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Microphysiological Systems to assess the functional capacity of cellular therapy products

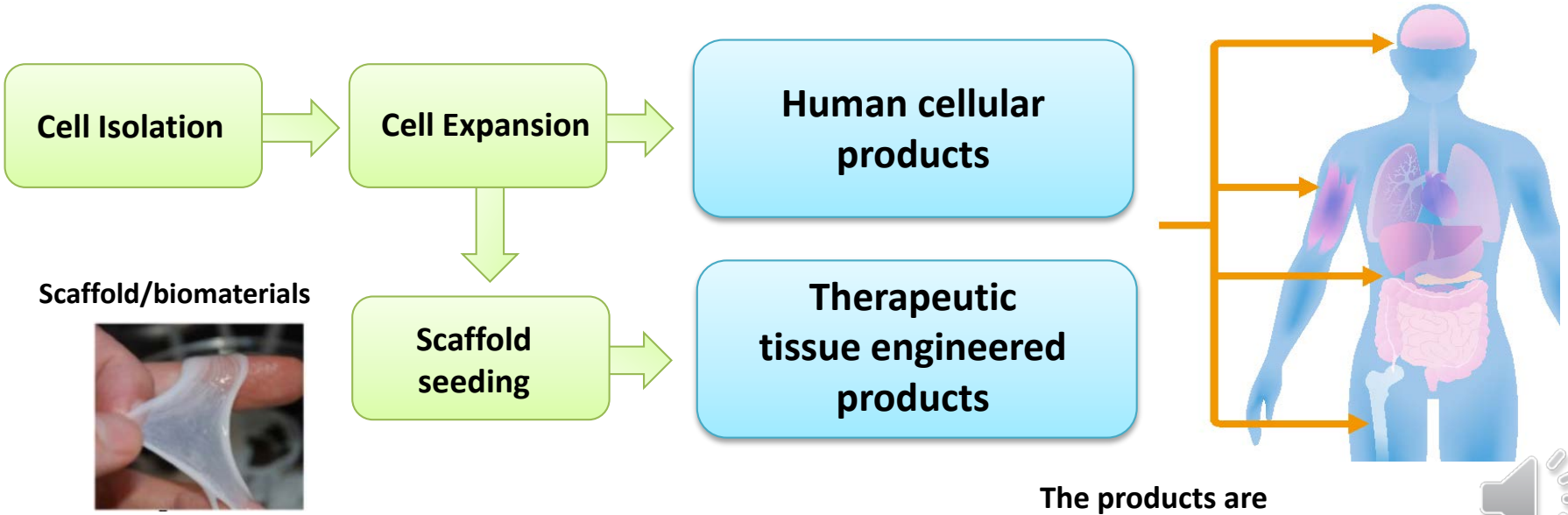
Kyung Sung

Cellular and Tissue Therapies Branch (CTTB)
Division of Cellular and Gene Therapies (DCGT)
Office of Tissues and Advanced Therapies (OTAT)
Center for Biologics Evaluation and Research (CBER)

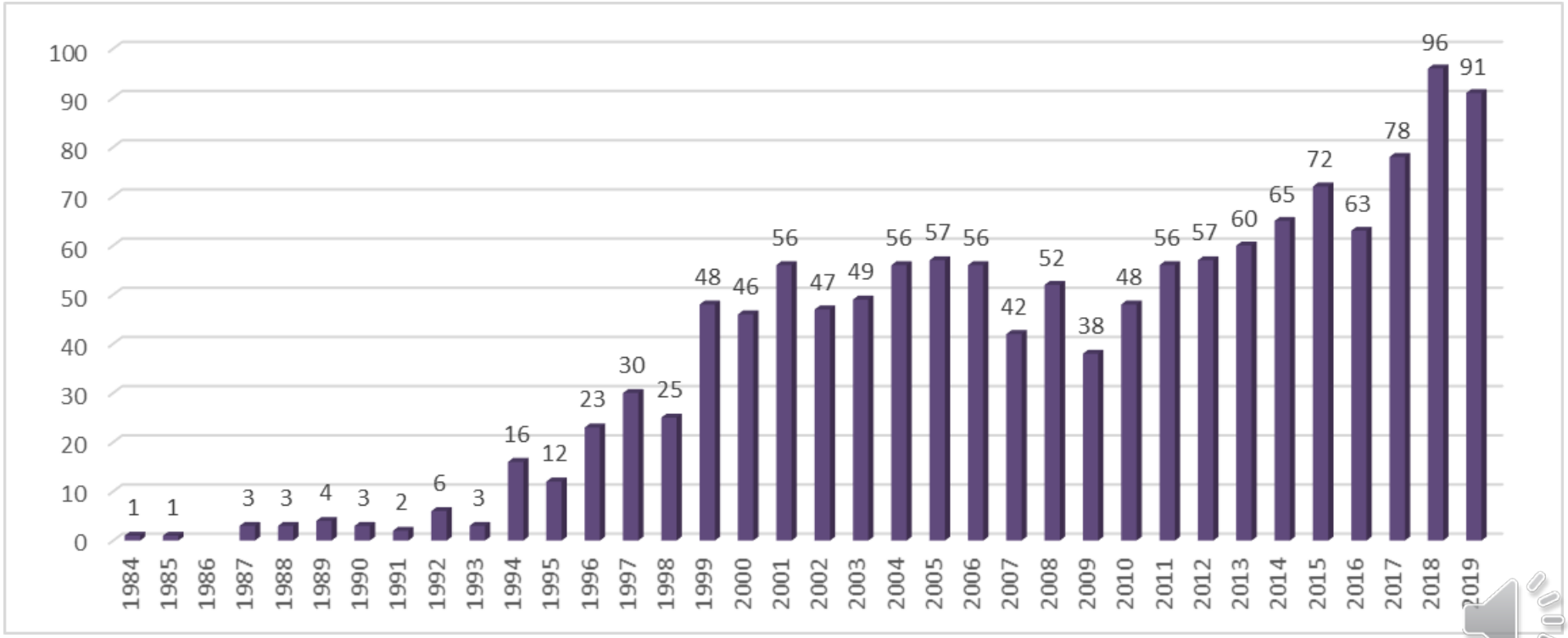
ILAR Workshop 2021

Regenerative Medicine Cellular Therapies

Regenerative medicine is the process of replacing or regenerating human cells, tissues or organs to restore or establish normal function.

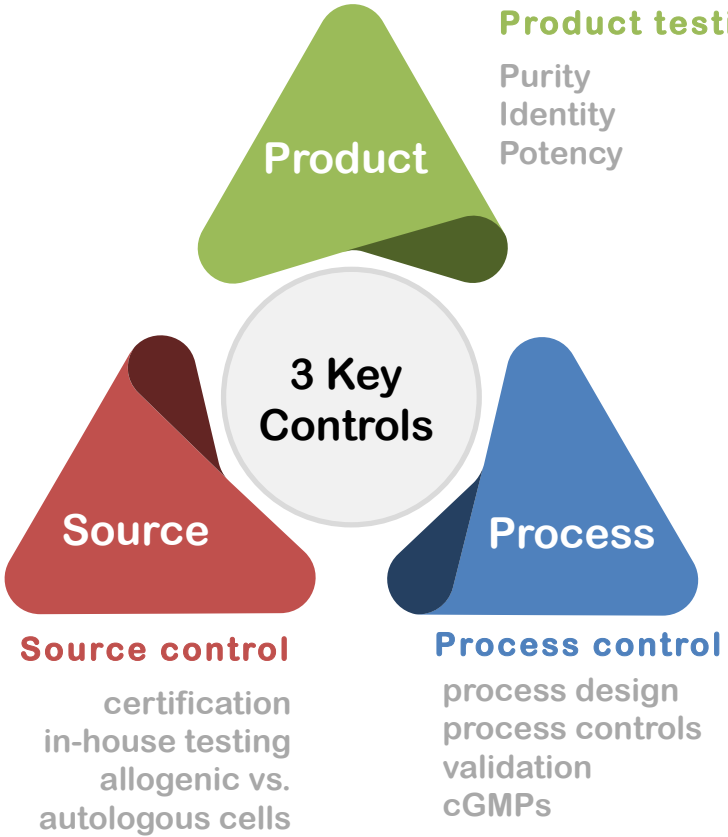


INDs with cell therapy development programs
CY 1984 - 2019



Chemistry, Manufacturing, and Controls (CMC)

- **CMC** = Product manufacturing and testing
- How do you make the product?
- What do you use to make the product?
- Product safety and Quality testing
- Product Stability
- Other controls – product container, labels, tracking



Challenges of Regenerative Medicine Cellular Products

Manufacturing & Regulatory challenges

- Cellular heterogeneity
- Patient to patient variability
- Limited shelf life/limited sample volume
- Limited availability of starting material for test method development
- A wide range of manufacturing protocols

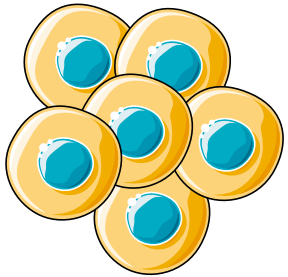
Isolated cells ? = **Manufactured cells**

New methods and quality attributes are necessary to reliably predict biological functions of manufactured products.

Current microphysiological system (MPS) research

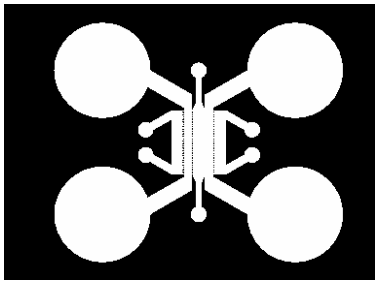
- **Develop and improve test methods for cell product characterization**
- **Identify product attributes that are predictive of safety and effectiveness**

3D aggregates



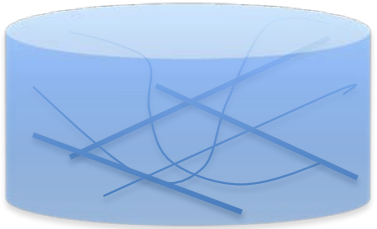
Chondrogenic potential

Co-culture



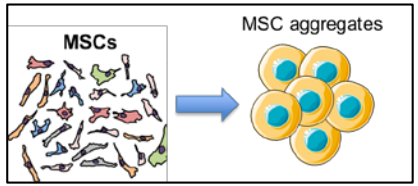
Vasculogenic potential

Biomaterials



Immunosuppresive potential

Chondrogenic capacity: MSC aggregate size matters

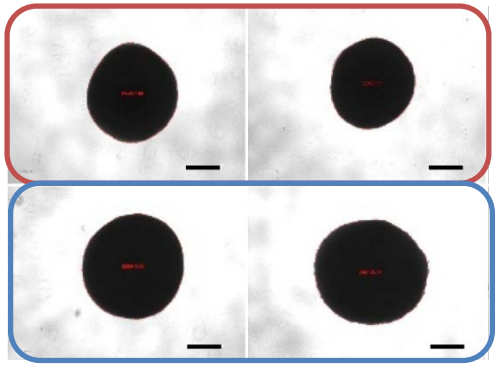


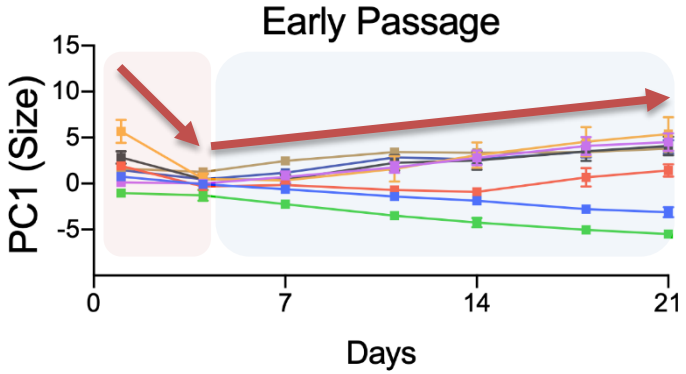
P2/3

MSC-A MSC-B

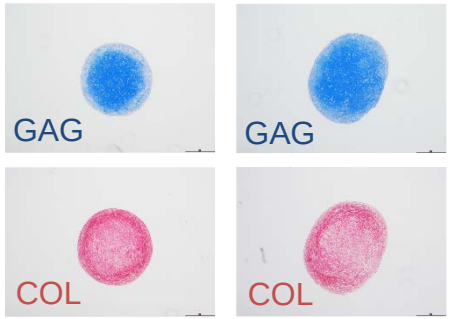
D7

D21





Size recovery

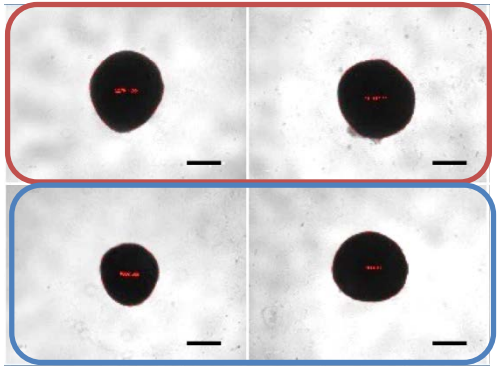


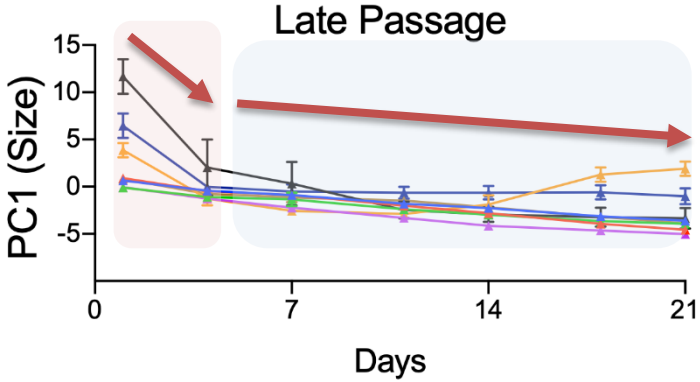
P5

MSC-A MSC-B

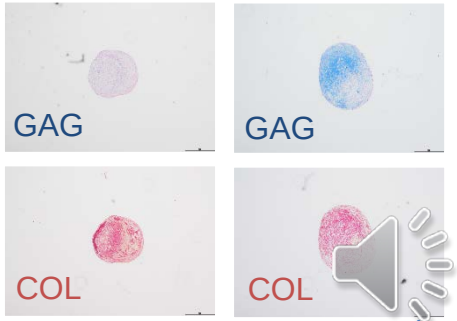
D7

D21

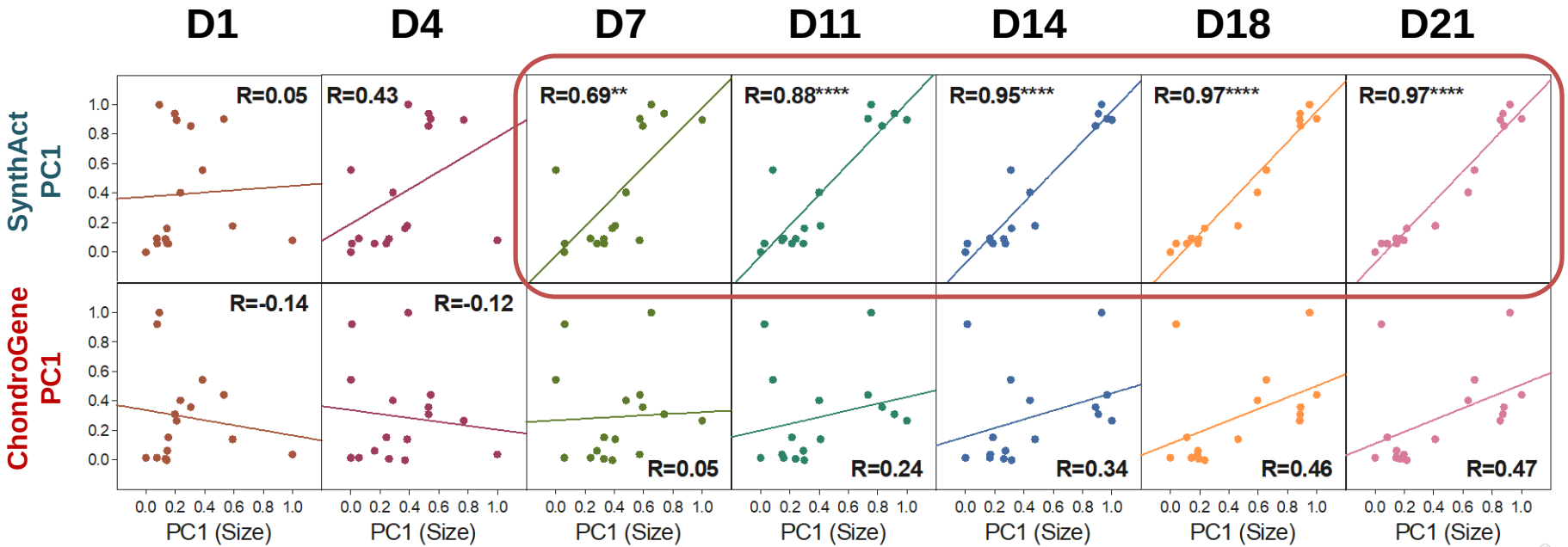




No size recovery



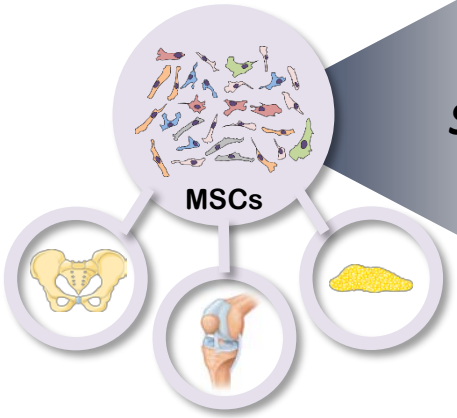
Synthetic Activity correlates with MSC Aggregate Size – Chondrogene expression does not



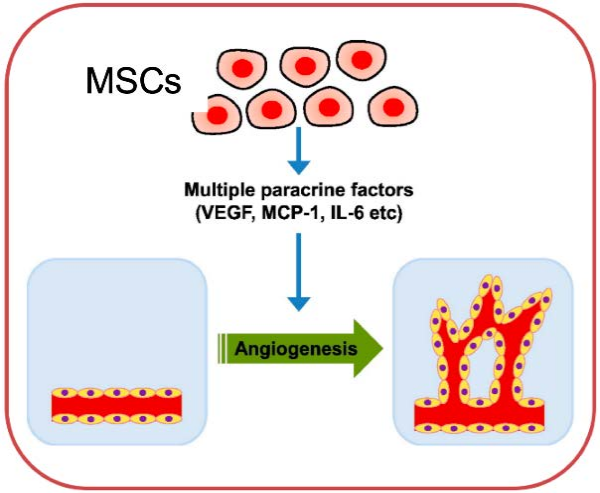
Lam, 2018, Stem Cells Translational Medicine

Paracrine Potential of MSCs

Differentiation Potential



Secretome



Kwon, 2014, Vascular Pharmacology

Clinical Applications

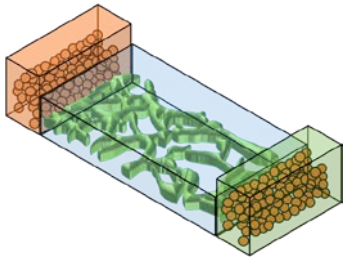
- *Wound Repair*
- *Immunomodulation*
- *Ischemic Reperfusion*

- *Are the paracrine/trophic action of MSC preparation also heterogeneous?*
- *Could paracrine potential of MSCs be robustly and objectively measured?*

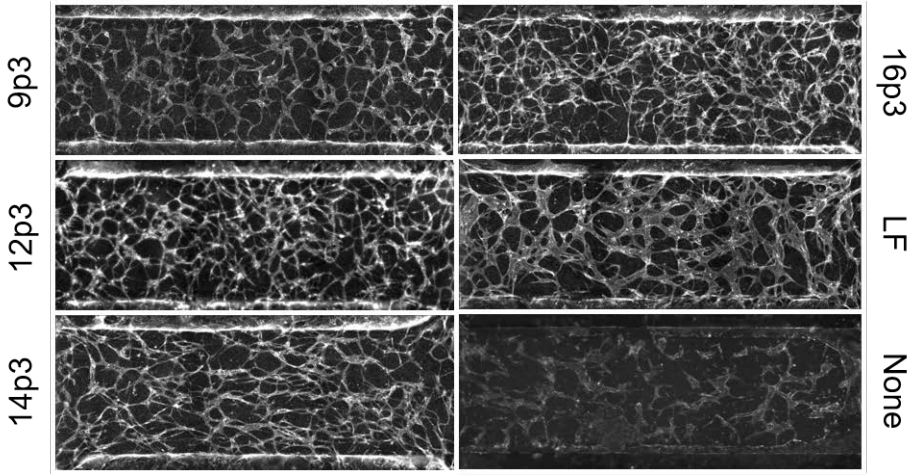
Vasculogenic Configuration

Group	Stromal
EC-only	Stromal: N/A
9p3; 9p5	MSC (RB9*)
12p3; 12p5	MSC (RB12*)
14p3; 14p5	MSC (RB14*)
16p3; 16p5	MSC (RB16*)
LFEC	Lung Fibroblasts

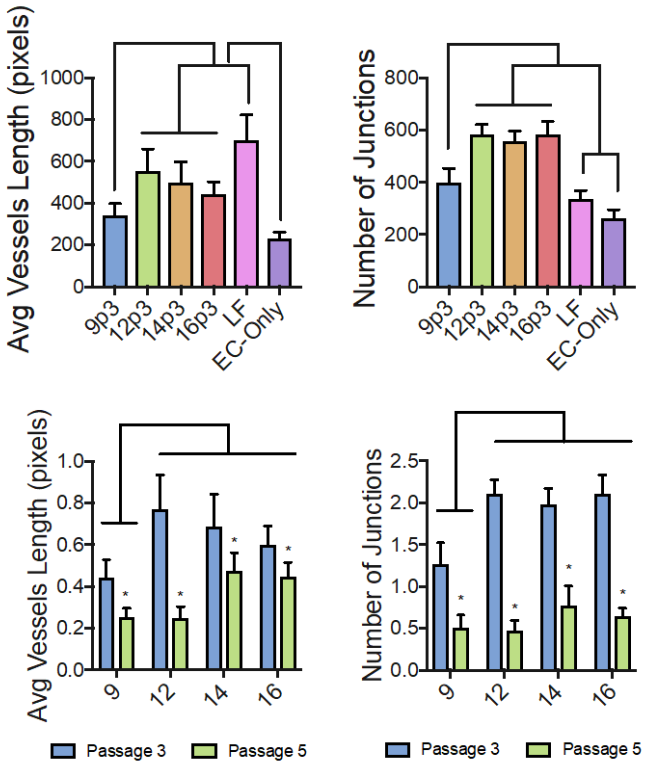
*passage 3 (p3) and passage 5 (p5)



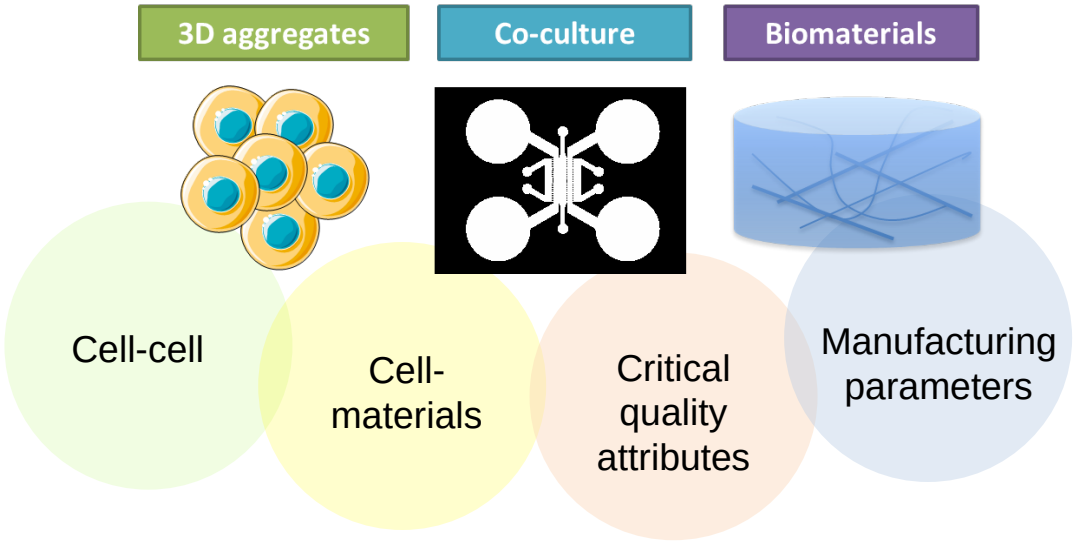
Vasculogenic metrics were different between MSC preparations and were passage-dependent



4 days



Conclusions



Well-designed MPS that recapitulate critical physiological conditions have the potential to contribute toward developing and improving test methods for product characterization and toward identifying product attributes that are predictive of safety, effectiveness, and potency.

Acknowledgements

The Sung Laboratory

Johnny Lam, *General Engineer (Staff Scientist)*
Chondrogenesis & Vasculogenesis

Fatima Abbasi, *Microbiologist*
Flow cytometry

Brian Kwee, *ORISE fellow*
Immunosuppression & Biomaterials

Gabriella Schito, *ORISE fellow*
Advanced manufacturing

Shekh Rahman, *ORISE fellow*
Placental drug transfer

Ashree Shah, *ORISE fellow*
Chondrogenesis

Collaborators

- CBER/OTAT: Steve Bauer, Brent McCright, Busik Park, Ge Ma
- CBER/OBRR: Indira Hewlett
- CDER/OTS: Alexandre Ribeiro
- CDRH/OSEL: Anant Agrawal, Jiwen Zheng, Shelby Skoog, Peter Goering, Alexander Nguyen, Eric Sussman, Asis Lopez
- CFSAN/OFS: Timothy Duncan, Yun Wang
- NCTR/OR: Nakamura Noriko, William Mattes
- CurioChips/Seoul National University: Noo Li Jeon, James Yu, Kyusuk Baek
- University of Wisconsin: David Beebe, Tony Jimenez
- University of Georgia: Ross Marklein
- Stanford University: Ngan Huang
- University of Maryland: John Fisher, Bhushan Mahadik

Funding

- Division of Cellular and Gene Therapies
- Center for Excellence in Regulatory Science and Innovation
- Challenge Grants
- Collaborative Nanotechnology Grants
- Perinatal Health Center of Excellence Grants
- National Center for Toxicological Research

Contact Information

- **Kyung Sung, Ph.D.**
  kyung.sung@fda.hhs.gov

- **Regulatory Questions:**
  OTAT Main Line – 240 402 8190
  Email: OTATRPMS@fda.hhs.gov and
  Lori.Tull@fda.hhs.gov

- **OTAT Learn Webinar Series:**
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