

Cellular Life Beyond an Individual's Death

Faculty Lecture Series
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Outline

- What are cell strains vs. cell lines?
- Basic history of cell culture
- Some famous human cell lines
 - HeLa
 - John Moore (Mo)
 - Others
- HeLa Genome sequenced (just this semester)
- Discussion

Can cells live outside the body?

You bet...

We call them cell strains and cell lines

Types of Cell Cultures- Human cell lines became possible in the 1950s, but other cells had been previously cultured (for about 50 years)

- Started in 1907; Ross Harrison growth of nerve fibers (from frogs)
- 1910-1923; Alexis Carrel and tissue culture (dog, cat, chicken, rat, guinea pig, human tumors (for several months))
- 1930s; Charles Linbergh; engineered devices to make cell culture easier
- 1950s: Bioreactors, large scale production \$\$\$

Cell Culture is a multi-billion dollar (per year) industry in the U.S. (alone)

- Research Tool
 - Cell biology
 - Virology
 - Cancer
- Major Production Tool
 - Cell-based vaccines
 - Monoclonal antibodies
 - Cell-based drugs

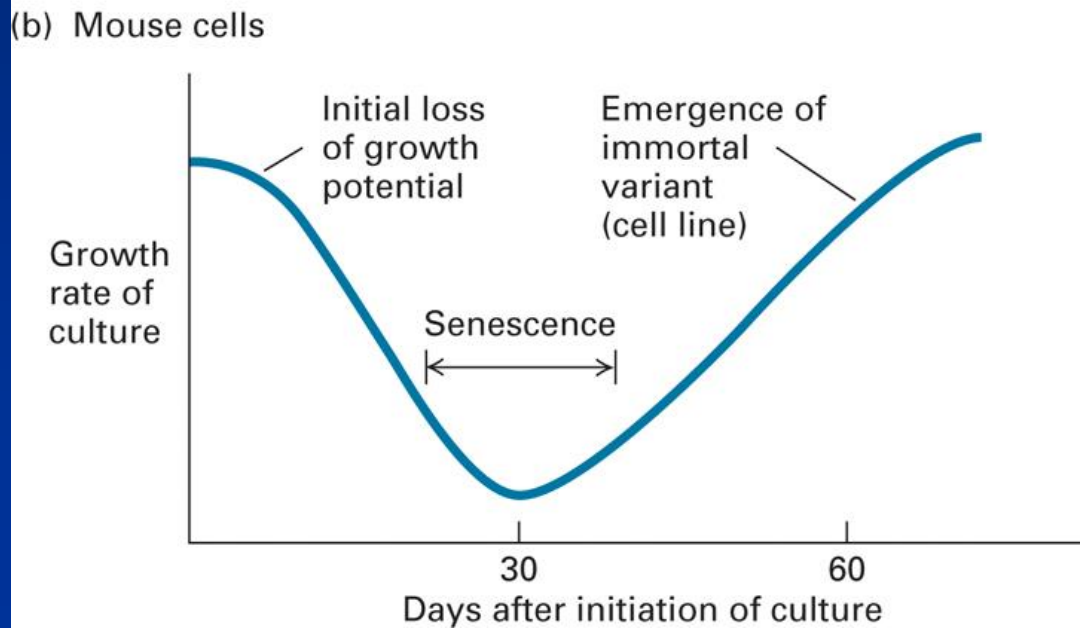
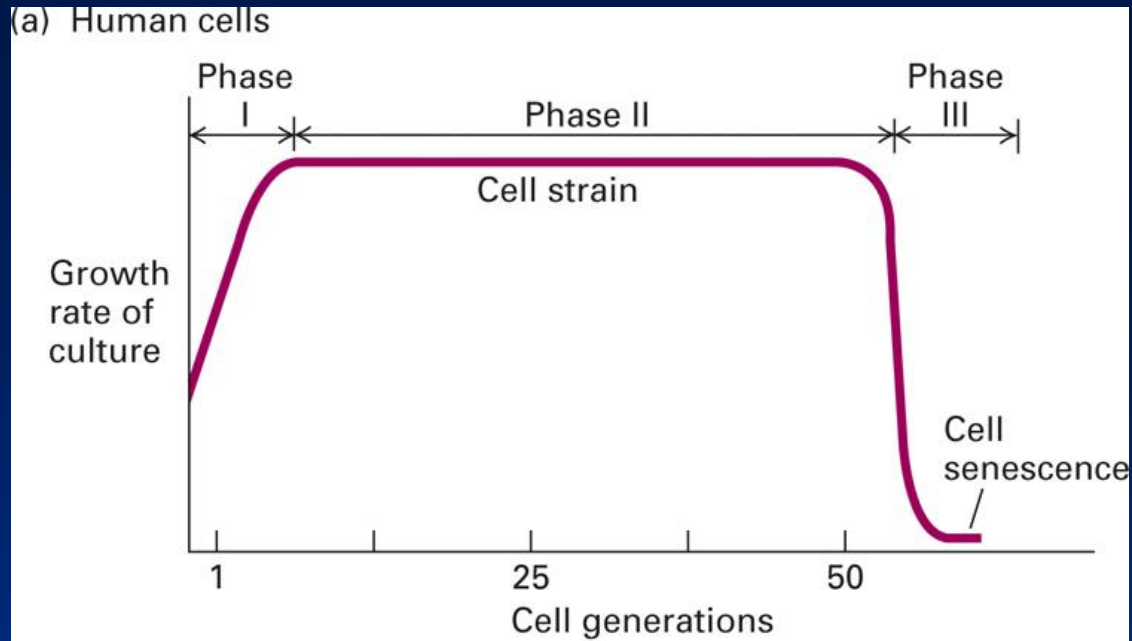
There are two main categories of cell culture

- Primary Cell Cultures
- Transformed Cell Cultures

Primary Cell Cultures (cell strain)

- Started from normal animal tissues (skin, kidney, liver)
- Specially treated to break cell-cell and cell-matrix adhesions
- Grown in nutrient rich media in dishes
- Divide a finite number of times (about 50) then stop growing
- Starting with 10 billion cells, 50 doublings can produce 10^{20} cells; weight of 1,000 people → cell strain (can be frozen)

Figure 9.1 Stages in the establishment of a cell culture.



Taken from:
Lodish et al, 2010

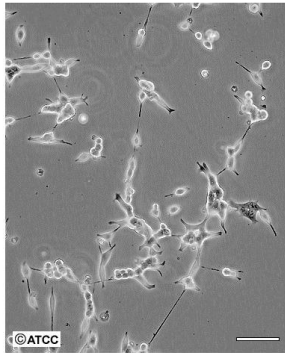
Transformed Cell Culture (Cell line)

- Transformed cells (cancer)
- Culture of cells with indefinite life span → immortal → cell line

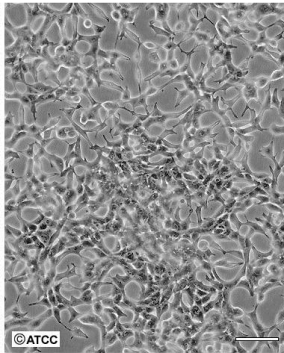
Cell Line	Biological Source	Cell Type	Price (atcc.org)
MCF7	69 year; human Caucasian female	invasive breast carcinoma	\$431
JURKAT	14 year old boy	T cell leukemia; peripheral blood	\$431
HEK-293	Human fetus	Epithelial	\$431
HT-29	44 year; human Caucasian female	Epithelial; colon adenocarcinoma	\$431
LNCaP	50 year; human Caucasian male	Prostrate; carcinoma	\$431
HeLa	31 year; human Black female	Cervix; adenocarconoma	\$431
WI-38	3 month; surgically aborted female Caucasian fetus	Normal lung fibroblast	\$431
MO	50 year, caucasian male	T lumphocyte; hairy cell leukemia	\$551

Cell Line Images (www.atcc.org)

ATCC Number: **CRL-1740**
Designation: **LNCaP clone FGC**

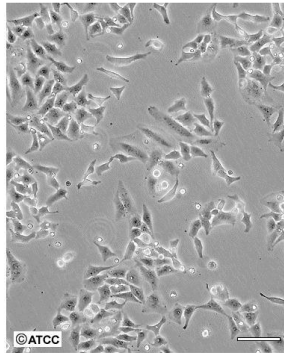


Low Density

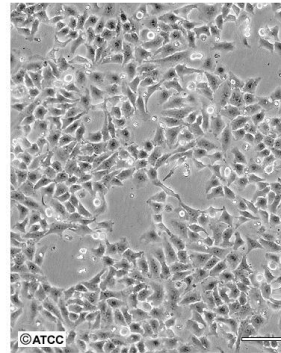


High Density

ATCC Number: **CCL-2**
Designation: **HeLa**

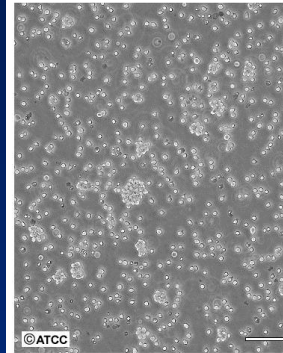


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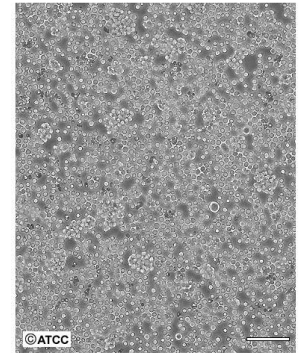


High Density

ATCC Number: **TIB-152**
Designation: **Jurkat (Clone E6-1)**

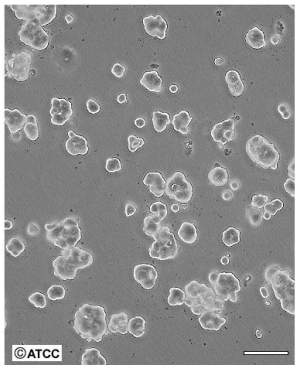


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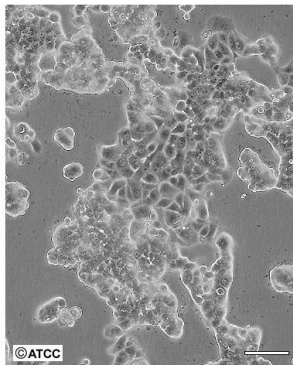


High Density

ATCC Number: **HTB-22**
Designation: **MCF-7**

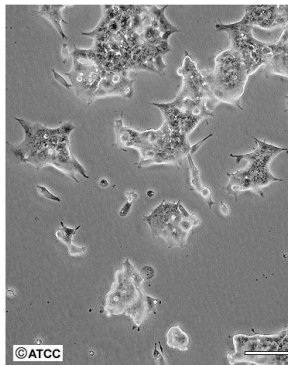


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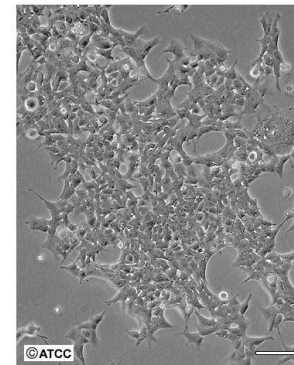


High Density

ATCC Number: **CRL-1573**
Designation: **293**

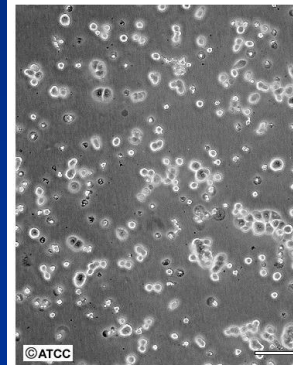


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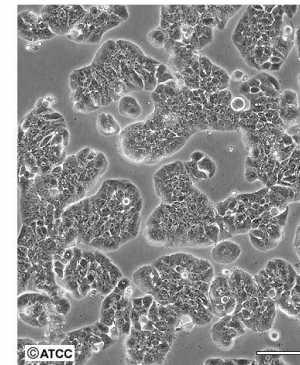


High Density

ATCC Number: **HTB-38**
Designation: **HT-29**



Low Density



High Density

Number of Scientific Papers from major cell lines



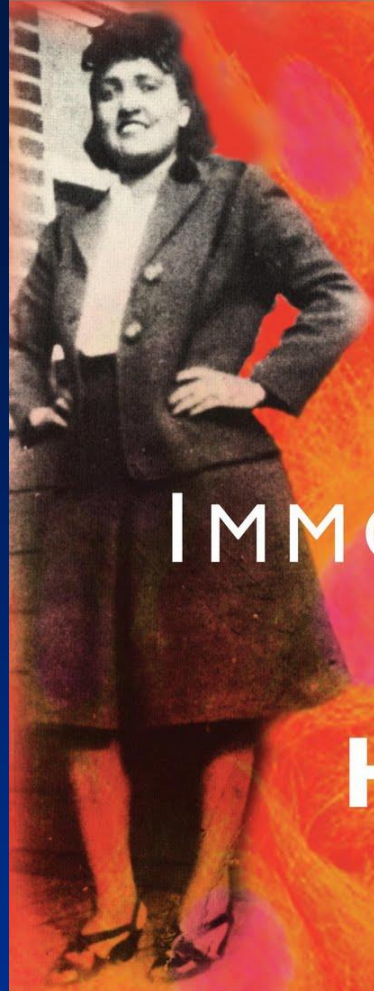
Taken from: Wired
magazine, January, 2010

How can you get these cells?

- There are easily over 4000 cell lines available for sale from a variety of companies/organizations
 - ATCC
Coriell Institute for Medical Research
 - European Collection of Cell Cultures (ECACC)
 - German Collection of Microorganisms and Cell Cultures (DSMZ)
 - Bioresource and Collection Center (FIRDI-Taiwan)

What was the first immortal human cell line?

- HeLa cell line (1951)
- From a malignant tumor (carcinoma) of the uterine cervix
- These cells are different from the normal cells they arose from.
- Henrietta Lacks was only 31 when she died...
- Usually she is not mentioned when her (cancer) cells are...



THE
IMMORTAL LIFE
OF
HENRIETTA
LACKS

Doctors took her cells without asking.

Those cells never died.

They launched a medical revolution
and a multimillion-dollar industry.

More than twenty years later, her children found out.

Their lives would never be the same.

REBECCA SKLOOT

Rebecca Skloot's
Book (2010)

A quick interview with Rebecca Skloot about her book, *The Immortal Life of Henrietta Lacks*

- <http://rebeccaskloot.com/>
- [Book trailer interview \(youtube\)](#)



Rebecca Skloot

<http://rebeccaskloot.com/faq>

- Completed a B.S. in Biology
- Planned to go to vet school, but changed to creative non fiction writing after a course in college
- “Letting go of a goal doesn’t mean you’ve failed, as long as you have a new goal in its place. That’s not giving up, it’s changing directions, which can be one of the best things you ever do in life.”

Where did HeLa cells come from?

- Henrietta Lacks; Turner Station, Baltimore

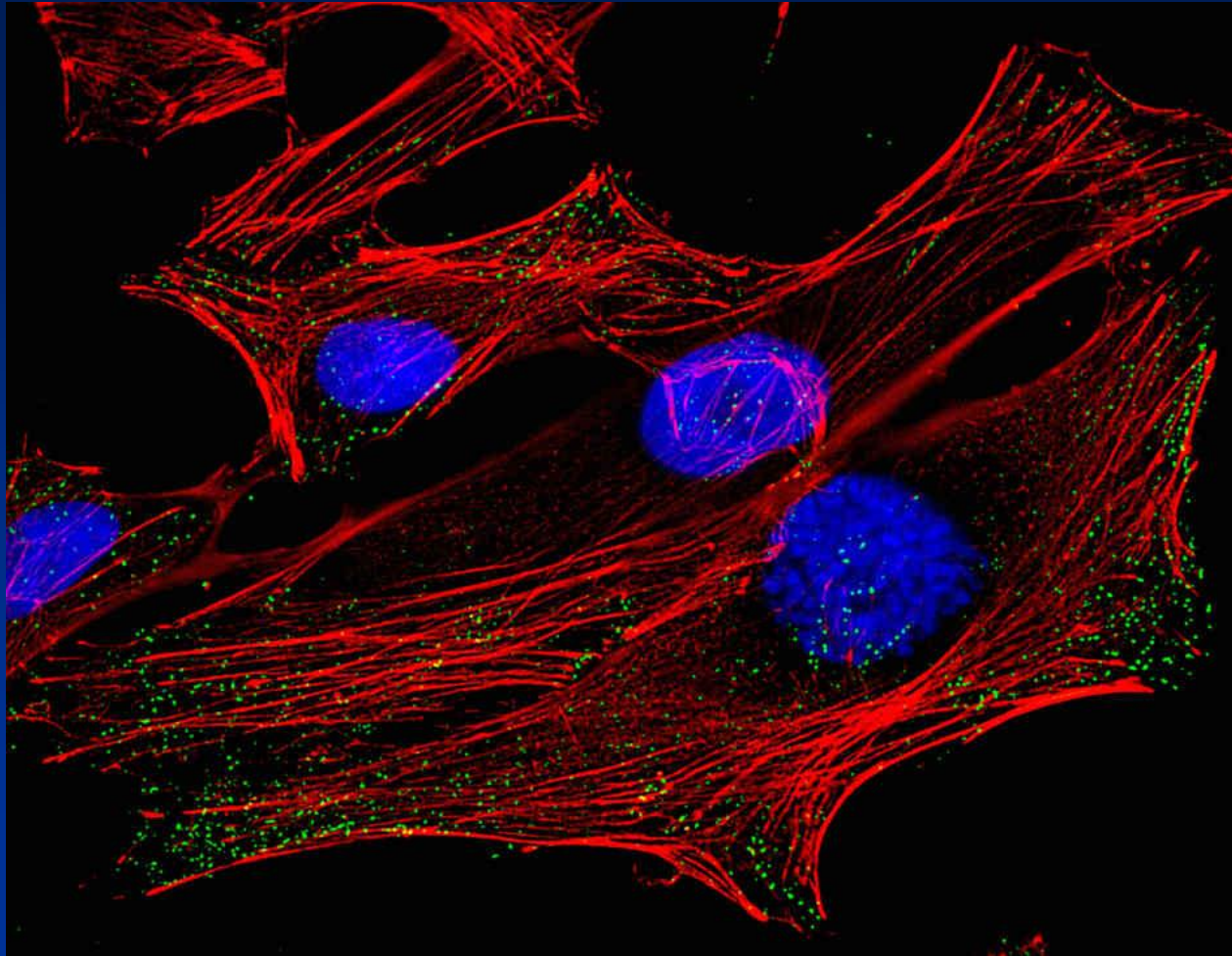


Taken from:
Skloot, 2010

Henrietta with her husband, David in 1945

- She was only 31 (5 children) when she died of cervical cancer...
- Cells taken at Johns Hopkins hospital; They just kept growing!

HeLa Cells



Taken from:
www.media.npr.org



Dr. George Gey



Margaret Gey and Minnie, a lab technician, in the Gey lab at Johns Hopkins, in 1951

Taken from:
Masters, 2002

Taken from: <http://elizabethh786.edublogs.org/2012/01/05/the-immortal-life-of-henrietta-lacks/>

Timeline | **The development of human cancer cell lines**

Ross G. Harrison develops the 'hanging drop culture' to study frog nerve-cell growth.

1907

Wilton R. Earle and George Gey generate a rodent continuous cell line.

1940

Klaus H. Rothfels and colleagues show interspecies cross-contamination.

1958

Walter Nelson-Rees shows widespread HeLa cross-contamination.

1974

Cross-contaminated cell lines are used at record levels.

2002

Montrose T. Burrows and Alexis Carrel grow chick embryo cells in tissue culture.

1910

George and Margaret Gey and Mary Kubicek develop HeLa, the first human cancer continuous cell line.

1951

Stan Gartler shows intraspecies cross-contamination.

1967

Dennis Gilbert, Stephen O'Brien and colleagues apply multilocus DNA fingerprinting to cell-line authentication.

1990

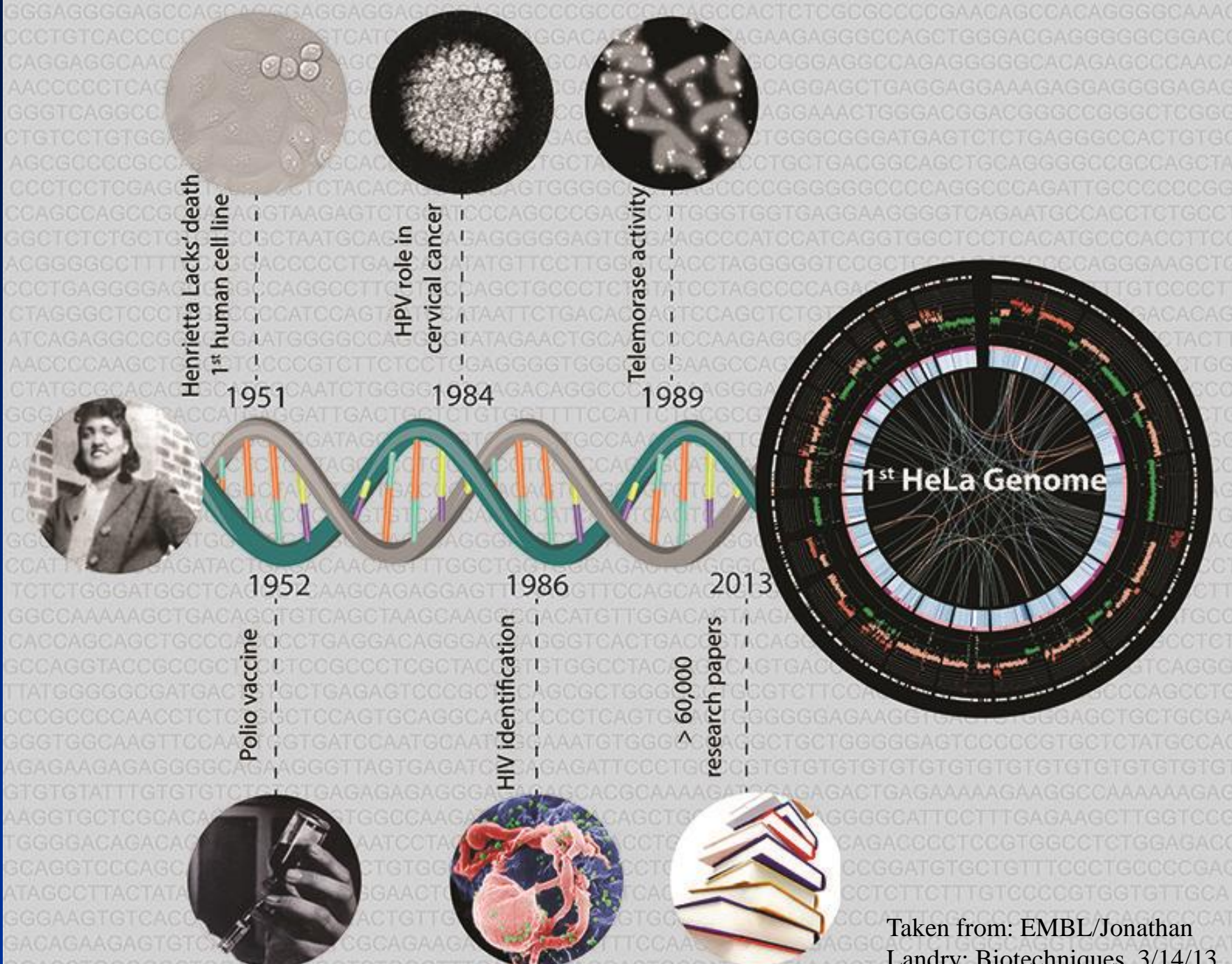
Taken from:
Masters, 2002

HeLa cells distributed

- Dr. George Gey sent them free to any researcher who wanted to use them
- The scientific community used them!

HeLa Cell Highlights

- 50 million tons of cells
- Enough for 1 billion people
- 11,000 patents
- >60,000 scientific papers
- At least 2 Nobel Prizes
- Assisted polio vaccine development, In vitro fertilization, many applications
- They have even been in space

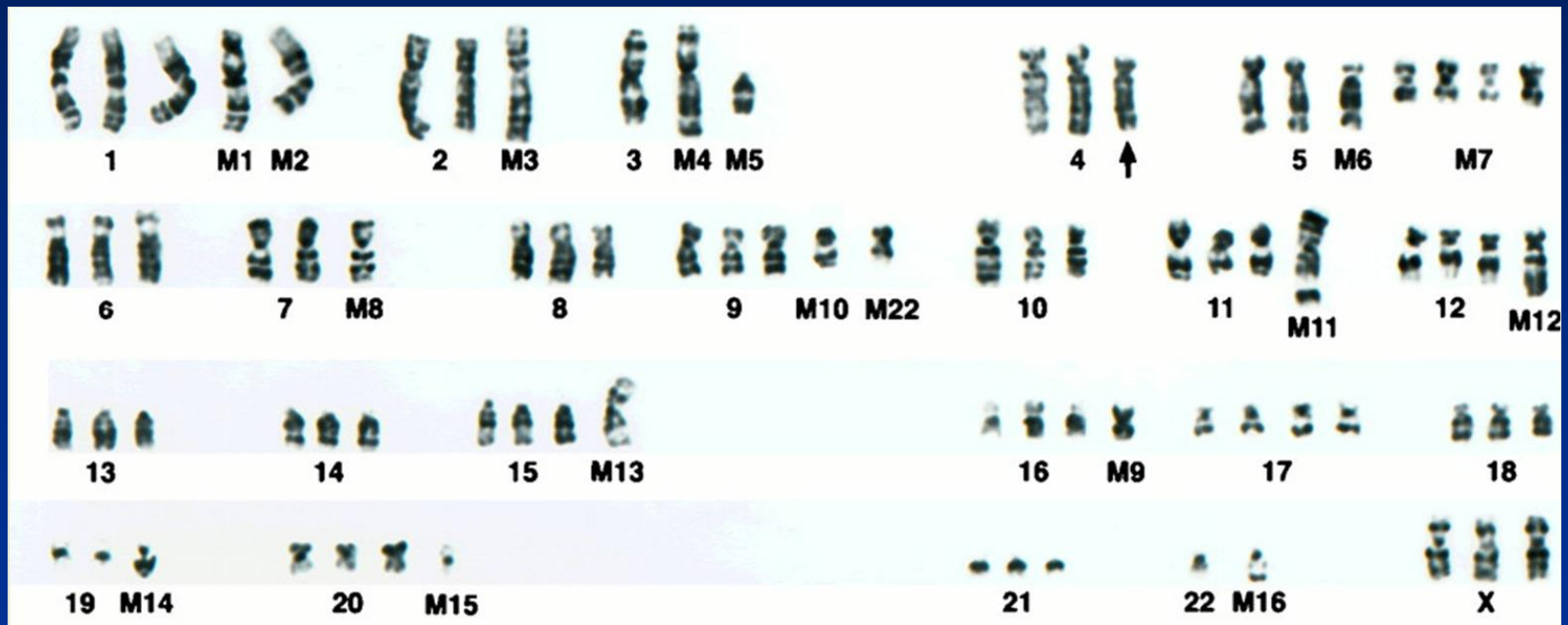


Taken from: EMBL/Jonathan
Landry; Biotechniques, 3/14/13

HeLa Genome Sequenced

- Many regions of the chromosomes were arranged in the wrong order
- Extra or fewer copies of genes → chromosome shattering exists in at least 2-3% of all cancers.

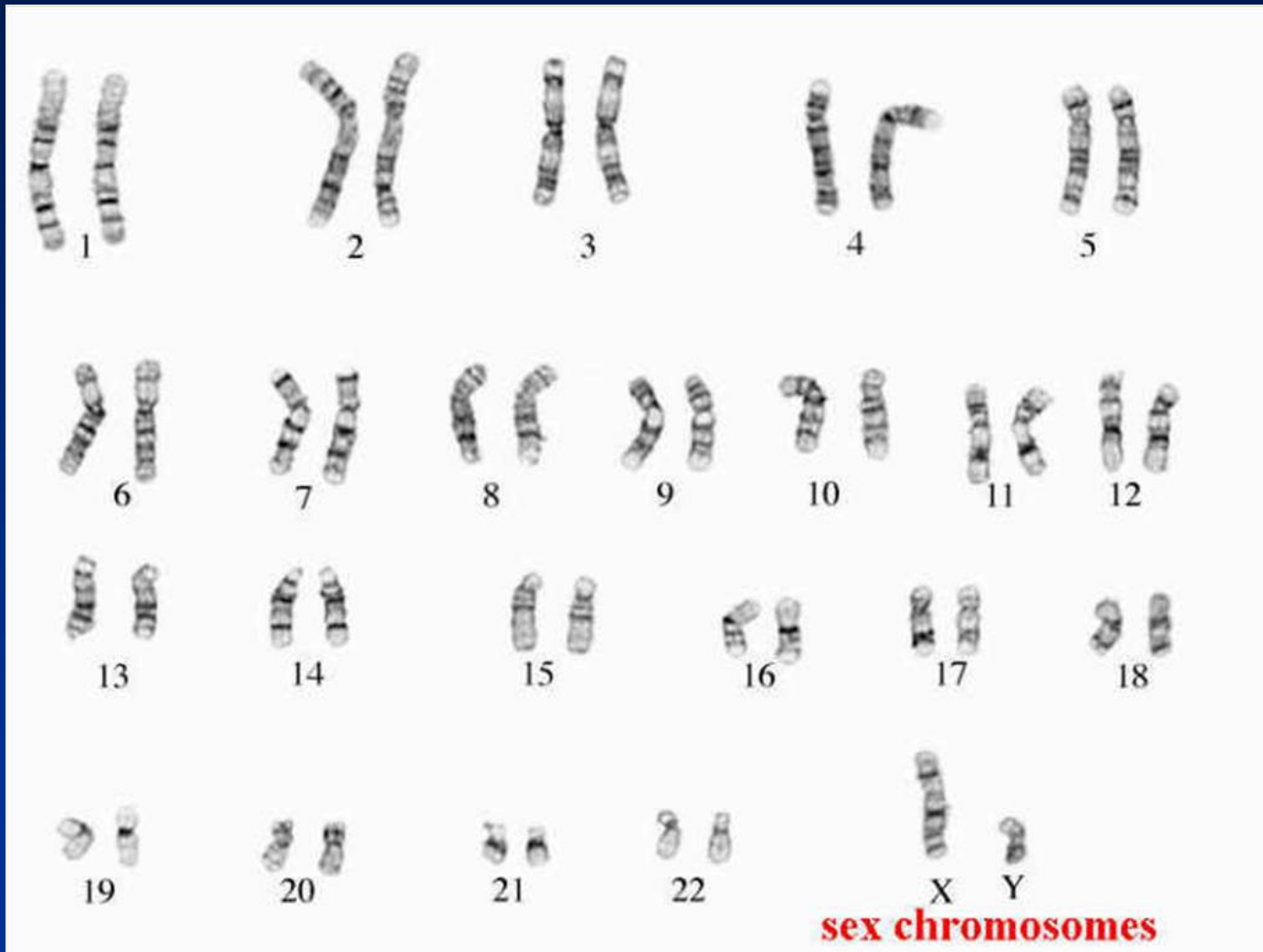
Abnormal Karyotype from HeLa cells HPV insertions



Taken from:

<http://www.htcl.cytspb.rssi.ru/tomors/HeLa-229.html>

Normal Karyotype



Taken from: Campbell and Reece, 2012

HeLa cells are very strange



Everything was going along fine until they discovered their HeLa cell line expressed Y chromosome markers.

Taken from:
<http://worldwide.promega.com>

What about the issue of tissue rights?

- Rebecca Skloot wrote a very interesting article in the New York Times (April 16, 2006), *Taking the least of you: The Tissue-Industrial Complex*

Highlights of the tissue rights issue

- The stuff you leave behind in the hospital or doctor's office does not always get thrown out.
- More than 307 million tissue samples from more than 178 million people stored in the U.S. and increasing by > 20 million samples each year (RAND Corporation, 1999).
- Do you have any rights to your biological “scraps”? (generally no)

John Moore's Story

- 1976, John Moore, Alaskan pipeline surveyor, developed hairy-cell leukemia
- Found Dr. David Golde; UCLA researcher
- Spleen removed; follow up visits to take blood, and other body fluids
- Cell Line Mo worth \$3 billion; protein that stimulates growth of white blood cells (fights infection)
- Moore sued Golde and UCLA in 1984
- Long case, in 1990 the supreme court of CA ruled against Moore; prevailed on 2 counts: lack of informed consent, and breach of fiduciary duty (died in 2001)

Bottom Line from Mo

“Any ownership you might have in your tissues vanishes when they are removed from your body, with or without your consent. When you leave tissues in a doctor’s office or a lab, you abandon them as waste. Anyone can take your garbage and sell it – the same goes for your tissues.”

-Rebecca Skloot

Lori Andrews, J.D.



Taken from: <http://ethics.sandiego.edu/>

- Director, Institute for Science, Law and Technology at the Illinois Institute of Technology
- Professor of Law
- Genetics rights and tissues issues
- People should control their tissues to protect themselves from potential harm.
- We decide who gets our money after we die... (but not so with our tissues).

Some interesting cases since Mo

- York v. Jones
 - People having property rights over their sperm, eggs, and embryos
- Greenbergs
 - Volunteered samples and money to help a researcher find a cure for their children's disease Canavan disease, but the researcher patented the gene without telling them.
 - No property claim upheld, but the “unjust enrichment” claim was upheld: undisclosed settlement for investing their “time and resources”.

But tissues are still yours if they
are inside your body

- If you know this, you can control your tissues and
- Play the market just as any biotech company

Ted Slavin Story (1980s)

- Was a hemophiliac, had been exposed to hepatitis
- He had antibodies to hepatitis in his blood, but was not sick with hepatitis
- Contacted laboratories to see if they wanted to buy his blood...
- Sold his serum for \$10 per mL; \$10,000 per L; income for the rest of his life.
- Gave his antibodies to Dr. Baruch Bloomberg, Nobel prize winning hepatitis researcher; He wanted a cure → 1st hepatitis B vaccine
- Started a company, Essential Biologicals, and recruited others

The Federal Policy for the Protection of Human Subjects (The Common Rule)

- 1981, for protection of the person
- Not their excised body parts
- Samples are exempt if they are anonymous
- What would a “good and complex consent process” look like?

Dr. William Catalona v. Washington University

- Prostate Cancer research
- Court case, 2003
- 4,000 prostate samples, 250,000 blood samples from at least 36,000 men
- Detailed consent forms
- But Washington University took possession of the samples (may be worth >\$15 million); as his intellectual property
- Patients requested the samples be transferred to Dr. Catalona → denied

Catalona and patients

<http://www.drcatalona.com/litigationConclusion.html>

- Ended at the U.S. Supreme Court, November 2008
- Washington University has outright ownership of the samples from the prostate cancer patients



Taken from: www.drcatalona.com

Havasupai Indians won fight to limit research of its DNA to Diabetes only

- Samples gathered for use on diabetes research; based on the population's need
- Were actually used to also study mental illness and geographic origin of the tribe among other things.
- Landmark case (2010) giving individual rights to a person's DNA sample
- University of Arizona spent \$1.7 million fighting lawsuits by tribal members
- Settled on \$700,000 to 41 tribal members and additional assistance in the forms of scholarships and health aid.

Havasupi Indians get their blood back! After their trust being violated...



Taken from: http://www.nytimes.com/slideshow/2010/04/21/us/0421DNA_13.html

Thought for Consideration:

Are these cases of life or death
and whose cells (molecules) are
these anyway?

Any Questions?



Taken from:
Gene Patent Cartoon by Cathy Wilcox

Should patients be paid for their
tissues/cells ? (series of papers in
Science July-September 2012

Should you be entitled to profits your
doctor makes on your cells?

Some Interesting Websites:

- <http://rebeccaskloot.com/>
- <http://henrietalacksfoundation.org/>
- <http://www.lacksfamily.net/>
- <http://www.helafoundation.org/>
- http://www.corning.com/lifesciences/us_canada/en/index.aspx

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