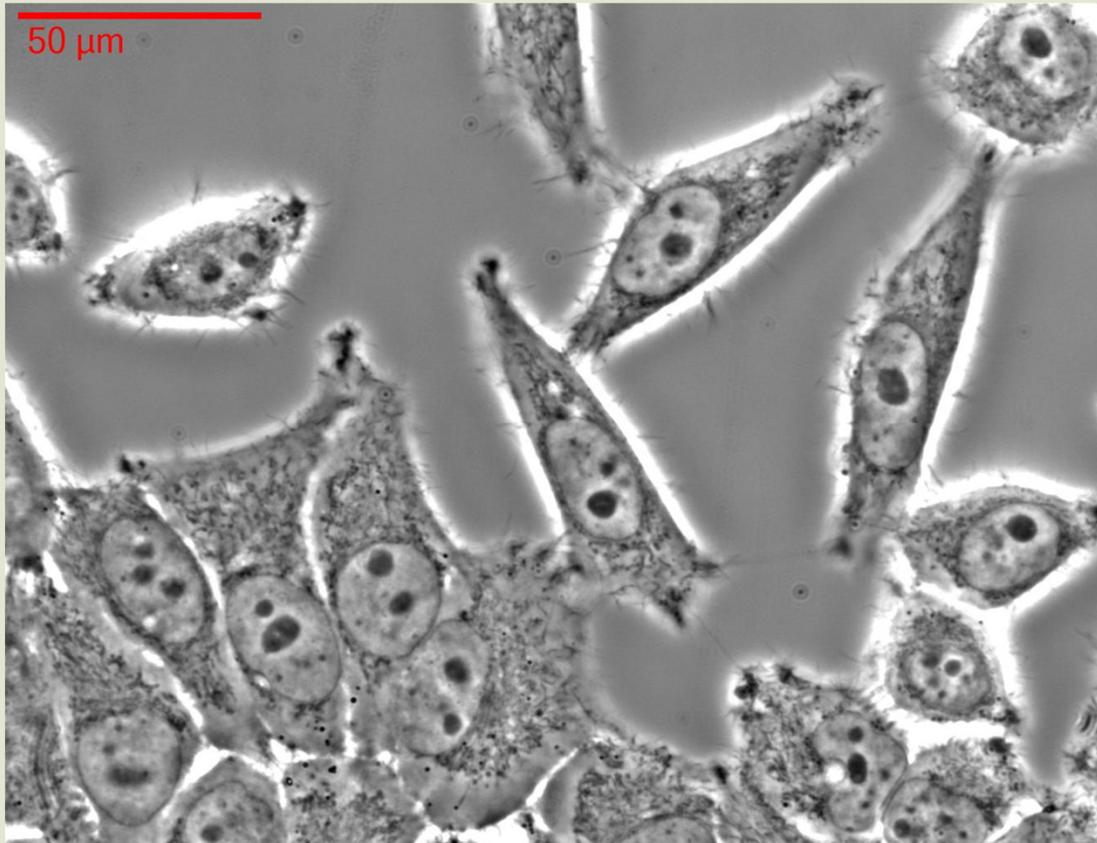


HeLa: Immortal Cells, Enduring Questions

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A HeLa cell is a type of cell from the first immortal human cell line grown in culture

- I. What is cell culture?
- II. Where did HeLa cells come from?
- III. Why are they so important?

cell culture: the maintenance and growth of the cells of multicellular organisms *outside the body* in specially designed containers and under precise conditions.



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Many types of studies are performed on cells in culture

- basic research on cell function
- basic research on gene function
- production of biological products (hormones, proteins, antibodies)
- testing of drugs, vaccines, chemical toxicity
- tissue engineering
- chromosomal or genetic analysis

Different types of cell culture allow scientists to explore different research questions

1. Primary cells

- Explanted directly from living tissue
- May be composed of different cell types
- Are similar to the same cells *in vivo*
- Divide/grow for a limited time and then senesce (Hayflick limit)

2. Immortal cell lines

- Derived from cancerous tumors or cells transformed *in vitro*
- Divide/grow indefinitely
- Are “abnormal” and differ from cells *in vivo*
- Allow researchers worldwide to use the same cells at the same time

Prior to the 1950s, scientists could not maintain human cells in culture for more than a few days

- optimum media conditions were unclear
- contamination was a problem



.....and then came
Henrietta Lacks and HeLa cells

Key players in the discovery of HeLa cells, the first immortal human cell line



Henrietta Lacks
(August 1, 1920 – October 4, 1951)

- January 1951 went to Johns Hopkins Hospital for treatment of a pain in her “womb”
- was diagnosed with “epidermoid carcinoma of the cervix, Stage I”
- no cancer was apparent just 3 months earlier

Key players in the discovery of HeLa cells



Richard W. TeLinde (1894 - 1989)

- interested in studying the progression of cervical cancer (carcinoma *in situ* vs. invasive carcinoma)



George Gey (1899 - 1970)

- spent decades trying to culture human cells

By 1952, HeLa cells were travelling by planes, trains, and automobiles (and pack mule) all over the world



- HeLa cells eventually even went into space

Technicians inspecting HeLa cells for shipment from the Tuskegee Institute



Within a few years companies began selling HeLa cells and the media required to grow them

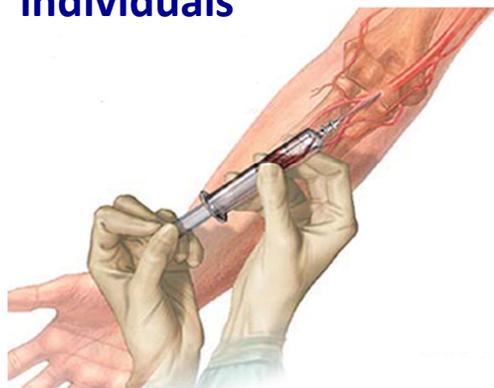
- led to standardization and optimization of cell culture
- allowed scientists quick and cheap access to HeLa cells
- launched the cell culture industry (today a multibillion dollar business)



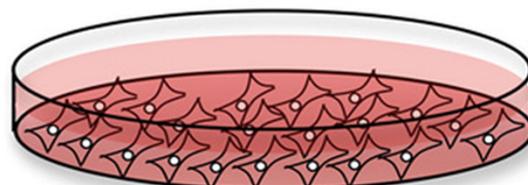
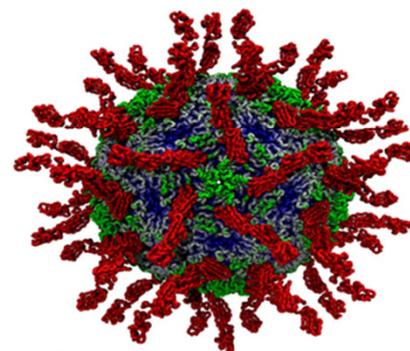
HeLa's first job: testing the polio vaccine (1952)

Neutralization test for vaccine efficacy

Blood samples from immunized individuals



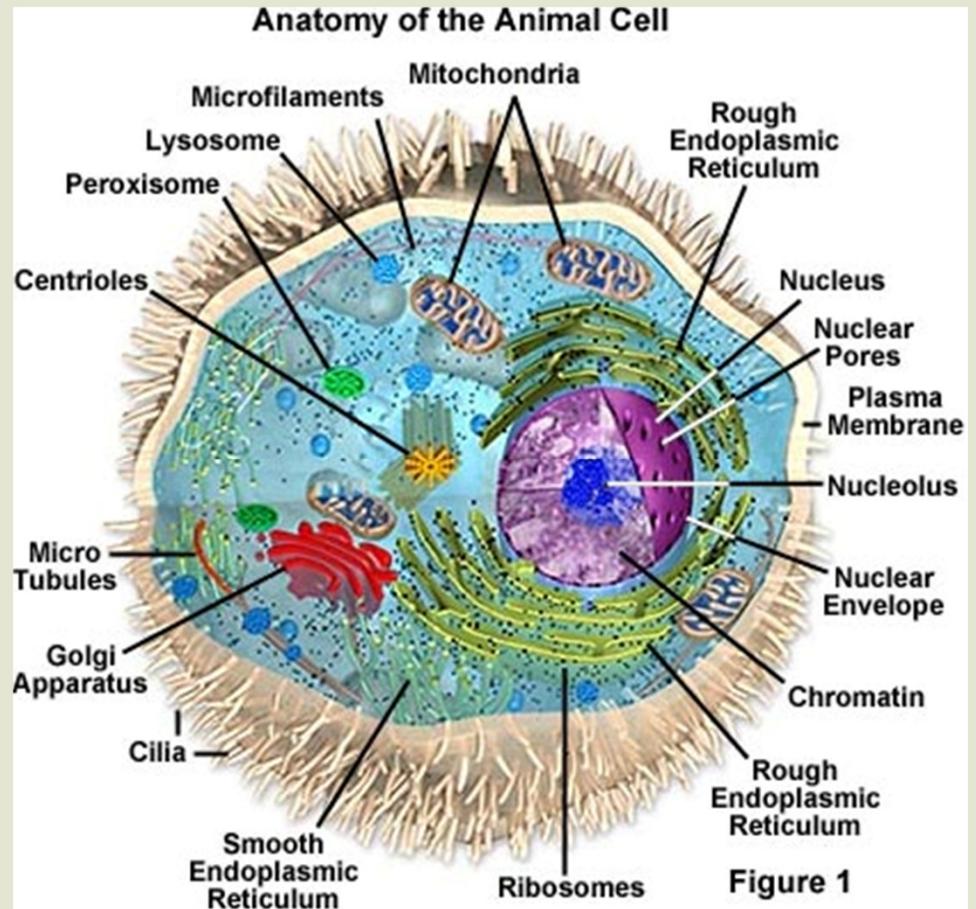
Live polio virus



HeLa cells

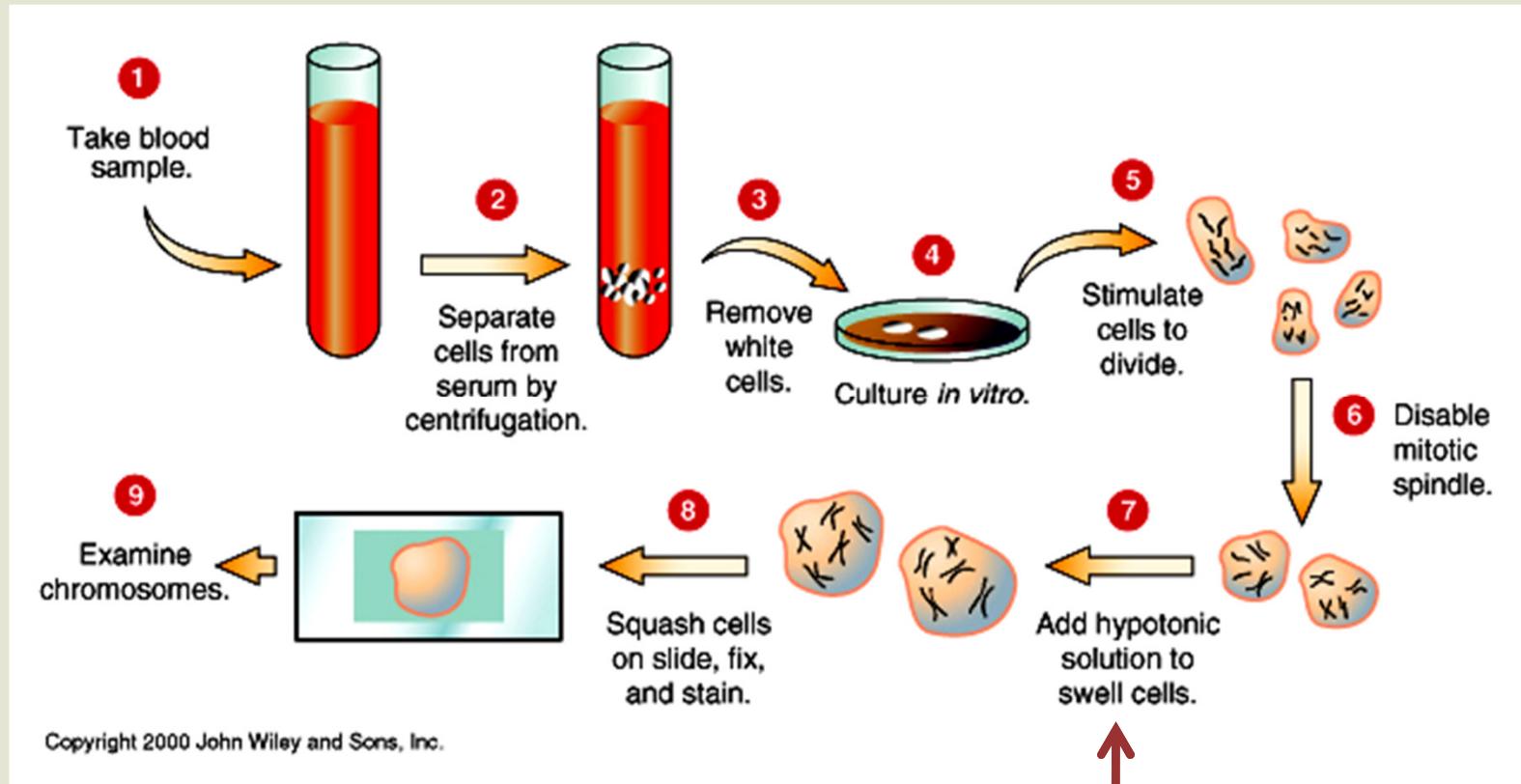
Much of our understanding of basic cell physiology and cancer biology is due to HeLa cell research

- many Nobel prizes have been awarded for research involving HeLa cells (5 since 2001)
 - telomerase activity
 - cell cycle regulation
 - protein transport
 - cell division
 - cell adhesion
 - signal transduction
 - apoptosis
 - virology



A lab accident using HeLa cells led to the discovery that normal human cells have 46 chromosomes

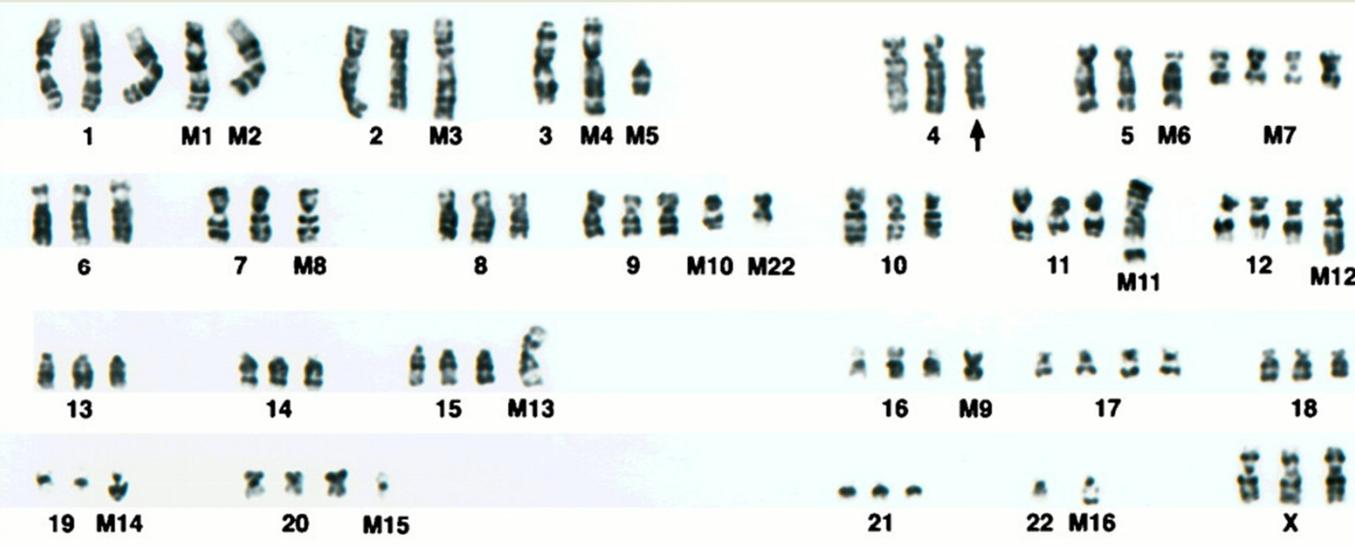
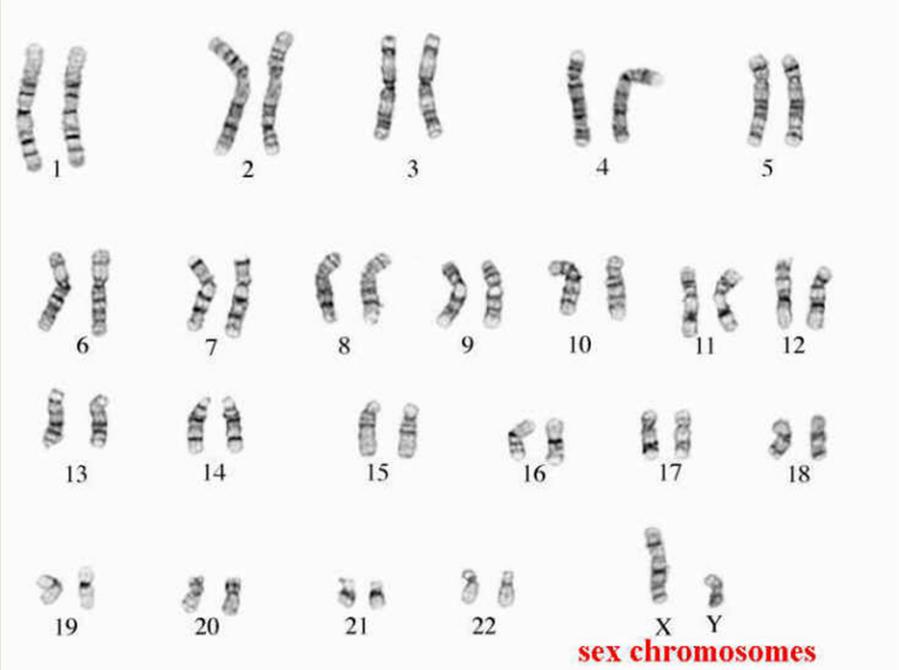
Karyotyping technique



T.C. Hsu (1952)

The scientific advances made possible by HeLa cells enabled scientists to understand their unusual properties

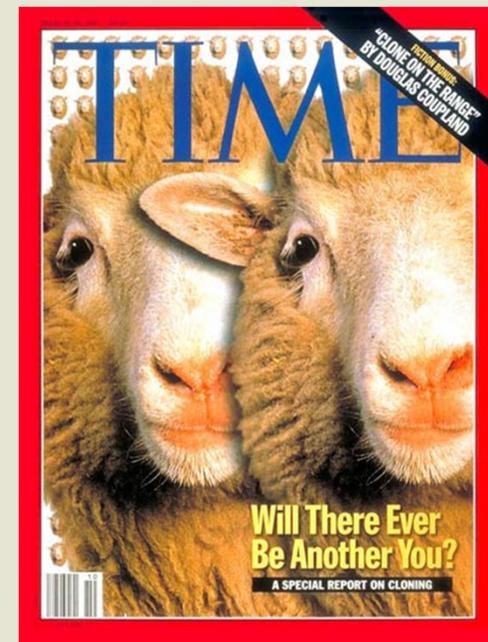
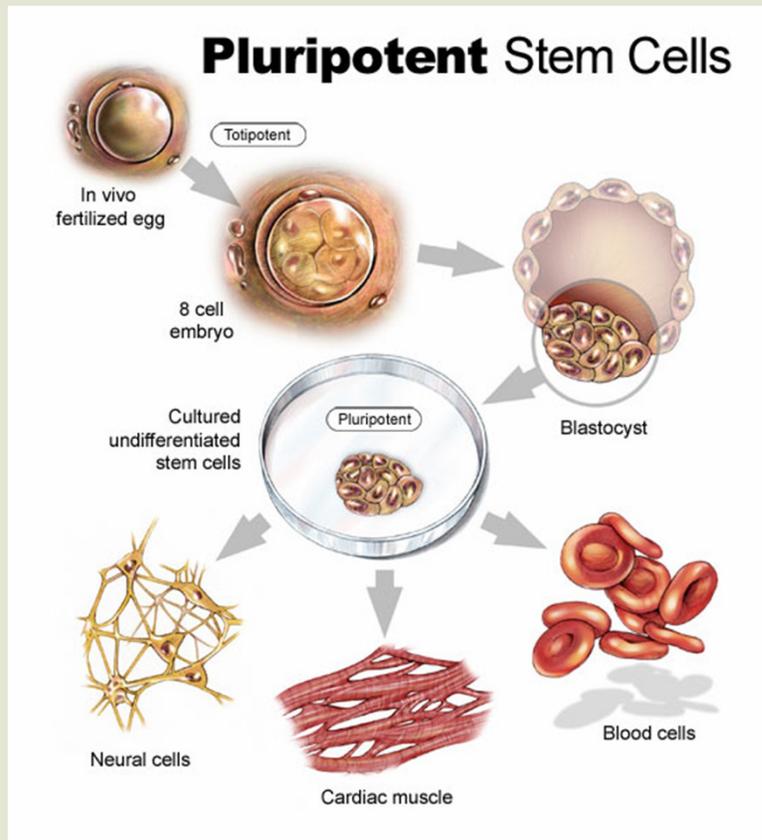
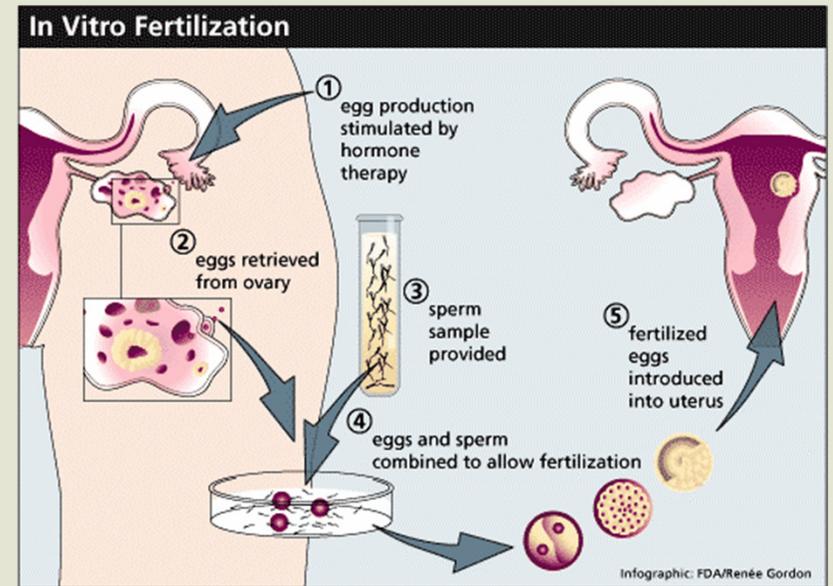
normal human cell



HeLa cell

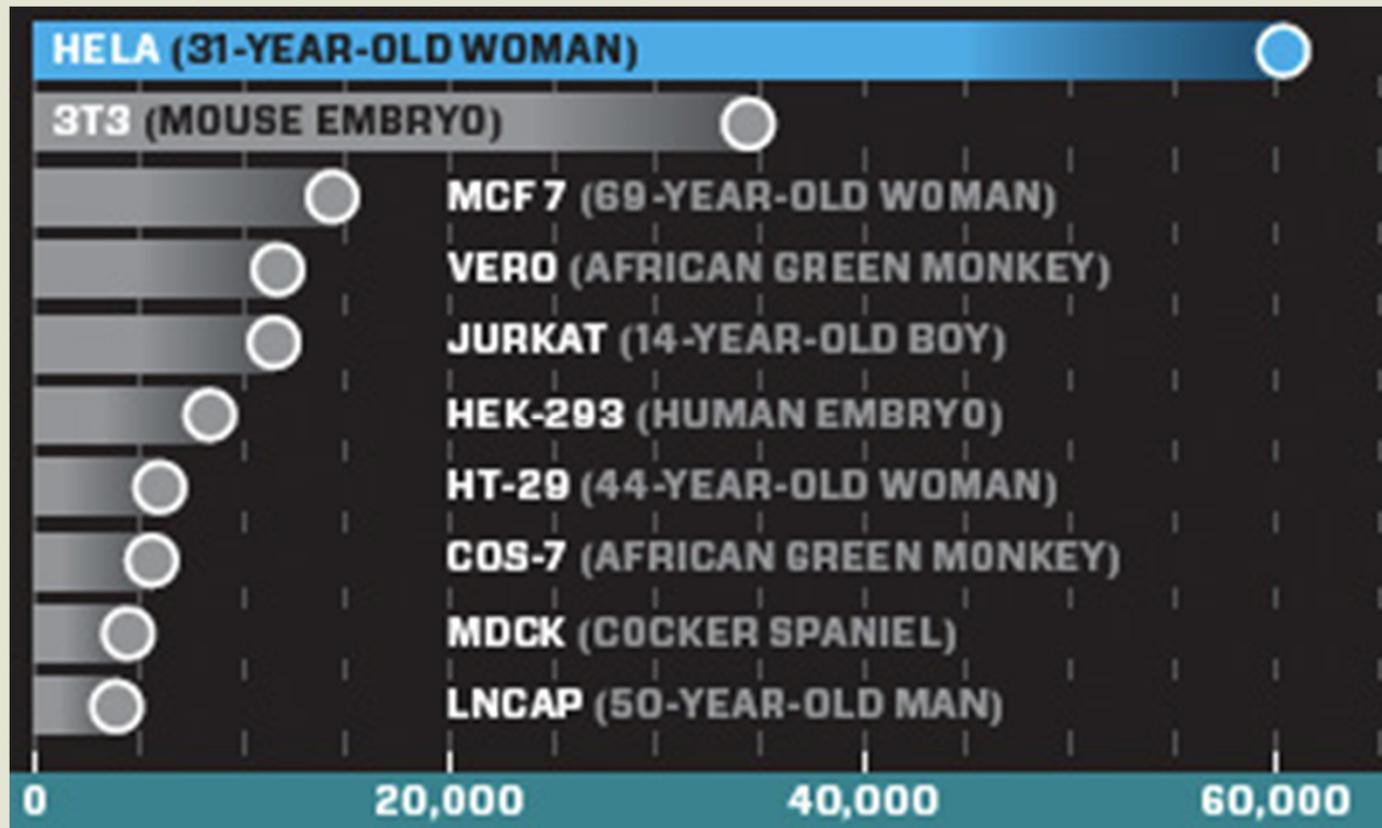
The karyotype of HeLa cells is extremely abnormal in part due to the presence of DNA from HPV

Techniques developed to isolate and then culture single HeLa cells to create a clonal population led to several important scientific and medical advances



HeLa cell research is ongoing today (and will continue into the future)

Number of scientific papers based on 10 popular cell lines



(*Wired* magazine online, January 2010)

It is estimated that 50 million tons of HeLa cells have been grown since 1951

What happened to Henrietta and her family?

I hereby give consent to the staff of The Johns Hopkins Hospital to perform any operative procedures and under any anaesthetic either local or general that they may deem necessary in the proper surgical care and treatment of

- consent form signed by Henrietta Lacks

Could Henrietta's story happen again today?

7) Johns Hopkins may dispose of any tissue or parts which are removed during the procedure. Johns Hopkins may retain, preserve and use these tissues or parts for internal teaching and other educational purposes without my permission, even if these tissues or parts identify me. However, Johns Hopkins may only use or disclose tissues or parts that identify me for research with my permission or with the approval of a review board governed by federal laws protecting these activities. If the tissues or parts do not identify me, Johns Hopkins may use them for scientific (research) purposes without my permission or action by a review board.

- excerpt from a current Johns Hopkins surgical consent form

Are there any laws governing human tissue research?

- Laws protecting *people*:
 - The Federal Policy for the Protection of Human Subjects (aka The Common Rule) established 1981
 - requires the establishment of Institutional Review Boards
 - outlines guidelines for informed consent
- Laws protecting *privacy*:
 - The Health Insurance Portability and Accountability Act of 1996 (HIPAA)
 - Defines boundaries for the use/disclosure of health records

Not really

Under the Common Rule, tissue research is considered human subjects research if the sample is individually identifiable, so informed consent is required

However, research is permitted without obtaining new consent if:

- samples are anonymized and minimal identifying information is provided
- the samples are “leftovers” from routine clinical care
- research presents only minimal risk to participants, does not adversely affect their rights or welfare
- the research could not practicably be carried out if consent was required
- the individuals caring for the patients are different from, and do not share information with, those conducting the investigation

Because the Common Rule was not written specifically for tissue donation, much is left to interpretation

Are there laws governing a person's ability to profit from their tissue?

- it is legal to sell tissue for research, education or art
 - eggs, sperm, and blood are routinely sold
 - it is illegal to sell tissue for transplantation or medical treatment
- Ted Slavin
 - contracted hepatitis B in the 1950s during treatment for hemophilia
 - his blood contained exceptionally high levels of hepatitis B antibodies, which are commercially valuable
 - in the 1970s he began selling his serum to laboratories and companies (\$10/ml)
 - donated his blood for free to a leading hepatitis B researcher

Do you still own your tissue once it has been taken for medical reasons?

Is tissue ownership an issue that affects many people?

- A 1999 report by the RAND Corporation gave a "conservative estimate" that more than 307 million tissue samples from more than 178 million people were stored in the US
 - increasing by more than 20 million samples each year.
- The tissue is stored in:
 - large tissue banks
 - specialized research collections
 - pathological specimen collected in hospitals/clinics
 - newborn screening tests kept in laboratories
 - forensic DNA banks
 - blood banks
 - umbilical cord blood banks
 - sperm, ovum, and embryo banks
 - individual investigator's collections

yes

Case Study 1: Washington University v. Catalonia (2006)

Dr. William Catalonia, a preeminent surgeon and expert on prostate cancer, was conducting research at Washington University (WU). During this research he collected tens of thousands of tissue samples (with appropriate patient consent) that were stored at WU. Eventually Dr. Catalonia moved his medical practice to Northwestern University (NU). He contacted his former patients and asked for permission to transfer their tissue samples to NU. Approximately 6000 men signed the new consent forms allowing Dr. Catalonia to move the samples and continue the research they originally donated the tissue for. WU filed a lawsuit to block Dr. Catalonia from taking the samples. WU asserted the men made a “gift” to the University (not Dr. Catalonia), and therefore the men cannot dictate what happens to their tissue samples.

Should the tissue donors have the right to control the location of their tissue samples?

Case Study 2: The Havasupai Tribe v. Arizona State University

In the 1990s, researchers from Arizona State University (ASU) collected blood samples from over one hundred members of the Havasupai Tribe of Indians in Arizona. The researchers hoped to find a genetic link to Type 2 diabetes, a disease that afflicts over half the tribe. While, many of the tribe members signed a consent form allowing the use of their blood to “study the causes of behavioral/medical disorders,” they maintain they believed the blood would be used only for diabetes research. After researchers were unable to identify any genes related to diabetes, they used the blood samples to study inbreeding in the tribe, the genetic causes of schizophrenia, as well as the ancestral origin of the Havasupai. The results were embarrassing to the tribe and contradicted the tribe’s oral history. The tribe then took legal action against ASU.

Should the Havasupai have the right to dictate what type of research is performed on their blood samples?

Case Study 3: The Texas Newborn Bloodspot Drama

Blood is taken from newborns (by heel stick) as part of mandatory testing for serious medical conditions such as cystic fibrosis, sickle cell anemia, and a number of metabolic disorders. Five drops of blood are placed on a paper card, and often times the cards are destroyed after a short storage period (although this varies). In 2002, Texas began warehousing the cards after de-identifying the samples. 8350 of the over 5 million samples collected were then given to scientists for wide-ranging research projects (from genetics of club feet to the effects of prenatal lead exposure). Parents were not notified since they did not have to consent in the first place for the newborn screening and the samples were anonymous. In 2009, The Texas Civil Rights Project and 5 families filed a lawsuit against the Texas Department of Social and Health Services.

Were the parents being overly litigious, or did they have a reason to be upset? What is “worse case scenario” for their children’s blood samples?

Case Study 4: Moore v. Regents of University of California

In 1976, John Moore began treatment for hairy-cell leukemia at the UCLA Medical Center. As part of the treatment, his spleen was removed, and Moore signed a consent form allowing the surgeons to "dispose of any severed tissue or member by cremation".

Moore's doctor, David Golde, discovered that Moore's spleen was biologically important and established a cell line (the Mo cell line) from it without notifying Moore. The cell line was patented and eventually licensed to a biotech company for commercial development. Golde became a paid consultant for the company and acquired stock, a deal worth more than \$3.5 million dollars. The Mo cell line was thought to be worth billions. Eventually Moore learned about the cell line and filed suit in 1984.

Should Moore have a received a share of the profits derived from the Mo cell line?

Case study 5: You (and your blood) v. your doctor

High cholesterol runs in your family, so you decide to be proactive and seek medical advice. The endocrinologist wants to start by taking a blood sample. Before treatment can begin, you must sign a consent form. The form is very simple as gives you two options:

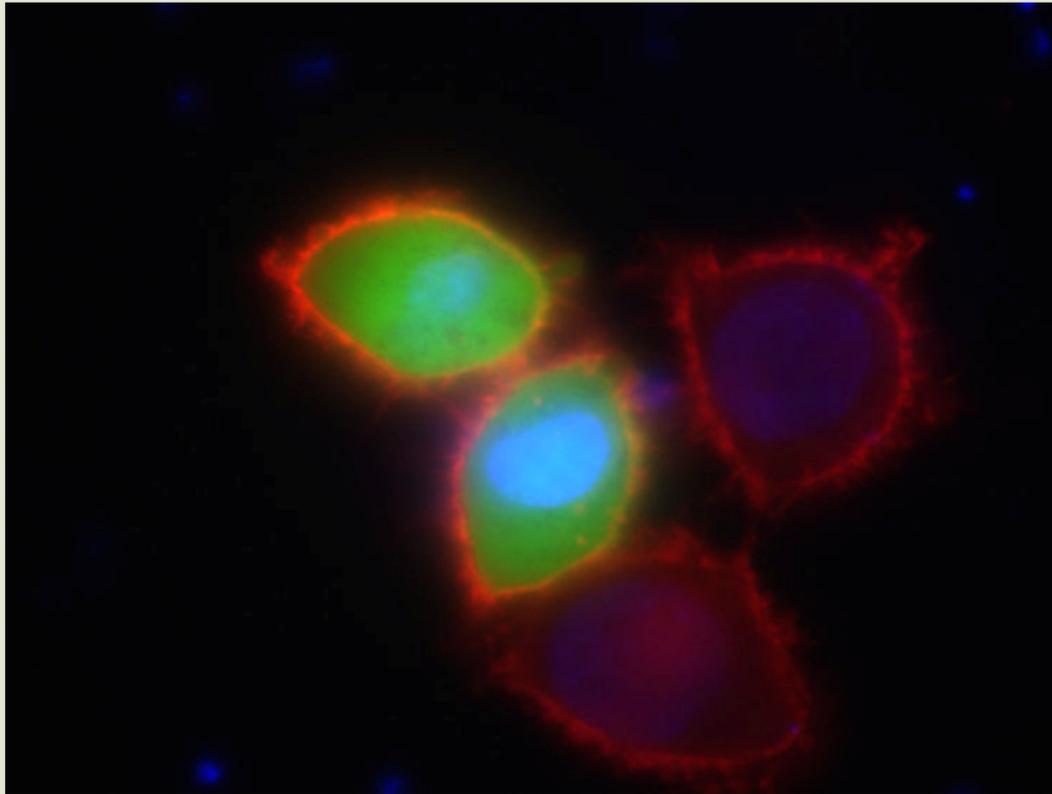
- I give permission for my blood to be used in biomedical research. I understand that all personal information will be removed and the sample will be made anonymous.

- My blood may not be used for research purposes.

Which box do you check and why?

How do you feel about the tissue you donated? Has the doctor taken a part of you?

Future goal for the use of human tissue in research:
Balance the needs of researchers with the needs of the
patient and public through open communication



One last picture of
HeLa

Photo courtesy of Myles Dillon of the Mowen Lab
at The Scripps Research Institute, La Jolla

Table 1. Approaches to Informed Consent for Research on Stored Biospecimens.

Approach	How Consent Is Obtained
Specific consent	Research participants are recontacted and asked to consent for each new use of their specimen or for information that is outside the scope of their original consent.
Tiered consent	At the time samples are collected, research participants are presented with a menu of options from which to choose, which may include general permission for future use, consent only for future uses related to the original study topic, consent for future uses unrelated to the original study topic, and specification that the investigators must obtain specific consent for any future use that differs from the original study.
General permission	At the time samples are collected, research participants are asked to permit all future uses that a qualified ethical review board determines to be scientifically meritorious and ethically defensible.
Presumed consent	At the time samples are collected, research participants are informed that their specimens will be used in future research unless they expressly deny permission.

Mello and Wolf, 2010. The Havasupai Indian Tribe Case — Lessons for Research Involving Stored Biologic Samples. *NEJM*. Volume 363(3), p 204–207

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