVF
hormone injections
more eggs
Needle to remove eggs
sperm added
eggs in vitro
egg + sperm
develops to blastocyst
remove cells
Decision to donate or keep eggs cryopreserved
"Bad Genes"
Implantation
Uterus
Flowresents Added for specific genes
Tested for "undesired genes"