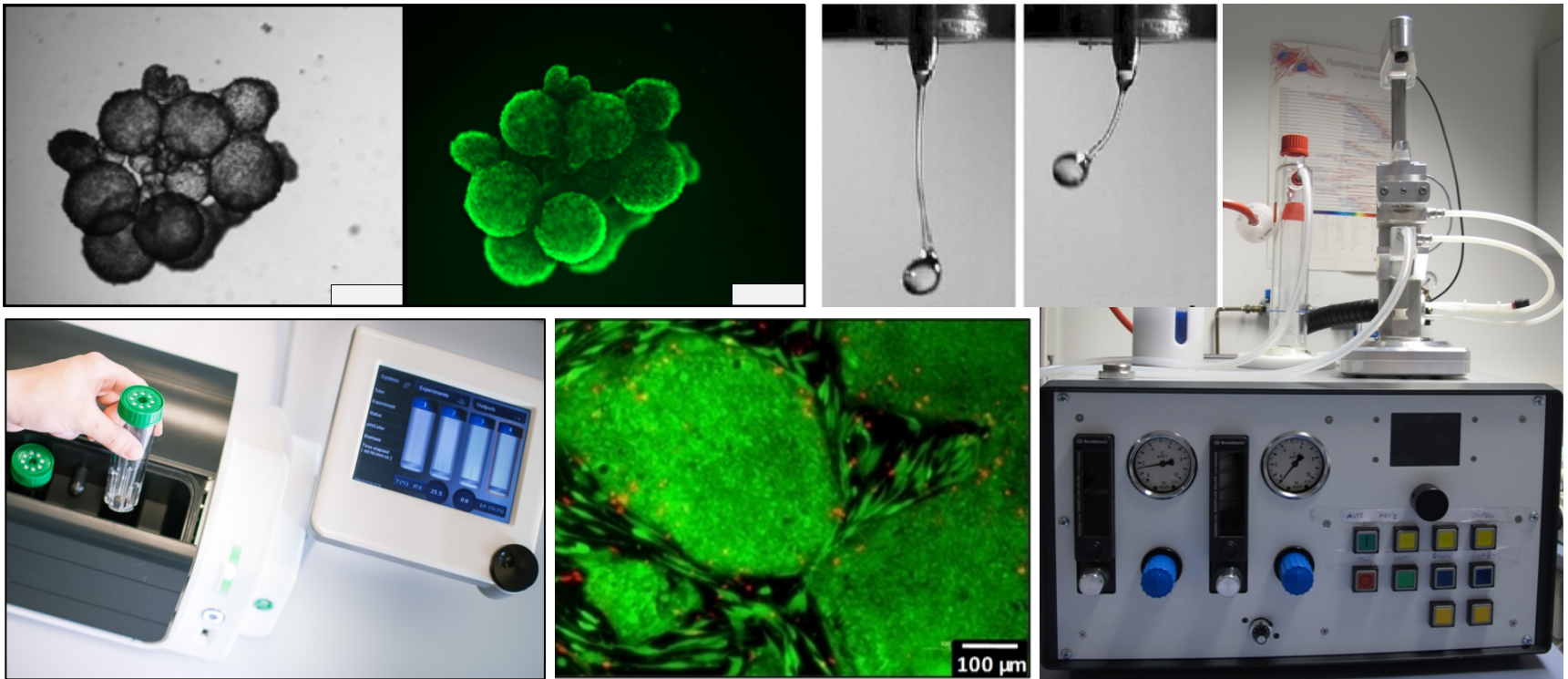


Entwicklung von Methoden zur verbesserten Expansion, Differenzierung und Kryokonservierung von humanen pluripotenten Stammzellen

Julia Neubauer

Fraunhofer-Institut für Biomedizinische Technik IBMT

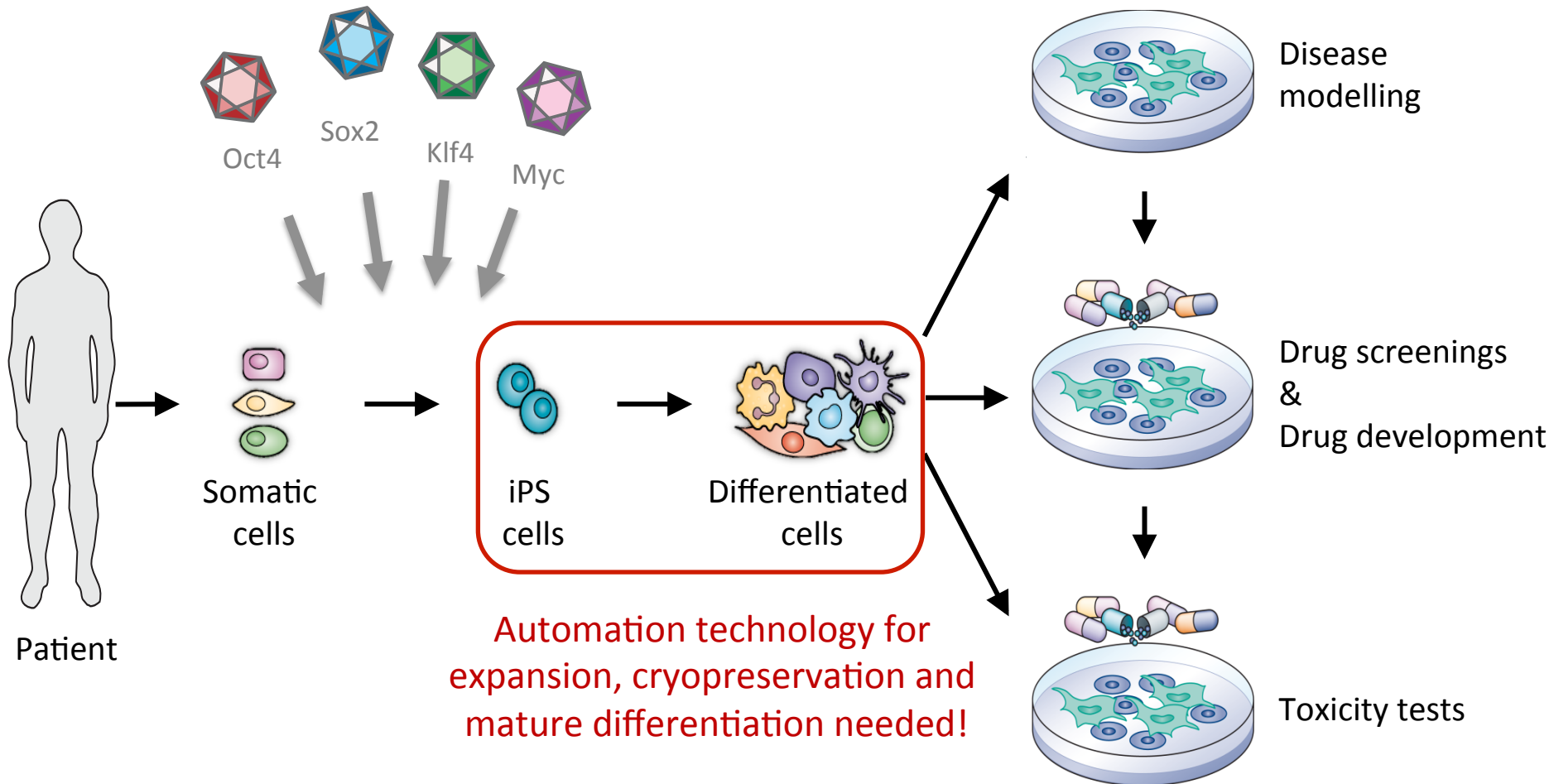


Fraunhofer - Society for applied research in Europe

- The Fraunhofer - Society promotes and conducts applied research in an international context, to benefit private and public enterprise and is an asset to society as a whole.
- 67 institutes and research units (IBMT is one of the 6 life science institutes)
- 24,000 staff
- more than €2.1 billion annual research budget totaling. Of this sum, around 1.8 billion euros is generated through contract research
- Non-for-profit organization
- Fraunhofer Institute for Biomedical Engineering (IBMT): www.ibmt.fraunhofer.de



Next generation drug development using iPS cell technologies



Bellin et al., Nat Rev Mol Cell Biol, 2012 - modified

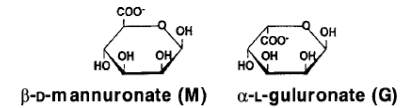
A novel, scalable bench top automation platform

Automation technology (OLS) + Biopolymer technology (Fraunhofer IBMT)



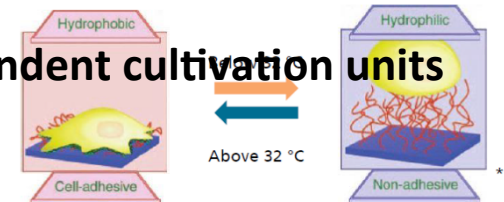
12 x Biolevitator automation platform

*Ottenbrite, R.M. et al., Biomedical Applications of Hydrogels Handbook, 2010, 19-43.

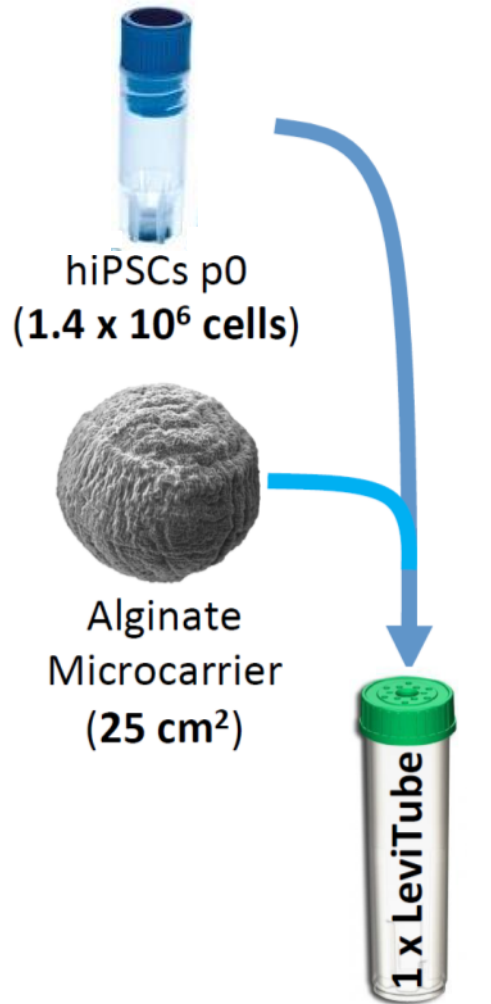


12 x 4 = 48 independent cultivation units

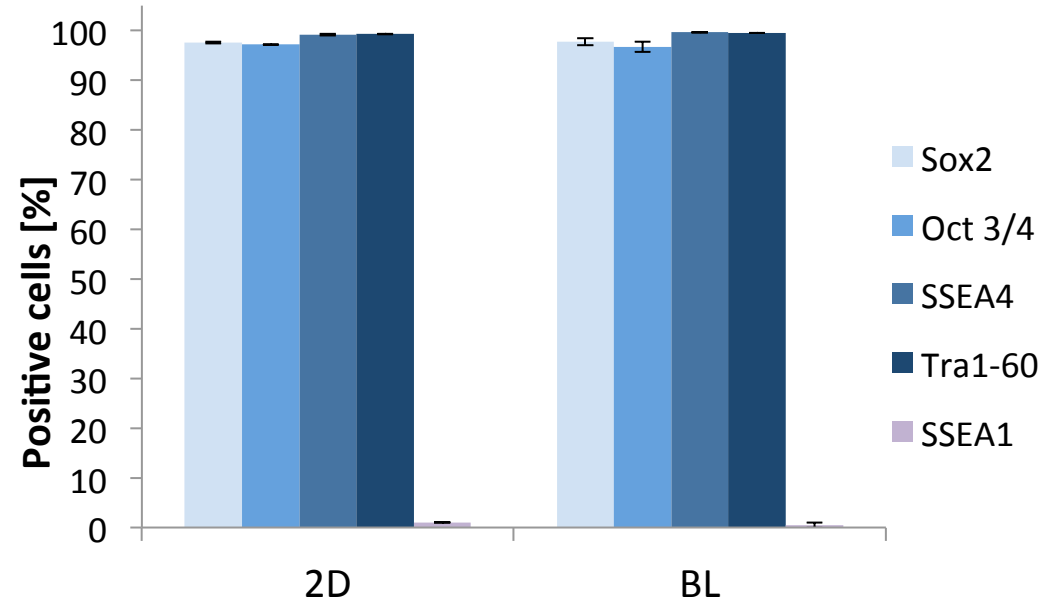
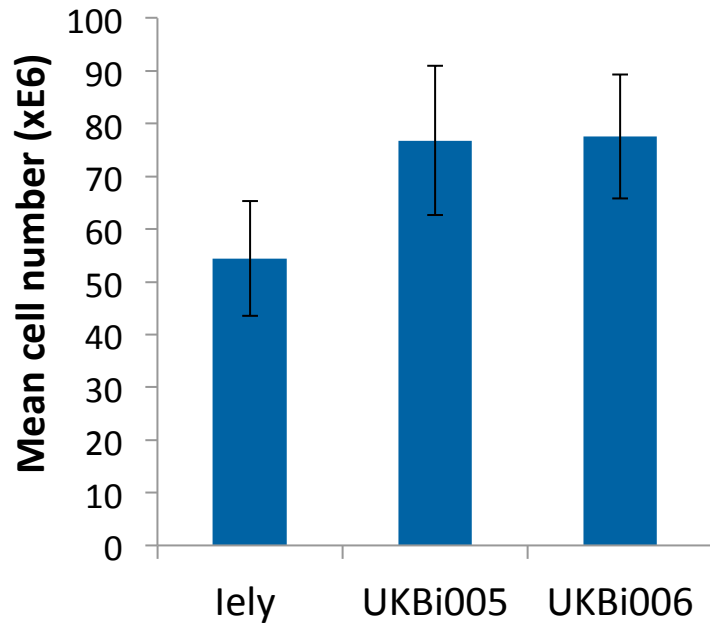
Stimuli-Responsivity



hiPS cell expansion on microcarrier in the Biolevitator



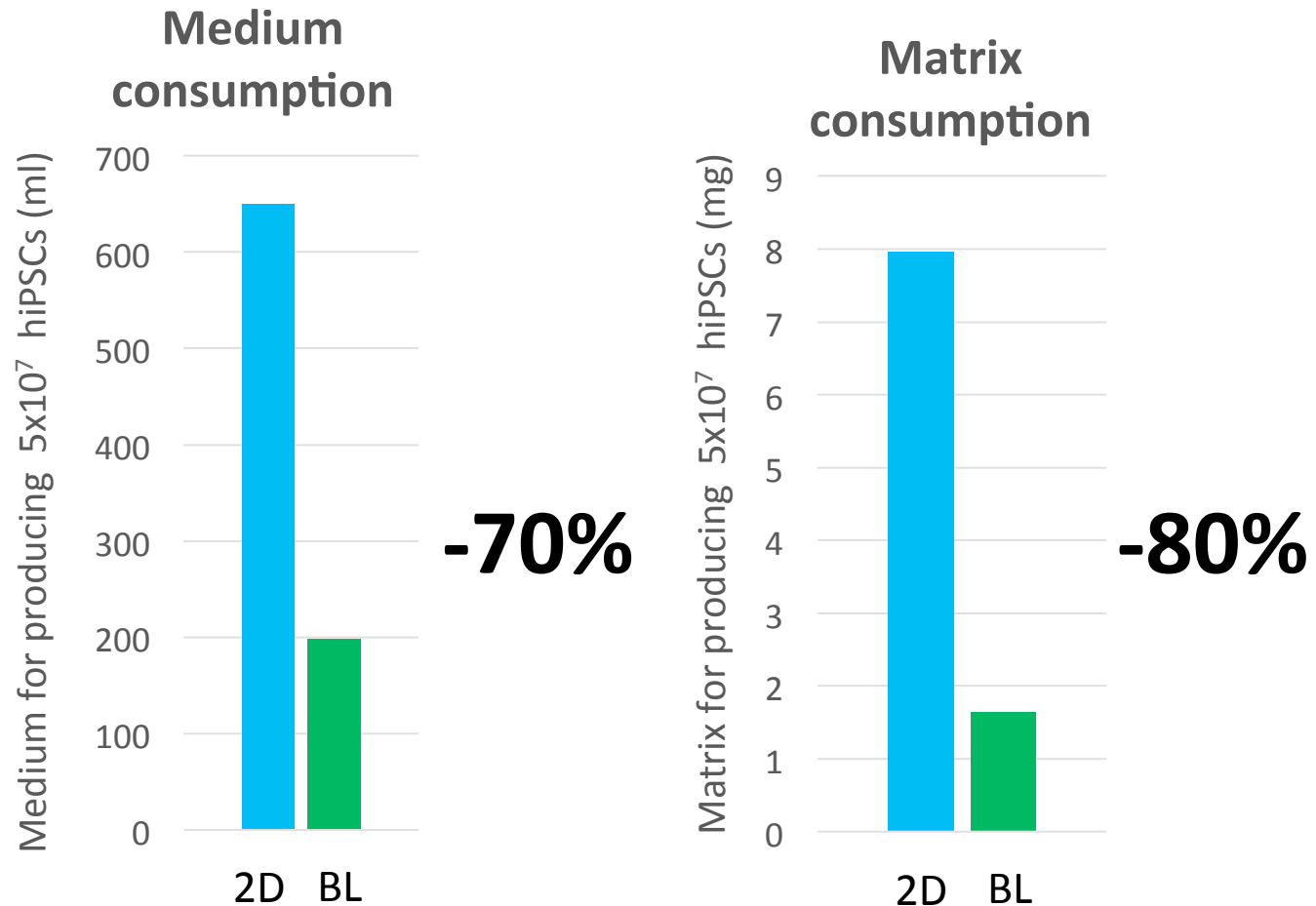
hiPS cell expansion on microcarrier in the Biolevitator



⇒ Production of more than 5×10^7 cells within 13 days

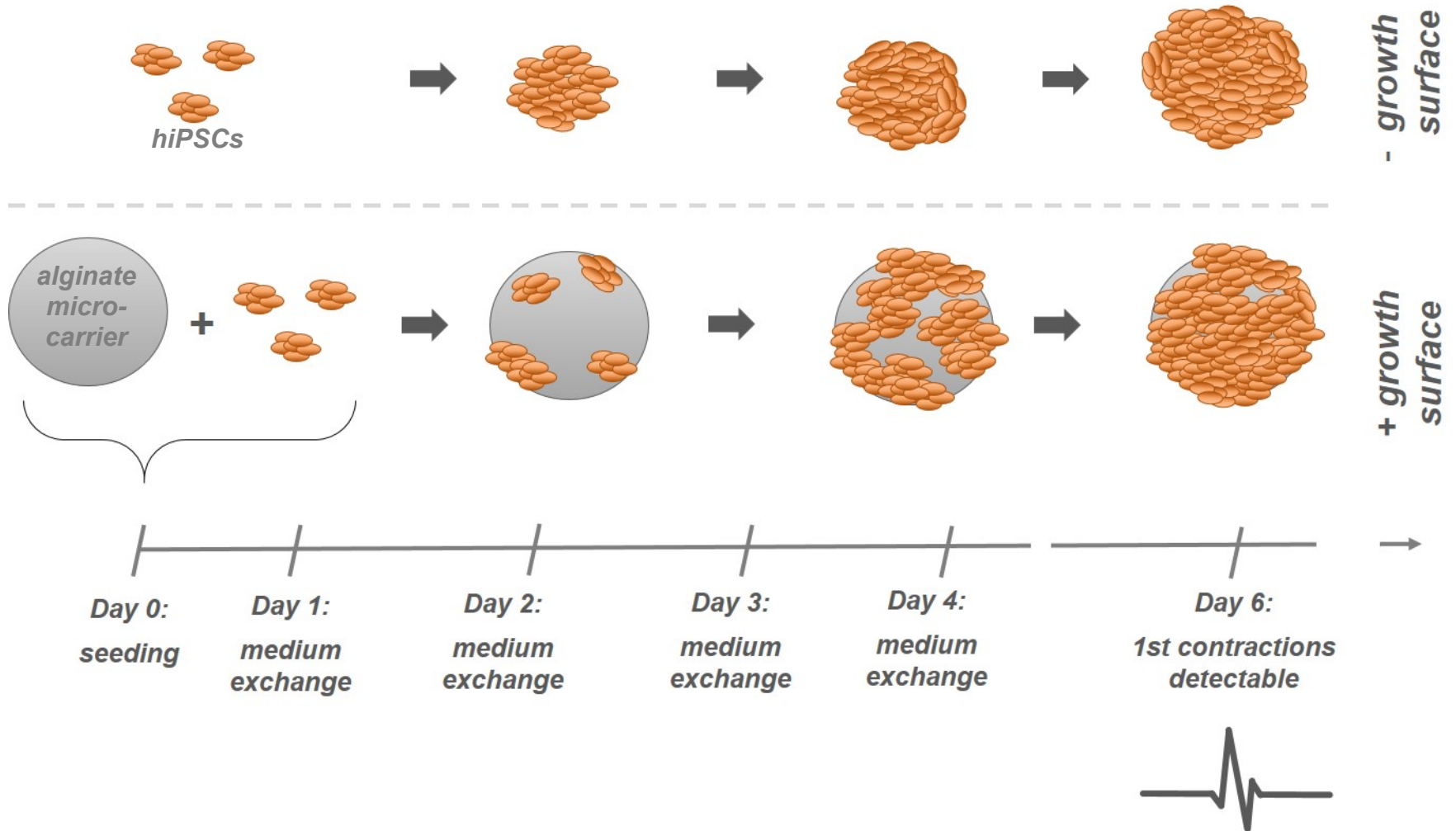
⇒ Maintained stemness

Impact on productivity



⇒ Significant reduction of expansion costs, because less passaging is necessary

Complete differentiation into cardiomyocytes on elastic alginate surfaces



Large-scale cardiac differentiation in Biolevitator

GOAL

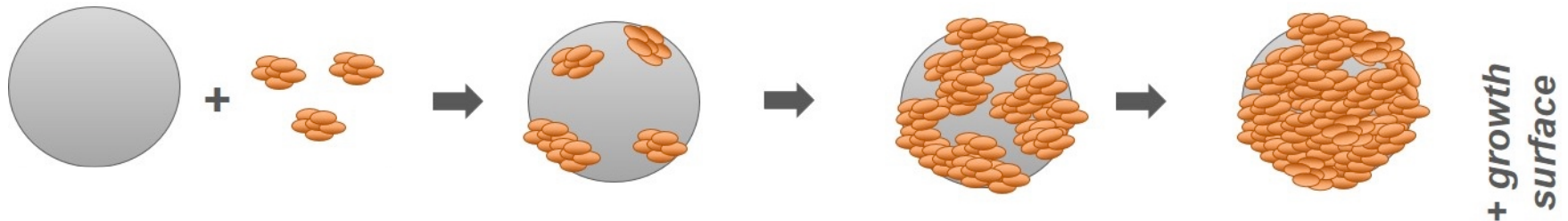


Large scale differentiation of **very mature** cardiomyocytes

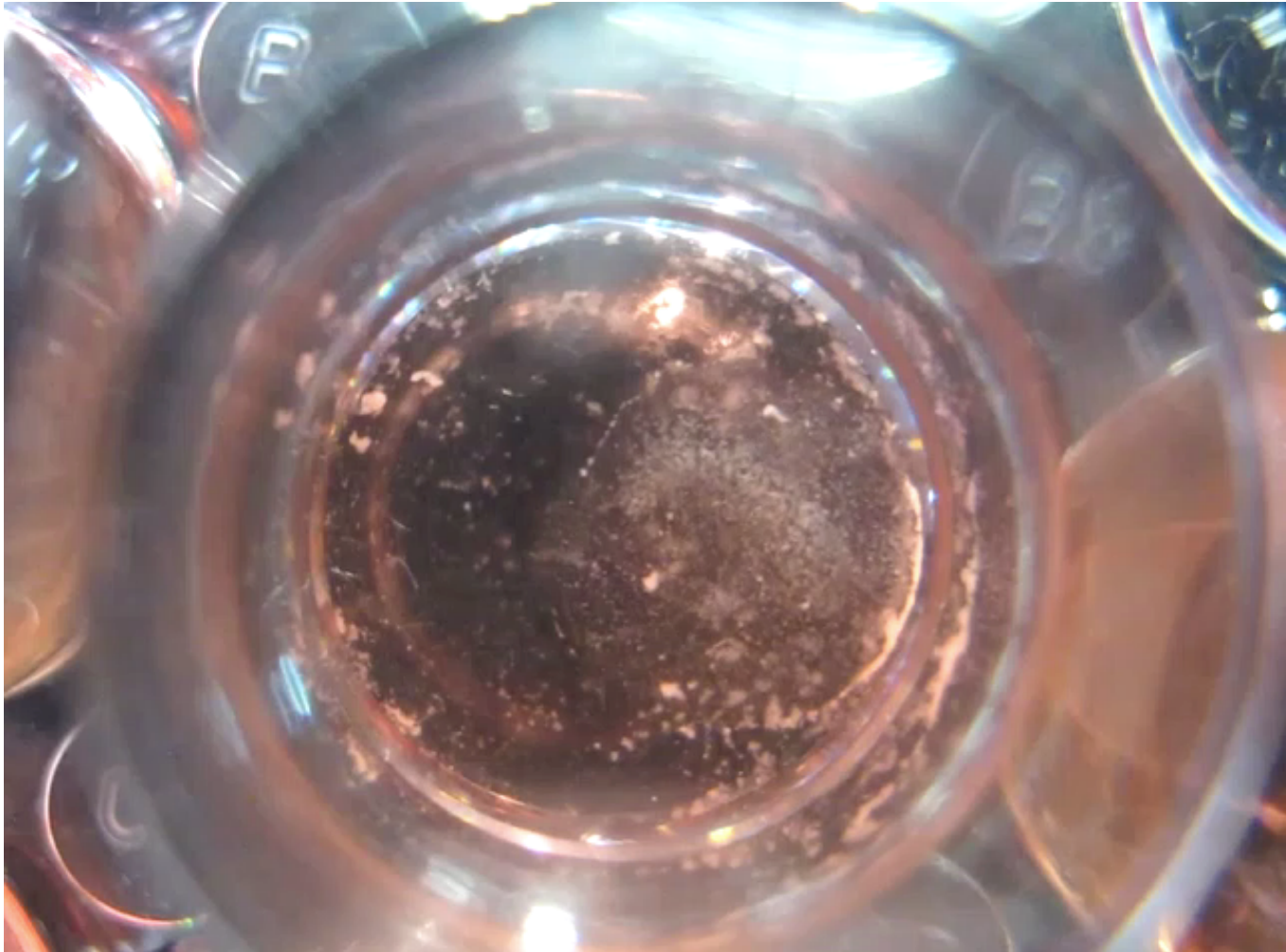


Needed?

Counter-Force during contraction
⇒ Impossible in aggregates
⇒ Elastic cell-matrix connection in Biolevitator

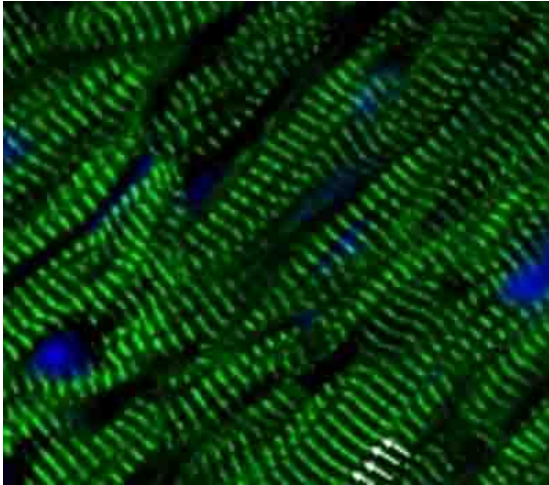


iPS derived cardiomyocytes on free floating elastic alginate surface

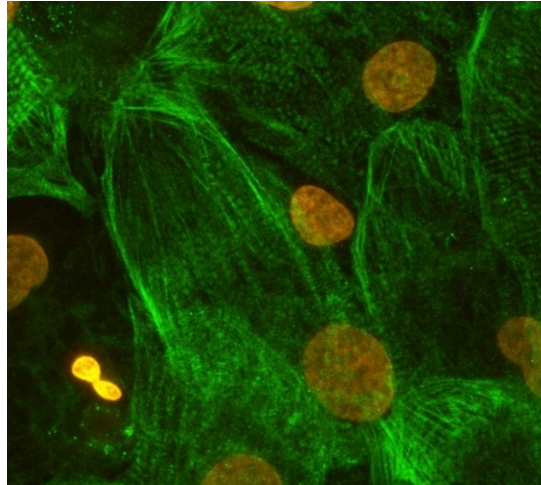


Maturation of cardiomyocytes on free floating elastic alginate surfaces

Primary cells



iPSC derived CMs cultured on polystyrene



iPSC derived CMs cultured on free floating alginate

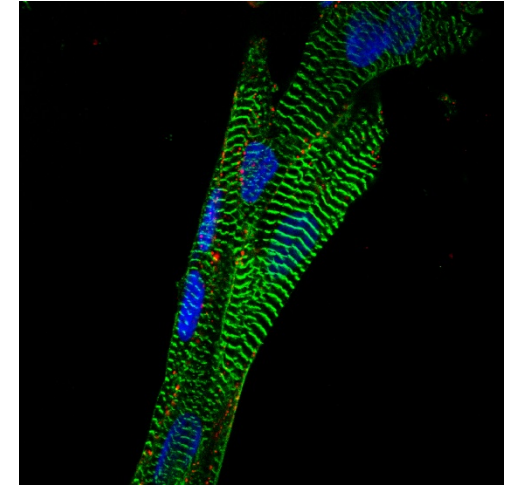
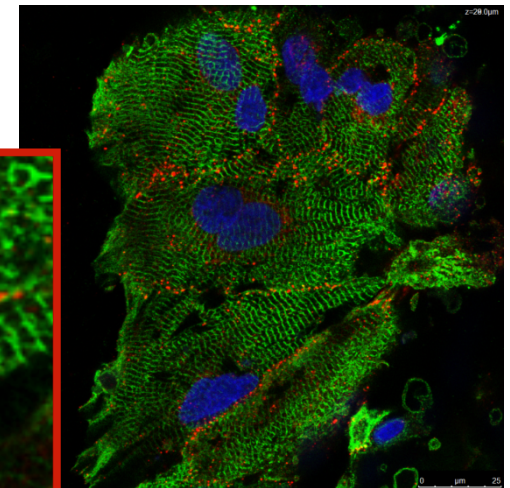
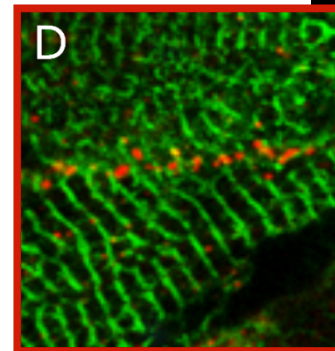


Image from Boyer JG et al, PLoS One. 2010
Mar 1;5(3):e9465, Fig 4

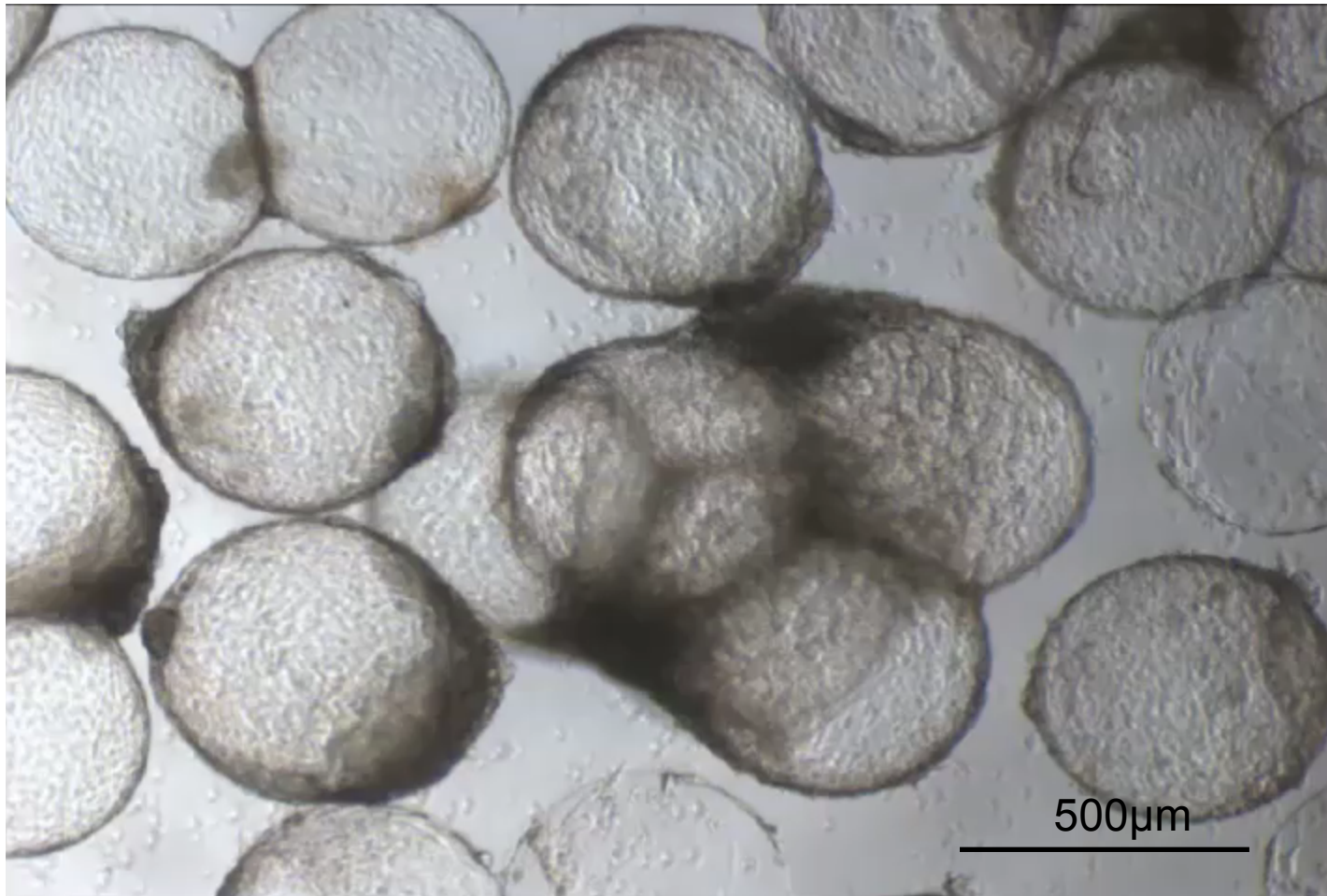
- Clear sarcomere structure
- Electrical coupling detectable

⇒ **High maturation status**

⇒ **Transfer to alginate microcarrier**



First results: Successful differentiation on elastic alginate surfaces



Procedures for improved expansion and differentiation of hiPS cells

Automation technology (OLS)

+ Biopolymer technology (Fraunhofer IBMT)

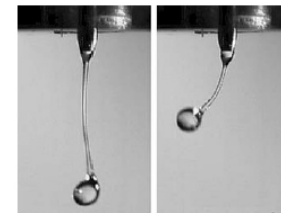
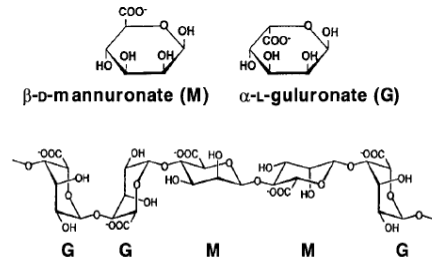


UHV
Alginate

Bead
production

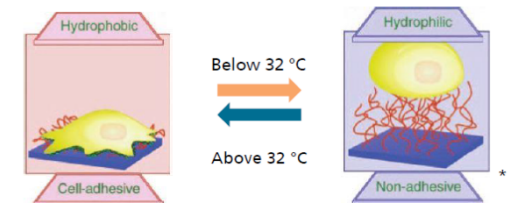
Biofunc-
tionalization

Stimuli-
Responsivity



■ Membranes 

■ Microcarrier 



*Ottenbrite, R.M. et al., Biomedical Applications of Hydrogels Handbook, 2010, 19-43.

Thank you for your attention!

