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The Rise of Research Biobanks

Henrietta Lacks

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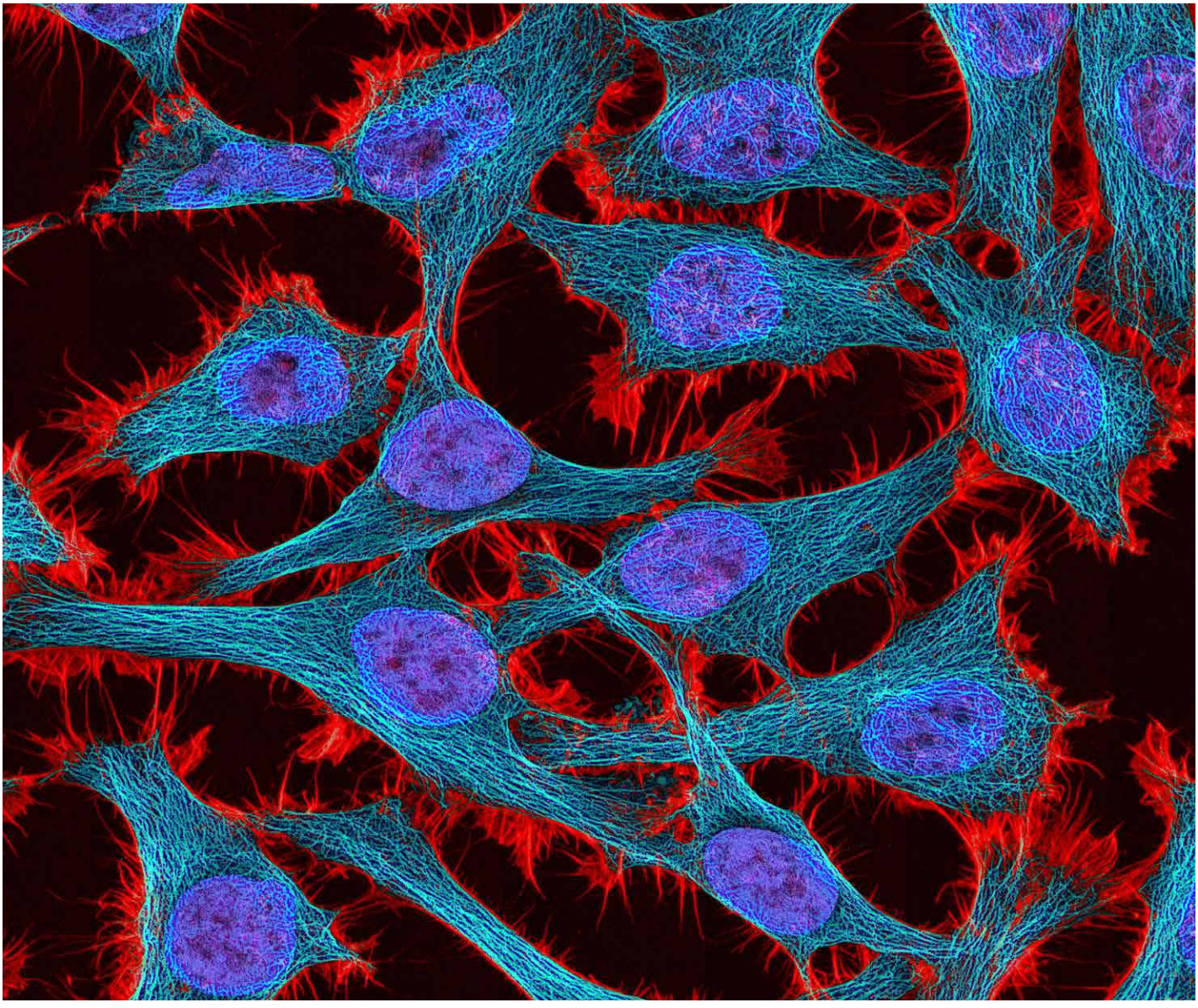
Cover Story



Above: National Center for Microscopy and Imaging Research

The Rise of Research Biobanks

How new technologies are challenging the ethics of patient consent »

> Those most involved in the research – that is, those involved with the collection of samples and the establishment and administration of biobanks – appear to be operating under the belief that the issues associated with the law and public opinion are either settled or manageable within existing frameworks.
>
> *– Timothy Caulfield, Canada Research Chair, Health Law and Policy, and Research Director, Health Law Institute, University of Alberta and Blake Murdoch, Research Associate, Health Law Institute*

In 1951, doctors at Johns Hopkins Hospital in Baltimore, Maryland, took cells from a biopsy of a 31-year-old woman's cervical cancer tumour and gave them to a researcher there without her knowledge or consent. The cells are called HeLa cells, named after the donor Henrietta Lacks who died the same year. As the first cells capable of dividing and surviving in culture indefinitely, HeLa cells launched a medical revolution. Over the decades, HeLa cells have enabled numerous significant medical breakthroughs, including the polio vaccine, cloning, in vitro fertilization, gene mapping, the AIDS cocktail, various chemotherapies and many more.

Henrietta's family never knew what the HeLa cells had been used for or how they were being used in health research until more than 20 years later. Her story captured widespread attention with the publication of Rebecca Skloot's book *The Immortal Life of Henrietta*

Lacks in 2010[1] and the subsequent film adaptation in 2017, highlighting the ethical and policy issues associated with using human biospecimens in health research and the issue of patient consent in particular.[2] HeLa cell lines are still in use today in medical labs across the globe, where scientists are investigating the intricacies of human disease processes, seeking to discover and develop new cures and treatments that may improve patient outcomes. Henrietta's cells have lived outside her body longer than they did inside and there are more HeLa cells living today than she had as an individual when she was alive.[3]

Back in the 1950s, obtaining patient consent for the use of human tissue in health research was not standard practice.[4] In the decades since, different countries have established various rules and regulations to deal with ethics and legality of protecting the rights and interests of biospecimen donors. Emerging trends such as the rise of biobanking and advances in computing power are challenging how to handle patient consent.

Pooling and analyzing vast amounts of biospecimens is an exciting modern method for finding cures and treatments for conditions and diseases that take a massive toll on human health. Advances in genetic, cell-line and tissue research combined with increased capabilities to harness information technology to analyze mountains of data generated by genomics, proteomics, metabolomics and other 'omics studies of biological processes have led to the proliferation of biobanks – repositories where human biological materials are stored and withdrawn for use in research. The biospecimens may be linked to donors' genetic information or other health and personal data.

In a recent review of how patient consent in health research is handled in various countries, two Canadian health law experts, Timothy Caulfield and co-author Blake Murdoch, found that despite the intensified global interest in biobanking, "many profound legal and ethical challenges remain unresolved. Indeed, there continue to be disagreements about how to best obtain consent and the nature of control over donated samples and health information."[5] Caulfield is a Canada Research Chair in Health Law and Policy and Research Director of the Health Law Institute at the University of Alberta and Murdoch is a Research Associate at the Health Law Institute.

Their bottom line: "the international research community has built a massive and diverse research infrastructure on a foundation that has the potential, however slight, to collapse, in bits or all together. Those most involved in the research – that is, those involved with the collection of samples and the establishment and administration of biobanks – appear to be operating under the belief that the issues associated with the law and public opinion are either settled or manageable within existing frameworks."[5]

Caulfield and Murdoch assert that the needs of the research community to produce new insights and treatments are not aligned with the rights of participants and that more robust consent and governance structures are required.[5] The spanner in the works is the increased use of broad consent, where participants sign off at the beginning that their samples can be used for unspecified future research. Broad consent certainly streamlines paperwork and administration for biobanks and ensures participants don't need to respond to continued requests for their consent for new studies over time, but it does not sufficiently address future risks and benefits.

Case in point: In 2013, German scientists at the European Molecular Biology Laboratory (EMBL) sequenced the HeLa genome without the consent of the Lacks family. Technically, consent was not required at that time and a press release from the EMBL asserted that nothing could be inferred about Henrietta's genome or of her descendants from the data generated in the study.[6] But a few scientists elsewhere uploaded the data to a public website called SNPedia that assembled, in a matter of minutes, a report that included personal information about Henrietta and her family that had the potential to reveal their risk of disease.[6]

The report was not disseminated and the scientists removed the information from public view and apologized to the Lacks family. But the controversy illustrated how unforeseen

Timothy Caulfield, Canada Research Chair, Health Law and Policy, and Research Director, Health Law Institute, University of Alberta

Blake Murdoch, Research Associate, Health Law Institute

technological advances could rapidly eclipse consent.[6] Shortly after that, the U.S. National Institutes of Health (NIH) reached an understanding with the family and established a new policy whereby NIH-funded scientists wishing to use the HeLa genome must apply, agree to terms set out in a data use agreement and deposit their data into a single database for future sharing.[4] A committee that includes Lacks family members oversees requests.[7]

In Canada, a policy called the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS) sets out the rules for how health research is handled here. Established in 1998, it is based on the fundamental value of respect for human dignity, expressed through three core principles: respect for persons, concern for welfare and justice. Jointly developed by Canada's three federal research granting agencies – the Canadian Institutes of Health Research (CIHR), the Natural Sciences and Engineering Research Council of Canada and the Social Sciences and Humanities Research Council of Canada – the TCPS is not a law or a regulation passed by the government. It is a policy that research institutions and researchers must adhere to as a condition of agency funding. The TCPS is an evolving document that undergoes review cycles and modifications over time. The second edition, the TCPS 2, has been in place since 2014. It is currently under review, with revisions expected in 2018.

One of the responsibilities of Susan Zimmerman, Executive Director of the Secretariat for Responsible Conduct of Research at the Canadian Institute of Health Resources (CIHR), is overseeing revisions and updates to the TCPS on behalf of the three agencies. "We think that the TCPS is the best of both worlds. It's enforceable, and because it's not a law or regulation,

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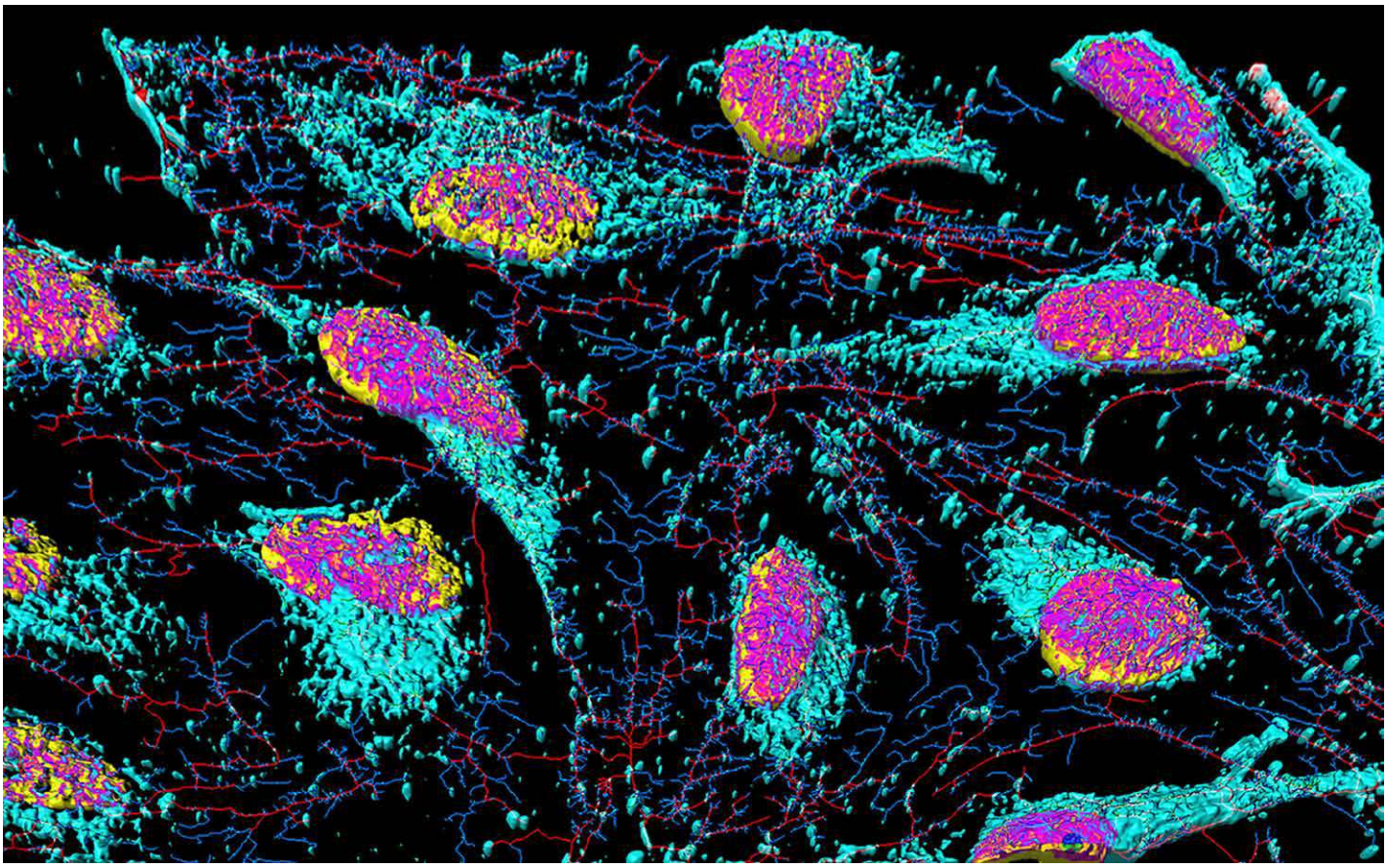

HeLa cervical cancer cells

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> *– Susan Zimmerman, Executive Director of the Secretariat for Responsible Conduct of Research at the Canadian Institute of Health Resources (CIHR)*

we can respond to rapid changes in the research sector and modify it," she says. "Researchers and research institutions take it seriously because their funding depends on compliance with agency policies. A complaint about a breach can trigger an investigation; funding agencies can impose a range of recourses, depending on the severity of the breach. Researchers can be admonished in a letter to their institution or have their funding revoked for up to five years, which can have a strong impact on their career as well as the reputation of the research institution."

In the TCPS 2, Chapter 3: The Consent Process states that patient consent must adhere to all three of these core principles: it must be voluntary, informed and ongoing. Voluntariness means that participants must be able to decide freely to participate or not and they can withdraw their consent and request the withdrawal of their data or human biological materials at any time, according to their values, preferences and wishes.[8] Informed consent means that participants are provided with full disclosure of all information necessary for making an informed decision to participate in a research project. For example, this generally involves including information about the research purpose, foreseeable risks and benefits, what materials or information will be collected and how it will be used, confirmation that their participation is voluntary and can be withdrawn at any time, how possible commercialization of research findings will be handled, how results will be disseminated, any payments and reimbursements, compensation for injuries, contact information, and in the case of clinical trials, information regarding when studies may be stopped or participants may be removed. Ongoing consent means that the consent is maintained throughout the research project: researchers have an ongoing duty to inform participants about any changes that may impact risks and benefits, ethical implications, or factors relevant to the circumstances of individual participants.[8]

The practice of de-identifying biospecimens has become a more common solution globally; however, de-identification is not a proxy for appropriate consent, says Zimmerman. De-identification addresses anonymity and privacy, but it does not adhere to the required principles for consent to be voluntary, informed and ongoing. As technology evolves and databases proliferate, privacy risks increase. As well, participants may find it objectionable for their materials or information to be used in subsequent research. For example, an individual may not want to participate in a follow-up study that links women of a certain age and income bracket in a particular neighborhood with a higher risk of a stigmatized condition like alcoholism.

Recognizing the rise of biobanking in Canada and how new technologies are allowing researchers to link information and perform an increasing number of projects with biospecimens, the Tri-Council's Panel on Research Ethics (PRE) recently created the Cell Line Advisory Subcommittee (CLAS). The CLAS is providing input to the TCPS 2 on

Henrietta Lacks' cervical cancer cells were donated by Johns Hopkins Hospital, to a researcher, without her knowledge or consent.
Photo courtesy of the Lacks family.

A BIOBANK EXAMPLE

Statistics Canada's biobank integrated within the Canadian Health Measures Survey stores DNA, whole blood, plasma, serum and urine biospecimens collected from more than 22,000 Canadians at the National Microbiology Laboratory in Winnipeg.

Read how researchers apply to access biospecimens for health research and how survey respondents are informed and can withdraw their biospecimens at **www.statcan.gc.ca/eng/help/microdata/biobank.**

Photo courtesy of the Public Health Agency of Canada

whether research involving de-identified human cells and cell lines from established biobanks need to undergo subsequent review by research ethics boards as new projects arise.

"The CLAS has made some recommendations that are focused on ensuring the facilitation of research using cells and cell lines," says Zimmerman. "The feedback we're getting from researchers are very appreciative of our efforts to clarify the guidance in this area. We don't want people to have to go through pointless probes of ethics reviews, but we do want them to be meaningful and ensure that not only are the human biological materials de-identified to protect the privacy of donors but also that there was some consent for their use." Consultations about proposed revisions affecting consent for cells and cell lines closed on January 5, 2018 and final recommendations will be put into place several months later. One recommendation is that de-identified cells or cell lines obtained from biobanks that can substantiate the ethical provenance of the samples will be exempt from further ethics reviews if the proposed research will not lead to re-identification.

The rise of biobanking has dramatically altered the ethical landscape around patient consent in health research. Canada's evolving TCPS framework sets Canada well above the global health research community for balancing the welfare, respect and rights of biospecimen donors with increasing quests by scientists to find new cures and treatments.

Would Lacks have granted consent if she had been asked back in 1951? We'll never know. But we can be sure that she would never have anticipated that her cells would enable so many breakthroughs and enlighten ethics discussions about patient consent today.

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JANE LANGILLE
Health and Medical Writer
Special to *CJMLS*

HELPFUL RESOURCES

The Tri-Council Policy Statement 2 (2014), available at www.pre.ethics.gc.ca. Refer to:

- Chapter 3: The Consent Process
- Chapter 12: Human Biological Materials Including Materials Related to Human Reproduction

CSMLS Code of Ethics, available at **www.csmls.org**
CSMLS Code of Professional Conduct, available at **www.csmls.org**

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