Learning Activity 1: Teaching Notes for Alternative Narratives for Henrietta Lacks and HeLa

HeLa Cells & HPV Genes: Immortality & Cancer Module

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This activity addresses the first two steps of the 7E model of learning proposed by Arthur Eisenkraft (Engage, Elicit, Explore, Explain, Elaborate, Evaluate, Extrapolate). Students *engage* in discussion and *elicit* prior knowledge from one another by reviewing congressional records, secondary literature, videos, and podcasts to trace the course of policies regarding human subjects and tissues as it applies to scientific advances in cancer research and vaccine development. The perspectives allow students to compare multiples narratives regarding altruism and gifting in biomedical research within the context of the commercialization of reagents and products related to tissue culture research.

This activity is a form of engagement, and formal assessment or evaluation is not necessary. Rather, the assigned resources address the establishment of the HeLa cell line and provide a cursory review of human subjects research, HPV infection, cancer biology, and stem cell research, stimulating students to ask questions about current practices and future research directions.

Instructors of cell biology courses will easily connect the notion of cell cycle control to this activity, while instructors focused on cancer, or infectious diseases, could use the activity as a springboard for conversations about HPV, genomic instability (TERC duplications), telomerase, and molecular biology techniques that address the cancer and immortality phenotypes. The last two references in Part II provides contemporary solutions including genoytyping to address the challenge of rapidly dividing cells (transformed, cancerous, or embryonic/pluripotent) contaminating cell cultures.

For students with limited biology background these topics can be explored using the HeLa Cells & HPV Genes Slide Set with more emphasis placed on the social context of the investigations. The activity can also be used in seminar courses to explore the relationship between science and other disciplinary areas such as politics, cultural studies, disability studies, and gender studies.

This assignment *elicits* alternative conceptions or understandings of how biomedical research is conducted and how tissues and DNA can be seen as public goods or commodities. The level of discussion and the complexity of questions will vary depending on academic background and interest. The activity is designed to have students frame the discussion through reflection and the generation of a set of questions that could be answered in future class sessions. This assignment also lends itself well to intersectional analysis by highlighting the complex network of factors that contributed to the development of the first human cell line as revealed in Part C. The narratives in this part of the activity are the less commonly heard and reveal the multidimensional nature of the HeLa narrative as complicated by race, class, ability, and gender.

Lastly, the resources offered in the assignment intentionally span congressional records, popular press (blogs and magazines), and news published in science journals. By showcasing how the narrative appears in these documents designed for different audiences and with variable access, students understand that knowledge itself can be considered a social justice issue.

STUDENT LEARNING OUTCOMES:

- Have an appreciation for the intersection of basic scientific research and clinical medicine
- Provide biological and social reasons to explain why Henrietta's cells were able to be cultured *in vitro*
- Pose questions about how genes and environment can influence cell division and "immortality"
- Explain how and why cell lines are used in biomedical research and list their limitations
- Offer more than one narrative for the establishment of the first human cell line
- Provide evidence for opposing views on privacy, compensation, and ownership of human biospecimens
- Recognize the influence that advances in basic science, medicine, business, human rights, and politics can have on one another.

FORMAT:
Portions of this case have been used in a cell biology course, a non-majors stem cell course, and a summer bridge course in the Equal Opportunity Program for liberal arts and design students at The New School. It has also been adapted for a junior level bioethics course and a first-year general education course at San Francisco State University. Some colleges and universities that have adopted Rebecca Skloot's book *The Immortal Life of Henrietta Lacks* have adapted this activity and others in this module in courses across the curriculum, while high school teachers have done the same under the Facing History and Ourselves educational project designed to promote tolerance and democracy to combat racism and prejudice.

Timing
As described below, the activity can take between 1-3 class sessions using a progressive disclosure approach in which the class is split into two large groups with even-numbered resources read by one half and odd-numbered read by the other half.

Using progressive disclosure, students read the articles during class in pairwise sets such that the congressional records (1,2) are read and discussed before receiving the next set (3,4) etc. Using this approach would require 2-4 class sessions to move through all 10 references.

Alternatively, reading can take place outside of class with each half of the class only reading odd or even-numbered references and again this can be broken up over a few days to achieve partial progressive disclosure. For instance, students could be assigned to read all references in Part I, and arrive to the first class session to discuss these and then be presented in class with, #5 and #6 to read and discuss, and then receive #7 and #8 and read and discuss. For instructors interested in using #9 and #10 to bring forth contemporary issues connected to stem cell derivation and characterization, these articles can be assigned for a future class session.

If short on time, or the readings prove challenging for introductory students, the Culliton and Katznelson articles can be replaced by the freely available BBC documentary film "The Way of All Flesh" directed by Adam Curtis; students can watch the 50-minute video outside of class or the instructor can use a five-minute excerpt at time stamp 18:58 addressing HeLa cell line contamination during class time. Additionally, there are two Newsy videos located under "Informed Consent Genetics Video" each of which is less than 5 minutes in length and now hosted on the site *Dailymotion*. One reviews the establishment of the HeLa cell line and the subsequent publication of its genome within the context of lack of informed consent and another listed in the resources, that details the assembly of the HeLa Genome Access Working Group on which two Lacks family members serve. For Part III, instructors can choose to view many of the resources during class time and refrain from assigning these resources outside of class.

If more time and learning activities are desired, the Erin C blog post and the Katznelson piece allow for further exploration in the classroom as instructors may choose to visit the websites of cell collections or DNA databases to demonstrate how these databases can serve as sources of information, such as the non-profit

private biological resource center, The American Type Cell Culture (ATCC). If instructors would like students to engage with these public databases, another session can be added.

If a more comprehensive overview is desired following this activity, instructors may ask students to review this one-hour lecture by David Spector from Cold Spring Harbor Laboratories. The lecture provides a succinct overview of the basic science of cell biology, cell division, and cell culture with a video of the cells dividing. At 23 minutes there is discussion of Chester Southam's research using human subjects in the identification of viral contagion for cancer by injecting the HeLa cells into inmates. At 38 minutes he discusses the complexity of profit making and the impact this had on the Lacks family in the context of informed consent and patients' rights providing a history of human research subjects guidelines. At 48 minutes he reviews the cases of John Moore, the Greenberg/Canavan Disease case, and the Catalona case regarding prostate cancer samples. At 56 minutes he discusses how the Skloot book resulted in actions that honor Henrietta Lacks.

Readings & Constructed Discussion
The assignment can involve small group work where each group of students is responsible for reporting out the findings of a particular news piece, radio segment, or video clip. The resources are intentionally chosen to cater to multiple intelligences. The first 8 readings reveal how stories are communicated within, and outside, the scientific community in a variety of media formats. The resources can be reviewed during, or outside of, class depending on the course structure. If striving for a constructivist approach to teaching and learning, instructors can divide the class in half and ask that one half read the odd-numbered articles (1,3,5,7,9) and the other half read the even-numbered articles (2,4,6,8,10). This approach promotes dialogue because the subdivision creates a situation where the two groups must discuss the same topic from different perspectives.

Each group will learn aspects of the HeLa line derivation through resources that bring the views of scientists, family members, policy makers forward, but the complete story must be put together through discussion. As just one example, the half of the class that is assigned the historical article published by Culliton in 1974 is also assigned the most recent article published by *Nature* regarding stem cell lines in 2015, but would be dependent on the other half of the class to learn of the proactive approaches being taken by the scientific community to reduce contamination and verify a cell line's provenance. Instructors may also choose to give students time in class to form small groups of 3-5 to discuss among themselves before providing a consensus overview to the remainder of the class. For small group work, see the resources at this site (Resource One: Group Role Profiles) for role responsibilities that ensure equity in groups, or assign an "equity monitor" who must ensure that all voices are heard in the group and that any missing voices are raised.

During the class discussion, the instructor acts as note taker, guiding the discussion by posting the groups' questions as they are posed and asking if another group can answer the question or challenge the points made using a different perspective. In this way the discussion can move from group to group rather seamlessly. The note taking can take the form of a concept map making explicit the connections, pushes and pulls in narratives that may appear to be in conflict, and help students synthesize a complex story from many vantage points.

Videos and Other Resources
Depending on the number of video clips and articles assigned in Part III the activity can take 1-4 class sessions. Showcasing videos or excerpts in class can illuminate more complexity. The resources listed here cater to multiple intelligences and different ways of learning using letters, radio, theater, video, poetry, microscopy, and art. If there is only one resource used it should be the Kumar Open Letter. Though it is short, it provides a broad narrative using intersectional analysis (race, class, gender, ability) to raise a call to action to educators. If this letter is used, instructors should have some familiarity with addressing race-related issues and the history of biomedical research as it relates to systems of oppression; some instructors have found the

tone of the letter off-putting but, after reading the **Primer** associated with this module, had a better appreciation for the letter's message. The Covert et al. theatrical educational slide show addresses these perspectives as well as commodification of the body and the role that power and privilege play in deciding who owns and profits from bodily goods. The BBC film by Curtis and the Radiolab segment highlight how HeLa cells were used to test the Salk polio vaccine that was never patented and "gifted" by Salk to the world. The World Stem Cell Summit excerpt and the Fabregas and Balis news piece broaden the discussion to other human subjects that may not have voice, such as Jimmy Sarkett, who was used a human incubator for the live polio vaccine when he was child afflicted with polio. The poem *For Elsie Lacks* by Sheri Davis-Faulkner and the Prezi student presentation by Hendren et al. extend that concern to those living with disability. The Helen Roe-Wilson project A Brush with Immortality, provides direct input from Lacks' family members on the narrative. The Weasel article uses a feminist lens to discuss the history of the human research subject and the HeLa cell line. When Weasel suggests that the cell line could have come from anyone, it is important to remember that some of her hypothetical patients would most likely not have experienced the biological and social factors listed above that led to the immortality phenotype; the conflation of race, class, and gender contributed to a lack of healthcare, and mistrust of the medical establishment. Verspaget fuses her own cells with HeLa cells to promote a philosophical discussion regarding ontology, alienability, and kinship. It is not uncommon for students to see Verpsaget's work as a challenge to racial boundaries and hierarchies, since it involves blood, a common icon for lineage. The lab techniques discussed in this art piece are highlighted in the cell culture video provided by the Association of American Medical Colleges. Lastly, the Benjamin TEDx video and the Curtis film touch on racial health disparities, vulnerable populations, and the need to design research studies in ethically responsible ways.

SIX "TEACHABLE MOMENTS": Language, Bioethics, Race, Social Justice, Gender, & Biology

Language

The congressional records use language suggesting altruistic donation, sacrifice, and gifting. Instructors should encourage students to notice this language and the impact it has on compensation schemes and ownership. It is no coincidence that both Ehrlich (1997) and Perriello (2010) have constituencies connected to the establishment of this cell line and that Adam Curtis' film *The Way of All Flesh* was released in 1997 and Rebecca Skloot's book *The Immortal Life of Henrietta Lacks* published in 2010. In a sense, the congressional requests for acknowledgement could be considered a form of reparations, or damage control, as the story entered the mainstream media.

Bioethics & Informed Consent

In bioethics four principles guide research practice: autonomy; nonmaleficence; beneficence; and justice. The process of informed consent is designed for potential research participants to exercise autonomy in choosing to participate in research based on an analysis of risk and benefit. The notion of justice is addressed through "just participant selection" such that the population that would benefit the most is selected for the research participant pool and that no one population experiences disproportionate risk or burden.

Instructors may need to remind students that protections for human subjects research in the US were not put into place until the National Research Act was signed into law in 1974. Following the publication of the Belmont Report, authored by a presidential commission, informed consent was effectively put into practice in 1981 as "The Common Rule." It is also important to note that this policy only regulates publicly funded research using human research subjects, not privately funded research. Thus, the informed consent process was not in place at the time that cells were removed from Henrietta Lacks' cervical cancer biopsy, though there was general consensus emerging post-WWII that research subjects should

participate voluntarily as stated in the Nuremberg Code (1948) and be informed as to risks and benefits as stated in the Declaration of Helsinki (1964).

Instructors may want to provide students with an abbreviated overview of quotes from significant policies as found in documents linked to the US Office Human Research Protections website (see International and within that Ethical Codes & Research Standards) and the update the update to the Common Rule in 2017):

> The voluntary consent of the human subject is absolutely essential.-Nuremberg Code 1948
>
> After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent.-*Declaration of Helsinki 1964*
>
> Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them.-*Belmont Report 1979*
>
> Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.-*The Common Rule 1981 (45 CFR 46)*

Race

Another challenge is raised when instructors address the historical aspect of the race-based categorization of cells as depicted in the Erin C blog post from 23andMe's "*Spittoon*" and the 1974 Culliton report in *Science.* Both pieces refer to genetic variants of genes that code for metabolic enzymes and the differential distribution of these variants in Caucasian and Black populations. In the Spittoon post, ErinC explains how cells could be traced back to an African American woman and provides an image of the molecular analysis of a metabolic protein variant. In the 1950s, there were a limited number of cell lines and most were established from tissues obtained from Caucasians. Thus, frequency distribution of two variants of G6PH was utilized as a means of identifying the HeLa cells line as Black. The "A" variant is the result of a genetic mutation that reduces the efficiency of the enzyme, but is believed to provide a protective effect against malaria, reducing infection rates by 46-58% (Ruwende et al., 2002). This variant is more *common* in individuals of African descent given their continued environmental exposure to mosquitoes harboring the protozoa *Plasmodium falciparum* responsible for malaria. Over time, African populations living in endemic malaria zones evolved to carry this gene variant as it improved survival.

The notion that cells can be defined as Black goes against research that demonstrates that race is socially constructed and not biologically based. Instructors should explain that frequencies describe general trends and that traits are not discontinuous in human populations such that one population carries a genetic variant at the exclusion of all other variants. The distribution of G6PH is the result of environmental factors that placed selection pressure on the population and, thus, altered the frequency of the variant in different human populations; this is similar to the explanation of the emergence of haplotypes that vary in frequency among human populations (Online Mendelian Inheritance of Man). So though the genetic structure of human populations corresponds to stressors specific to geographic locations, this structure does not support essentialist conceptions that racial categories are discrete or informative.

Instructors not familiar with genetic variation as it relates to human populations may find the "Race: Are We so Different?" and Race: The Power of an Illusion projects useful. This former was developed with

funding from the National Science Foundation and the American Anthropological Association while the latter is used in many high schools as an educational unit on the social construction of race. Additionally, instructors concerned about reifying essentialist beliefs regarding biology and race, may want to review science education articles the demonstrate how biology textbooks, learning materials, and instruction can inadvertently solidify students preconceptions that race is a biological category (Donovan, 2013; Donovan, 2015; Donovan, 2016).

The race-based analysis of the HeLa cell line was only possible given the small number of cell lines at the time and the limited population sampling represented in these lines. Because there were only 18 cell lines in existence and all but Henrietta's were derived from Caucasians, generalizations about the distribution of gene variants among populations allowed the tracing of cell line provenance back to HeLa. It might be instructive to explain the law of independent probabilities at this juncture. Because the probability of having a specific G6PH variant is independent from having a specific PDM enzyme variant, researchers multiple these probabilities to determine the probability of any given cell line carrying both specific variants. Given the population frequencies of these variants, the chance of two unrelated cell lines having the same genotype was negligible. Students in a genetics course might appreciate a connection to the law of independent assortment. This same logic is used in paternity testing and criminal investigations using DNA analysis, however in these situations up to 20 different genetic sequences, or loci, are analyzed. These genetic loci exhibit DNA sequence hypervariabilty across human populations due to evolutionary processes and, thus, used to create a unique genetic profile, or DNA fingerprint. Because 20 loci are used, the probability of obtaining a single specific variant for each location must be multiplied, again making it highly unlikely that two DNA profiles would be identical. It is of note that until Jan 2017, only 13 short tandem repeat (STR) loci were used but, in 2010, a Working Group was assembled to address whether the addition of three more loci could encourage "international data sharing efforts by having more loci in common with other countries for comparison purposes." The decision to add seven more loci was approved in 2015, and implemented in January 2017.

Again, language plays an important role in framing the provenance of the HeLa cell line as it invokes hierarchies related to race and gender. Feminist scientist Lisa Weasel writes:

> "For now, knowing this history (which incidentally many scientists may not), we must question what it means to propose that cells taken from the cervix of an African-American woman without her consent are now proposed to represent a separate species—and not one more highly evolved because of its ability to live under such a variety of conditions, to offer such an essential function in so many scientific experiments around the world, but a less advanced scientific species, placing a piece of what once was Henrietta, a mother of five alive and well in the kingdom "animalia," suddenly now amongst the likes of algae, amoebae, and euglena in the kingdom protista. And if any question exists that gender is absent from this intersection with race, the proposal that the new species be named "Helacyton gartleri," after Stanley Gartler, one of the white male researchers who brought the cells to prominence in the laboratory, should quickly dispel that notion. In fact, in their proposed description of this new species, the authors specifically state, "The gender, like that of cytos, is neuter"8 (Van Valen and Maiorana 1991)."- (Weasel, p 189, 2004)

Medical anthropologist Hannah Landecker in her book *Culturing Life* (**Part III #12**) also highlights the impact that language has on the narrative of the HeLa cell line and the person from which they were derived. She reminds us that the language used in the laboratory does not hold the same meaning

outside the laboratory. Using words like “contamination” when discussing a cell line that has overtaken other cell cultures, “promiscuous” when discussing a cell line infected with a sexually transmitted virus, and “aggressive” to describe a cell line derived from an African American woman, could be construed as racializing the cell line through the use of language often associated with acts of discrimination against African American women.

For instructors familiar with eugenics history or Social Darwinism, making the connection to words used to promote eugenics practices might be helpful. The term “unfit” was often used in conjunction with “promiscuity” during the eugenics movement and this coupling continues today. Additionally, James Watson, co-discoverer of the structure of DNA has, on more than one occasion, remarked that people of color have an elevated sexual appetite. For students with a background in gender studies, race studies, or social justice, Watson’s ideas echo those who showcased Sarah Baartman, known as the Hottentot Venus, in public venues as a highly sexualized African woman. So though using words like “contamination” and “promiscuous” may seem benign in the lab, it may unintentionally register differently in the minds of students and be linked to these other discriminatory remarks. Sharing the historical and contemporary use of these terms will help students not as familiar with racial stereotyping to understand how language can influence social policies.

For instance, Weasel’s interpretation of Van Valen and Maiorana’s proposal to reclassify the HeLa cell line as a strain of a microbial species is aligned with earlier eugenics philosophy that human races represented an evolutionary path(see **Essential Resources/Contamination**). Instructors should note that the proposal had to be self-published in *Evolutionary Theory & Review,* suggesting that the proposals was not taken very seriously nor widely supported. However, there are important aspects of the proposal to review beyond Weasel’s feminist critique. That the proposed nomenclature for this cell line/ microbial strain would stem from that of the scientist, Stanley Gartler, who identified the HeLa cell culture contamination reifies the power dynamics at play in biomedical research, placing the researcher at a level of higher importance than the person from which the cells were derived. The kind of social messaging that such a move would produce echoes the ideology of the eugenics movement that stratified humans based on their race and/or ability.

Social Justice

Students gradually realize that even if they thought they knew something about Henrietta Lacks, or HeLa cells, there are many things they do not know. They may also learn that their peers hold differing views on the history of this case. For example, in biology courses, some students refer to the cells as Helen Lane’s, in gender courses there is immediate outcry surrounding the word “gift” in the congressional record, and in classes where students are familiar with issues of intersectionality (race, class, and gender) past race-based abuses of the Public Health Service emerge; namely the investigation of the STD study in Guatemala, Mississippi Appendectomies in the Deep South, La Operacion in Puerto Rico, and the Tuskegee Syphilis Trial. These cultural views and history should be acknowledged if students are to build mental schemas that layer new knowledge onto prior knowledge. Without acknowledgement, students may feel that the discussion is not relevant to them and their community. This acknowledgement of past abuses is perhaps most important in biology courses, where issues of social justice are rarely discussed. Given the comment posted on the IMDB regarding the documentary film *La Operacion* “All empires need at least one laboratory. That is what Puerto Rico has been to the United States since mid-1898,” it is not difficult to understand that discussion of the derivation of the HeLa cell line should occur within the larger context of inequities of power in biomedicine and health. There are some instructors who may feel that raising these issues would “turn students off” from science and medicine, but research studies demonstrate that if trust relationships are established, students will pursue science education in an effort to promote innovation and justice. Thus, acknowledging the abuses of the past and pointing to regulations, structures, and proposals to prevent them from occurring in the future is

a step in rebuilding that trust. This sentiment is echoed in the Letter from the Presidential Commission for the Study of Bioethical Issues in their report on the egregious activities of the US Public Health Service regarding the study of sexually transmitted diseases in Guatemala. This letter and that work are discussed further in Learning Activity 2 and is a nice follow up to this Learning Activity.

> The best thing we can do as a country when faced with a dark chapter is to bring it to light. The Commission has worked hard to provide an unvarnished ethical analysis to both honor the victims and make sure events such as these never happen again.--September 2011. Presidential Commission for the Study of Bioethical Issues. Letter Exchange between the Commission and President Barack Obama. *In* Ethically Impossible: STD Research in Guatemala from 1946-1948: v-vi. Link

Though these past abuses are important to the larger context, it is important to remind students that the care that Henrietta was receiving for late stage cervical cancer was the best care available at the time. Unlike the Guatemala case or the Tuskegee case, deliberate actions to cause illness or withhold treatment did not occur in her case. That said, the history is part of her community's collective knowledge and serves as an important backdrop to her story. Though Hopkins was one of the only Charity Hospitals in the area, Henrietta loathed to be treated thereMany African Americans arriving with late stage diseases often did not leave the hospital alive leading to rumors and mistrust. That they came to the hospital late in disease is not irrelevant. The lack of routine healthcare in the African American community combined with the medical research abuses of the past caused those in the community to view Charity Hospitals as a last resort.

Part II also raises contemporary issues regarding ownership and access to the HeLa cell line bringing this historical case study into the present, with the establishment of a controversial gatekeeping committee for HeLa cell line use. There are those that argue that the creation of such a committee for a single human bioresource introduces problems associated with exceptionalism. Others argue that to acknowledge this contribution and to police its use with input from family members is a more generalized acknowledgement of human subjects contributions to biomedical research. As mentioned earlier, in this latter view, the new process for HeLa cell line use is seen as a trust building activity.

Gender

Clearly gender as described above plays an important role in any narrative about Henrietta Lacks, and this highlighted in the primer regarding HPV testing and cervical cancer screening and the stigma that is disproportionately placed on women (Shire, 2014). However, instructors should take note of the intentional use of resources designed to highlight women in journalism, science, and policy. As references, I chose books authored by women to provide the history and narrative of this cell line and its connection to stem cell research, all of which are in the bibliography of the Primer for this module (Skloot, Benjamin, Landecker, Weasel, Ikemoto). I also chose several news articles that highlight the important "corrective," or paradigm shifting work, that is often needed in basic scientific research. These choices include the work of: Amanda Cape Davis in cell contamination (NCBI, 2014) ; Maura Gillison in the area of HPV and head and neck cancers (Scudellari, 2013; Jennifer Doudna with CRSPR and its connection to the basic science of DNA repair mechanisms that go awry with cancer; and Elizabeth Blackburn and Carol Greider with their work on telomeres and telomerase. The work of female artists is also showcased including the work of Charnell Covert and Deborah Laufer in theater, Wilson-Roe in painting and mixed media, and Verspaget and Piccinini in bioart all of which are listed in the Essential Resources for this Module. In an effort to provide younger students with role models and narratives that speak to women in science and women who are at the intersection of science and policy, arts, and social sciences, I encourage instructors to make note of these choices in class.

Biology
After the students have engaged in discussion for Parts I and II, they may begin to ask biology-based questions. The progressive disclosure approach is designed to create a need to learn the biology to answer their own questions. For example, students ask “Why were her cells able to grow and not anyone else’s?” This question can be addressed by directing students to the HeLa entry in the ATCC collection. Instructors may need to use the accompanying Slide Set and Primer to address this question within the context of HPV infection and genomic instability leading to active telomerase activity.

Because students are aware of HPV as a result of immunization with the HPV vaccine and routine cervical cancer screening using Pap smears, instructors should point out that HPV infection and the progression to cancer is influenced by social factors. In the case of the HeLa cell line, instructors should reveal the unique set of biological and social factors that resulted in a highly virulent strain of HPV causing an aggressive form of cervical cancer from which immortal cells could be cultured. Namely that Henrietta:

- lived when segregation was rampant, leaving her with few opportunities for regular healthcare.
- lived in a patriarchal society where adultery was difficult to challenge, leaving many individuals vulnerable to multiple sexually transmitted infections (Henrietta lived with gonorrhea, syphilis and HPV infection); co-infections are known reduce the efficacy of immune function in clearing infections and cancer.
- did not receive regular Pap smears as a diagnostic for cervical cancer screening . These were not widely instituted until the 1960s. Thus, unchecked or removed, the HPV virus continued to integrate into her genome leading to genomic instability and telomerase RNA related genomic repeats (TERC), and ultimately the immortality phenotype characteristic of aggressive cancers.
- admitted herself to the hospital with late stage cervical cancer because of fears of past abuses in medical care and research in the African American community.

Some of the background for the role of HPV 18 in promoting cervical cancer can be found in Rebecca Skloot’s book *The Immortal Life of Henrietta Lacks, in* Chapter 27, “The Secret of Immortality” or in the Slide Set associated with this module. What this activity does is bring a more interdisciplinary intersectional analysis to the causation of Henrietta’s cancer and the cell immortality phenotype.

In the activity itself, viral infection is raised in the Culliton reference (#6) but is not described as HPV, while the Marrow review (#9) specifically addresses the HPV DNA integration sequence. Instructors should note that though Weasel also includes information on HPV and its role in conferring the immortality phenotype on the HeLa cells, the reference is a bit dated as it was published in 2004, when less was known about the number of cancer promoting HPV strain types. She mentions only HPV18 in relationship to cancer, but there are a growing number of strains that have been associated with oncogenesis and categorized into low and high-risk strains, and a number of vaccines include protection to an array of them. Similarly in the Radiolab interviews (Part III #12), Skloot mentions that there is no known reason for the immortality phenotype, but this is not entirely true. Instructors should be aware that HeLa cells are known to have multiple copies of HPV18 integrated into the human genome. This viral integration leads to genomic instability, including gene duplication of TERC DNA sequence that codes for the RNA component necessary for telomerase function. Telomerase enzyme function is normally turned off in fully differentiated cells of the adult and thus, these cells have a finite life span, or number of cell divisions, before losing vital information and undergoing programmed cell death. HPV integration activates the expression of telomerase in cervical cells and increases the transcription of its accessory RNA, leading to full enzyme activity allowing for DNA bumper sequences to be added to the tips of chromosomes, preventing them from losing vital information with each cell division. Thus, HPV is an important promoter of the immortality phenotype, the ability of a cell to reproduce indefinitely in culture.

Many companies have designed diagnostic tests to identify the TERC gene duplications in cervical cells (Animation Link).

For more general discussion of cancer progression and cell cycle control, a wonderful animation by Bohan is available from the Essential Resources associated with this Module (Animation Link).

The overall goal sof this activity are to highlight the intersectional (race, class, ability, and gender) dimensions of human research subjects, encourage students to want to learn more about the biological and social factors that led to the development and use of the HeLa cell line, and consider future biomedical research endeavors using human clinical specimens or donations. A timeline of Human Subjects Research and Biomedical Research are available from the **Media and Infographics** section of *Stem Cells Across the Curriculum*.

Questions that May Arise During Discussion

1. What biological characteristics do HeLa cells possess that make them useful for cell culture research?
2. Who are the people involved in moving cells from a clinic, to the lab, and ultimately to the market?
3. Are patients adequately informed about benefits and risks of tissue collection and donation?
4. What are the policies regarding DNA or cell donation outside of the clinical setting as seen with the Genographic, 23andMe, and Apple's Research Kit projects?
5. Should people have a choice in how their individual bodies may serve biomedical research, or should tissue banking be considered a social good?
6. What kinds of information or data need to be made available for individuals to consider participating in biomedical research? Do protections for privacy and anonymity exist?
7. Why do we need a diverse supply of cell lines for research?
8. What is being done about the cell contamination problem?
9. Did HeLa cells lead to the development of the HPV vaccine and better diagnostics?

CONTEXT & EXTENSIONS:

If used in a freshman seminar, *People's Science: Bodies and Rights on the Stem Cell Frontier* by Ruha Benjamin could be assigned, as it depicts the ways in which biomedical research is viewed by various stakeholders including those who advocate for disability justice, the social model approach to health, and economic equity. If used in a policy or ethics course, the article published by Truog and colleagues entitled "Paying Patients For Their Tissue: The Legacy of Henrietta Lacks" and the responses to this proposal in the journal *Science* could be assigned or the historical review of human subjects research policy by VanderWalde and Kurzban entitled "Paying Human Subjects in Research: Where Are We, How Did We Get Here, and Now What?" published in the *Journal of Law Medicine and Ethics.* If used in an anthropology, ethics, law, or race studies course Hannah Landecker's "Between Beneficence and Chattel: The Human Biological in Law and Science" published in *Science in Context* or her book *Culturing Life: How Cells Became Technologies* provide a critical view on science and medicine practices using a cultural perspective. If used in a gender studies course or global studies course the article by Lisa Weasel entitled "Feminist Intersections in Science: Race, Gender and Sexuality Through the Microscope " published in *Hypatia* could be assigned. If the activity is used in a biology course, readings regarding the cell contamination problem can be assigned and a short piece by O'Brien reviews the more contemporary work of Masters et al. in addressing the problem. Most of these readings are listed in Learning Activity 2 of this Module.

1. Benjamin, R. 2013. People's Science: Bodies and Rights on the Stem Cell Frontier. Stanford University Press: 272. Link
2. Landecker, H. 1999. Between beneficence and chattel: The human biological in law and science. *Science in Context.* 12 (1): 203-225. Link

3. Landecker, H. 2007.Culturing Life: How Cells Became Technologies. Cambridge: Harvard University Press. Link
4. Truog, R. et al. 2012. Paying patients for their tissue. The legacy of Henrietta Lacks. *Science.* 337: 37-38. Link
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LAB DEMONSTRATIONS and EXTENSIONS:

The gene for the G6PD enzyme resides on the X chromosome and consists of 13 exons and 12 introns, and is the most polymorphic DNA locus in humans with over 400 allelic variants. The variants have been characterized based on a) differential enzyme activity, b) electrophoretic mobility patterns, c) physiochemical behavior (thermostability, chromatography, and enzyme kinetics). All of the genetic variants are described as being Type A while the wildtype sequence is referred to as Type B. Because women carry two X chromosomes they can genetically be AA, BB, or AB, while males with one X chromosome, will genetically be either Type A or Type B, with Type A being more frequently associated with African American populations. Thus, a lab component could be added to more traditional biology courses that allows students to replicate the G6PD electrophoretic results mentioned in the piece by ErinC in the 23andMe blog "Spitoon." Alternatively, students can explore the databases to learn how researchers are gathering data about specific cell lines and genetic variation in human populations (OMIM 305900). They may be surprised to learn of a G6PD specific database maintained by Dr. Andrew C.R. Martin's group.

Students can also explore the American Type Tissue Culture (ATCC) collection and search for the HeLa cell line: choose Cell Lines under Products pull down menu and use the CCL-2 accession numbers for HeLa. There they will learn that the cell line requires Biosafety Level 2 facilities, is cancerous due to a dysregulated protein kinase C independent pathway that uses c-jun/AP-1, has genomic instability in M regions, and information about HPV 18 infection status and G6DH variants. Additionally, students can explore the role of hTERT immortalized cell lines on the ATCC site.

Lastly, if the course intends to explore the role of HPV in genomic instability a more elaborate discussion of diagnostic screening tests can be reviewed with an emphasis on oncoFISH cervical, which distinguishes persistors of HPV infection with cervical dysplasia from those that will most likely regress by using fluorescent probes to visualize and quantify the number of TERC repeats (the DNA sequence that codes for an essential telomerase adaptor RNA) in cervical cells.

NOTE of IMPORTANCE REGARDING INTERSECTIONAL ANALYSIS

As many will be unfamiliar with intersectional analysis and the alternative narratives of Henrietta Lacks, instructors are strongly encouraged to review the Pedagogies and Philosophies document on the *Stem Cells Across the Curriculum* website and the Primer associated with this module. The Primer provides a comprehensive view of many of the topics that will emerge during discussion with learners from diverse backgrounds. An account of this approach using their entire *Stem Cells Across the Curriculum* resources was published by Chamany in 2016 the *Studies in Social Justice* journal and accessible here.

FURTHER LEARNING: Instructors and students would benefit from accompanying this engagement activity with Learning Activity 2 and 3 or assigning the Primer associated with this Module. The Supplemental Materials include a list of Discussion Questions. Additionally slide sets, infographics, video, timelines, and artwork can be found on the module site as well as the **Media and Infographics** section of *Stem Cells Across the Curriculum*.