

# **Simple Complexity in an Evolving World: Rising to the Challenge**



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# Office of Cellular, Tissue and Gene Therapies



- ❖ **Efforts in counterterrorism**
- ❖ **Repair, Replace, Restore, Regenerate**
  - ❖ **Human Tissues**
    - ❖ **Finalize rules for framework**
  - ❖ **Hematopoietic Stem cell transplantation**
    - ❖ **Reviewing data for possible ‘deemed’ licensing for stem cell facilities**
  - ❖ **Other Stem Cells (Neural, pancreatic, mesenchymal)**
    - ❖ **Guidance for stem cells**
    - ❖ **Outreach to stem cell providers**
  - ❖ **Tumor vaccines**
    - ❖ **International Workshop, April 2003**
    - ❖ **Development of guidance**

# Office of Cellular, Tissue and Gene Therapies



## ❖ Federal “Stone Soup”

### ❖ Education

- ❖ Comprehensive Clinical Course, ASGT

- ❖ ICH Gene Therapy Workshop

### ❖ Partnerships

- ❖ Adenovirus Standard (finished and shipping, 2002)

- ❖ NIH Stem cell task force (ongoing)

- ❖ Xenotransplantation Assay development (ongoing)

## ❖ Patient Centered Therapies

# **“PATIENT CENTERED THERAPIES”**



- ❖ Patient defines therapy**
- ❖ Market share/niche**
- ❖ Delivery infrastructure evolving**
- ❖ Financing, product development evolving**
- ❖ Patient need drives the process**

# Prototype Patient Centered Therapy



- ❖ **X-linked Severe Combined Immunodeficiency Syndrome (X-SCID)**
  - ❖ **Lack of gamma-c chain with consequent lack of cytokine receptors needed for T-cell function**
  - ❖ **Death within first year of life from severe recurrent infections**
  - ❖ **Transplant of HLA-identical marrow >90 % survival; haploidentical transplant 50-70 %**
  - ❖ **Survivors may still need gamma globulin, unknown long term survival**

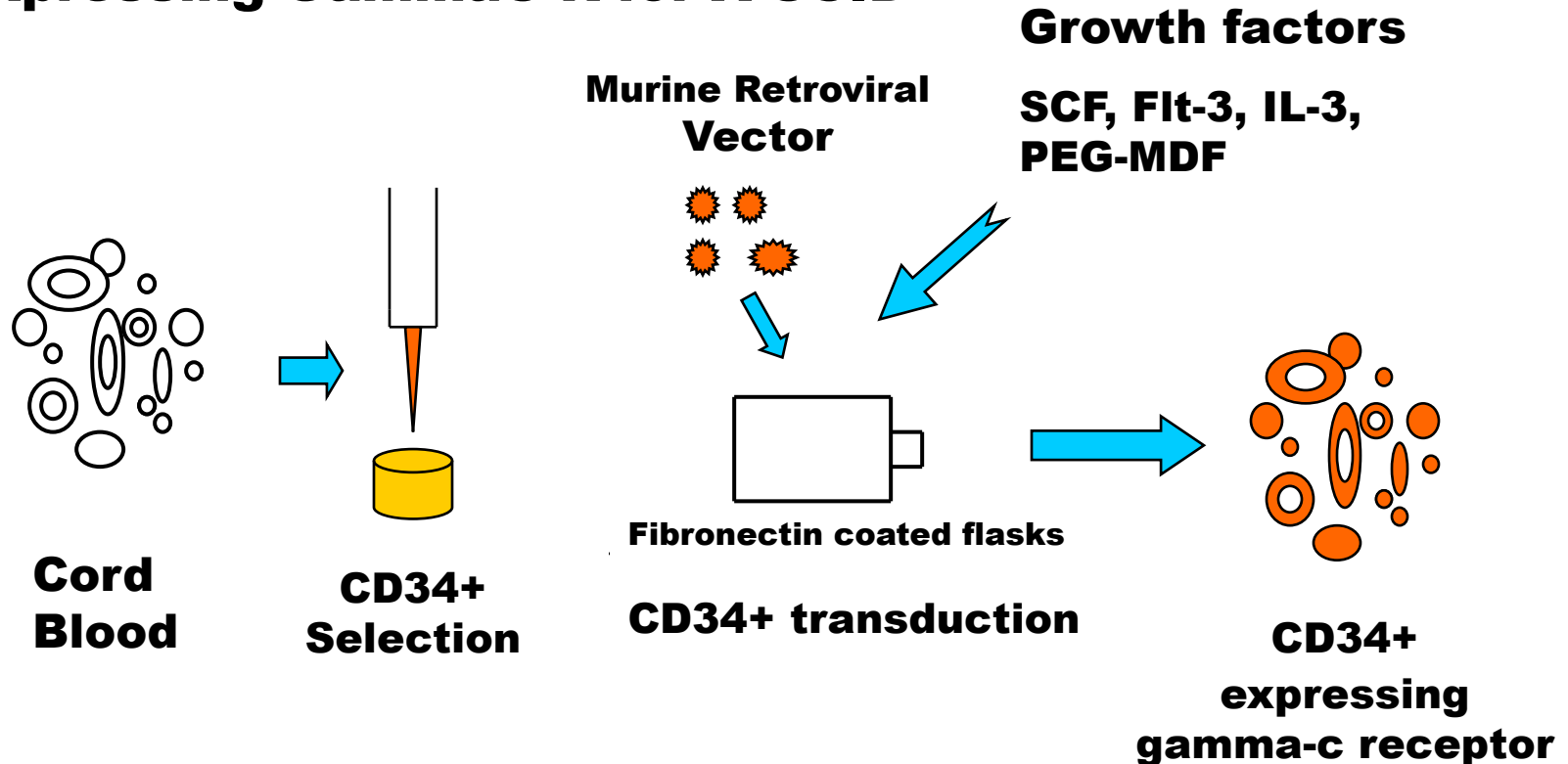
# Gene Therapy For X-SCID



- ❖ In France, 9/11 children showed evidence of immune reconstitution following gene therapy
- ❖ Late August 2002, one successfully treated child developed leukemia-like symptoms
- ❖ FDA Biologics Response Modifier Advisory Committee (BRMAC) reviewed case on 10 October 2002
- ❖ Consensus of BRMAC
  - ❖ Gene insertion gave both therapeutic effect and caused insertional mutagenesis
  - ❖ Because of potential superior immune reconstitution with gene therapy, studies should proceed with caution with stringent testing for clonal expansion of T-lymphocytes
  - ❖ Revision of informed consent process for ALL retroviral gene therapies

# Complexity of (a) Gene Therapy Product

## Ex Vivo Transduced CD34+ Cells Expressing GammaC-R for X-SCID



# Complexity continued...



## ❖ Cord Blood

- ❖ Donor screening, adventitious agents, purity, potency

## ❖ Devices

- ❖ Monoclonal antibodies, surface markers, extracellular matrix

## ❖ Retroviral Vectors

- ❖ Cell substrates, adventitious agents, reversion to wild type

## ❖ Specified Products (SCF, Flt-3, etc)

- ❖ Purity, potency, novel use (ancillary, not as primary effector)

## ❖ Cellular Product

- ❖ Characterization, potency, evidence of gene transduction



...learning the lessons of the past  
will enable the future:

*“What can be imagined, will be  
done”*



*...with hope*

*...humility*

*...patience*

*...compassion*