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.

(a) Human cells

Phase I

Phase II

Phase III

Cell strain

Growth rate of culture

Cell generations

(b) Mouse cells

Initial loss of growth potential

Emergence of immortal variant (cell line)

Senescence

Growth rate of culture

Days after initiation of 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
<table>
<thead>
<tr>
<th>Cell Line</th>
<th>Biological Source</th>
<th>Cell Type</th>
<th>Price (atcc.org)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCF7</td>
<td>69 year; human Caucasian female</td>
<td>invasive breast carcinoma</td>
<td>$431</td>
</tr>
<tr>
<td>JURKAT</td>
<td>14 year old boy</td>
<td>T cell leukemia; peripheral blood</td>
<td>$431</td>
</tr>
<tr>
<td>HEK-293</td>
<td>Human fetus</td>
<td>Epithelial</td>
<td>$431</td>
</tr>
<tr>
<td>HT-29</td>
<td>44 year; human Caucasian female</td>
<td>Epithelial; colon adenocarcinoma</td>
<td>$431</td>
</tr>
<tr>
<td>LNCaP</td>
<td>50 year; human Caucasian male</td>
<td>Prostate; carcinoma</td>
<td>$431</td>
</tr>
<tr>
<td>HeLa</td>
<td>31 year; human Black female</td>
<td>Cervix; adenocarcinoma</td>
<td>$431</td>
</tr>
<tr>
<td>WI-38</td>
<td>3 month; surgically aborted female Caucasian fetus</td>
<td>Normal lung fibroblast</td>
<td>$431</td>
</tr>
<tr>
<td>MO</td>
<td>50 year, caucasian male</td>
<td>T lymphocyte; hairy cell leukemia</td>
<td>$551</td>
</tr>
</tbody>
</table>
Cell Line Images (www.atcc.org)
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.*
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

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!

Taken from: Skloot, 2010
HeLa Cells

Taken from: www.media.npr.org
Margaret Gey and Minnie, a lab technician, in the Gey lab at Johns Hopkins, in 1951

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.
- Wilton R. Earle and George Gey generate a rodent continuous cell line.
- Klaus H. Rothfels and colleagues show interspecies cross-contamination.
- Walter Nelson-Rees shows widespread HeLa cross-contamination.
- Cross-contaminated cell lines are used at record levels.


- Montrose T. Burrows and Alexis Carrel grow chick embryo cells in tissue culture.
- George and Margaret Gey and Mary Kubicek develop HeLa, the first human cancer continuous cell line.
- Stan Gartler shows intraspecies cross-contamination.
- Dennis Gilbert, Stephen O'Brien and colleagues apply multilocus DNA fingerprinting to cell-line authentication.

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
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)
“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.

- 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).

Taken from: http://ethics.sandiego.edu/
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 Biologica, 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…

Thought for Consideration:
Are these cases of life or death and whose cells (molecules) are these anyway?
Any Questions?

They're our breast cancer genes—we identified them.

It's kind of you to let us have the disease for free.

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://henriettalacksfoundation.org/
- http://www.lacksfamily.net/
- http://www.helafoundation.org/
References

• American Type Culture Collection. [www.atcc.org]
• Lacks Family Foundation, 2012. [www.lacksfamily.net]