Microenvironment induces epigenetic reprogramming and promotes cell plasticity

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Induced pluripotent stem cells (iPSC) revolutionized the field of regenerative medicine and disease modelling, but its clinical viability has been hindered by limited reprogramming efficiency and the usage of exogenous factors. Here I will present a vector free approach to induce plasticity in somatic cells through epigenetic reprogramming[1]. A combination of extracellular matrix (ECM) proteins are covalent conjugated on polyacrylamide (PA) gel to create controlled biophysical and biochemical cues. Confined substrate promotes epigenetic reprogramming and pushes varied cell types towards pluripotent phenotypes in the absence of exogenous factors. The reprogrammed cells express pluripotent markers, forming spheroids or aggregates that are prone to 3D bio-assembly in various biomaterial substrates and are capable of performing trilineage differentiation. The onset of mechanical induced epigenetic reprogramming correlates with elevated autophagy activities, which promote cytoplasmic remodeling by reducing cell size and complexity. Moreover, confined substrate priming improves reprogramming efficiency substantially when incorporate with standard reprogramming through viral transduction.

References

[1] Romanazzo, S. et al. *Adv. Drug Deliv. Rev.,* **2020**, *161*, 124-144