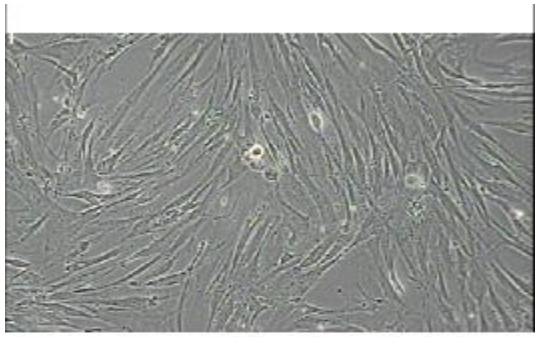
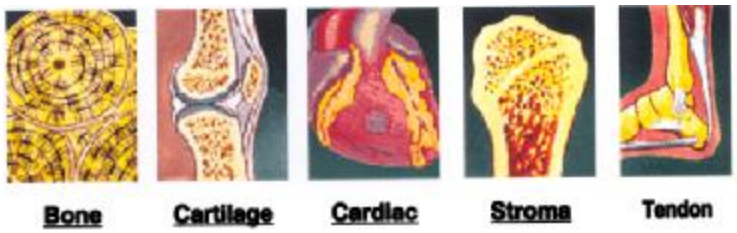
Issues to consider for safety testing

- Mahendra Rao

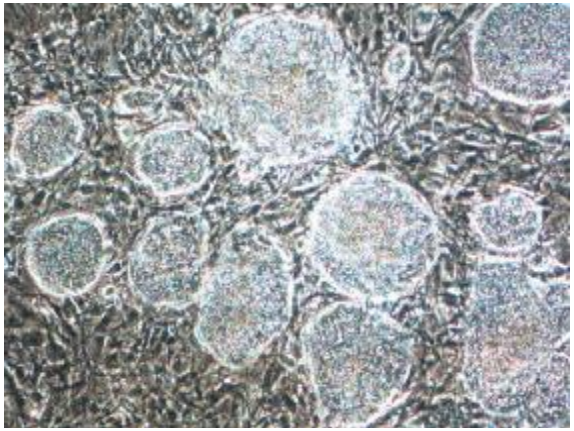
Stem cells come in many flavors



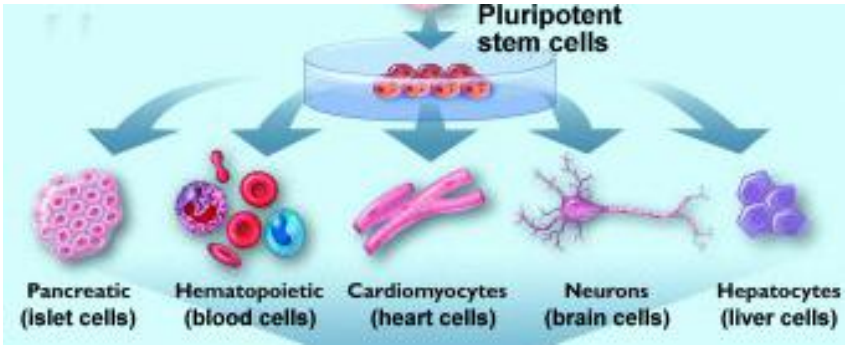
Somatic Stem Cells



Differentiated Cells

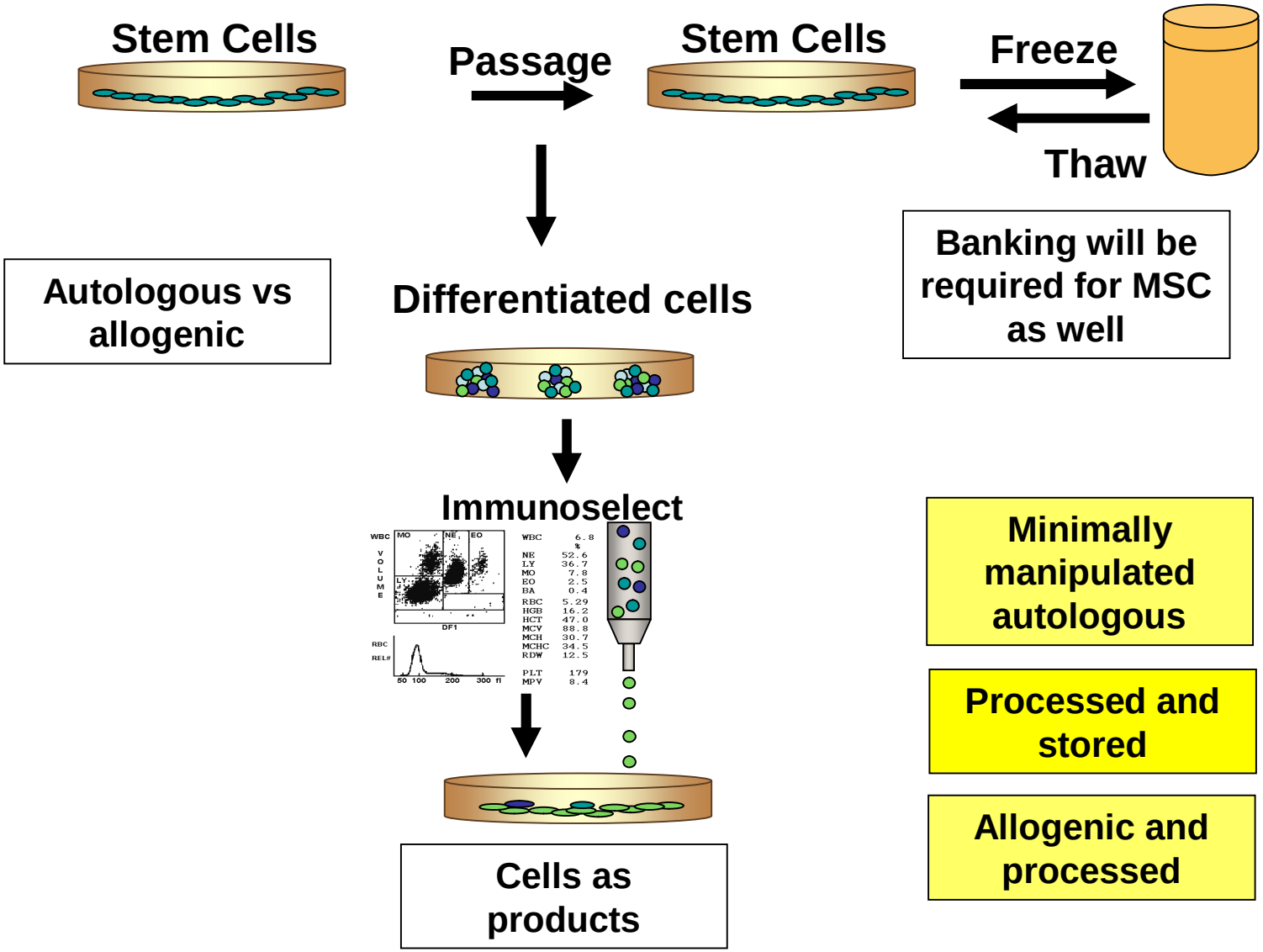


Embryonic Stem Cells

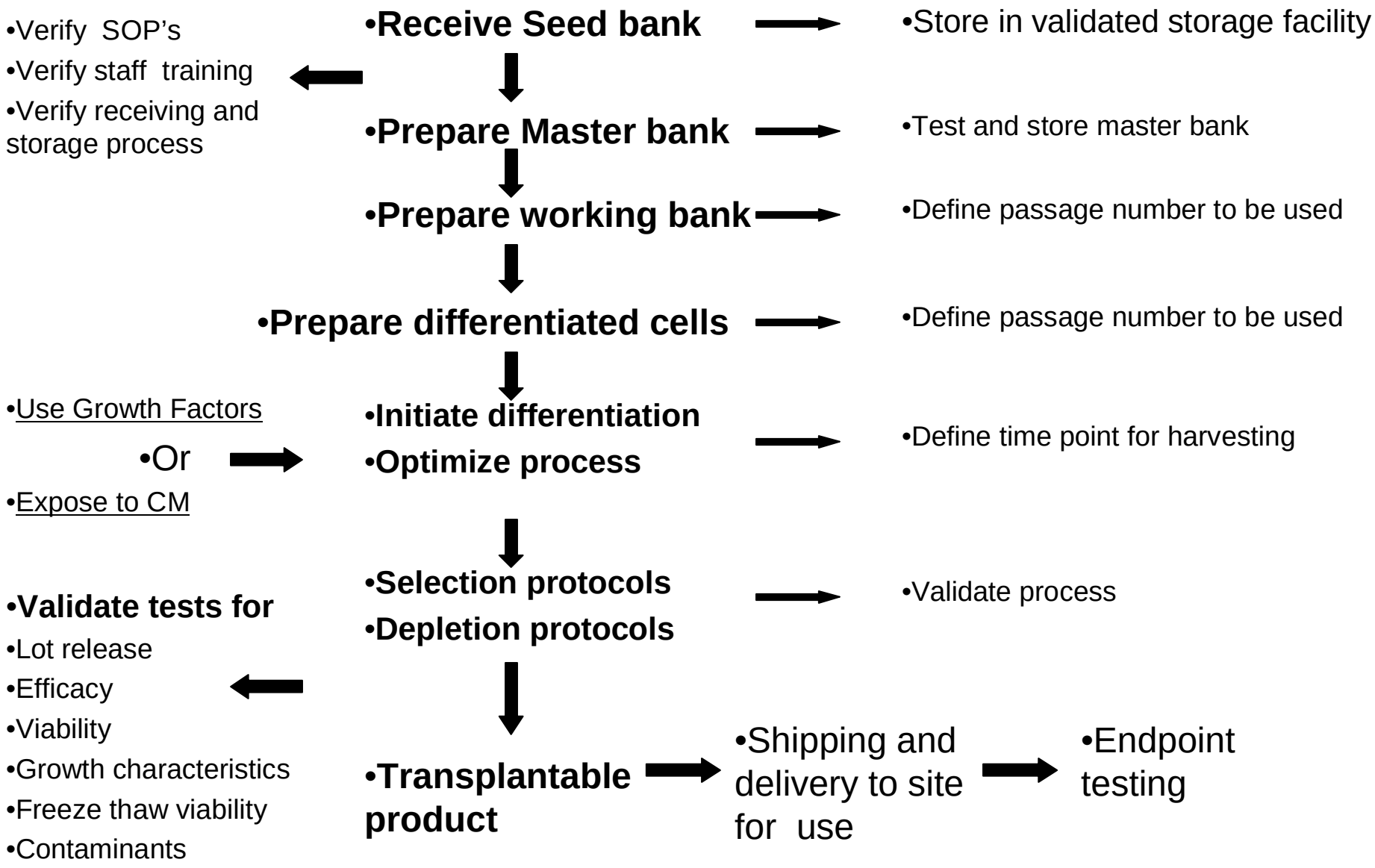


Three Different Models for therapy

Self -renewal and differentiation of stem cells



Demonstrating scalable production



Animal Studies

- Receive control and working bank cells

Safety studies

- **Rodent Studies**
- Biodistribution
- Dosing
- Survival and peristence
- Tumorigenicity
  - Working Bank
  - Differentiated product

- **Primate studies**
- Device and Injection compatibility
- Possible 2nd species studies
- Surgical safety

Efficacy Studies

- **Rodent Studies**
- Efficacy studies in disease model

- **Primate Studies**
- Efficacy studies in disease model

Additional Tests

- Immune compatibility
- Immune dosing
- In vivo monitoring protocols

Developmental efforts

- TH ferritin ESC line and GFP line
- Transient hESC product labeling for animal testing

Safety Issues

- Karyotype stability
- Contaminating cells
- Tumorigenicity from residual ESC
- Atypical growth of partially differentiated cells
- Adverse immune response
- Ectopic distribution
- Issues with combining gene therapy and cell therapy
- Surgical procedure issues (device, volume of injection)

- Predictive tests for safety
- One animal species or more
- Models for immune response
- Standardizing tumorigenicity assays- when and what to test
- How long to follow up
- Uncertainty of epigentic effects
- Appropriate Potency assays when mechanism of action unknown
- Equivalence data