MEDICAL RESEARCH

The vaccine chronicles

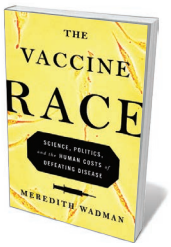
Ewen Callaway extols a study on the creation of a cell line key to combating rubella.

A rare probity permeates Meredith Wadman's *The Vaccine Race*, the riveting story of a human fetal cell line, the scientists who established it and the front lines of vaccine research where it was deployed. In the epilogue, Wadman tracks down 'Mrs X', the Swedish woman whose aborted fetus gave rise to the cell line without her knowledge. Wadman promised never to make her name public or to contact her again.

The book — the first from Wadman, a former *Nature* journalist — invites comparison with Rebecca Skloot's 2007 *The Immortal Life of Henrietta Lacks* (Crown). Skloot also explored the social, ethical and historical legacies of research on human subjects and their discarded tissues. Her book drew much of its power from chronicling the author's relationship with, and advocacy on behalf of, Lacks' family. Wadman stands back from sources and material to guide readers through a narrative that is no less captivating.

The cell line at the centre of *The Vaccine Race*, WI-38, was established in the 1960s by Leonard Hayflick, a driven cell culturist at the independent Wistar Institute in Philadelphia, Pennsylvania. The institute was becoming a global hub in the war against polio and other viruses under its larger-than-life director Hilary Koprowski. Although Koprowski saw cell culturists as "supporting actors" to the institute's star virologists, Hayflick's lab work soon caught his attention.

In the late 1950s, all available lab cultures of human cells were derived from tumours such as the cervical cancer that killed Henrietta Lacks in 1951 and gave rise to her immortal HeLa cells. In search of normal human cells unlikely to be infected with viruses, Hayflick turned to fetuses. (Abortion was then illegal across the United States, but some hospitals occasionally performed 'therapeutic abortions' from which the human fetal cells came.) Hayflick coaxed different bits of fetal tissue — cells from muscles, kidneys, hearts and lungs — to divide in laboratory dishes. Unlike cancer cell lines such as HeLa, which has unstable chromosomes, these cells contained the normal number of chromosomes even after months of dividing in culture. Eventually, however, the cell lines began dying off.



The Vaccine Race: Science, Politics, and the Human Costs of Defeating Disease
MEREDITH WADMAN
Viking: 2017.

Hayflick theorized that healthy cells could undergo only a limited number of cell divisions. That sparked the field of cellular ageing. (Jack Szostak, Elizabeth Blackburn and Carol Greider, who determined aspects of its biological basis in DNA caps called telomeres, won the 2009 medicine Nobel.)

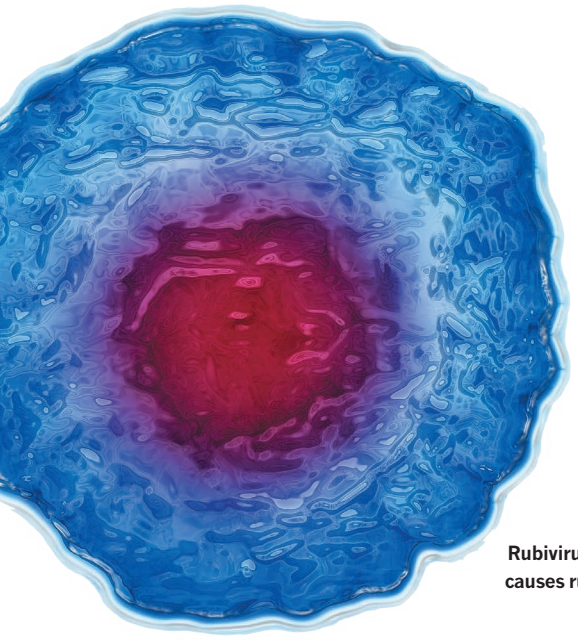
Koprowski soon got other ideas for the fetal cell lines. Hayflick showed that the cells could be infected with human viruses, including polio. That made them an ideal tool for studying infections and producing vaccines — killed or weakened viruses that summon an immune response against a pathogen. The first successful polio vaccine, developed by Jonas Salk in 1952 (T. Tansey *Nature* **520,** 620–621; 2015), had been made by infecting monkey kidney cells with polio, then killing the virus. However, incompletely killed batches of polio vaccine paralysed hundreds of people. Many scientists, including Koprowski, were pursuing a less dangerous, more effective polio vaccine composed of virus weakened after being passed repeatedly through monkey cells. But the discovery that monkey cells can carry hard-to-detect viruses prompted Koprowski to champion Hayflick's human fetal cell lines as vaccine factories.

WI-38 emerged from a collaboration between Hayflick and Swedish physician-scientist Sven Gard. Abortion was legal but restricted in Sweden, and doctors were willing to provide patient medical histories to let regulators gauge whether fetal cells might be predisposed to turn into tumours. In 1962, lung tissue from Mrs X's aborted fetus reached Hayflick; he created hundreds of ampoules of WI-38 cells and froze them in liquid nitrogen. The resulting Wistar polio vaccine found use in Europe. But the cells' biggest success was in heading off rubella. In the 1940s, it had been found that pregnant women who got rubella often gave birth to blind infants; doctors later tied the infection to deafness, heart defects and fatal brain inflammation. There were US epidemics every 6–9 years, and one was on the horizon when Wistar researchers started work on a vaccine in the 1960s.

Here, Wadman turns her attention to vaccinologist Stanley Plotkin. She is at her best in these passages, soberly describing ethically dubious clinical trials in orphans, intellectually disabled children and other vulnerable populations. Plotkin's rubella vaccine was not the first choice of the US government, in large part because of concerns about using a vaccine made from human cells. But it soon became clear that competing vaccines made with animal cells caused worrying side effects and did not lead to long-lasting immunity. In 1978, the United States licensed Plotkin's vaccine.

Hayflick rejoins the narrative in the final section. Wadman's reporting chops shine when she describes the acrimonious and career-crippling legal dispute that emerged between Hayflick and the US government over the ownership and resale of WI-38 cells after he moved to Stanford University, California, in 1968. That clash led him to resign in 1976, and to withdraw from consideration for a job directing the newly established US National Institute on Aging in Bethesda, Maryland. Wadman's retelling does not completely exonerate him. But in 1980, not long after the dispute spilled into the news, the US government passed the Bayh–Dole Act, making it possible for federally funded life scientists to pursue commercial applications for their research, in many cases with financial rewards for them and their universities.

WI-38 cells are still used to make vaccines for rubella and other illnesses. Last year, Wadman filed a freedom of information request to find out how many of them remain in the non-profit tissue repository that holds Hayflick's remaining stocks. Reassuringly, there are still plenty to go around. ■



JAMES CAVALLINI/SPL

Rubivirus, which causes rubella.

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