Systems

Engineered Manufacturing Systems (Test-Beds)

MSCs for immune modulation and musculoskeletal applications	T cells and NK cells for immunotherapy applications	iPSC-derived cardiac, neural, and immune cells

- Integrated, closed manufacturing system with real time analytics of CQA/CPP for scale-up or scale-out manufacturing
- Education and workforce development
- Social and regulatory policy, healthcare economics
- Predictive systems analysis of therapeutic cells and supply chain
- Best practices, consensus analytics, and industry standards

Products & Outcomes:
- Transformative innovations in cell manufacturing technologies
- Best practices/standards
- Well-trained workforce

Industry, Clinicians, Patient Advocates, NIST, FDA, & Reimbursement Experts

Requirements

Barriers
- Predictable safety and efficacy
- Lack of quality-driven manufacturing
- Regulatory pathway, and standards
- Large-scale, low cost, manufacturing
- Lack of trained workforce

TECHNOLOGY INTEGRATION

System Requirements

Technology Building Blocks

Enabling Technologies

Engineered Manufacturing Systems (Test-Beds)

Marrow stromal cells (MSCs)	Therapeutic T and NK cells	iPSC-derived cells

Deliverables:
New tools and technologies

Thrust 1
- Multi-omics integration
- Big data analytics tools
- Supply chain simulations

Thrust 2
- Disease/tissue-on-a-chip
- Biosensors, imaging, for in-line monitoring
- Potency and Safety Assays

Thrust 3
- Biomaterials and bioreactors
- Integration of sensors for feedback controlled Automation/Process Control

Barriers
1. Lack of physiologically relevant potency/safety assays; difficult supply chain/logistics
2. Lack of real time monitoring of CQAs and CPPs during manufacturing
3. Difficult scale-up/out; lack of process controlled automation

TECHNOLOGY BASE

System Requirements

Fundamental Insights

Fundamental Knowledge

Deliverables:
New scientific knowledge

Thrust 1
- New systems-driven multi-omics pipeline for cell characterization
- Process/supply-chain and logistics requirements for living cells and reagents

Thrust 2
- Minimal models of tissue/disease
- *In vitro* vs. *in vivo* safety/potency
- New sensor modalities

Thrust 3
- Effects of materials and bioreactors on cell quality and scaling of manufacturing
- Integration of quality attributes into control algorithms

Barriers
1. Lack of critical quality attributes & critical process parameters & optimized supply chain
2. Poor understanding of *in vitro/in vivo* correlation of cell properties/function
3. Lack of understanding of scaling and automation effects on cell quality

KNOWLEDGE BASE