POTENTIAL USE OF TISSUE GENE, AND CELL THERAPY PRODUCTS: REPAIR, REPLACE, RESTORE, REGENERATE

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Office of Cellular, Tissue, and Gene Therapies
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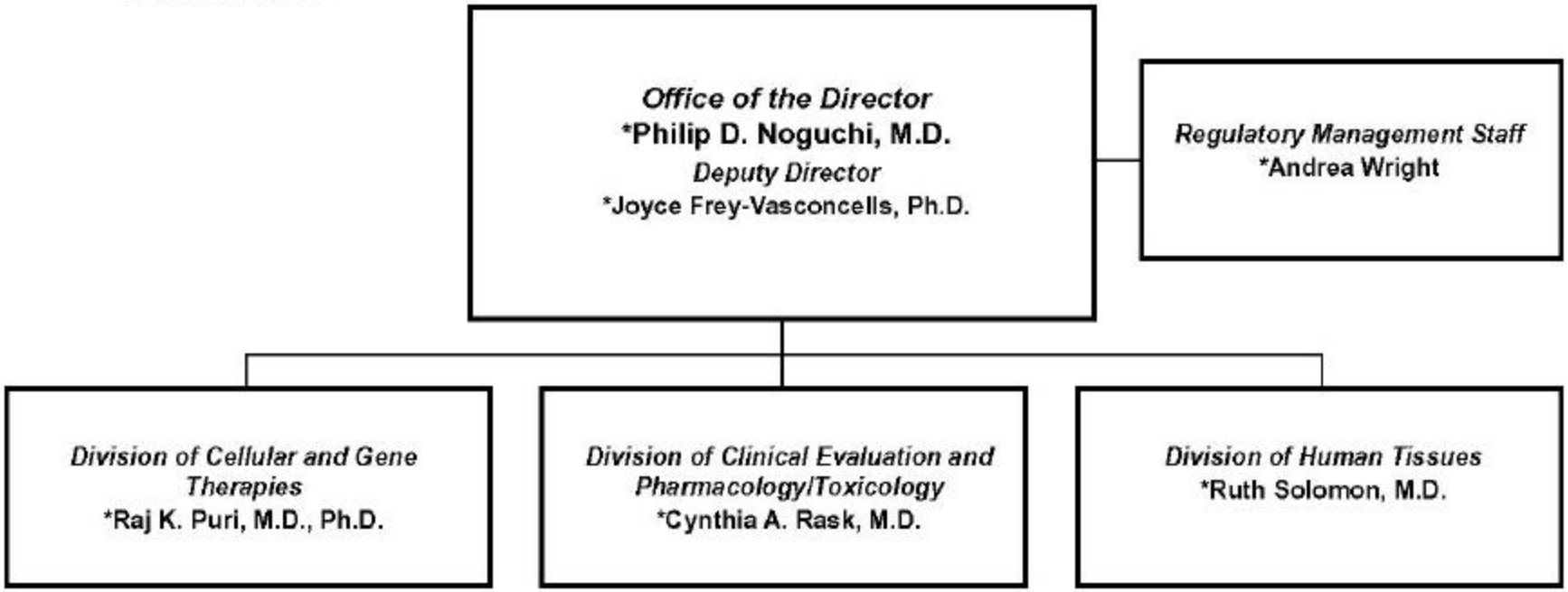
- Regulatory/review responsibility for tissues, cellular, gene therapies, and xenotransplantation products
- Regulatory programs and scientific research to assure the continued safety, identity, purity, and potency of these products
- Collaborative reviews for combination products that consist of cells/tissues combined with a drug or device

CBER
OFFICE OF CELLULAR, TISSUE AND GENE THERAPIES



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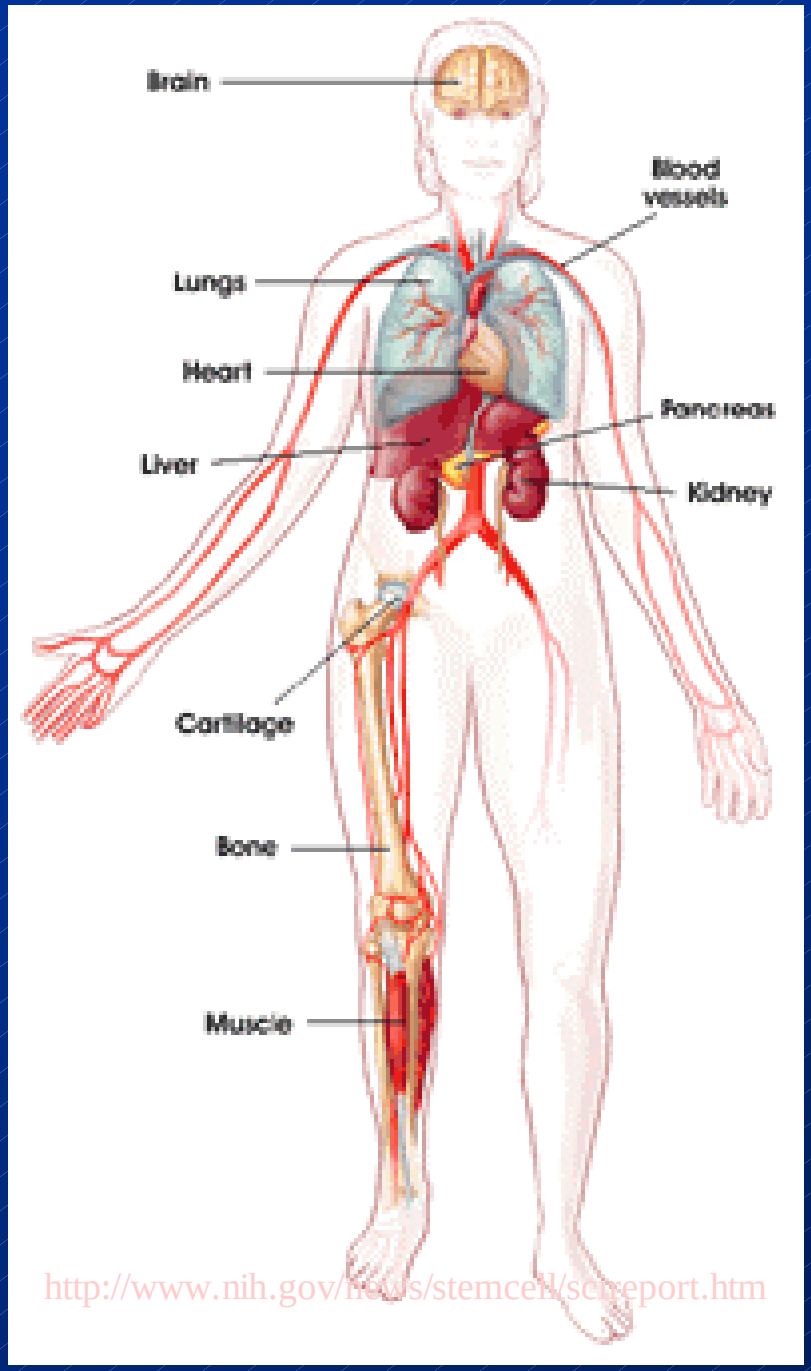
OCTGT Counterterrorism Approach: Potential Uses

- Goals
  - OCTGT perspectives on importance of novel approaches for treating terrorism-related injuries, long-term consequences
  - Stimulate thoughtful consideration of unmet needs in this area

OCTGT Counterterrorism Approach

- Encourage and facilitate development of cellular, tissue, and gene therapy products as medical countermeasures



http://www.nih.gov/news/stemcell/scireport.htm

Repair

Replace

Restore

Regenerate

OCTGT Counterterrorism Approach

Repair, Replace, Restore, Regenerate

- **Biological, radiological, chemical, traumatic injuries**
- **Address with tissue, cell, gene therapy-based products**

Repair, Replace, Restore, Regenerate

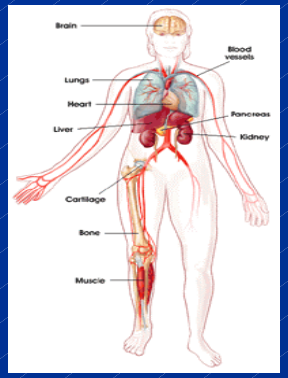
- **OCTGT Products**
  - **Tissues**
  - **Cellular Therapy**
  - **Gene Therapy**
  - **Cellular + Gene Therapies**
  - **Tissue Engineering**
    - Combination Cell/Tissue with Device/Gene Therapy/Recombinant Protein

Use of Human Cells, Tissue and Cellular and Tissue-based Products(HCT/Ps)

- Musculo-skeletal
- Ocular
- Skin
- Hematopoietic stem cells
  - peripheral/cord blood derived
- Bone marrow stem cells

Useful and Needed as Countermeasures

- Adequacy of supply?
- Not all conditions amenable



Repair, Replace, Restore, Regenerate

- UNMET NEEDS: sufficient medical counter-measures for acute and long-term consequences
- Acute needs
  - E.g.: live skin replacement for burn victims, bone repair or organ replacement for trauma victim
- Long-term needs
  - E.g.: complete immune reconstitution, cell or gene therapy for cancer subsequent to irradiation

Potential Uses: Address Unmet Needs

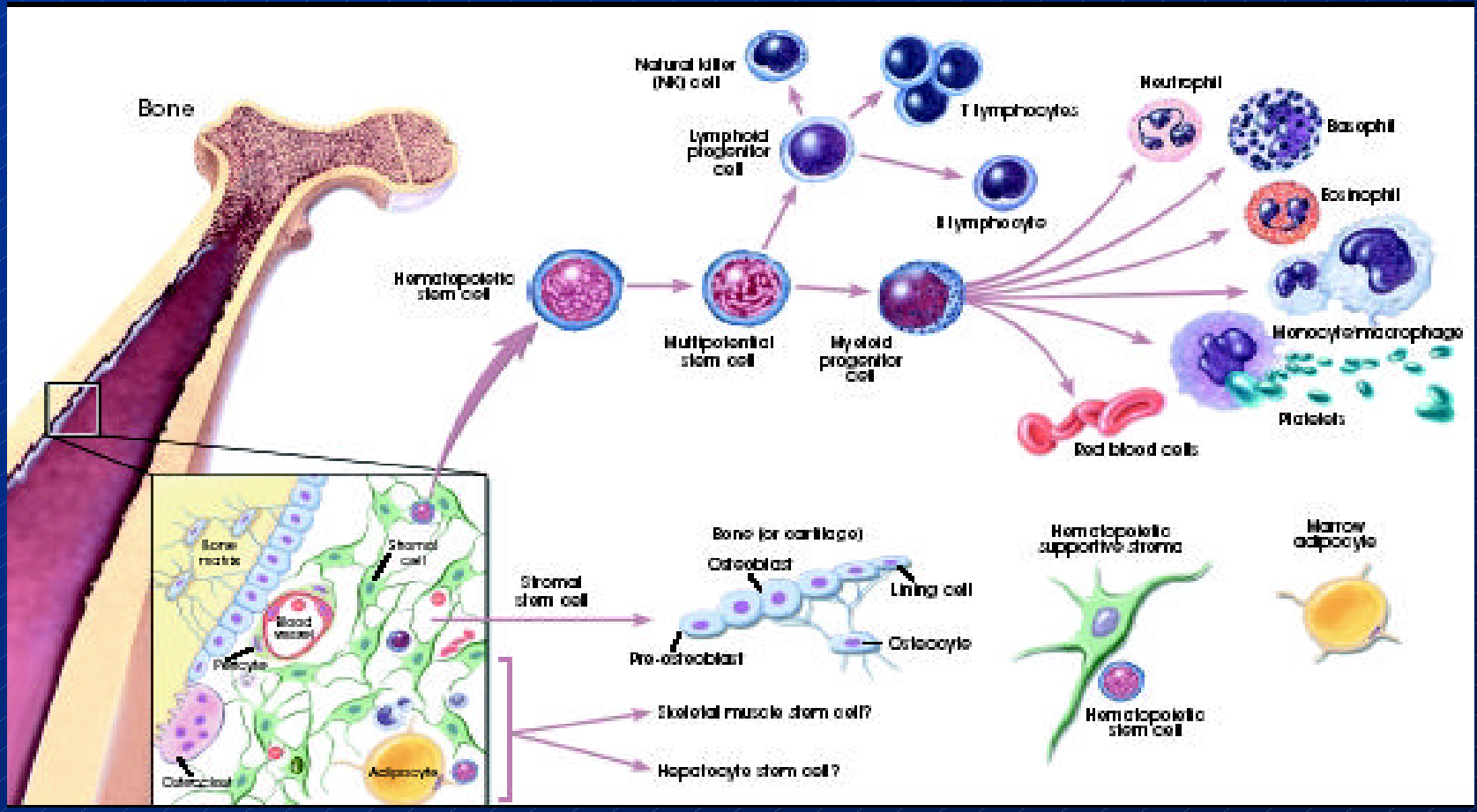
- Cellular Therapies
  - Hematopoietic Reconstitution
  - CNS Repair
  - Cardiac Repair
  - Stem Cells
- Tissues and Tissue Engineering
  - Skin
  - Bone
  - Organs
    - Xenotransplantation

Potential Uses

- **Stem Cell-Based Therapies**
  - **Stem cells, directed to differentiate into specific cell types, offer the possibility of a renewable source of replacement cells and tissues to treat diseases including, spinal cord injury, burns, heart disease**
  - **In vitro differentiation**
  - **In vivo differentiation**

Potential Uses

Bone marrow stroma/Mesenchymal stem cells Facilitate hematopoietic reconstitution



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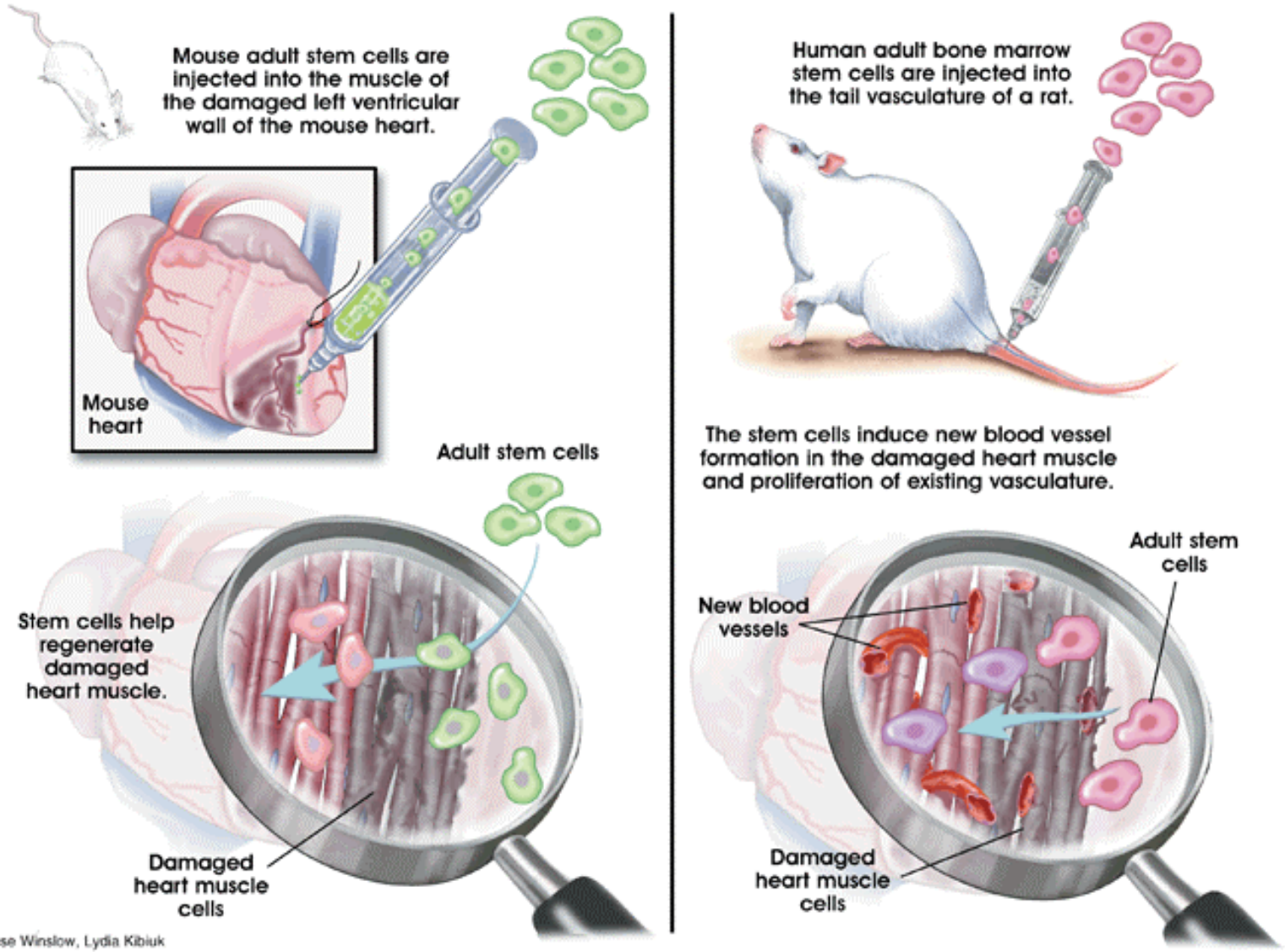
Potential Uses



http://stemcells.nih.gov/infoCenter/stemCellBasics.asp#6

Potential Uses

Adult Stem Cell

- Satellite cells = Muscle stem cells
- Divide in response to injury
  - Self renew and differentiate
    - more stem cells, new muscle cells
- Wnt signaling pathway stimulates muscle forming processes
  - Polesskaya et al., *Cell* 113:841–852, 2003

Potential: repair damaged muscle

Potential Uses

Human embryonic germ cells

- **partially restore paralyzed rat motor activity**
- **migrate into the spinal cord of paralyzed rats**
- **prevent existing host neurons from dying**
- **secrete factors for regrowth of connections between nerves and motor neurons**
  - **Kerr et al., *J Neurosci* 23:5131–5140) 2003**

Potential: repair spinal cord damage

Potential Uses

Dental pulp stem cells

- **Origin: baby teeth**
- **Progeny express molecular markers for dentin, bone, fat, and nerve cells**
- **Accessible source of stem cells to repair damaged teeth, regenerate bone, and treat nerve injury or disease**
  - **Miura et al., *PNAS* 100:5807–5812, 2003**

Potential: repair bone, dental, and nerve injuries

Potential Uses

Genetic modification of stem cells

- **Homologous recombination in human embryonic stem cells**
  - **OCT4, HPRT1**
- **Modify hESC-derived tissues for use in treating patients.**
  - **Zwaka and Thomson, *Nat Bio* 21:319–321, 2003**

Potential: alter stem cells to match recipient, enhance performance, etc

Potential Uses

Genetic modification: Gene Transfer

- ***Ex vivo*** **transformation with gene transfer vectors**
- ***In vitro*** **transformation with gene transfer vectors**
- **Enhance function, performance, longevity, other characteristics of cells or tissues**

Repair, Replace, Restore, Regenerate

- Tissues available and useful
  - Limited supply, unmet needs remain
- Great potential for cell, gene, or combination products
  - Much product, clinical, pharmtox development needed
  - Consider need in different terrorism scenarios
    - likely numbers, storage, delivery, etc

CBER/OCTGT Contact Information

- PHONE: 800-835-4709 or 301-827-2000
- INTERNET: http://www.fda.gov/cber
- Send e-mail to: OCTMA@CBER.FDA.GOV or MATT@CBER.FDA.GOV

- CBER Regulatory and Guidance Documents on the Internet at: http://www.fda.gov/cber/guidelines.htm

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- 301-827-0684

Information on HCT/Ps

- Website at www.fda.gov/cber/tiss.htm
  - Form 3356 – Registration/Listing
  - Published documents and letters
  - Meeting minutes/summaries/transcripts/presentations
- E-mail address for registration questions tissueregs@cber.fda.gov
- HCTERS Queries – information on registered establishments http://intranet.fda.gov/cber/tissue/hcters.htm