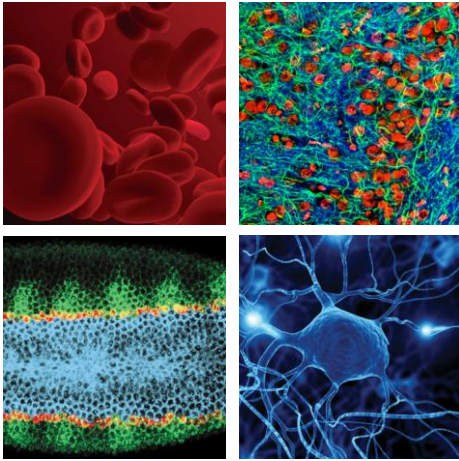


# About Life Technologies Corporation



- Publicly traded as LIFE:NASDAQ
- 50000 Products in 110 Countries
- 10,000 employees globally; over 900 in Molecular Cell Biology Division; only 80 isolating primary cells from fresh human organs and tissues
- Member of the DOW Jones Sustainability Index

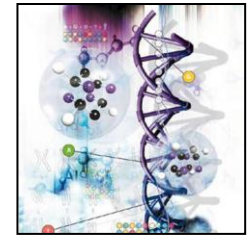
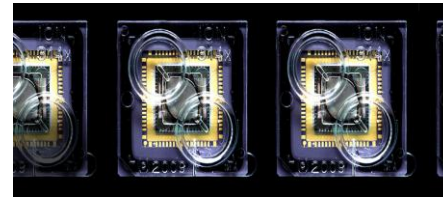
*life*  
technologies™

# What We Do – Life Technologies

**Our Mission: To Improve the Human Condition**

## **4 Major Areas of Business**

**1) Personalize Medicine (genome analysis)**



**What's our DNA?**

**2) Q-PCR Diagnostic Testing (Forensics, Clinical Diagnostics, FDA, etc.)**

**PGM – Ion Torrent**

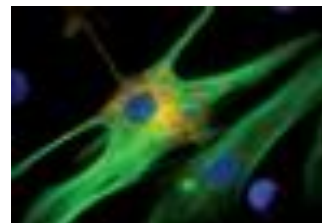


**3) Drug Development and BioProduction**



**4) Cell and Molecular Biology**

**(Includes: Primary Cell Culture Systems and Cell Therapy)**



# North America *Primary Cell* Developments & Research

- We *design (ds)*, *develop (dv)*, *manufacture (mfg)*, and *distribute (dt)* to researchers worldwide for nearly every stage of medical research

Eugene, OR – Aorta, CA, PA, neo-skin, adult skin umbilical cord, and cornea

- Primary cells (ds, dv, mfg, dt)
- Media, Supplement & Reagents (ds, dv)

Grand Island, NY  
- Media, Supplement, Reagent (mfg, dt)

Madison, WI

Frederick, MD  
- Media, Supplement, Reagent (dt)

Durham, NC - Liver  
- Primary cells (ds, dv, mfg, dt)

Austin, TX



# Primary Cells vs Cell Lines

## What are “primary cells”?

(Also called “normal” cells)

Cell-type specific applications

- Isolated from tissue
- Availability: dependent on source of tissue and expertise
- Represent tissues of origin
- Have not been immortalized

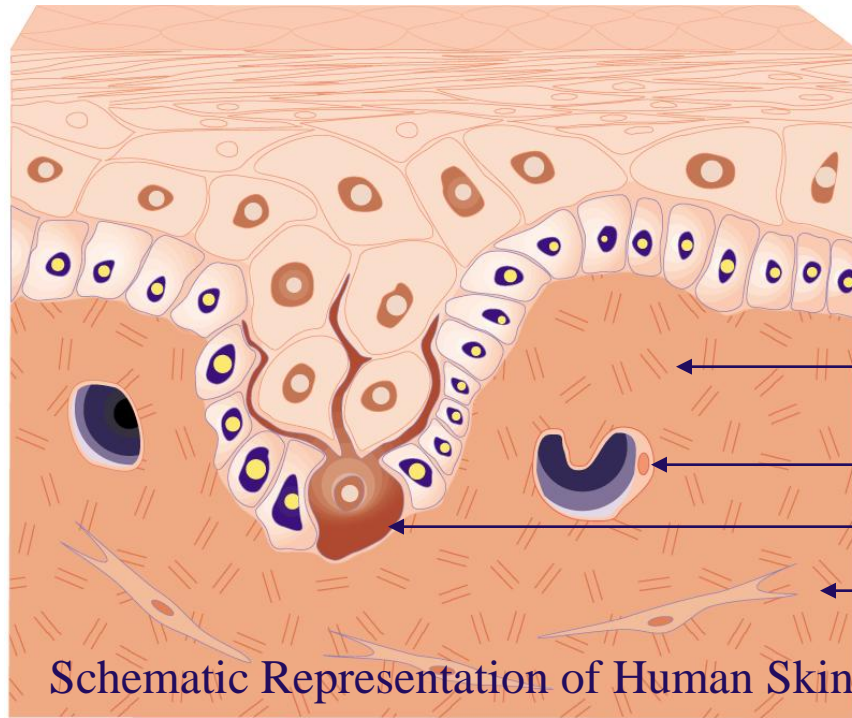
## What are “continuous cell lines”?

(Also called “immortalized cells)

General cell functionality

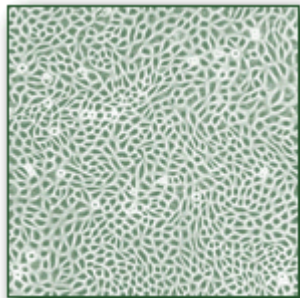
- Availability: readily available
- Immortalized *in vitro*, or
- Cells derived from tumor tissue and serially propagated in culture for an extended period of time
  - Retain very few *in vivo* characteristics
  - Often overexpress certain genes (oncogenes)
  - Increased levels of proteases, and altered cell surface markers.

# Skin (tissue source: neonatal foreskin, adult skin, anatomical donor skin)

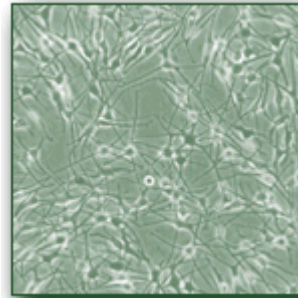


- ← Cornified keratinocytes
- ← Suprabasal keratinocytes  
*Transient amplifying cells*
- ← Basal keratinocytes
- ← Basement membrane
- ← Collagen fibers
- ← MicroVascular Endothelial Cell
- ← Melanocyte
- ← Fibroblast

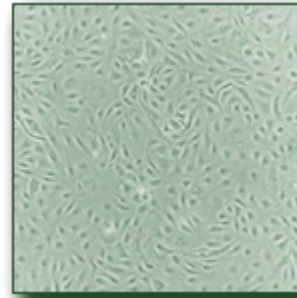
Schematic Representation of Human Skin



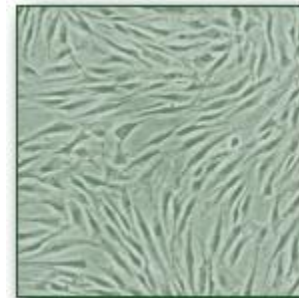
**HEK**  
(Human Epithelial  
Keratinocytes)



**HEM**  
(Human Epithelial  
Melanocytes)



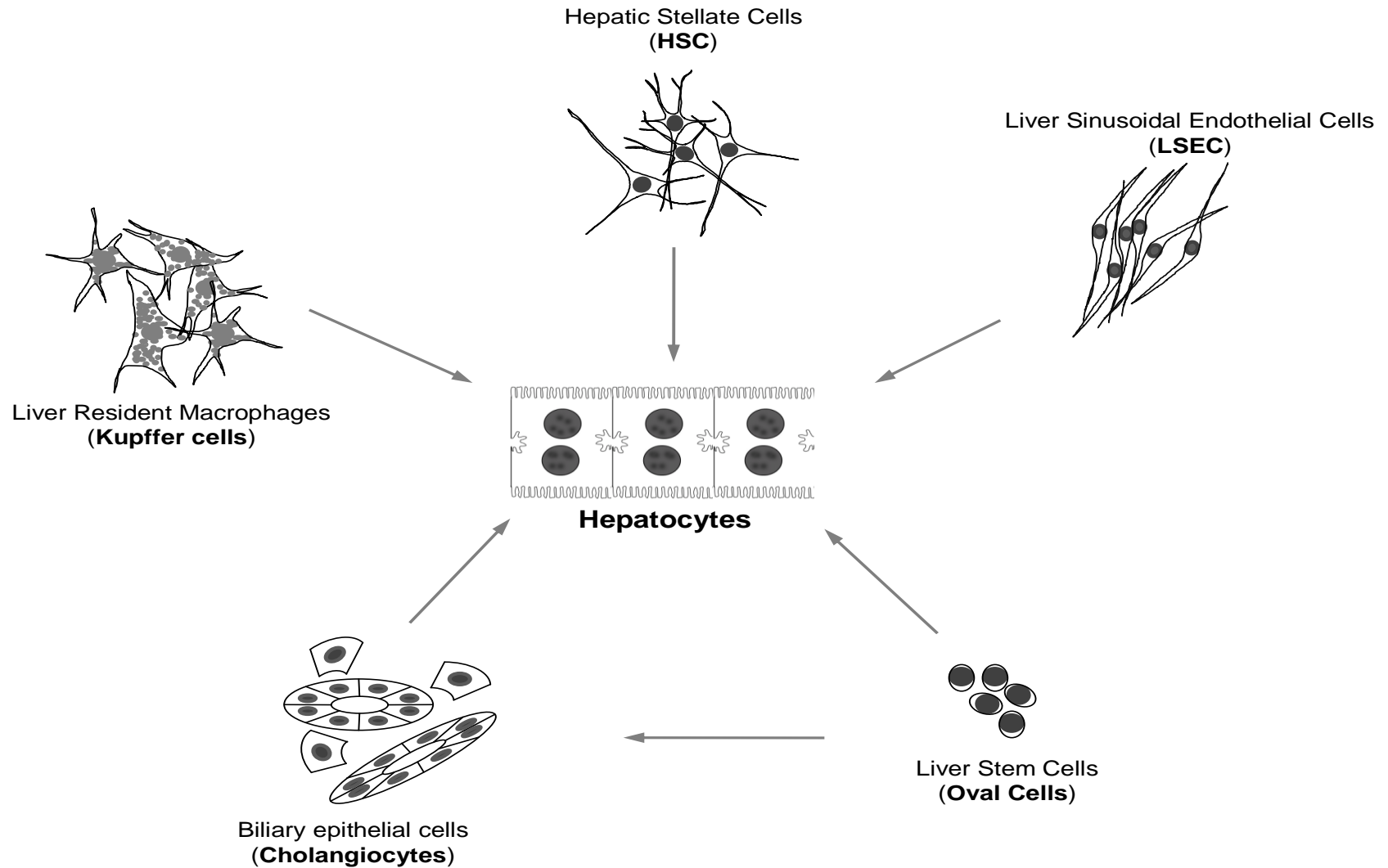
**HMVEC**  
(Human Microvascular Endothelial  
Cells)



**HDF**  
(Human Dermal Fibroblasts)

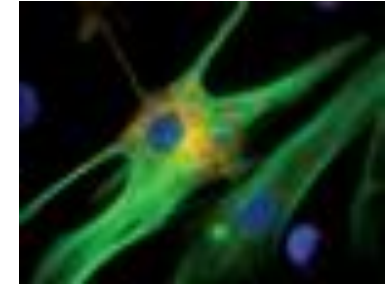
Cultured  
Cells

# Types of Liver Cells

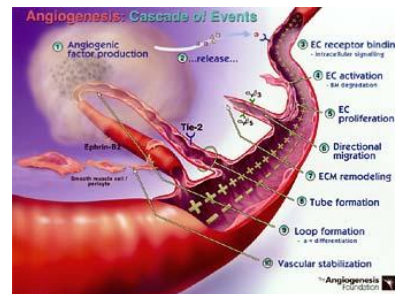


## Skin

- Keratinocytes
- Melanocytes
- Fibroblasts
- Dermal microvascular endothelial cells



## Cardiovascular Tissue



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- Endothelial cells from aorta, pulmonary artery
- Smooth muscle cells from aorta, pulmonary artery, coronary artery

## Cornea

- Corneal epithelial cells



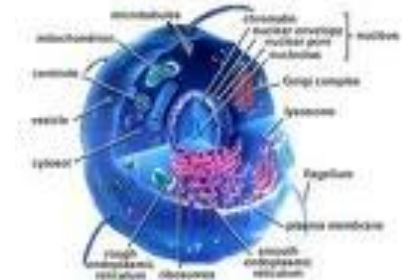
# Helping to Improve the Human Condition

*How Tissue donation today can help millions tomorrow*



## Basic Biology of Cells

- > Growth factors
- > General studies of cells



## Mechanisms of Wound Healing/Tissue Repair

- > Progress towards truly personalized medicine

## Advances in Pharmacokinetics

- > Genomic analysis progress towards truly personalized medicine



## Epithelial grafting

- > Development techniques for 3 dimensional grafts for treatment of severe burns and chronic wounds

## In-vitro models for toxicology

- > The development of alternatives to the use of animals in testing consumer products

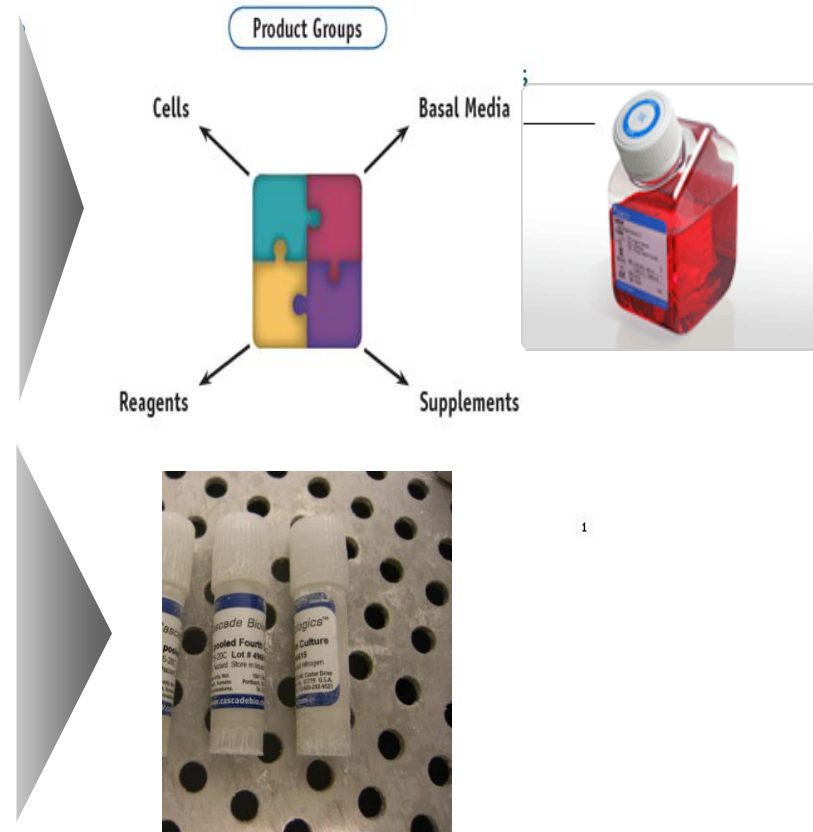
# Optimal Primary Cell Confluence is achieved through a System of Cell and Liquid Developments

## • Cell Systems

1. Liquid media LifeTech develops and manufactures to support primary cells *in-vitro* are also used in FDA regulated diagnostics such as:

- Drug development
- Clinical trials
- Cosmoceutical toxicology tests

2. Cryopreserved vials of primary human cells that mimic the human *in-vivo* environment using a defined group of medias, supplements, and reagents.



# Primary Cell *Developments* from Organ & Tissue Donation

- Primary Cell Systems

- Cell Growth Medium, Supplements, and Reagents for Scientists to grow normal, non-diseased cells for research
- Various cell types derived from tissue such as:
  - > Aorta, Pulmonary Artery, Coronary Artery

- > Cell development progression time period: 3 months

Whole Heart

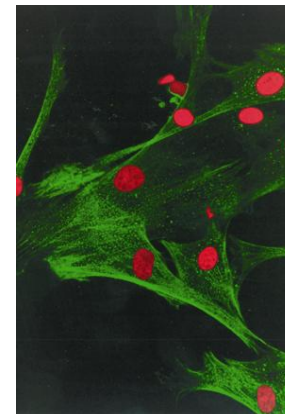
(procurement)

Aortic, Pulmonary & Coronary Artery Smooth muscle

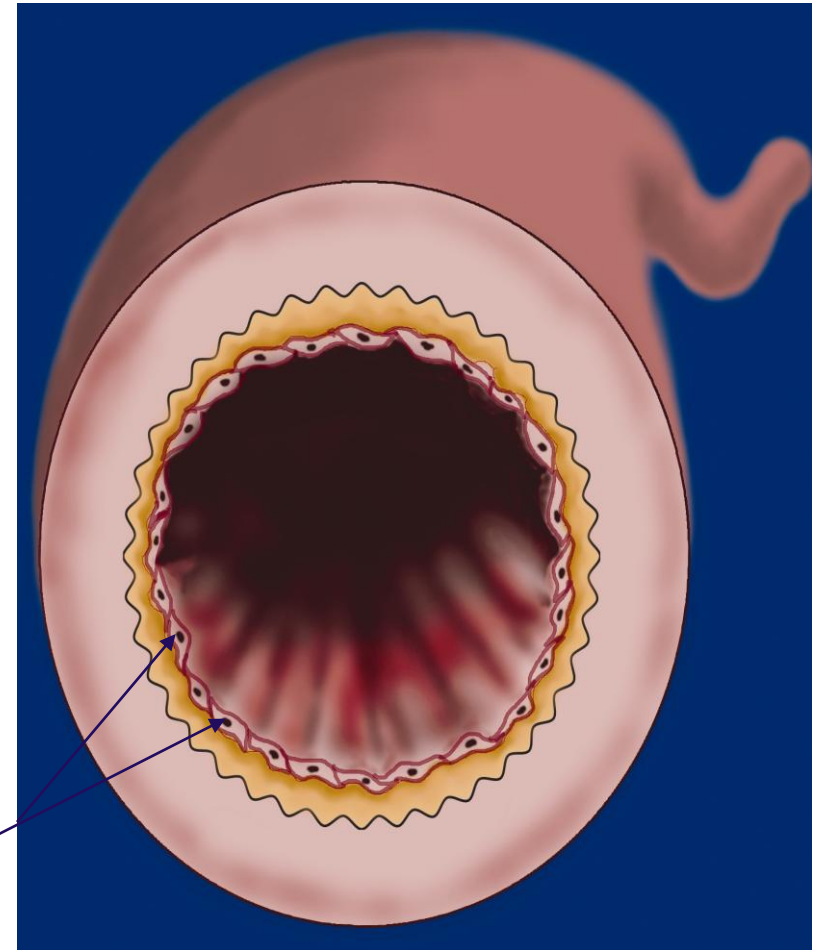
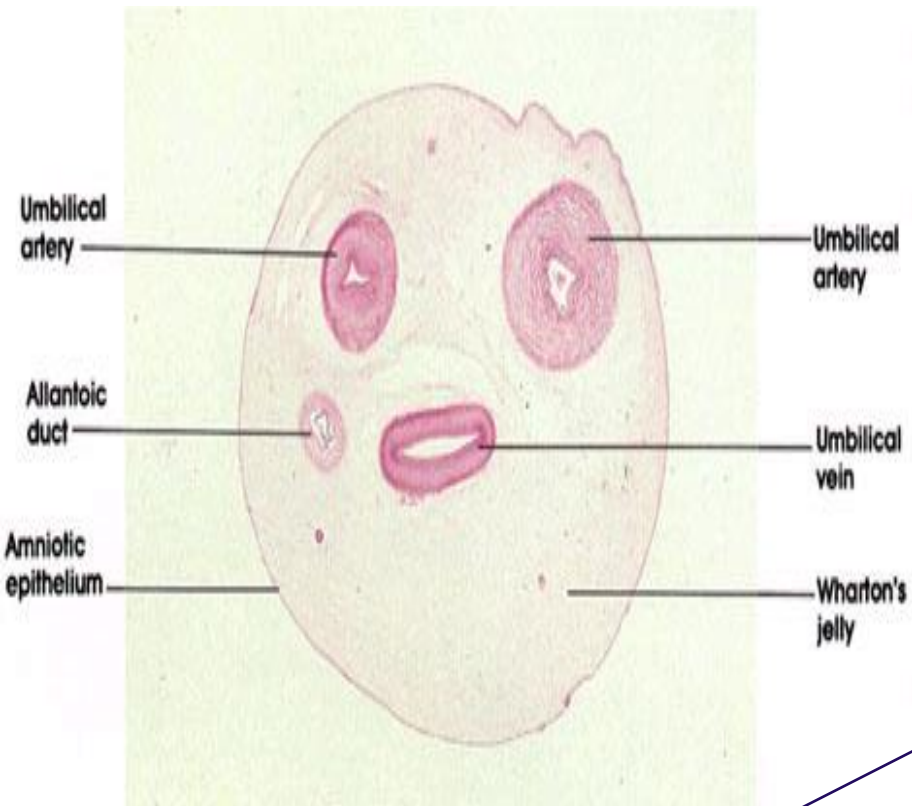
(enzyme digestion - cell proliferation)

Human Aortic Smooth Muscle Cells

(cell characterization – product for researchers)



# Histological image of an umbilical cord and an illustrated vessel



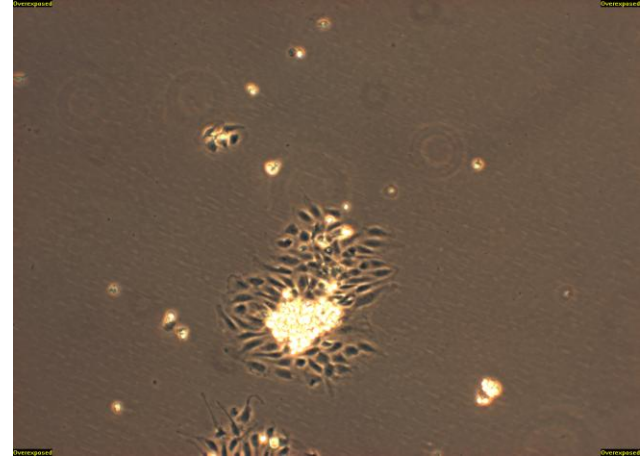
**Endothelial cells**  
(Extremely delicate)

# Workflow: Preparation of Umbilical Vein Endothelial Cells from (human) Adult Umbilical Cord

**Step 1:** Tissue is cannulated & incubated in enzymatic solution

**Step 2:** Tissue is further digested with enzyme solutions

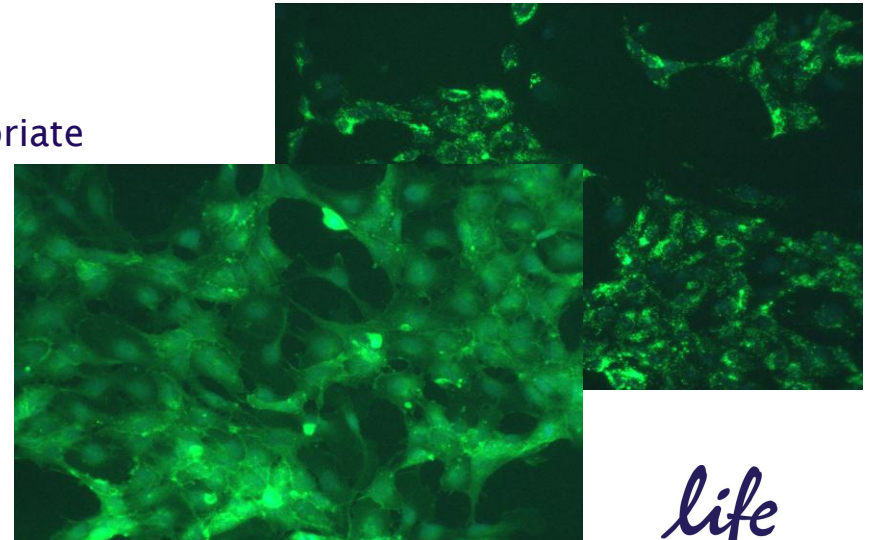
**Step 3:** Endothelial layer is released for the cell type of interest



## Steps 4

-Cells are subsequently re-suspended in the appropriate medium & supplement and seeded in culture flasks

**Time period: 2-3 months**



# Processing Liver Cells

Post Filter Cells are evaluated for Quality

Then the cells undergo a series of clean up spins

Final Cell quality is then evaluated at which point acceptable

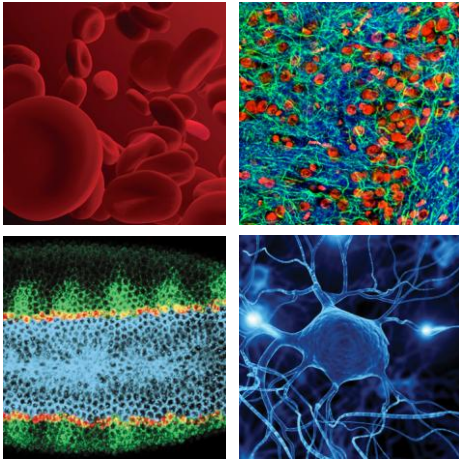
hepatocytes can be used by Scientists in the following forms:

Fresh Suspensions

Fresh Plated Cells

Cryopreserved Cells

# Case study 1

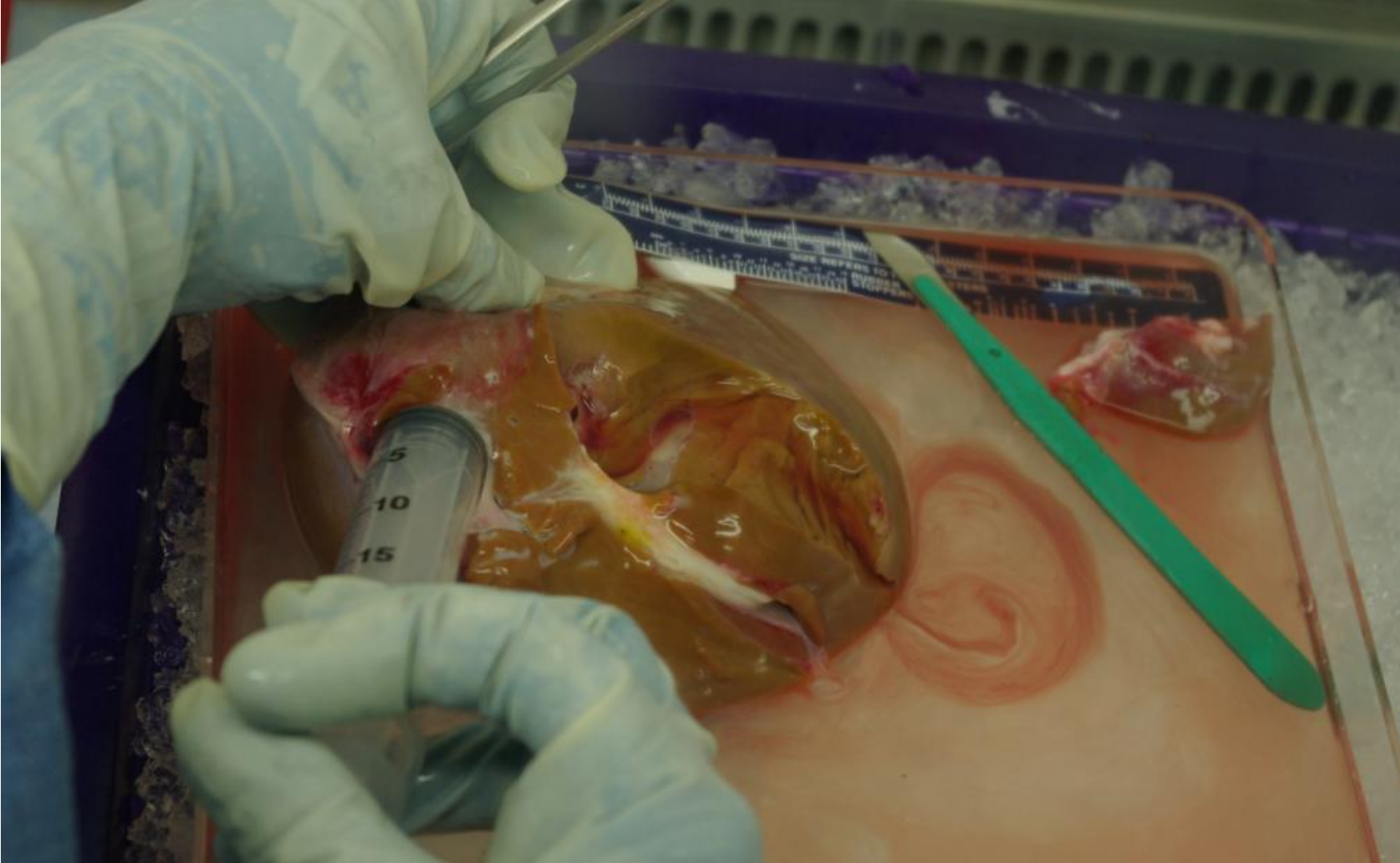


- Good donor specs
  - Young, low BMI, low CIT
- Excellent flushing
- Excellent vasculature
- Good cut
  - End of lobe, capsule intact

**Final – 3.8 Billion, 94%, A-**

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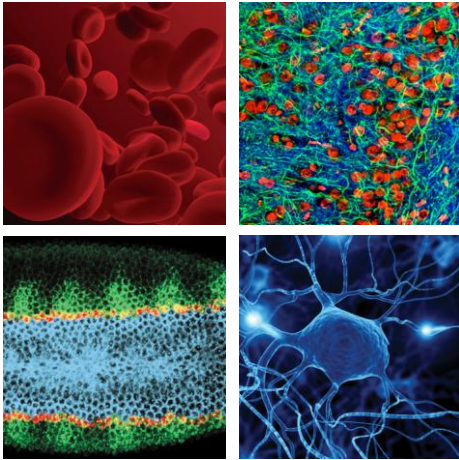
# Flushing upon arrival



# Perfusion of the Tissue



# Case study 2

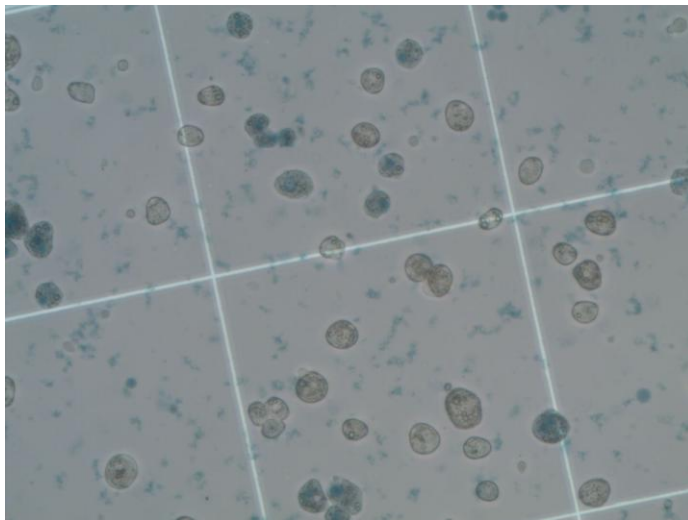


- Fair flushing
- Good vasculature
- Donor had history of diabetes, cardiac disease, GI disorders
- 11 Different medications

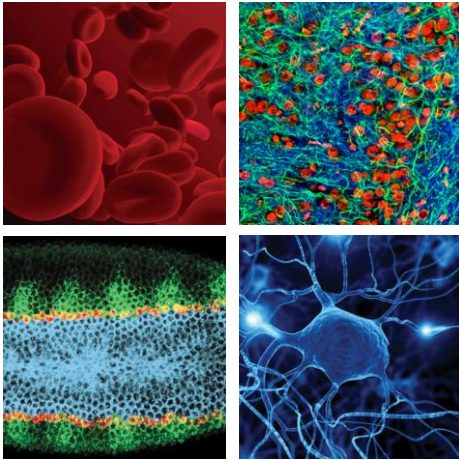
**Final – 694 Million, 79%, B+**

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# WLT Results – 8### – worked well



# Case study 3

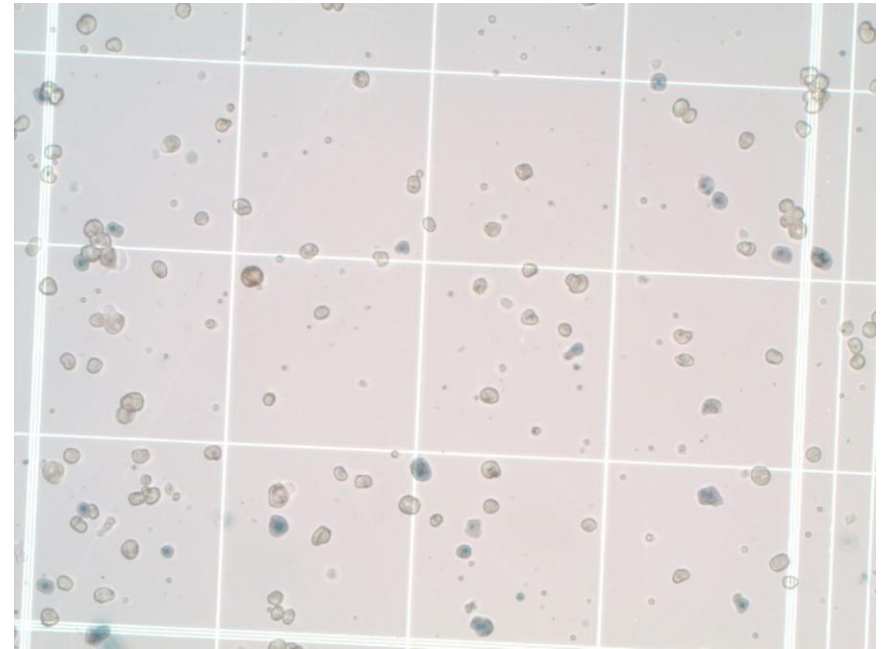
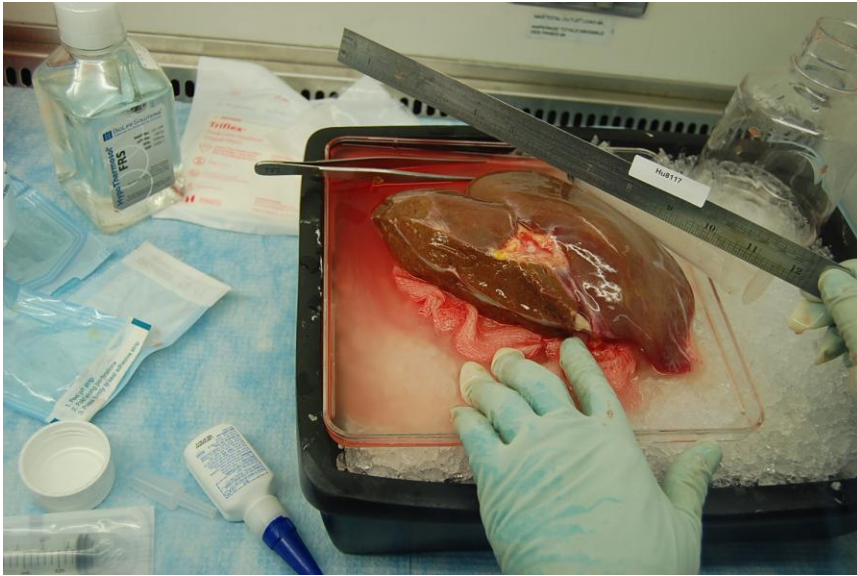


- Fair flushing
- Good vasculature
- Blood clots present throughout tissue and under capsule

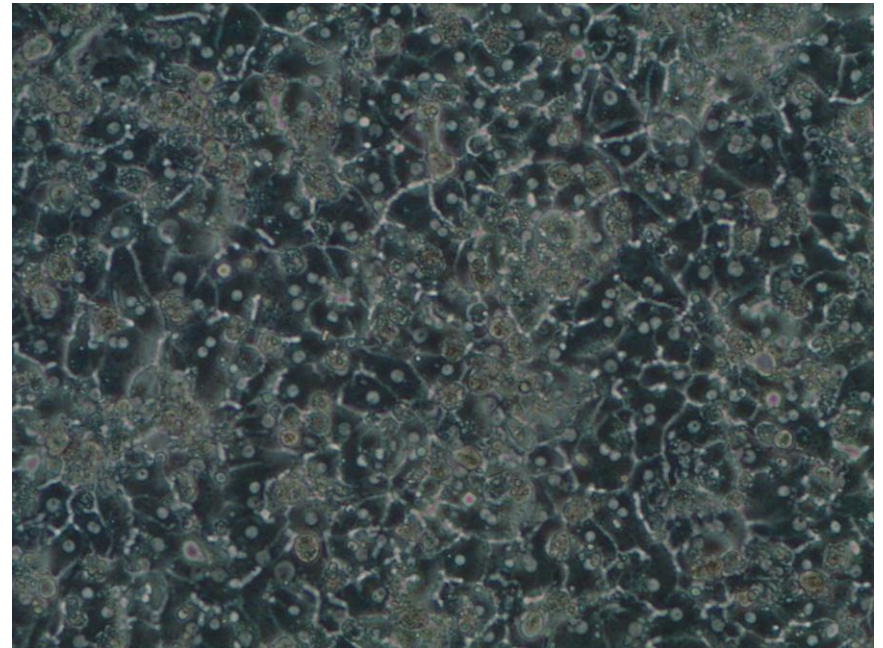
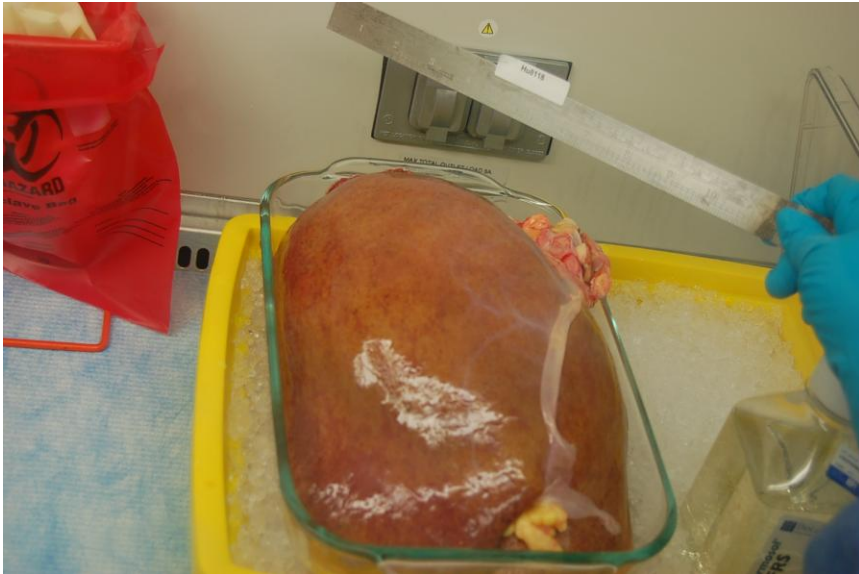
Post Filter – 150 Million, 37%, B-

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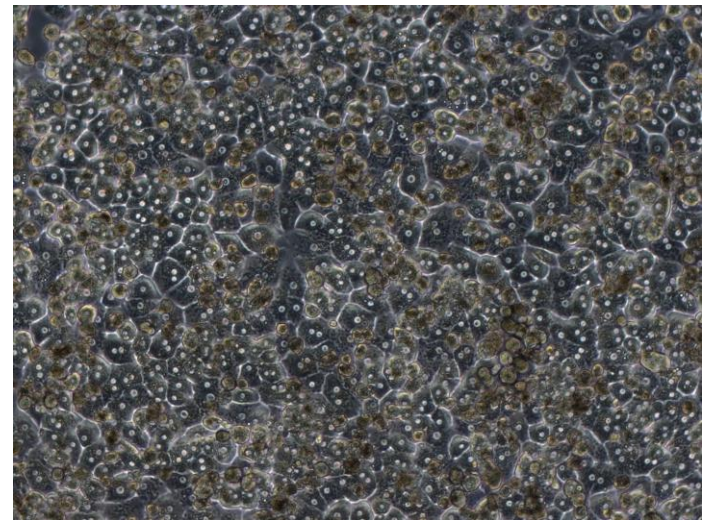
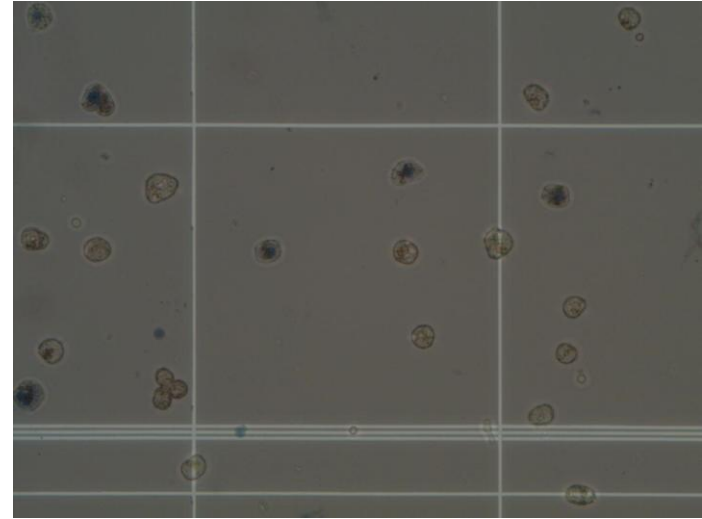
# 8### – did not work very well, but got some cells



# 8### – did not work well, but still got cells



# 8### – worked well



# 8### – did not work at all





# Donor Organs for Research (cont)

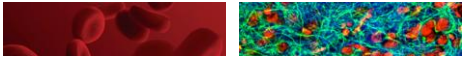
- Cardiovascular tissue
  - Medical History (Donor Variables)
    - > AGE: ( $\leq 55$ )
    - > Diabetes: Duration, IDDM vs NIDDM
  - Labs
    - > None
  - Tissue Appearance
    - > Length: 4" aorta; 1" CA and PA
  - Preservation
    - > DCD or BD
    - > Downtime: N/A
    - > WIT: N/A CIT:  $\leq 48$ hrs
    - > Temp: Always kept at refrigerator temp
    - > Medium: UW
- Cardiovascular tissue (cont)
  - Preservation (cont)
    - > Perfusion: No flushing
  - PMH to consider (Donor Variables)
    - > COD
    - > Heart disease
    - > Smoking
    - > ETOH
    - > High Risk Behavior

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# Thank you



Deven Richardson: IIAM - MERIN event presentation

June 07, 2011

