



Advanced Cell Technology

(OTCBB: ACTC)



Advanced Cell Technology

CAUTIONARY STATEMENT CONCERNING FORWARD-LOOKING STATEMENTS

This presentation contains “forward-looking statements” as defined under the federal securities laws. Actual results could vary materially. Factors that could cause actual results to vary materially are described in our filings with the Securities and Exchange Commission. You should pay particular attention to the “Risk Factors” contained in documents we file from time to time with the Securities and Exchange Commission. The risks identified therein, as well as others not identified by the Company, could cause the Company’s actual results to differ materially from those expressed in any forward-looking statements.



Advanced Cell Technology

Human Embryonic Stem Cells

The Opportunity:

- **All Somatic Cell Types**
- **Ease of Gene Targeting**
- **Regenerative Gene Expression**

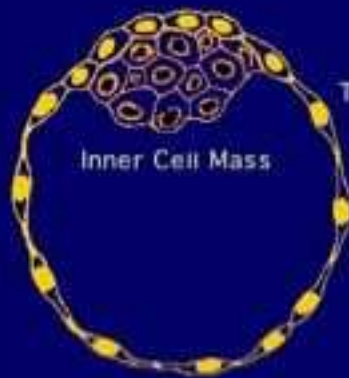
Photo: Martin Pera



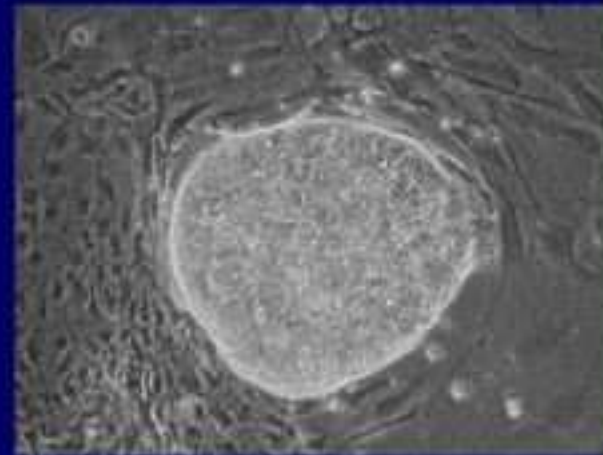
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Human Embryonic Stem Cells

What Are ES Cells?



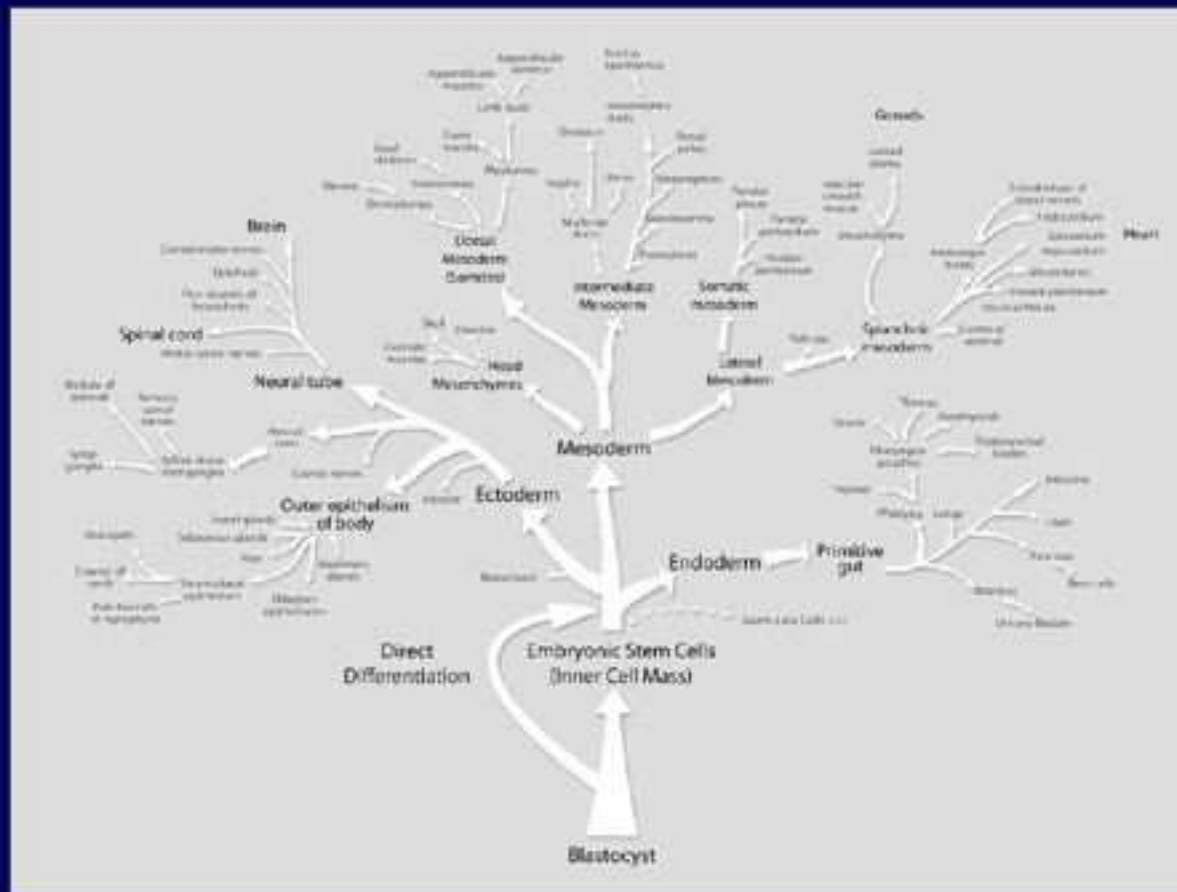
Trophectoderm





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ACTCellerate Cell Lines

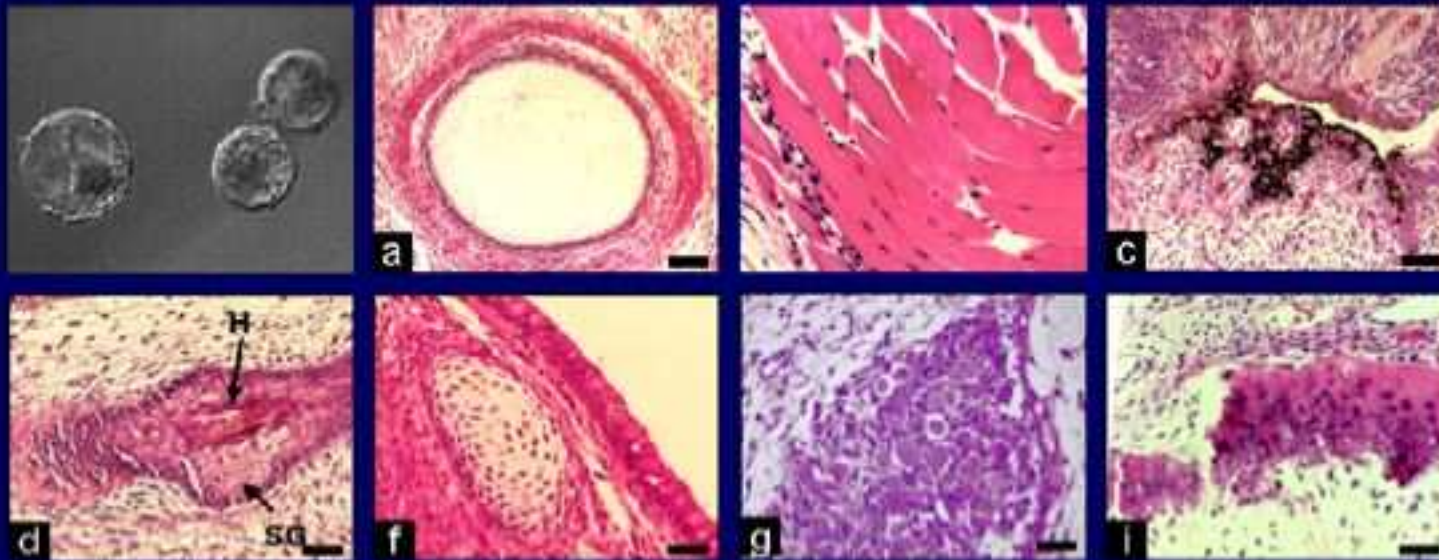




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Human Embryonic Stem Cells

"Regenerative" Gene Expression



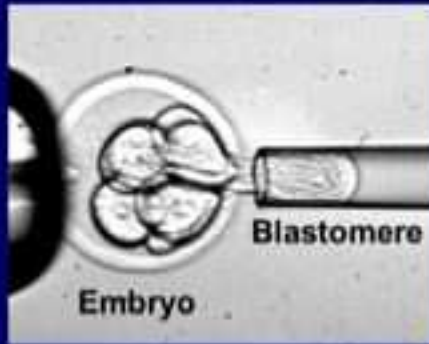
Cibelli et al, Science 2002



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Technology Platform

Blastomere Biopsy



Embryo

Embryo transfer or
Cryopreservation

Blastomere

Human ES Cells or
Direct Differentiation

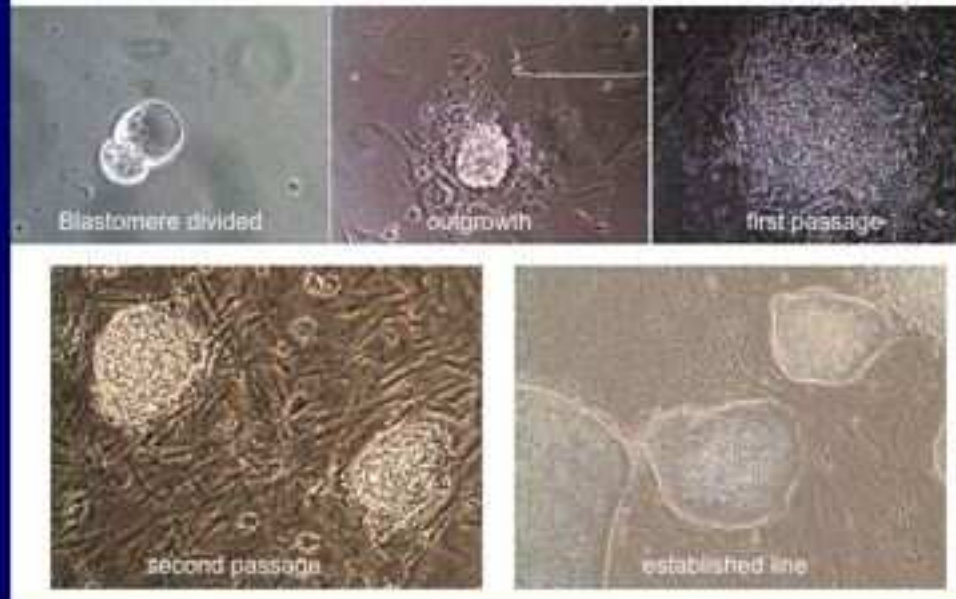
Klimanskaya et al, Nature (2006)



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Technology Platform

Stages of derivation of hES cells from single blastomere





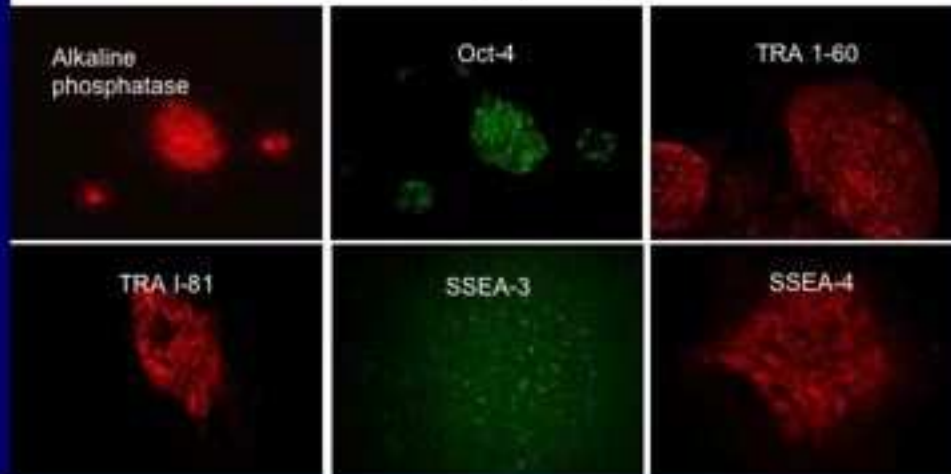
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Histocompatibility

Federal Policy and New Lines

Characterization of Single Blastomere-Derived hES Cell Lines

Markers of pluripotency

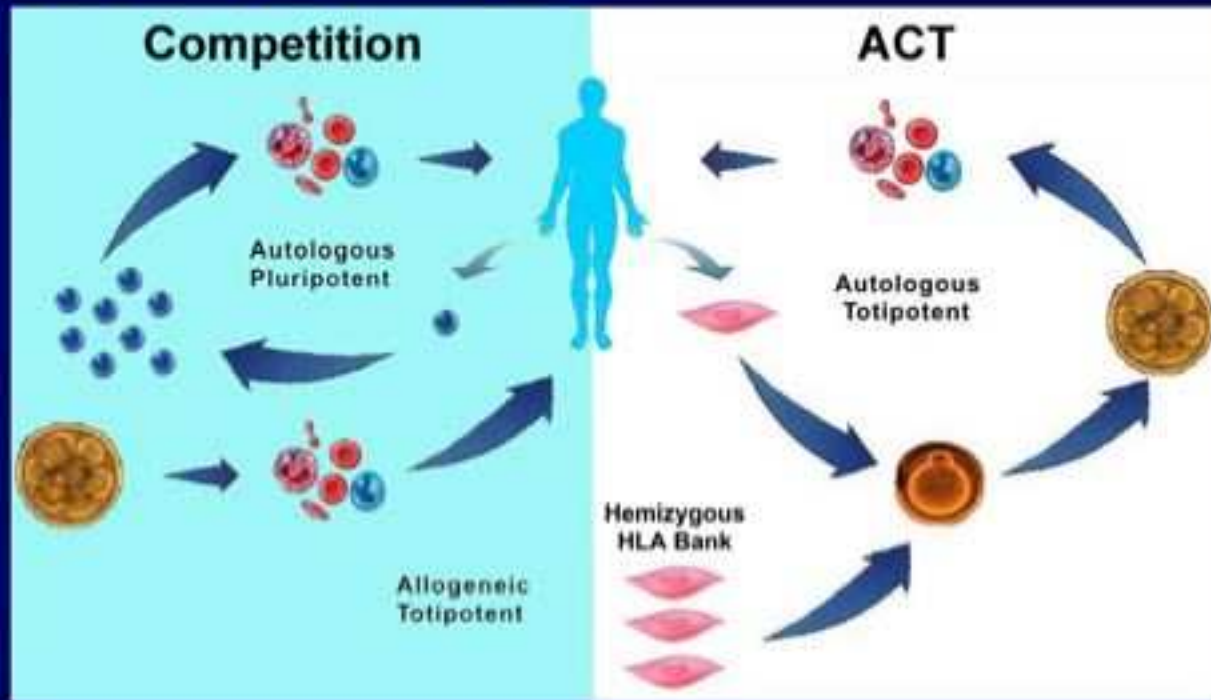




Technology Platform

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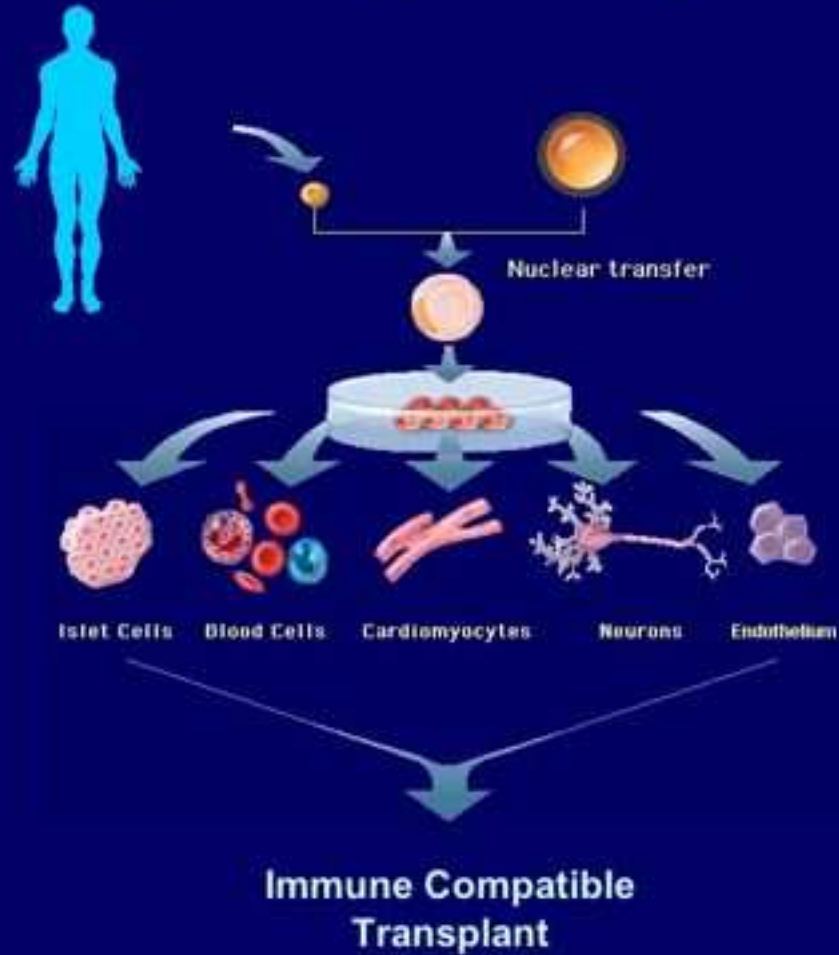
Histocompatibility Strategies





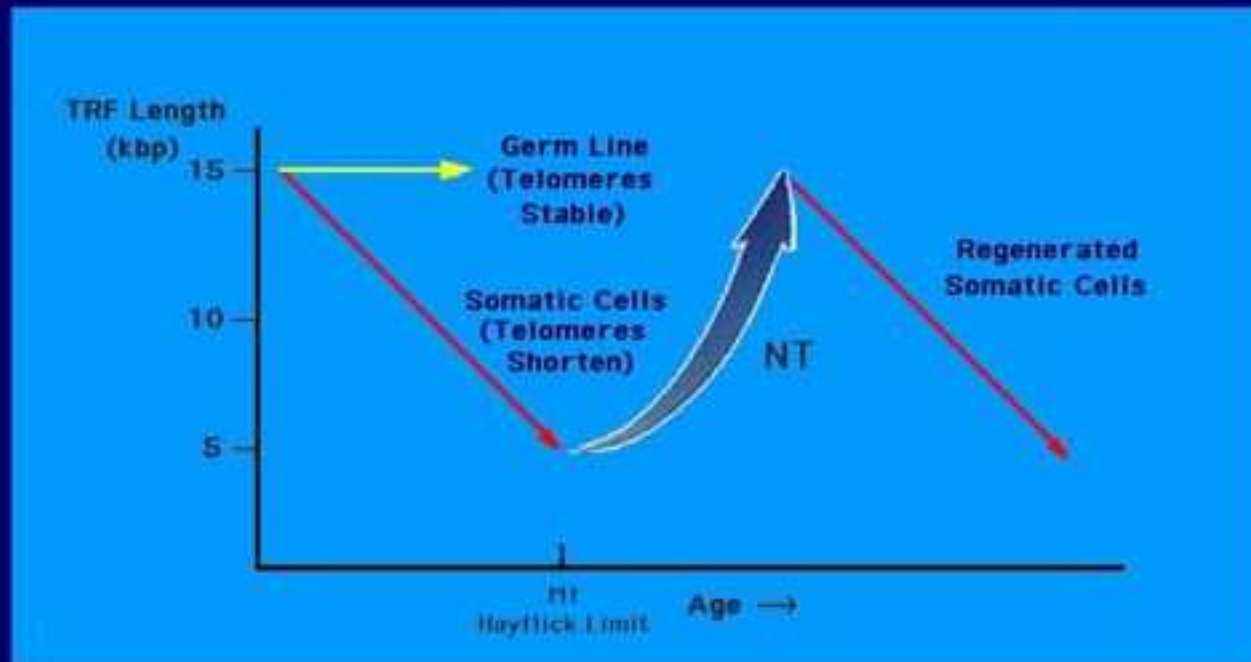
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Histocompatibility Strategies



Histocompatibility Strategies

Restoration of Cell Lifespan

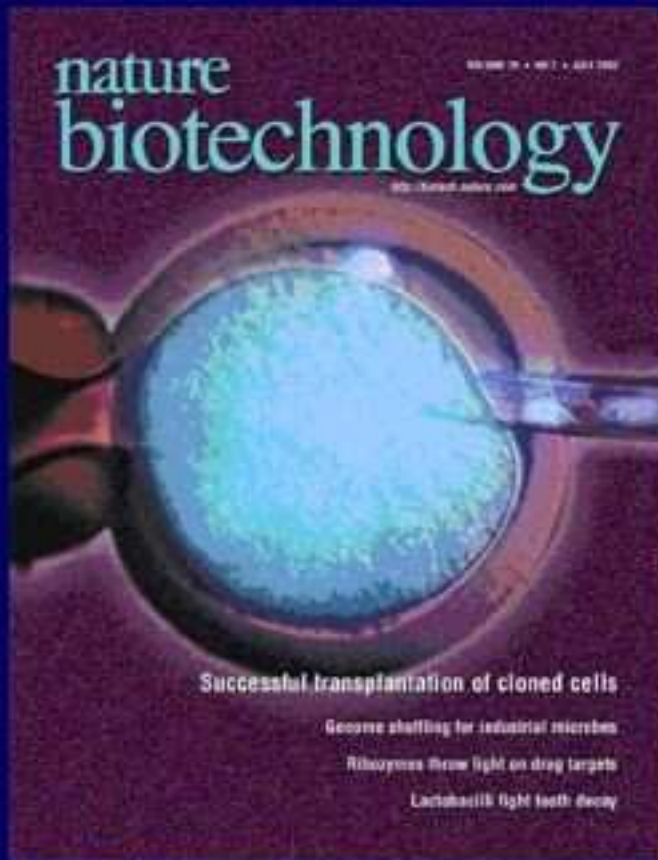




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Technology Platform

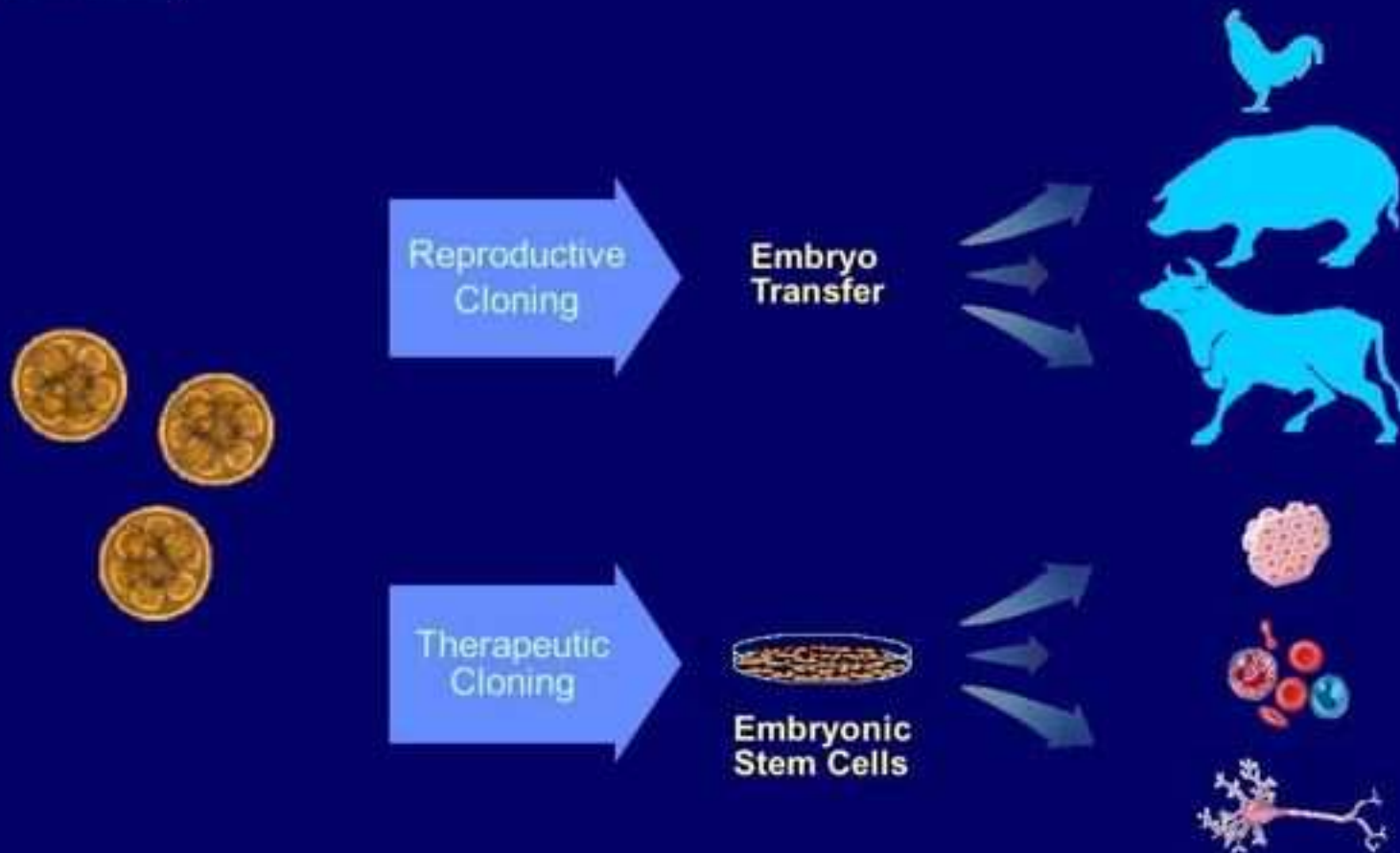
Cloned Cells Are Not Rejected





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Histocompatibility Strategies





Histocompatibility Strategies

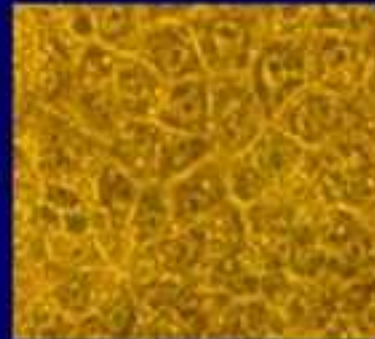
Therapeutic Cloning: Evidence from Bovine, Murine, and Human Systems



Bovine Fibroblasts



Blastocyst



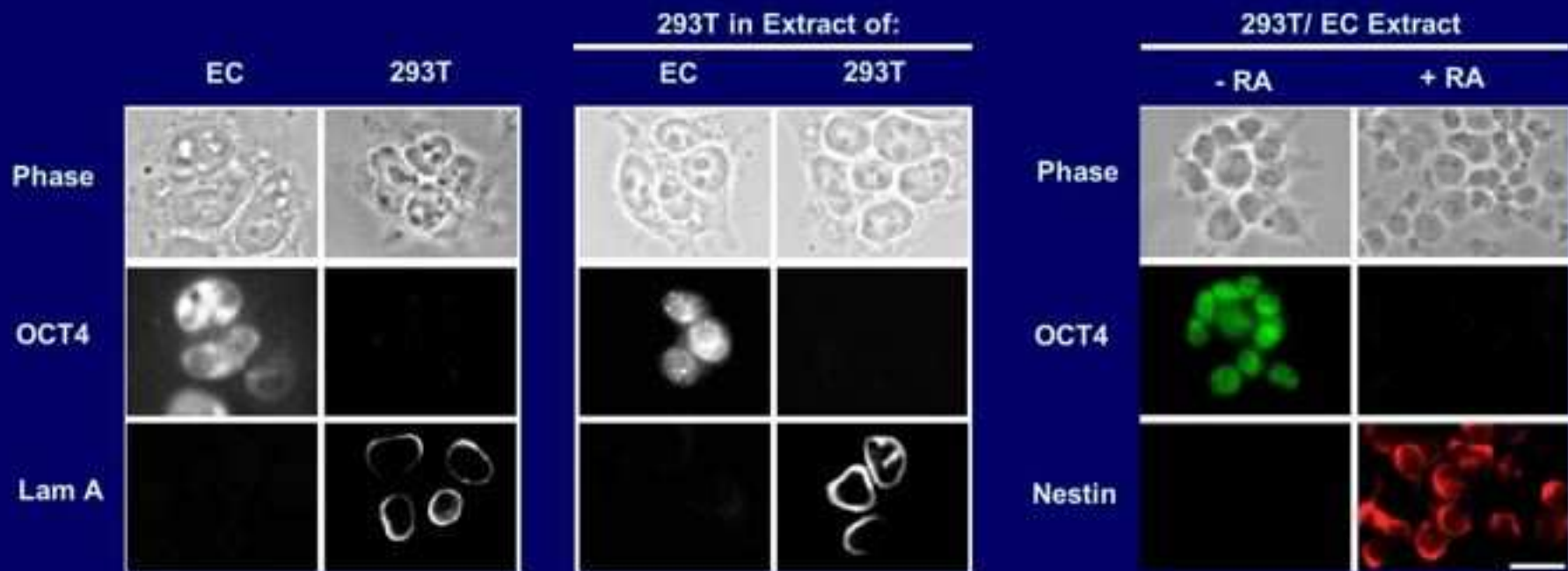
Embryonic Stem Cells



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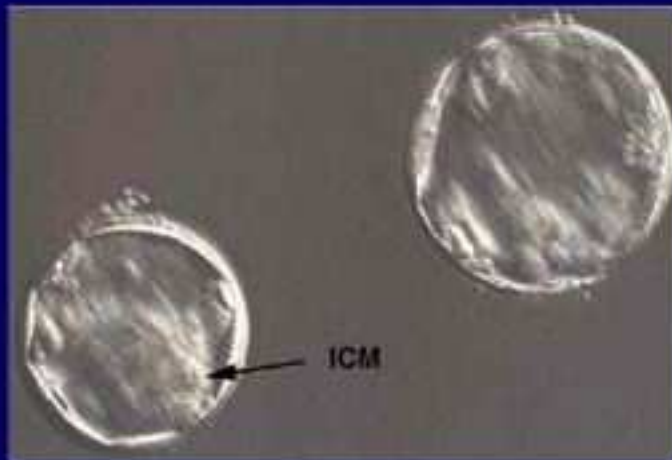
Histocompatibility

Fusion-Mediated Reprogramming

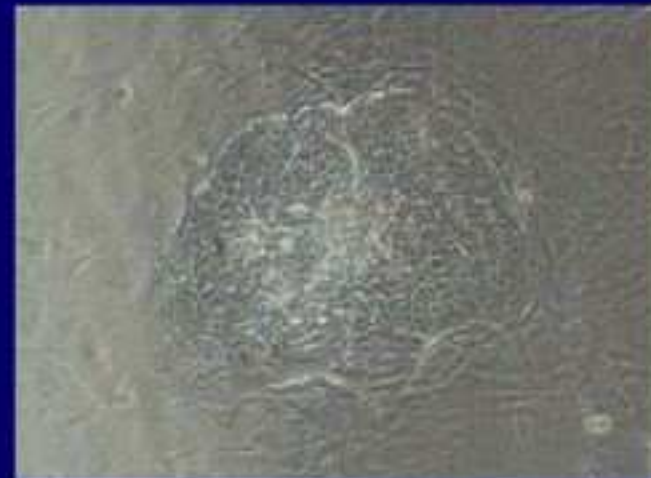


Taranger et al, (2005) Mol. Biol. Cell 16: 5719

Parthenogenesis



Human Parthenote

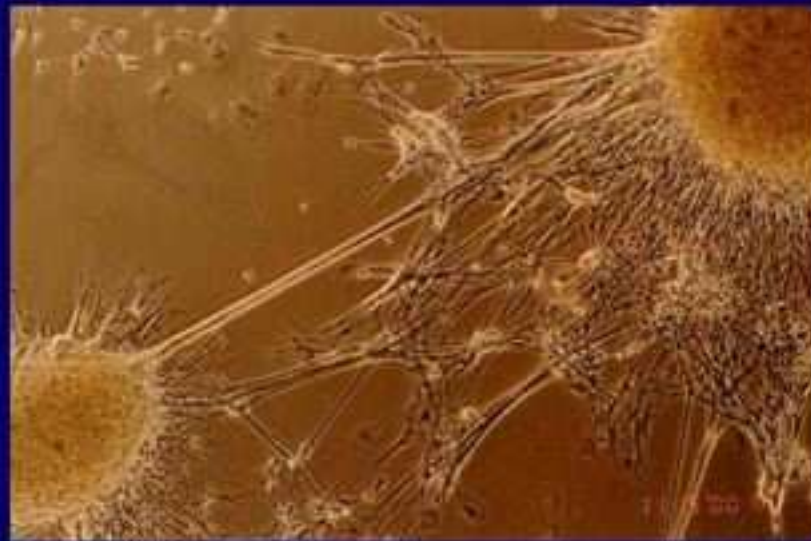
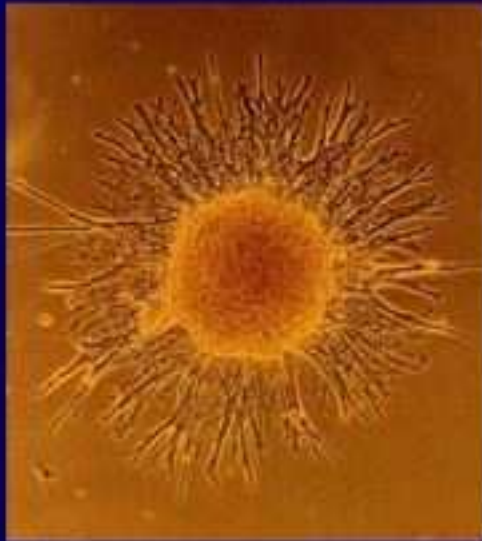


Primary ES Cells



Technology Platform

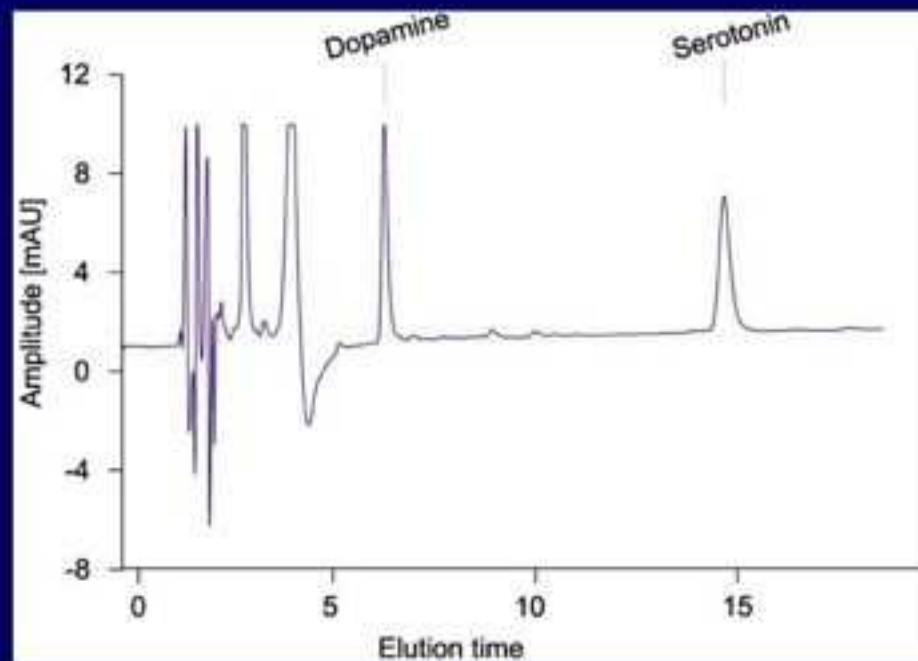
Potential for Neurons





Technology Platform

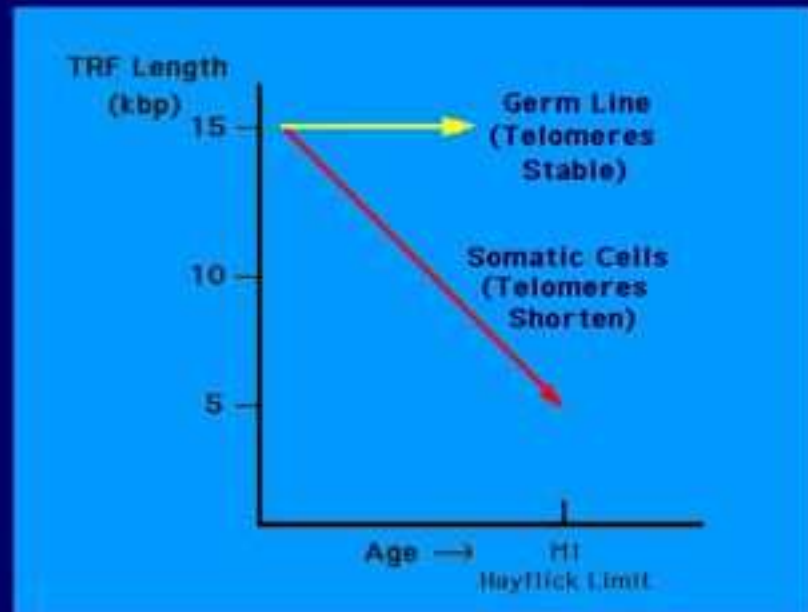
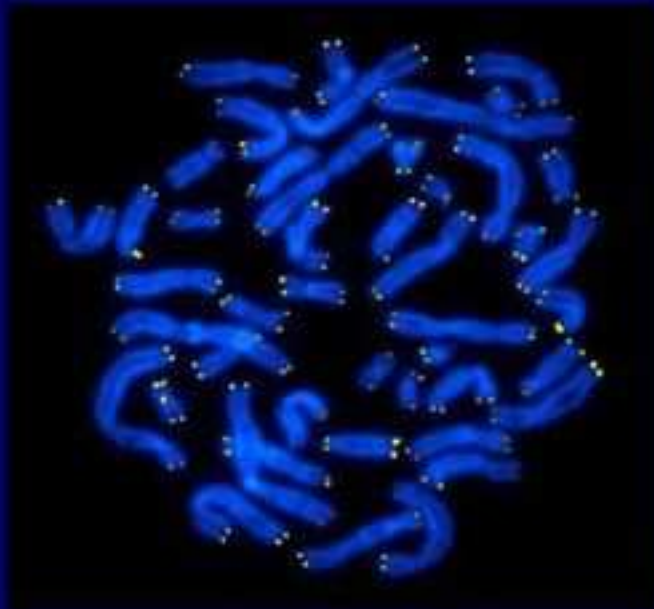
Potential for Neurons





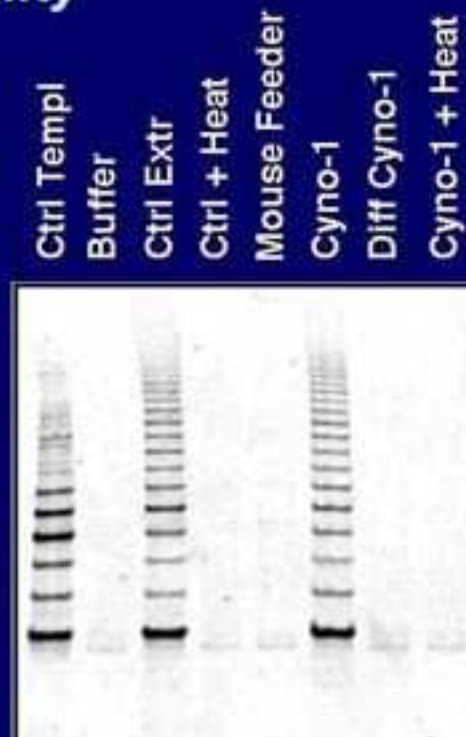
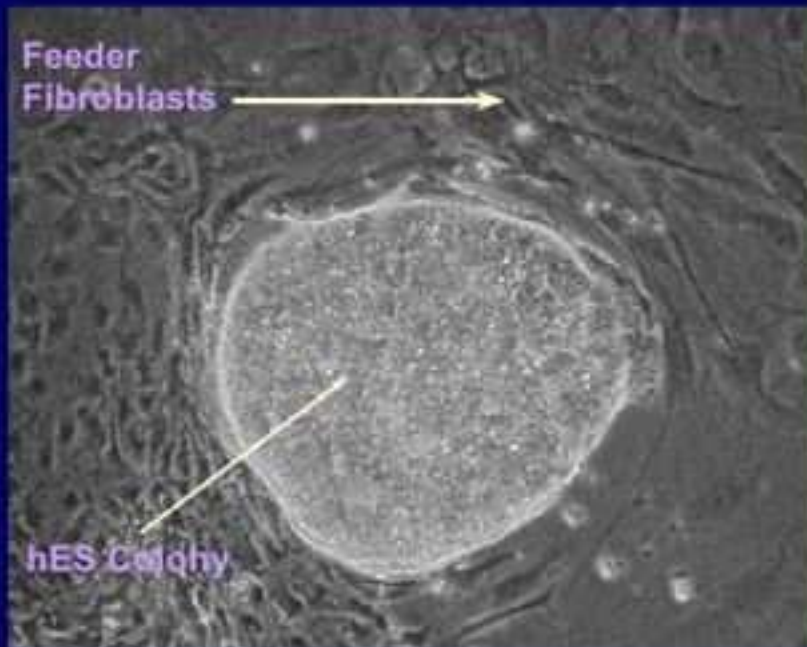
Technology Platform

Gene Targeting in Immortal Cells



Complex Mixture of Cell Types

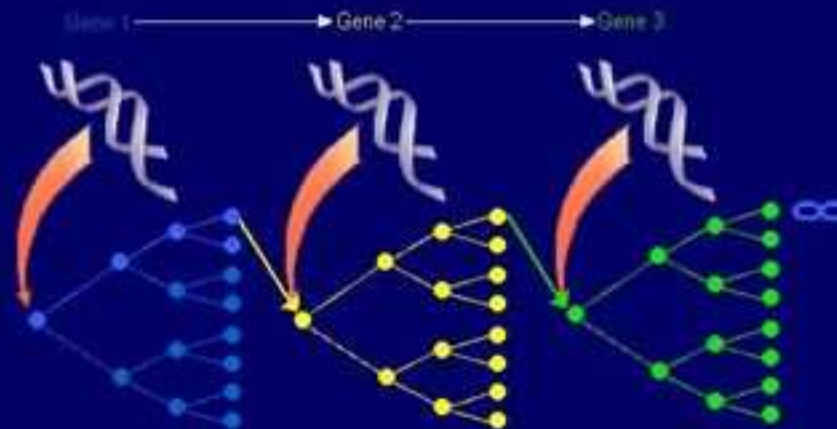
ES Cells Possess a Regulated Immortality





Complex Mixture of Cell Types

An Immortal Substrate Facilitates Gene Targeting



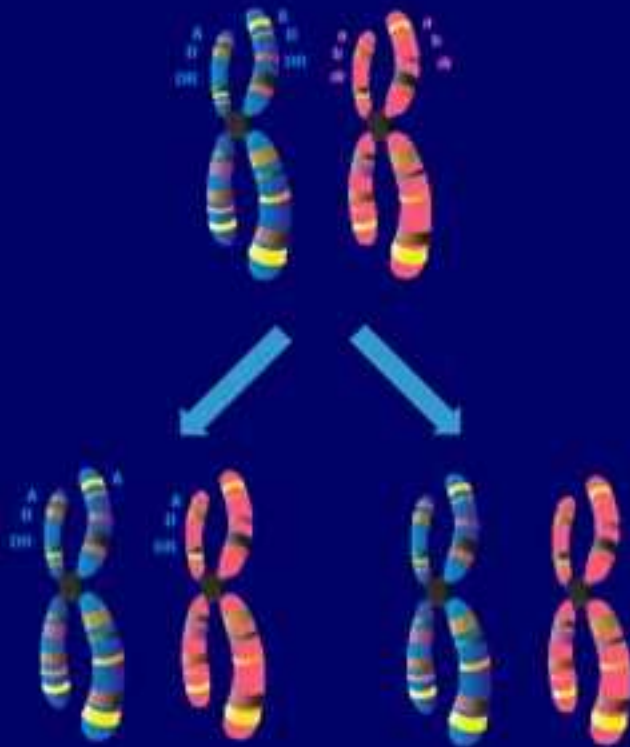
Gene Targeting Technologies



Histocompatibility

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Reduced Complexity Library



Matching A&B Only:

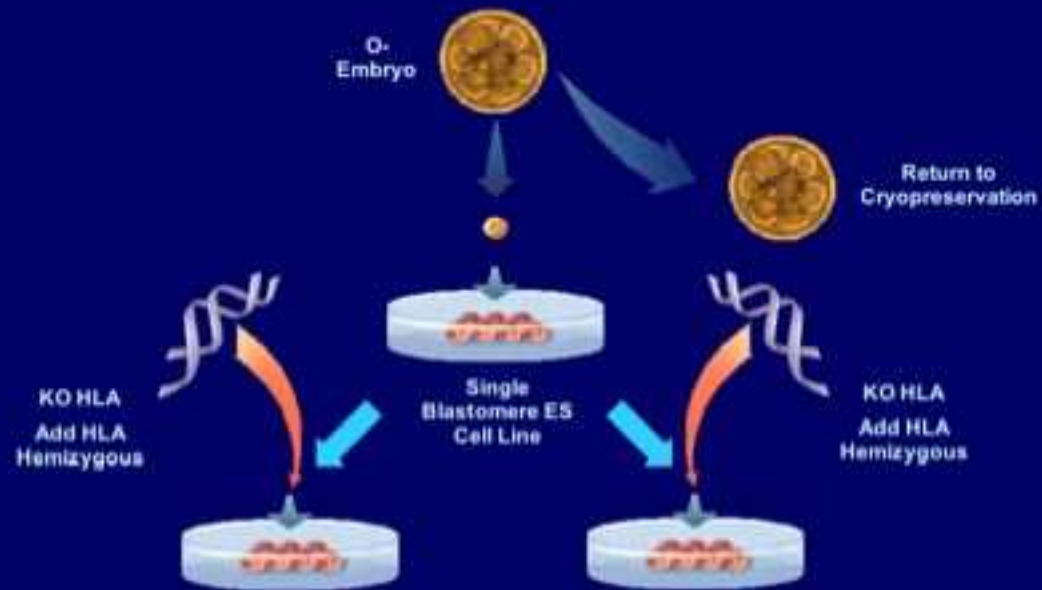
Complexity of Heterozygous 767,746
Complexity of Homozygous 1,708



Histocompatibility

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Reducing the Complexity of HLA Genes

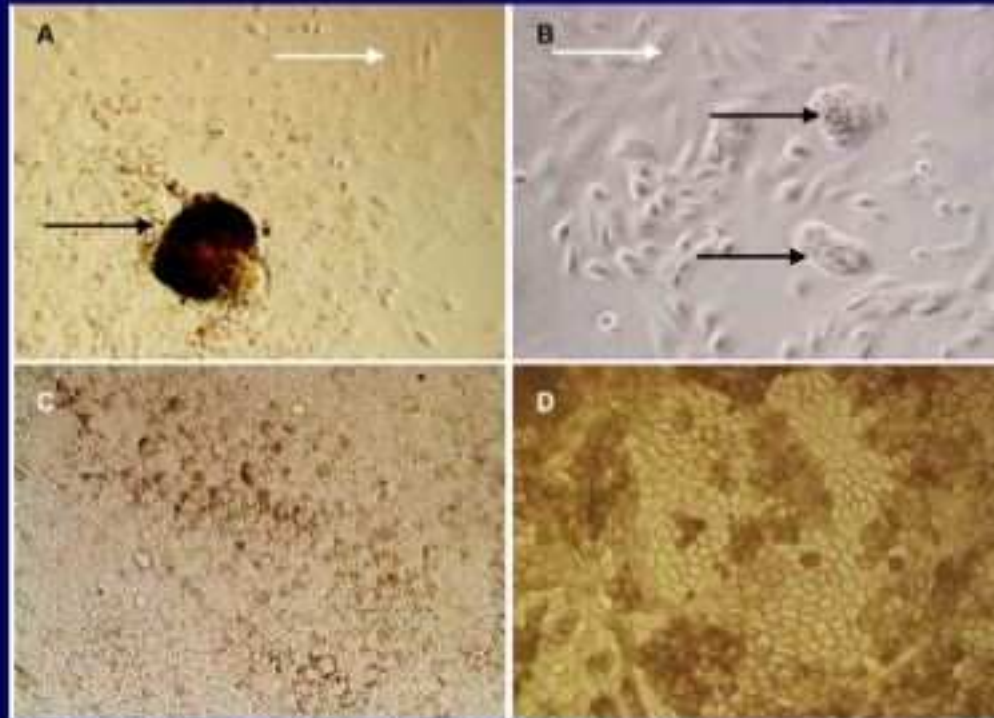




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Product Development

Development of hES-Derived RPE

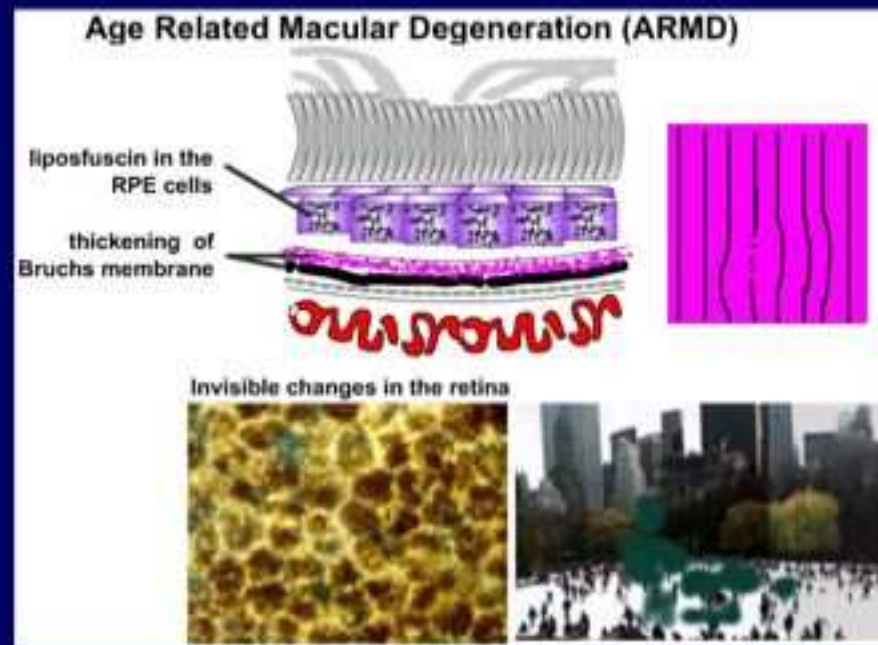




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Product Development

Development of hES-Derived RPE





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RPE & Hemangioblast Cells

WA09 RPE used for transplantation in RCS rats

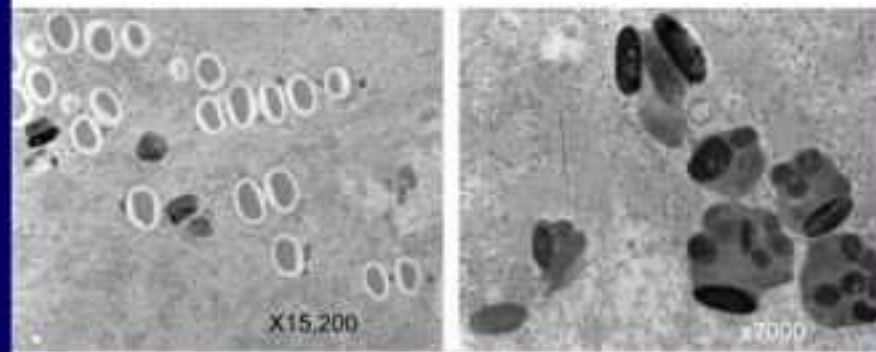




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RPE & Hemangioblast Cells

Phagocytosis of latex beads





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Product Development

Development of hES-Derived RPE

**All hES cell lines in our experiments
reproducibly generated RPE
which could be passaged, characterized and expanded**

Wicell hES cell lines

WA01, WA07, WA01 – three lines, 23 experiments

Harvard hES cell lines

HUES1, HUES2, HUES3, HUES5, HUES6, HUES7, HUES8, HUES10
– 6 lines, 22 experiments

ACT hES cell lines

MA01*, MA03, MA04, MA09*, MA14, MA40, MAJ1
- 7 lines, 25 experiments and going on

* -- single blastomere-derived hES cells

hES-RPE cells express RPE markers, show typical RPE morphology
and behavior(transdifferentiation and differentiation in culture),
and no longer express markers of hES cells

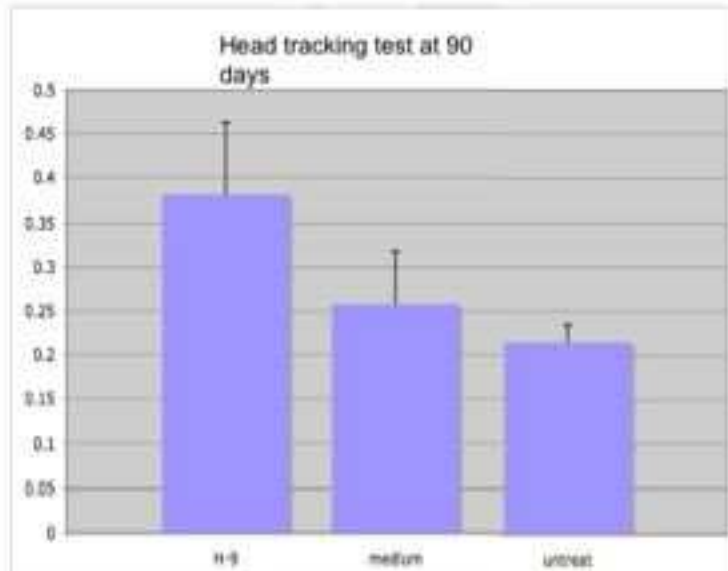


Product Development

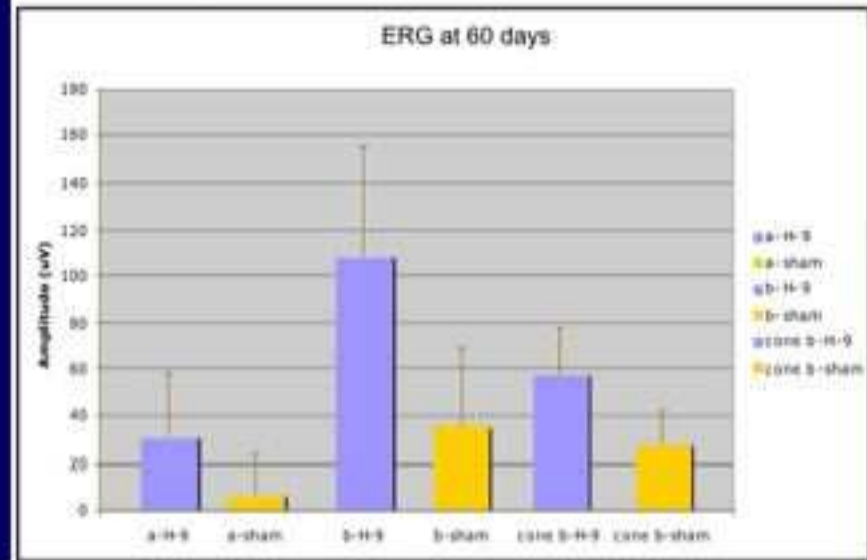
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Development of hES-Derived RPE

Animal studies – RPE transplantation into subretinal space of RCS rats



Animal studies – RPE transplantation into subretinal space of RCS rats

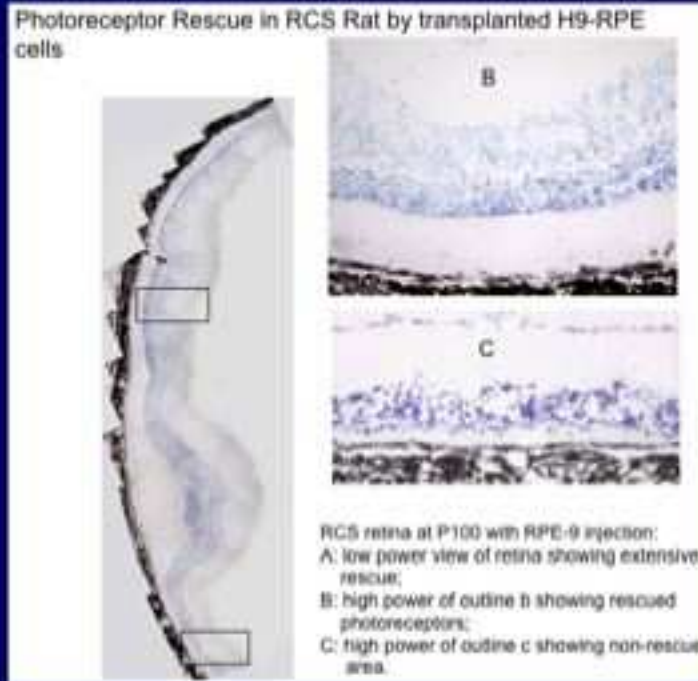




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Product Development

Development of hES-Derived RPE

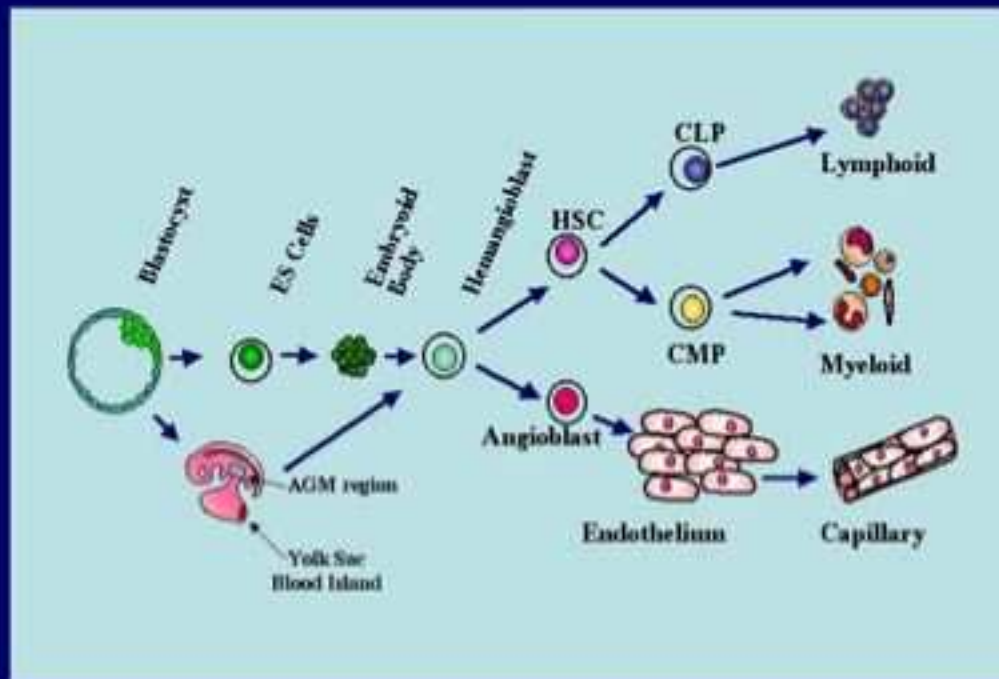




Product Development

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The Opportunity in Hemangioblasts

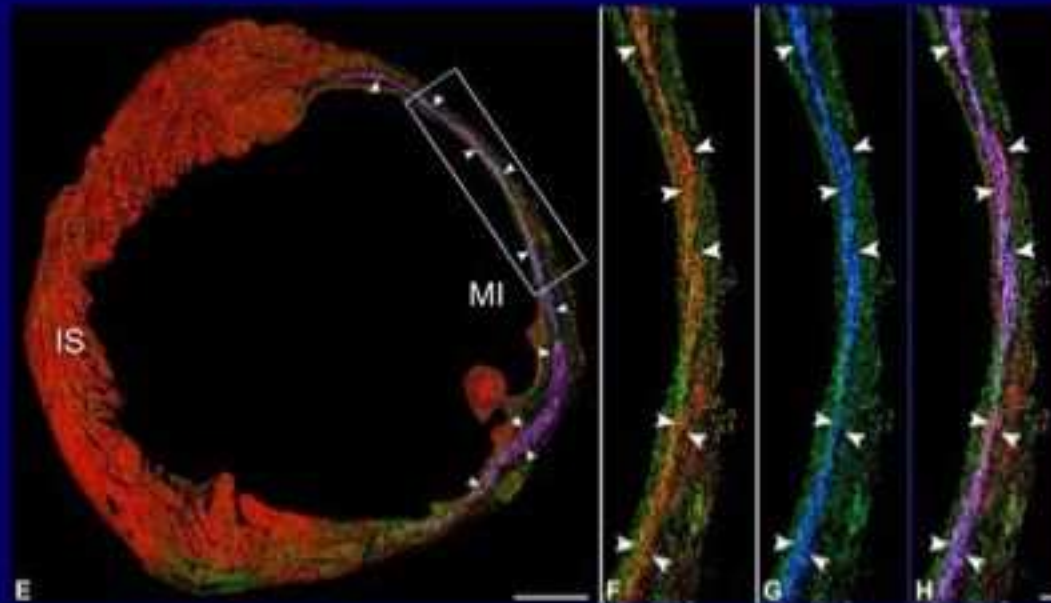




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Product Development

Large Markets: Age-Related Heart Disease

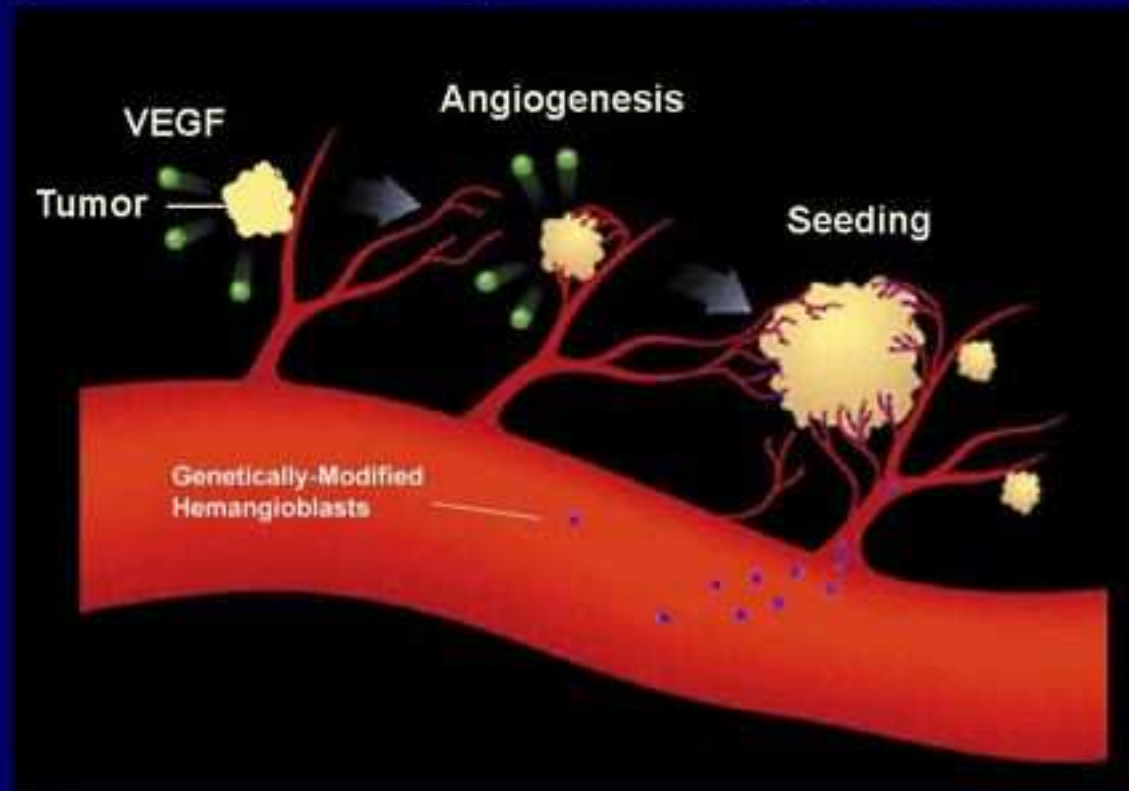


Lanza et al, Circ. Res. 2004



Identifying Near-Term Clinical Applications

Genetically-Modified Hemangioblasts May Target Cancer

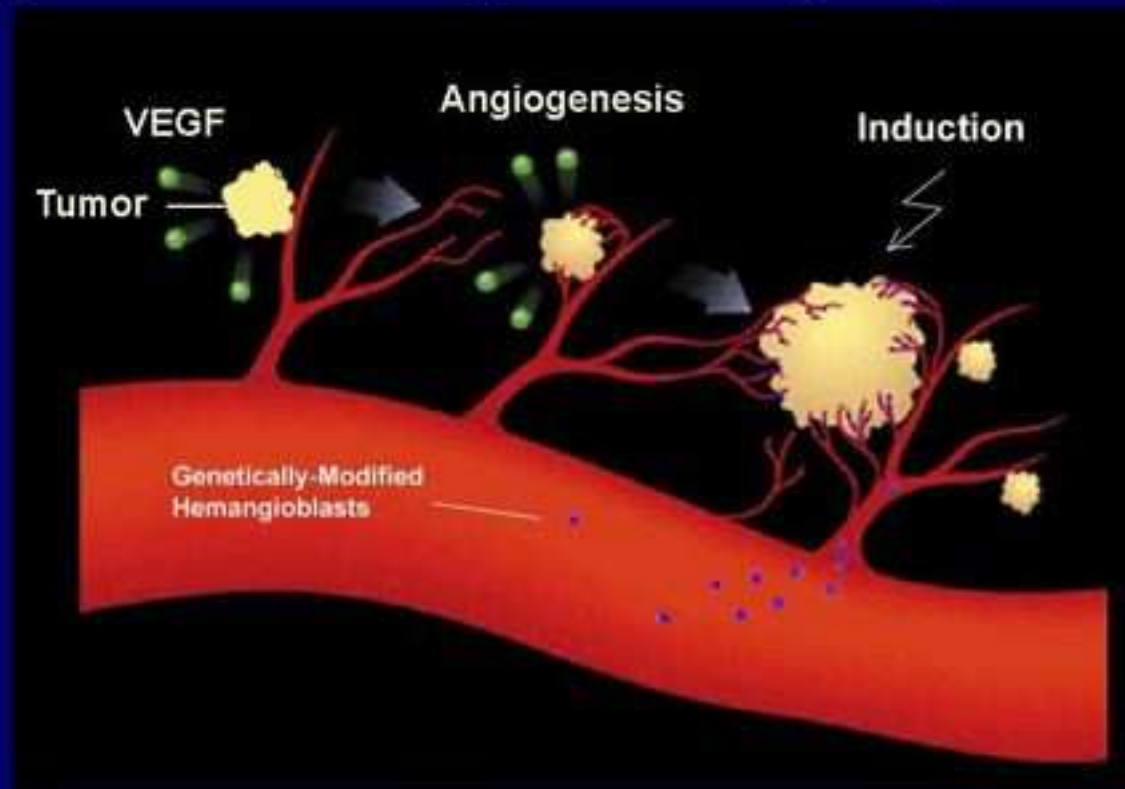




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Identifying Practical Applications

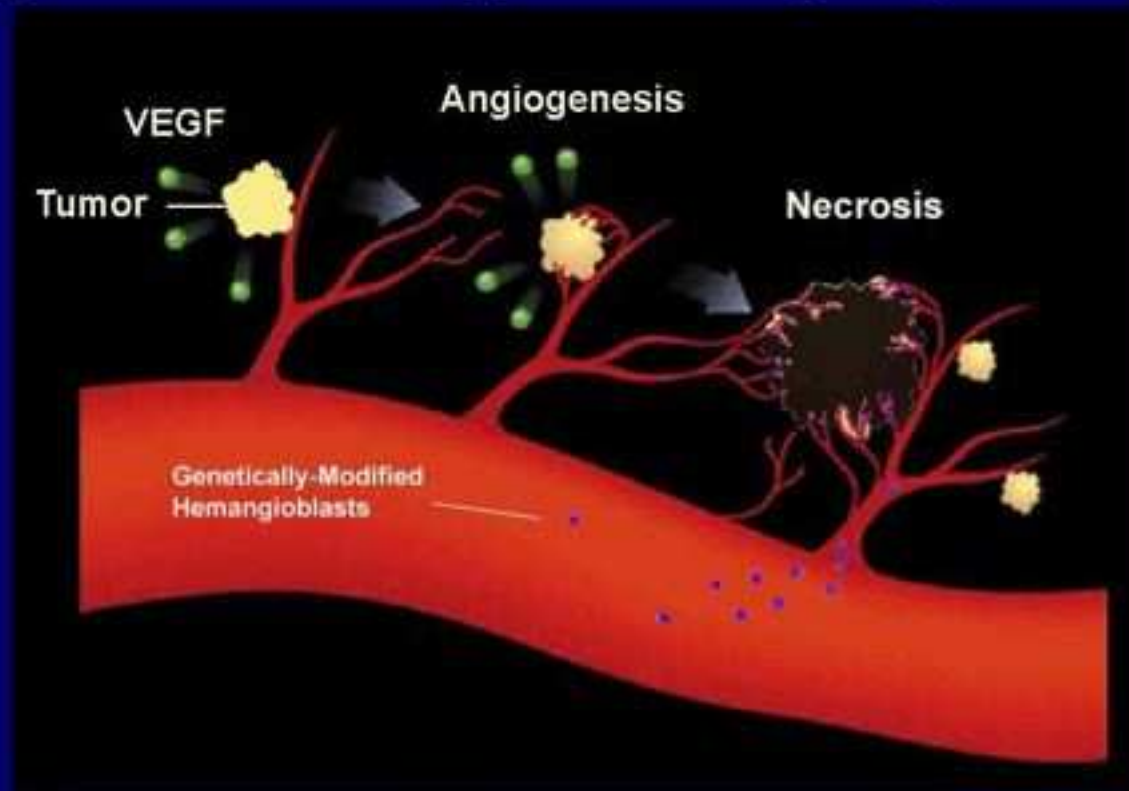
Genetically-Modified Hemangioblasts May Target Cancer





Identifying Practical Applications

Genetically-Modified Hemangioblasts May Target Cancer

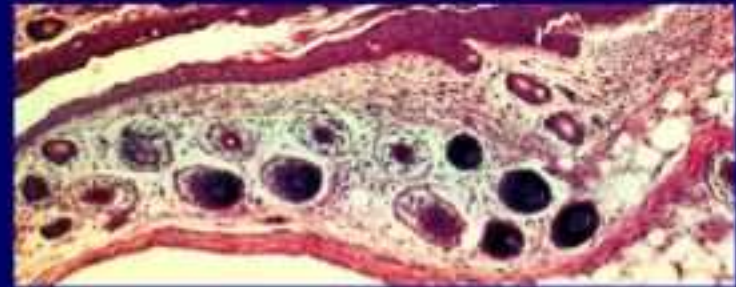




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Regenerative Dermatology

- **Full Regeneration in Embryonic Skin**
- **Easiest of cells to manufacture and scale under GMP**
- **Application in scarless wound healing, skin aging & elastogenesis**





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Product Development



- **Increased discovery rate**
- **Identifies scalable cells**
- **Increased purity for genomics**
- **Identification of potential applications**



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Product Development



Human Embryo-Derived Cells



hES Cell Line



Scaling in Rollers

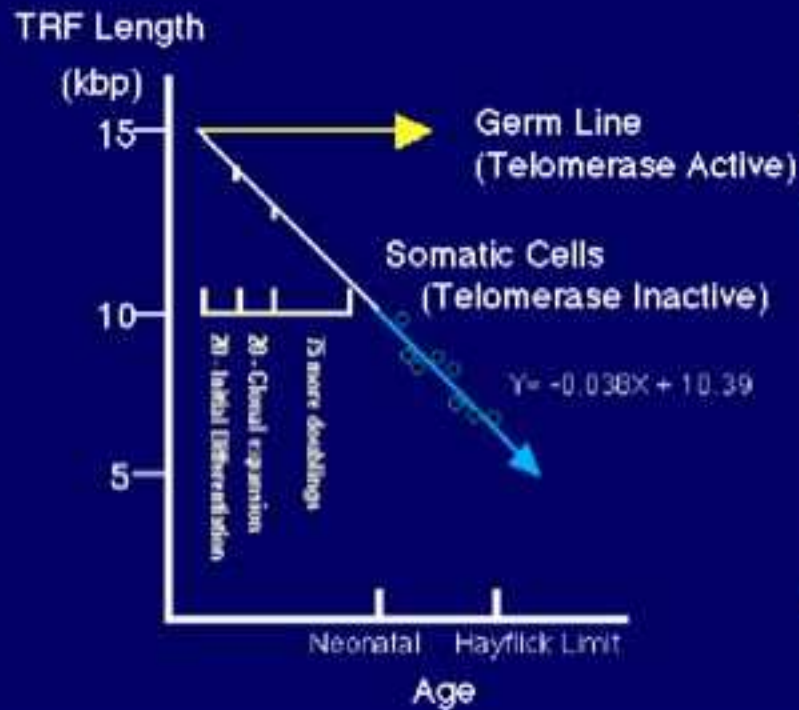


Gene Expression
Profile



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Product Development



population doublings:
22 34 43 53 65 72 82 90





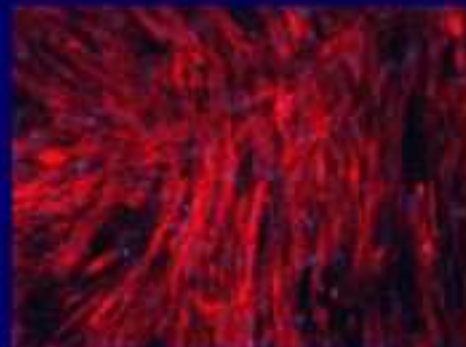
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Product Development



ACTC162

Cardiac Progenitor



MYH7

**Cardiac
Muscle**

ACTC
MYH7
MYL4
MYH3
TNNT2

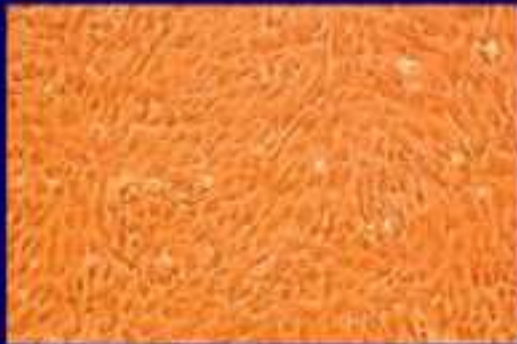
Neuronal

NEF3
NEFL
MEIS1
CDH2
SILV



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Product Development



ACTC61 (P7)

**3-4th Rhombomere
Cranial Neural Crest**

- **Potential for Cranial Neural Crest:**
- **Capacity to migrate**
- **Differentiate with cues from environment**
- **Recruit vascularization & innervation**
- **Potential to differentiate into skin, cartilage, bone, nerves, and sensory organs such as the middle and inner ear.**
- **Applications in cranial/ facial congenital abnormalities, trauma or other reconstructive surgery of skin/cartilage, or bone of the face and neck, neuropathies, skin aging, hearing loss, pigmentation disorders.**



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Product Development

- **Manufacturing - Simple in vitro expansion**
- **Stability of karyotype**
- **Production from ES, ED, EG**
- **Standard cryopreservation protocol**
- **Skin - Animal scarless regeneration**
- **Skin - Animal models of angiogenesis**

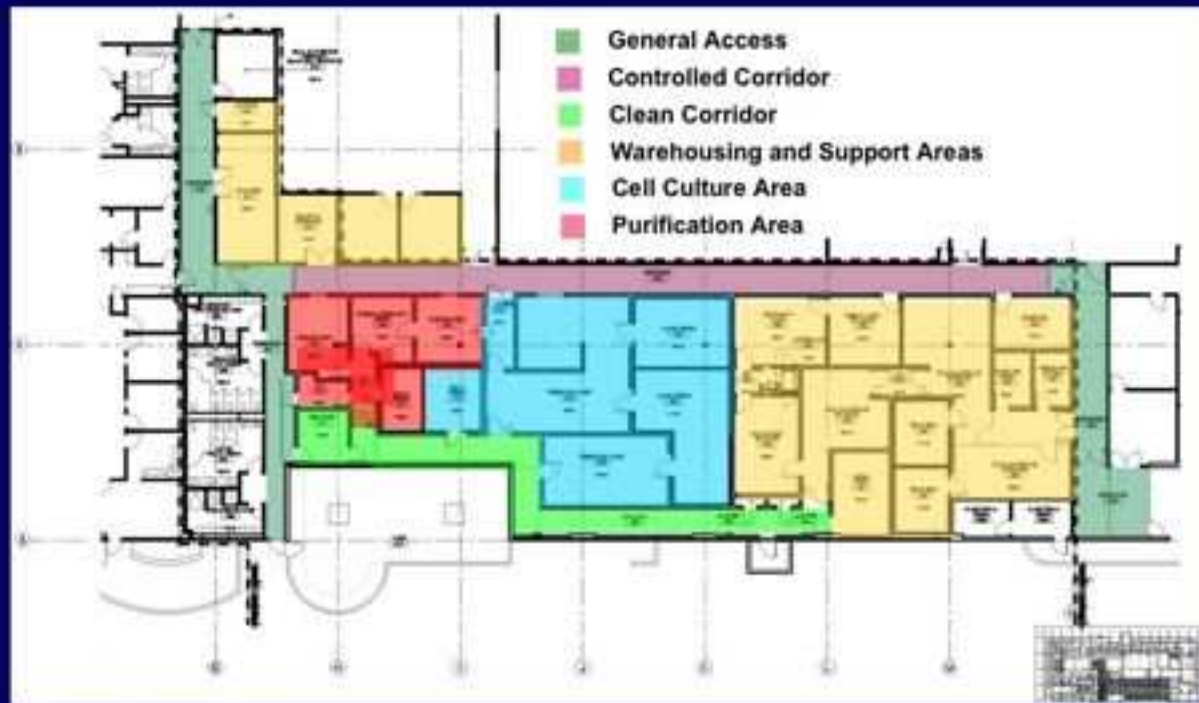


Scaling in Rollers



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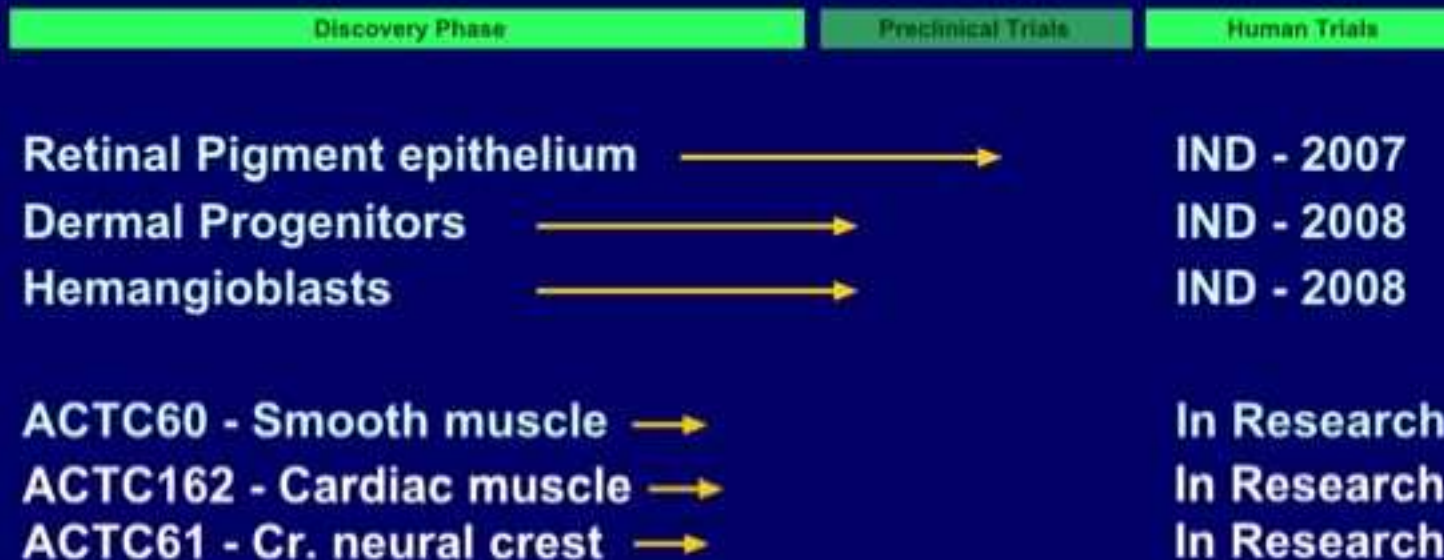
ACTCellerate Cell Lines





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Product Development





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Summary

- **Blastomere-Derived RCL Bank Strategy**
- **Initial Product Focus in Retina, Vascular, and Derm**
- **ACTCellerate as an IP Strategy and Pipeline**



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