The National Academies of SCIENCES ENGINEERING MEDICINE

HEALTH AND MEDICINE DIVISION

Board on Health Sciences Policy

Applying Systems Thinking to Regenerative Medicine- A Workshop

October 22-23, 2020

#RegenMedForum

Focus on critical quality attributes

Impractical

Too much emphasis on a single attribute

Appropriate attributes, criteria too low

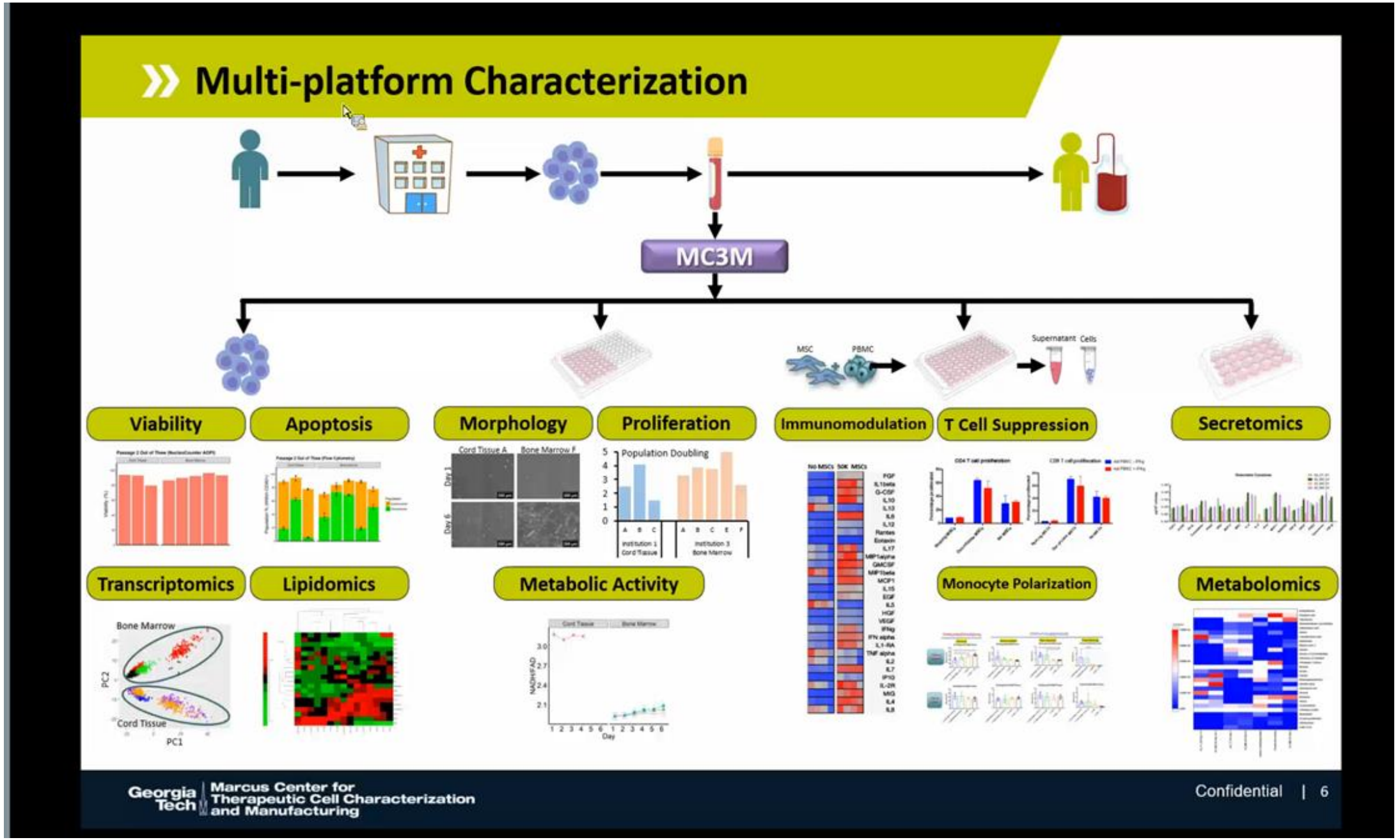
Appropriate attributes, appropriate criteria

ISCT Liaison Meeting October 19, 2016 Tom Finn, Ph.D. Product Reviewer Office of Tissues and Advanced Therapies FDA/CBER

Attributes that predict clinical effectiveness and outcomes:

It remains challenging to characterize the functional attributes of chimeric antigen receptor (CAR)-engineered T cell product targeting CD19 related to potency and immunotoxicity ex vivo, despite promising in vivo efficacy in patients with B cell malignancies.

Xue et. al. *Journal for ImmunoTherapy of Cancer*2017.



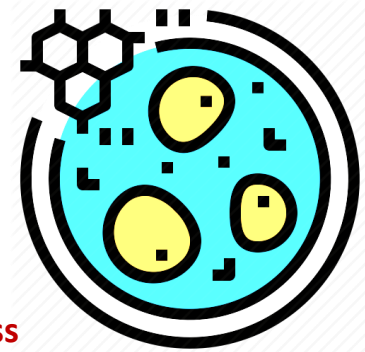
Shown at CBER Advanced Technologies Symposium July 9th, 2019

From, CMaT and Marcus Center, @Georgia Tech

Cell Therapy: Interaction of Multiscale Dynamic Complex Systems

DONOR/SOURCE CELL

Immune system
Disease status
Prior therapies
Age
Sex
Ethnicity
Lifestyle
Environment
Collection Process
Storage/shipping



+

Process
Operator
Reagents
Technologies/Tools
Storage/Shipping

MANUFACTURING

CELL PRODUCT

Source/Donor
RNA
Proteins
DNA
Lipids
Metabolites

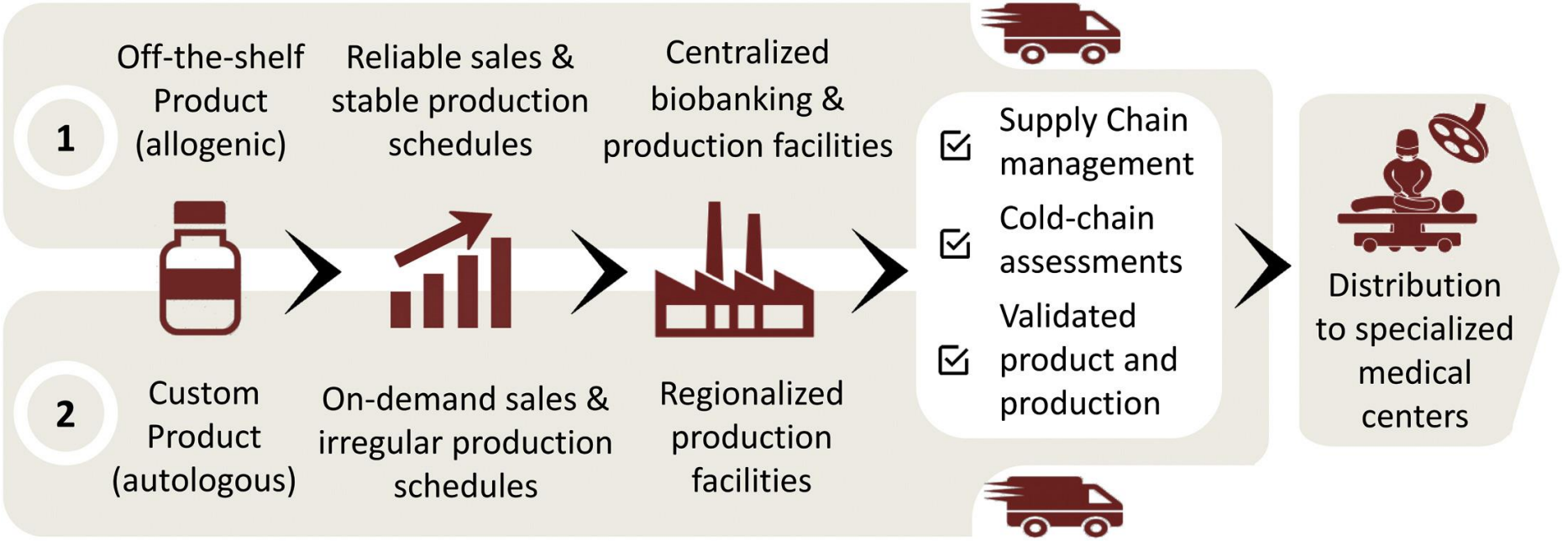
PATIENT

Immune system
Disease status
Other treatments
Age
Sex
Ethnicity
Lifestyle
Environment

From, CMaT and Marcus Center, @Georgia Tech, www.cellmanufacturingusa.org

Regen-Med therapies have complex and risky supply chain: Optimization, redundancy and failure modeling is critical for success

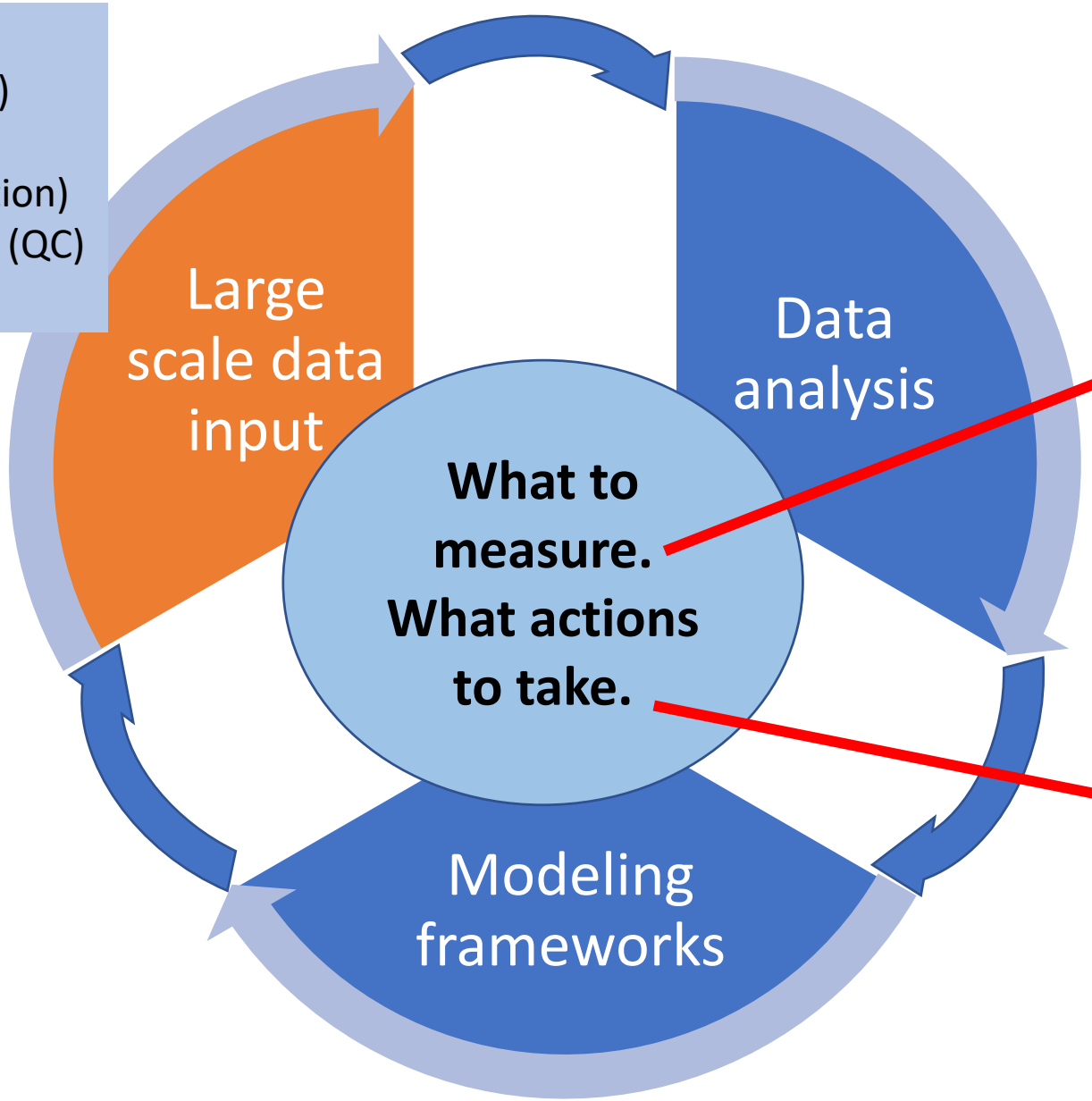
- **Nascent Reagent Supply Chain**
  - Single suppliers
  - Inadequate QC
- **Patient Queuing and Production scheduling**
  - First come, first serve
  - Disease status
- **Complex Transportation Logistics**
  - Cold chain
- **Data Management, Data Collection. and QMS Systems**
  - A SYSTEM of integrated data and decision process
- **Centralized, vs Regional vs Bedside Manufacturing**
  - Economy of scale
  - Cost
  - Demand fulfillment



Cell Stem Cell, Volume 19, Issue 3, 1 September 2016, Pages 293-297

A Systems Approach

- Omics data (MOA)
- Clinical indicators (Patient stratification)
- Starting materials (QC)



- Critical quality attributes of the product.
- Critical process parameters for manufacturing

- Patient queuing
- Manufacturing decisions
- Product release

Applying Systems Thinking to Regenerative Medicine

For discussion:

1. *How can the use of data and theory help identify mechanistically relevant quality attributes for regenerative medicine products, and corresponding critical process parameters for their reproducible manufacturing? How are these advances being used by the industry today?*
2. *What are challenges in the development of data-intensive analytical methods and theoretical models? Where additional advances are needed? Do we have the needed workforce?*
3. *How might these data and theoretical approaches influence the regulatory process?*
4. *How can we use systems modeling and AI to optimize and manage the complex supply chain for regenerative medicine products?*
5. *What should be the best practices for data sharing, data collection, and clinical trial designs (collecting longitudinal mechanistic data from patients), to enable systems thinking across the regenerative medicine ecosystem?*

Planning Committee Members

Anne Plant (co-chair)
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Gamma Biosciences

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Akron Biotech

**at the time of planning committee approval*

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Reminders

- Please ask questions by typing them into the box below the webcast.
- Please include your name and affiliation with your question.
- We will do our best to address as many questions as possible during the panel discussion period.
- This workshop spans two days- October 22 and 23- and we hope you can join us both days to continue the discussions.