



Examining the Immortal Legacy of HeLa

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Disclosures

- I have no relevant commercial financial disclosures
- I am a gynecologic oncologist
- I have used the HeLa cell line in research

The Problem of Human Disease

- Cancer
- Infection
- Autoimmune disorders
- Neurologic degeneration
- Cell biology
- Human reproduction
- Aging
- Radiation/toxin research

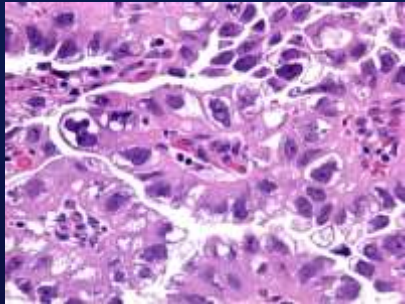
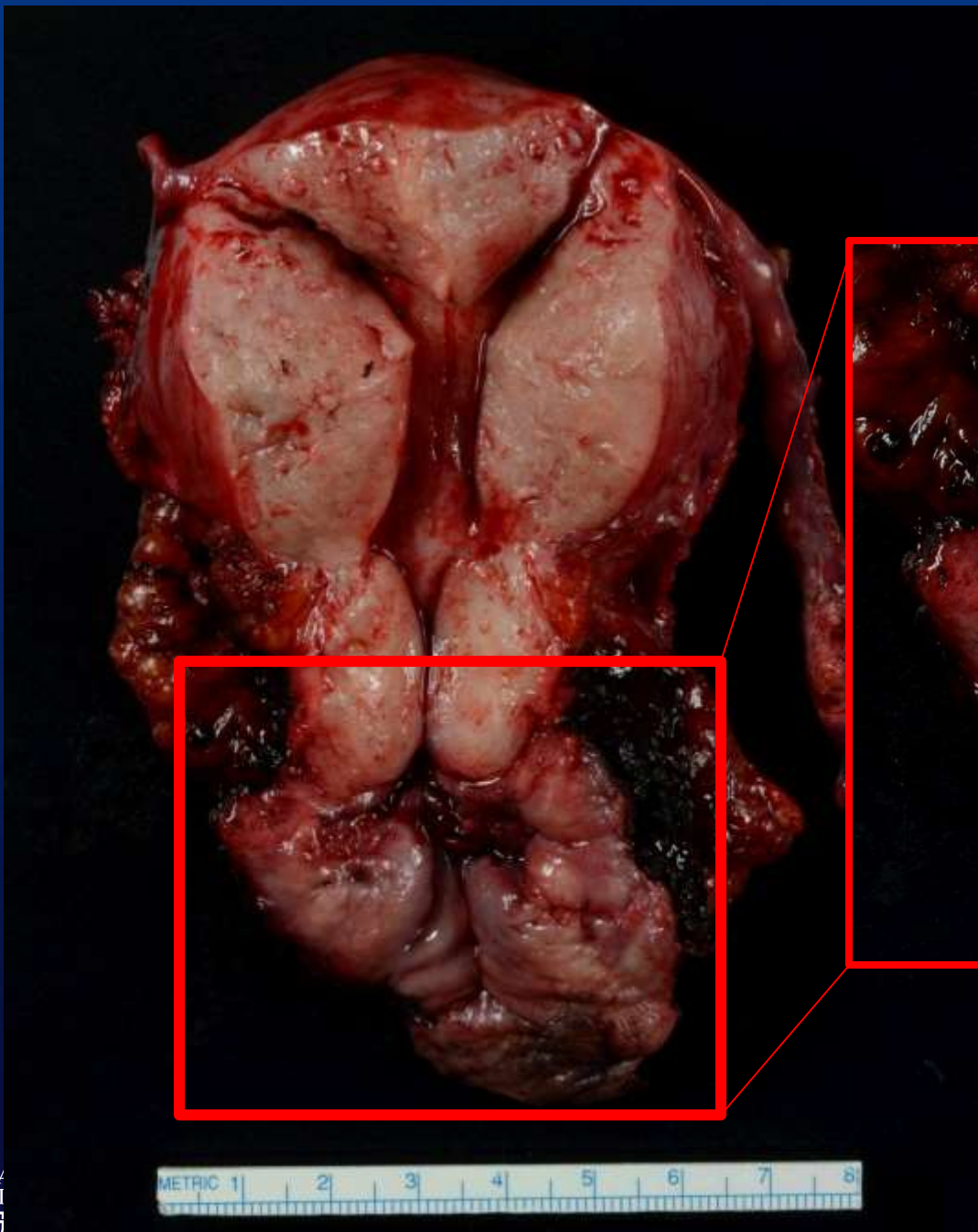




Who was Henrietta Lacks?

- 31 year-old African-American woman
- Born in Roanoke, VA (Aug 1, 1920)
Died in Baltimore, MD (Oct 4, 1951)
- 5 feet tall
- Mother to 5 children
- Tobacco farmer
- Diagnosed with an aggressive locally-advanced cervical cancer in 1951—died 8 months later





Henrietta Lacks' Cervical Cancer

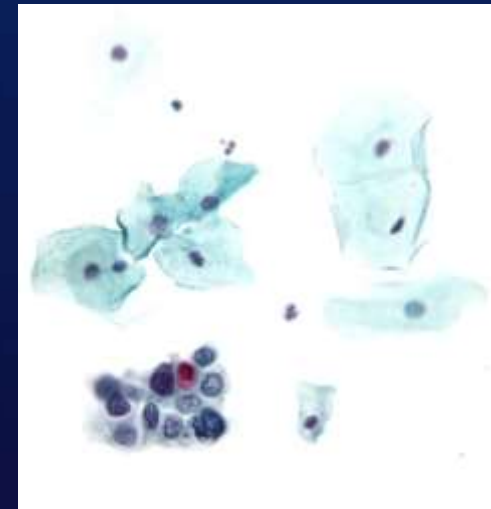
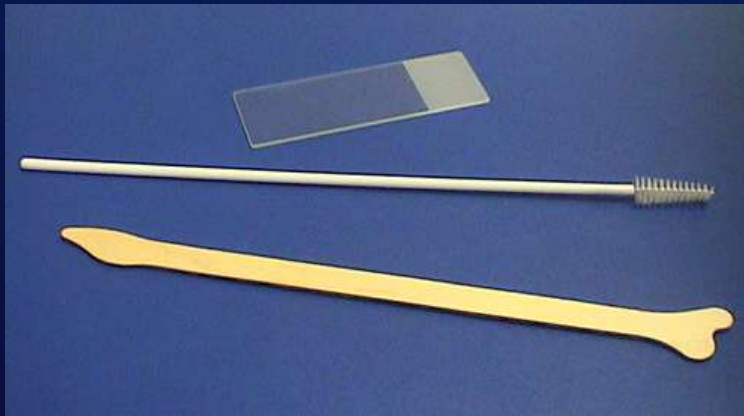
- Aggressive + large → Exam showed a normal cervix 3 months prior to diagnosis
- Initial diagnosis: Portion of tumor removed as a biopsy
- Treatment → Radiation
 - Consent for treatment signed
 - 2 “dime-sized” pieces of tumor shaved off before radiation
 - Given to Dr. George Otto Gey → History

But First--Why Didn't Henrietta Lacks Have Cervical Cancer Screening?



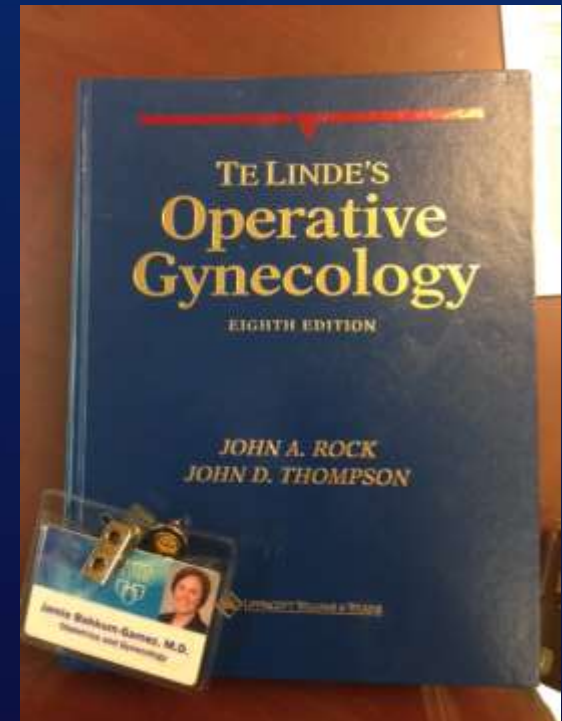
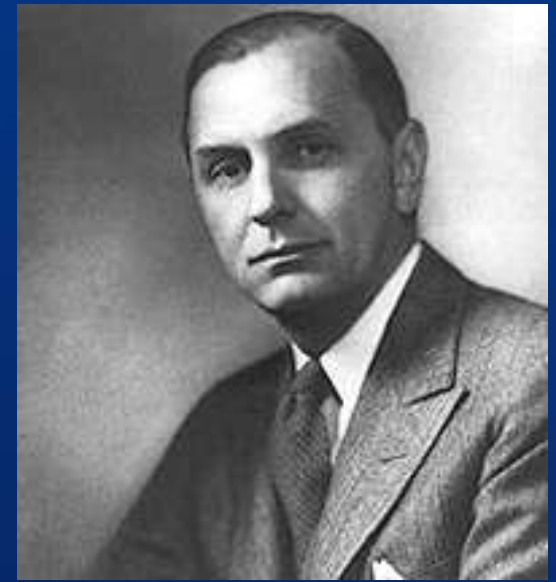
Dr. George Papanicolaou

- Pap smear
 - Concept—1929
 - Published—1941
 - Henrietta Lacks diagnosed—1951
 - Deaths in the US from cervical cancer decreased by 75% in the last 50 years



Richard TeLinde, MD

- Johns Hopkins (1930-1960)
- Shaped contemporary Gyn Onc as a practice
- Life's work to decrease death from GYN cancer, especially cervical cancer
- Practiced in an era of common practice for physicians to use patients for research without their knowledge
- Justified by free care in indigent populations



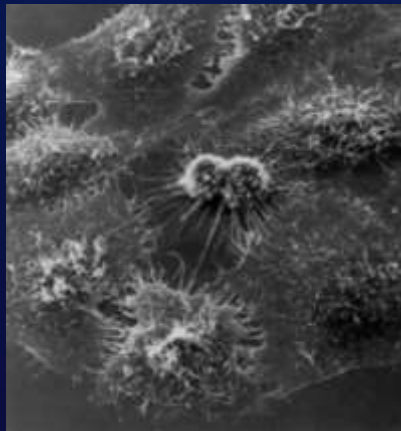
George Otto Gey, MD

- Cell biologist, cancer and virus researcher
- Johns Hopkins University (1933-1970)
- Life's work to generate human cell lines to cure cancer
- 1941 – NIH successfully cultured mammalian cells in vitro (mouse)
- Human cell cultures died quickly
- Hundreds of failed attempts with human tissue...Until HeLa



HeLa Cells are Uniquely Virulent

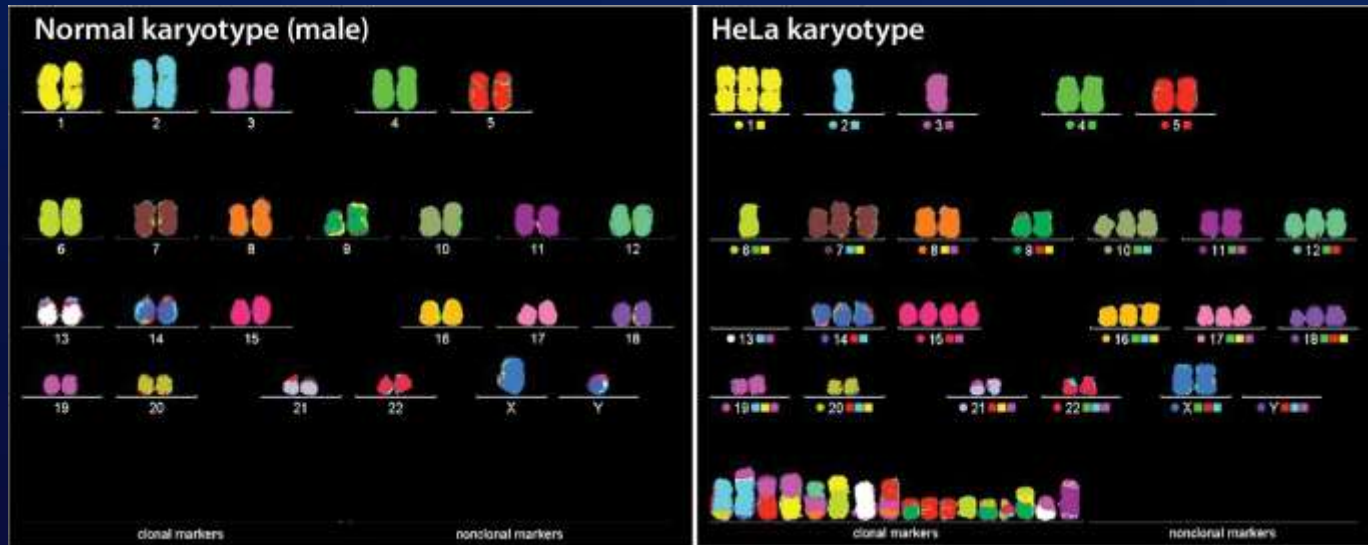
- Did not need glass surface for growth
- Could grow in constantly-stirred media in a roller drum
- Easily transferred on hands and unwashed pipettes
- Could float on dust particles...?
- Shared widely with researchers all over the world



First photomicrograph of HeLa; taken by Dr. Gey

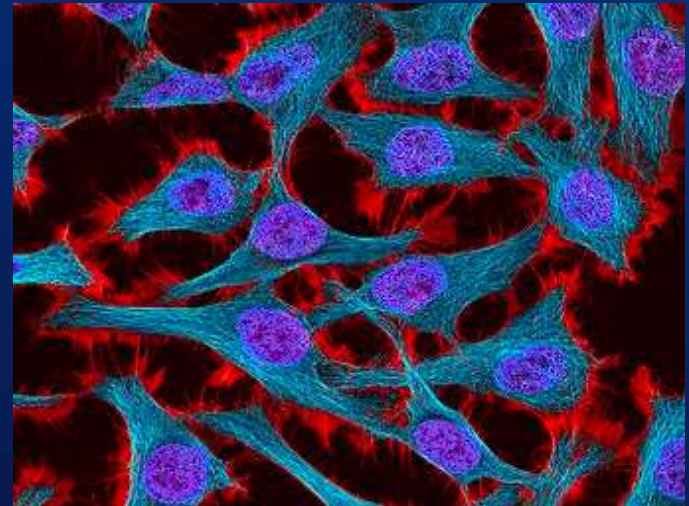
What was Special about Henrietta Lacks' Cervical Cancer Cells?

- HeLa
 - Human papilloma virus (HPV) 18+
 - Virulent growth; cell doubling in 20-24 hrs
 - Grows well with minimal nutritional support
 - 76-80 chromosomes; (normal=46; up to 5 extra copies of portions of some chromosomes in HeLa)



Since 1951, What Has HeLa Accomplished?

- >70,000 peer-reviewed scientific research publications
- Broad fields
- Biotech development and revenue immeasurable



- 32,755 publications on misidentified cell lines
- Cited by ~500,000 subsequent publications

HeLa May Ultimately Eradicate Cervical Cancer

- HPV 18 discovered in 1984 using HeLa cells
- Knowledge used to develop HPV vaccines
- First vaccine FDA-approved 2006 (4-valent)
- Nobel prize 2008
- 9-valent HPV vaccine FDA-approved Dec 2014
- Impact of vaccine not yet seen on cervical cancer death rate

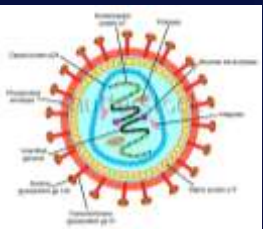


Dr. Harald zur Hausen

What Other Medical Successes Did HeLa Cells Contribute to?



- Earliest work toward success of the Human Genome Project (1960s)
- Development of the field of virology
 - HIV, herpes, Zika, measles, mumps, influenza
 - Discovery of CD4 as a receptor for HIV
 - Development of HIV drugs
 - Zika cannot multiply in HeLa cells
--Potential to aid in vaccine or therapy development



<https://www.statnews.com/2017/04/14/henrietta-lacks-hela-cells-science/>



What Other Medical Successes Did HeLa Cells Contribute to (cont)?

- Led to first clone of a human cell
- Discovery that humans have 46 chromosomes
- In vitro fertilization (IVF) development
- Discovery of how cells age and telomerase
- Contributed to breakthroughs in the study of leukemia, hemophilia, Parkinson's, several genetic diagnoses, radiation and other toxins



One of the Earliest HeLa Successes— Polio Vaccine

- 1930s-40s—Early vaccine development, paralysis and death in unacceptable #s of vaccinated children
- Vaccine testing in primates—expensive, paralysis and death also common
- Cell culture—ideal cell for poliovirus vaccine testing: Rhesus monkey cells
 - Limitation: needed large volume of cells—limitation
 - 1948—poliovirus shown to infect human cell culture



One of the Earliest HeLa Successes— Polio Vaccine

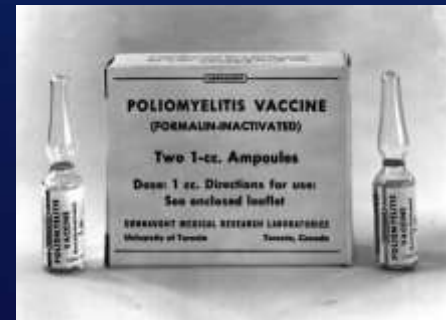
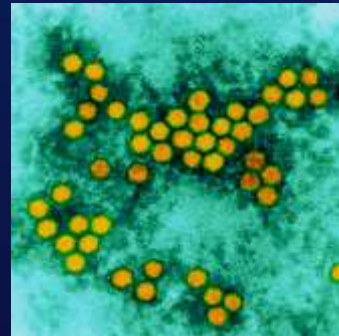
- 1951—Poliovirus easily infected HeLa
- 1952—Tuskegee University Carver Research Foundation building selected as HeLa cell culture factory site
- 1953—HeLa cultures established at Tuskegee and replaced primates in early polio vaccine development



Dr. Jonas Salk

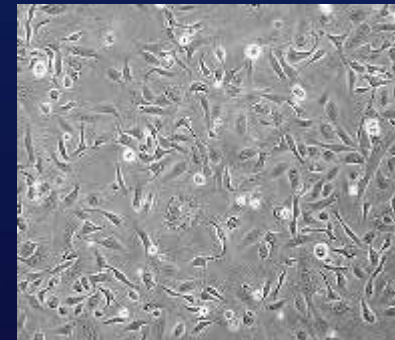
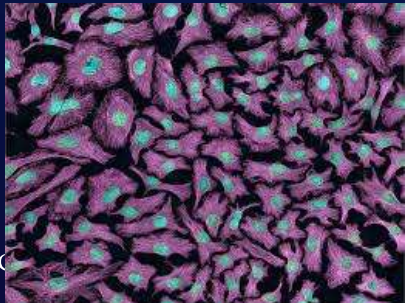


Dr. Albert Sabin

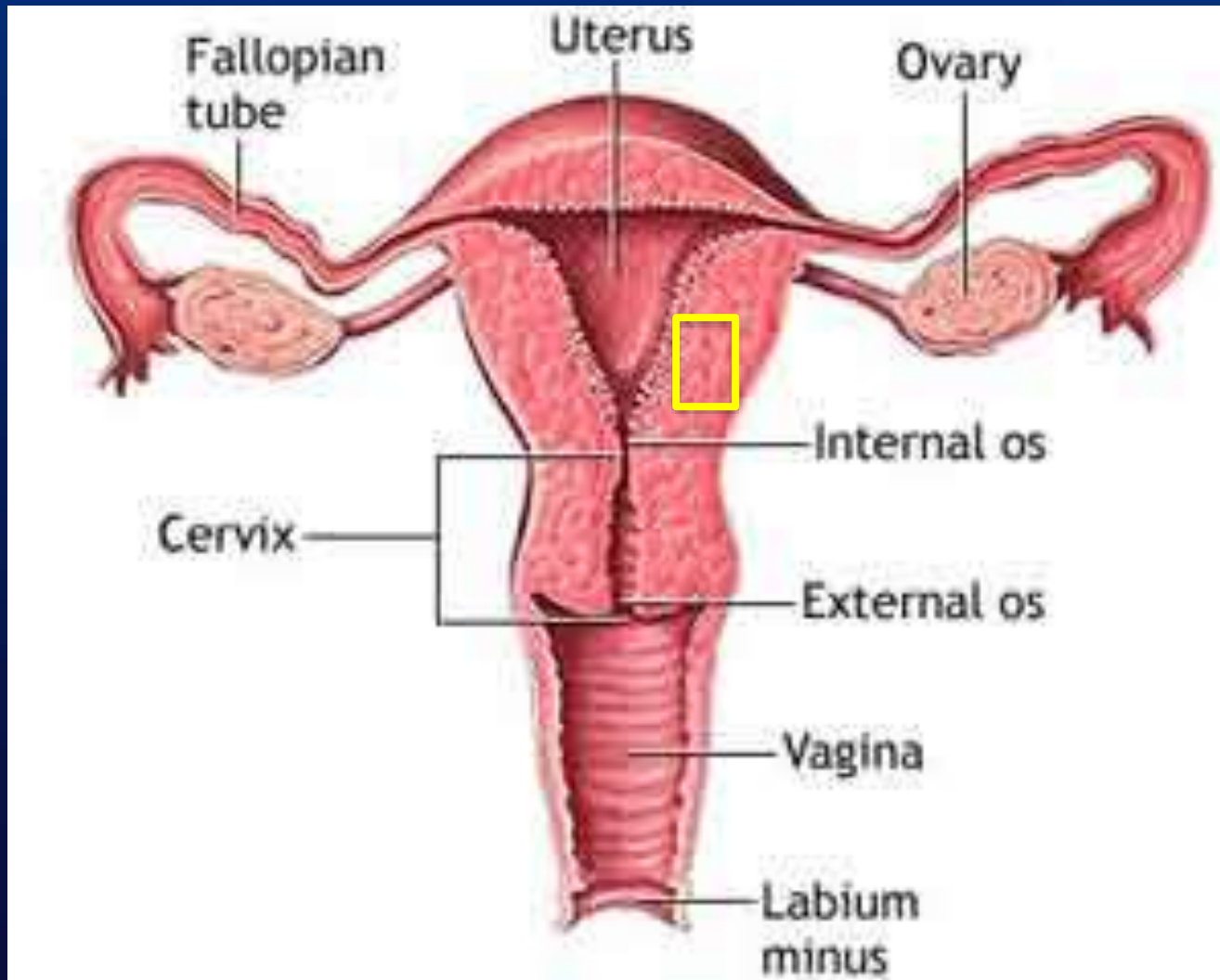


When Did I First Meet HeLa?

- 2003
 - Second year of OB/GYN residency
 - Basic science research
 - Studying expression of a MIS type II receptor in ovarian cancer cell lines
 - HeLa cells easiest to grow—“Cell Culture 101”
 - Post-It note from prior lab bench occupant had the name “*Henrietta Lacks*” written out



My research required benign tissue as well



2003, Mayo Clinic

- In 2003, Mayo had a “blanket IRB” for surgical waste tissue
- Mayo stopped doing this ~10 years ago
- Why?
 - It didn't protect our human subjects adequately
- Today, all research tissue collected from patients at the time of surgery is done so with their signed consent

An Evolution of Informed Consent: How Has *OUR* Protection as Patients and Human Subjects Evolved?



Events of the 20th Century that underscored the need for human subject protection



1943—Dr. Josef Mengele begins human experiments at Auschwitz

1945 — WWII ends

Nov 1945 — Nuremberg Trials

Oct 1946— Doctors' Trials

1948— Nuremberg Code

1951 — HeLa cultured

1954 — Injected into cancer patients

1956 — Injected into prisoners

1963 — Injected into healthy women



10 Principles of the Nuremberg Code (1948)

1. Voluntary consent of human subjects
2. Study should yield fruitful results for the good of society and not obtainable in any other way
3. Prior animal experimentation results
4. Avoid unnecessary physical and mental suffering
5. No experiment where death or disabling injury is expected to occur
6. Degree of risk does not exceed that of the humanitarian importance of the study question

10 Principles of the Nuremberg Code (cont)

7. Proper protection against even remote possibility of injury, disability, or death
8. Study should only be conducted by scientifically qualified persons
9. Human subject has the right to quit the study at any time
10. Scientist in charge of the study must be prepared to end the study at any stage if there is probable cause to believe the study will result in injury, disability, or death to the human subject.

Events of the 20th Century that underscored the need for human subject protection



1932—Tuskegee syphilis experiment begins

1943—Dr. Josef Mengele begins human experiments at Auschwitz

1945 — WWII ends

Nov 1945 — Nuremberg Trials

Oct 1946— Doctors' Trials

1948— Nuremberg Code

1947—Penicillin standard of care for syphilis

1951 — HeLa cultured

1954 — Injected into cancer patients

1956 — Injected into prisoners

1963 — Injected into healthy GYN patient

1972—Tuskegee syphilis experiment ends

1979—Belmont Report



Belmont Report – Ethical Principles and Guidelines for Research Involving Human Subjects (1979)

Written by National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research

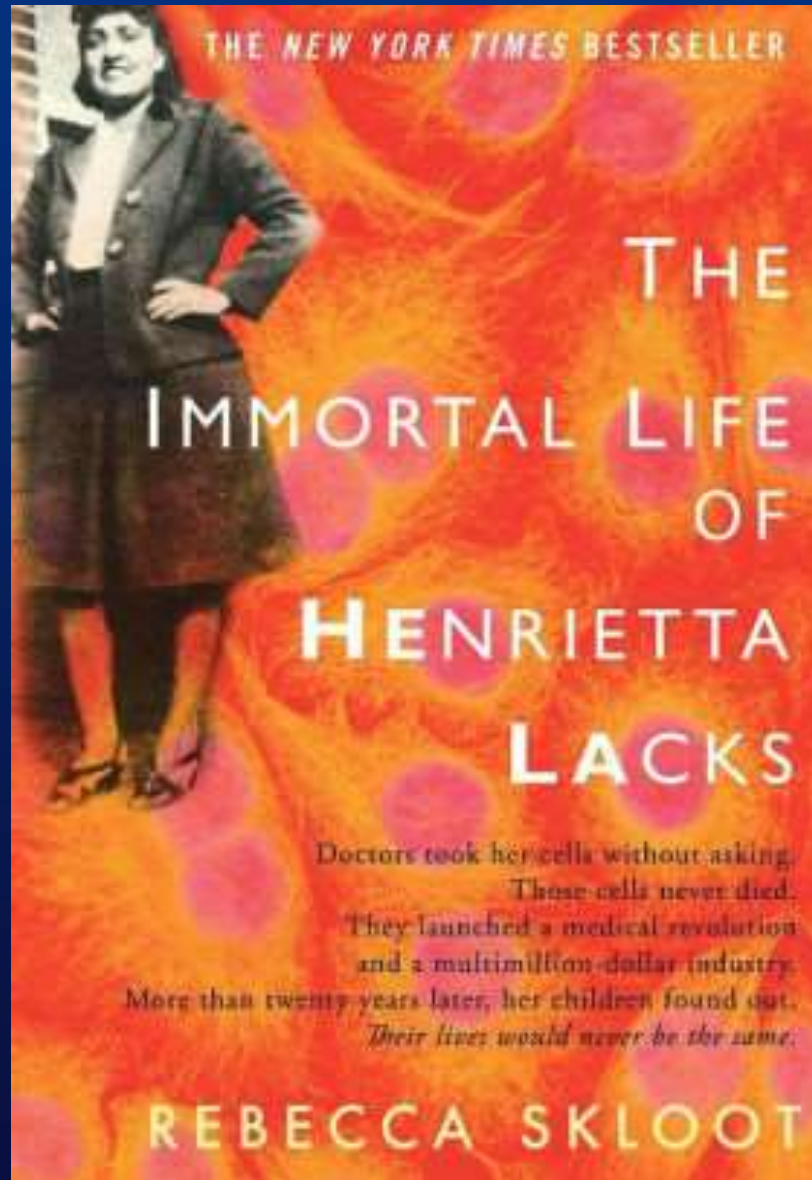
1. Boundaries between Practice and Research
2. Basic Ethical Principles
 1. Respect for Persons
 2. Beneficence
 3. Justice
3. Applications
 1. Informed Consent
 2. Assessment of Risk and Benefits
 3. Selection of Subjects



45 CFR 46, Subpart A: Common Rule—1991

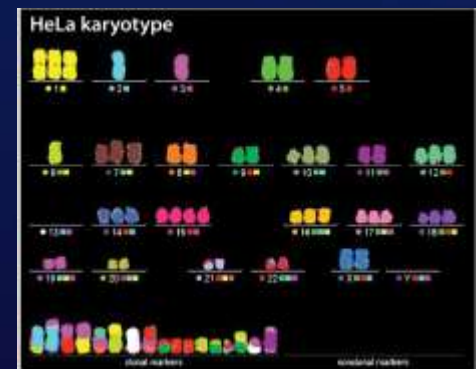
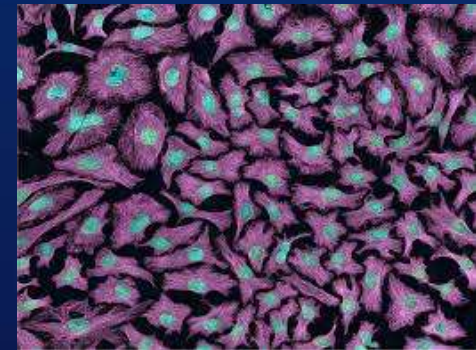
- Federal Policy for the Protection of Human Subjects
- Response to revelations of extreme research abuse of vulnerable populations
- Aim to protect against physical harm
- *Human subject*: living individual about whom an investigator obtains
 - A) data through intervention or interaction with the individual or
 - B) **identifiable private information**
- Guides informed consent, IRB-approval

2010



HeLa 2013

- HeLa genome sequenced and published in 2013
 - March—European Molecular Biology Laboratory
 - August—University of Washington
- Sequence publication routinely required by publishing journals
 - Enhances replicability of results
- Identifiable data:
 - Link to subject
 - Lacks' family genome within the sequence

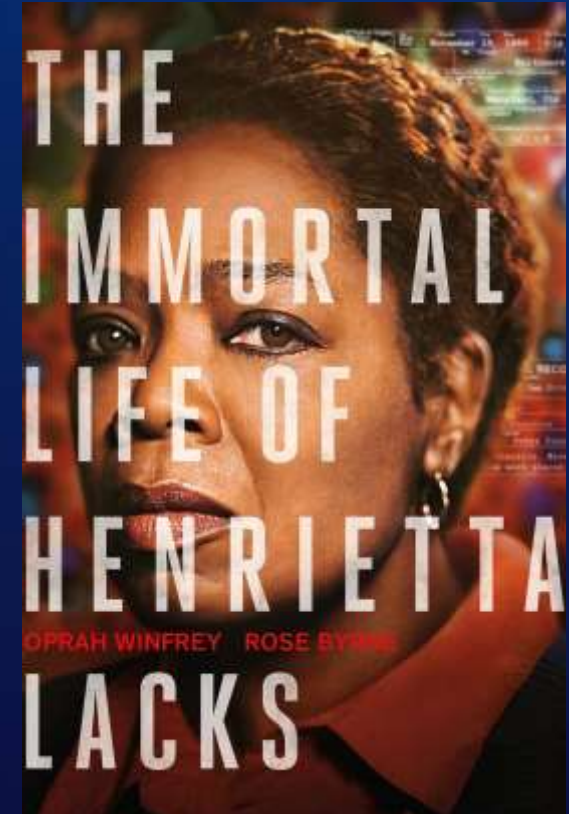


National Institutes of Health (NIH) Response and Intervention

- HeLa genome published without Lacks' family knowledge—quickly removed from public access
- HeLa Genome Data Use Agreement established—August 7, 2013
- The HeLa Genome Data Access Working Group of the Advisory Committee to the Director (ACD)
 - Reviews requests from research community for access to HeLa datasets
 - ACD makes recommendations to NIH Director
 - NIH Director decides whether access granted
 - **2 members of Lacks family on the ACD**

Henrietta Lacks' Exceptional Story

- Rare that N=1 makes such an impact
- Generated public dialogue
- In turn, federal dialogue
- And further federal response in 2015



Common Rule (1991)—Evolution of the Human Subject

- Biospecimens (tissue, blood, etc) can be determined to not involve human subjects *if* collected for:
 - Indications other than proposed research (clinical care, prior trial to which patient consented) *and*
 - De-identified
- Identifiability pivotal → **DNA data cannot truly be anonymized**
- Sept 2015: Notice of proposed rulemaking (NPRM) to overhaul the Common Rule

2015 Overhaul of Common Rule

- Why?
 - Changing research landscape
 - Volume and diversity of studies
 - Analytic sophistication
 - Growing use and global sharing of massive electronic genomic datasets
 - It is possible to discover the identities of individuals whose genomic data had otherwise been considered de-identified
- Revised Common Rule
 - Published in Federal Register Jan 19, 2017
 - Went into effect July 19, 2018



In Conclusion

- Henrietta Lacks made history on levels that transcended her consent for cancer treatment
- HeLa cells have impacted the study and cure of human diseases in immeasurable ways
- The definition and protection of human subjects is at the core of ethical human research
- Dialogue and evolution of the Human Subject and Informed Consent will continue

Thank You

