“HeLa Cells 50 Years On: The Good, The Bad, and The Ugly” (2002), by John R. Masters

Published in 2002, prostate cancer researcher John R. Masters authored a review article ”HeLa Cells 50 Years On: The Good, The Bad, and The Ugly” that described the historical and contemporary context of the HeLa cell line in research in Nature Reviews Cancer. The HeLa cell line was one of the first documented immortal cell lines, isolated from cervical cancer patient Henrietta Lacks in 1951 at The Johns Hopkins Hospital in Baltimore, Maryland. An immortal cell line is a cluster of cells that continuously multiply on their own outside of the original host. Though the HeLa cell line has contributed to many biomedical research advancements such as the polio vaccine, its usage in research has been controversial for many reasons, including that Lacks was a Black woman who did not knowingly donate her cells to science. In the article “HeLa Cells 50 Years On: The Good, The Bad, and The Ugly,” Masters describes that, despite the benefits of the HeLa cell line, it has caused significant negative impacts on research due to its propensity to contaminate other cell lines, which can potentially invalidate research findings.

In the review article, “HeLa Cells 50 Years On: The Good, The Bad, and The Ugly,” Masters summarizes major breakthroughs that occurred as a result of the use of the HeLa cell line. At the time of publication, Masters worked for the Institute of Urology at University College London in London, United Kingdom. In 2021, Masters held the three titles, which were Professor of Experimental Pathology, Director of the Prostate Cancer Research Centre, and Head of the Research Department of Urology.

The term cell line refers to a group of cells that multiply on their own outside of an organism. Healthy human cells have finite life spans because they have internal controls that regulate how many divisions each cell can undergo. However, some cancer cells are immortal, meaning they do not die after a set number of divisions, as a result of alterations that happen when cells become cancerous. That property of cancer cells makes them more durable than normal cells for scientific research. Many medical researchers use laboratory-grown human cancer cells as a model to understand how cells work and test theories on the causes and treatments of diseases. One of the first human immortal cell lines was the HeLa cell line. In the article, Masters describes how the HeLa cell line came from a cancer sample from the cervix of Lacks, who, in 1951, was diagnosed and treated for terminal cervical cancer at The Johns Hopkins Hospital, before she died later that same year.

Masters describes how, as other researchers created new human immortal cell lines, they found that the HeLa cell line contaminated many of their cell lines. He describes how HeLa cells began to compete with the cells in later developed human immortal cell lines and overtook and replaced those cells because of how aggressive Lacks’s cancer had been. As such, what researchers thought were new human immortal cell lines were in fact more HeLa cells. Cross-contamination occurs in cell lines when the cells from one cell line are inadvertently mixed with the cells of another cell line. Cell line cross-contamination compromises the comparison of results between different laboratories because it diminishes reproducibility of data, which is important for researchers to validate their findings. If an experiment generates different results each time it is performed, then the data is not reliable, and the findings are not valid.

Masters splits the article into five sections. In the first section, he describes the historical context during which Lacks’s physician Howard Jones collected her cervical cancer cells and researcher George O. Gey produced the HeLa cell line. In the second section, titled “The Good,” Masters details how the HeLa cell line has contributed to scientific breakthroughs and discoveries such as

the polio vaccine or understanding how diseases like tuberculosis, Ebola, and HIV infect the human body. In the third section, “The Bad,” Masters describes the HeLa cell line cross-contamination that occurred. In the fourth section, “The Ugly,” Masters documents how cross-contamination went unchecked by the scientific peer-review process and led to publications with problematic data. The peer-review process involves subjecting an author's scholarly work and research to the scrutiny of several experts who work in the author's field to ensure a work's validity and suitability for publication. Finally, in the fifth section, “The Future,” Masters concludes the article by arguing for greater peer review and quality control.

In the first section, Masters describes the process by which the HeLa cell line was obtained, as well as its historical context. Prior to 1951, cancer researchers had been trying to develop what Masters refers to as human cancer in a test tube. At the time, no laboratory had been able to grow human cells for more than a few weeks because those cells would stop replicating and die. On 8 February 1951, at The Johns Hopkins Hospital, researcher Gey received a sample of Lacks’s cells from her cervical tumor. Masters asserts that in 1951, there was a war on cancer in the United States and a worldwide hunt for the virus that some scientists like Gey attributed to causing human cancer. Therefore, locating and studying a human cancer cell line would enable scientists to identify the mechanisms that cause cancer.

Despite Gey’s scientific contributions, Masters asserts that by naming the cell line HeLa after Lacks – “He” for the first two letters of Henrietta and “La” for the first two letters of Lacks – Gey failed to preserve her complete anonymity, which he states was regrettable because there is no record that Lacks granted consent to the collection and use of her cells for science. Nevertheless, Masters states that it was not customary in 1951 to ask for written consent from patients. At the time, there was no legal precedent that would hold Gey responsible for his actions. As of 2021, there are strict requirements to ensure that physicians and researchers acquire and document patient consent, which Masters argues is due at least in part to the HeLa cell line story. Obtaining patient consent ensures that the patient is protected and is aware of the potential risks, benefits, or long-term consequences of their healthcare decisions.

In the second section, “The Good,” Masters describes why the HeLa cell line was and has been significant to medical research. He claims that the HeLa cell line and other cell lines have contributed to contemporary knowledge of every fundamental process occurring in human cells. Masters also asserts that the capability to expand scientific knowledge will continue to be dependent on cell lines. Masters also states that after the creation of the HeLa cell line in 1951, in just a few years, Gey distributed the cell line worldwide, and HeLa became the laboratory model for the study of not only cancer, but also biochemical pathways of normal and diseased human cells.

Continuing in his second section, Masters claims that despite being established in 1951, the HeLa cell line’s genetic information had remained remarkably stable even after years of continuous cultivation. That stability enabled scientists to conduct new studies with what were essentially the same cells every time they did an experiment. That also enabled scientists to publish reproducible data. According to Masters, at the time of the article’s publication in 2002, HeLa was still the most widely used human cancer cell line, even though scientists had developed thousands of continuous cell lines from virtually all types of human cancer cells in the late twentieth and early twenty-first centuries. Masters asserts that the importance of the HeLa cell line has grown since its creation, claiming that every year between 1980 and 2000, the number of citations for HeLa on MedLine, a bibliographic database of life sciences and biomedical information, had increased, with four times as many citations in 2000 as in 1980. Masters notes that there are even more publications that use HeLa cells without acknowledgement.

In the third section of the article, “The Bad,” Masters describes the interspecies and intraspecies cross-contamination that occurred in biomedical laboratories worldwide, where scientists found multiple humans’ cells in one cell line. Masters claims that it took more than fifteen years after the distribution of HeLa cells worldwide before the full extent of that dilemma was uncovered. That means for over fifteen years, scientists had been collecting data that was not reproducible, even though they did not realize that. Masters states that reports of widespread cell line mislabeling in laboratories led to the establishment of a bank of authenticated cell lines at the American Type Culture Collection in 1962, eleven years after scientists first created the HeLa cell line.

Continuing in his third section, Masters states that cell researcher Stan Gartler suspected that those authenticated cell lines were mislabeled and were actually more HeLa cells. According to Masters, Gartler used the principle of genetic polymorphism to prove that. Genetic polymorphism, also referred to as biochemical polymorphism, results from variations in genetic material between members of a single species that cause these members to have different forms. An example of genetic polymorphism is how individuals can be grouped into the biological sexes of male, female, or intersex. Individuals of each group, male, female, or intersex, have variations in their genetic material that cause their appearances to vary.

According to Masters, in 1967 Gartler introduced the concept of genetic polymorphism to the study of human cell lines. Masters states that because there can be different forms of proteins and those forms vary across individuals, it is possible to use genetic testing to distinguish between cell lines derived from different individuals of the same species because proteins come from genes. Glucose-6-phosphate dehydrogenase is found in one of two forms in an individual, A or B. According to Masters, the A form is almost exclusively found in individuals of African descent. When Gartler tested those so-called authentic cell lines, they were all found to express the type A form. Masters demonstrates that because the type A form was rare among the general population, which was mostly white at the time of Gartler's research while Lacks was of African descent, Gartler asserted that all those alleged authentic different cell lines were all actually HeLa cells. Therefore, Masters states that though the American Type Culture Collection had been developed to be a repository of authentic cell lines, it was actually providing mislabeled cell lines.

Finally, in the third section, Masters includes a table of better-known HeLa cell cross-contaminants in his article, asserting that though Gartler's finding was true, too many scientists had done research and written grants and publications based on those mislabeled cell lines and were not willing to admit that there was a problem because their results would be void and they would have to retract their findings. In the 1970s, researcher Walter Nelson-Rees developed methods to authenticate cell lines. Masters claims that Nelson-Rees ruthlessly and relentlessly exposed HeLa cross-contaminants.

In the fourth section, "The Ugly," Masters asserts that the scientific community became ignorant, complacent, deceptive, and unchecked regarding their use of cell lines in their research. As of the article's publication date in 2002, Masters estimates that scientists falsely label up to twenty percent of cell lines, primarily due to intraspecies contamination. Masters also asserts that the scientific community has allowed chaos and fraud to persist in research and, as such, scientists continue to use mislabeled cell lines. Masters places partial blame on scientific journals and their editors, which he claims do not take responsibility for the widespread publication of false data. Masters also places blame on certain cell-line banks, which he asserts are aware of the problem but continue to sell cells under false descriptions. Masters ultimately claims that if twenty percent of cell lines are mislabeled, then twenty percent of publications are using false data.

In the final section, "The Future," Masters ends with the claim that HeLa cells are more important today than when Gey first grew them. However, he also states that the HeLa cell line has shown that there are serious consequences when peer review and quality control fail. Such consequences include the potentially invalid experimental results produced by contaminated cell lines.

As of 2021, the article, "HeLa Cells 50 Years On: The Good, The Bad, and The Ugly," has primarily been cited by cancer researchers and those investigating the integrity of biomaterials and data. Researchers Jeffrey L. Furman and Scott Stern cited the article in their American Economic Review article, "Climbing Atop the Shoulders of Giants: The Impact of Institutions on Cumulative Research in 2011." In that article, they discuss the maintenance and integrity of biomaterials and data when those are shared across researchers, claiming it is a central challenge in biomedical research. Some researchers are working to validate cancer cell lines and assess which cell lines should still be used for cancer drug development research.

Scientists and researchers still cite Masters' article when describing the history of HeLa, cross-contamination, and mislabeled cell lines. After he published "HeLa Cells 50 Years On: The Good, The Bad, and The Ugly" in 2002, Masters published two other articles on HeLa cells in 2004 and 2010 in which he asserted that scientists should suspect all cell lines are contaminated with HeLa cells until proven otherwise.

Despite advances in techniques used to authenticate cell lines, there are still mislabeled cell lines that circulate in the scientific community. The article has helped encourage broader awareness of mislabeled cell lines, as well as promoted efforts to improve the peer review and quality control process.

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