

## Screening of better cell responses to the nanotopography using gradient nanopatterns

Kyu Back Lee

Department of Biomedical Engineering, School of Health Science, Korea University, Seoul, 02841, Republic of Korea.

### Abstract :

Surface nanotopography has been reported as an important physical parameter in the stem cell niche for regulating cell fate and behaviors for various types of cells. Substrates featuring arrays of increasing nanopillar or nanohole diameter were devised to investigate the effects of varying surface nanotopography on the responses of various cells such as human embryonic stem cells (hESCs), fetal liver kinase 1-positive mesodermal precursor cells (Flk1+ MPCs), mesenchymal stem cells (MSCs) and endothelial colony forming cells (ECFCs). hESCs demonstrate a propensity to organize into more compact colonies expressing higher levels of undifferentiated markers towards a smaller nanopillar diameter range ( $D = 120\text{--}170\text{ nm}$ ). Cell-nanotopography interactions modulated the formation of focal adhesions and cytoskeleton reorganization to restrict colony spreading, which reinforced E-cadherin mediated cell-cell adhesions in hESC colonies. hESCs also generate clusters of pancreatic endocrine progenitors (PDX1+ and NGN3+) on the nanopattern with nanopore diameter range ( $D = 200\text{--}300\text{ nm}$ ). The nanopattern-derived clusters generated islet-like 3D spheroids and tested positive for the zinc-chelating dye dithizone. The spheroids consisted of more than 30% CD200 + endocrine cells and expressed NKX6.1 and NKX2.2. In addition, pancreatic beta cells expressing insulin and polyhormonal cells expressing both insulin and glucagon were obtained at the final stage of pancreatic differentiation. Flk1+ MPCs showed increased cell proliferation and colony formation on the nanopattern plates. Nanopatterns with nanopillar diameter range ( $D = 200\text{--}280\text{ nm}$ ) increased cardiomyocyte differentiation and expression of the early cardiac marker gene *Mesp1*. Vinculin and p-Cofilin-mediated cytoskeleton reorganization was observed, and the induced cardiomyocytes had cardiac sarcomeres with mature cardiac gene expression. Nanopatterns with much smaller nanopillar diameter range ( $D = 70\pm 10\text{ nm}$ ) activate transcriptional coactivator with PDZ binding motif (TAZ), which stimulates osteogenesis of MSC. TAZ activation via the nanotopological cue was mediated by actin polymerization and Rho signaling. The FAK and MAPK pathways also play a role in TAZ activation. Nanopillars with nanopillar diameter range ( $D = 120\text{--}200\text{ nm}$ ) caused the cell area and perimeter of hECFCs to decrease and their filopodial outgrowth to increase. The structure of vinculin was modulated by nanostructural stimuli. The gradient nanopattern plates generate size-specific nanostructural stimuli via ROCK signaling for manipulation of the response of hECFCs

### Biography:

Kyu Back Lee is a professor in Department of Biomedical Engineering in Kora University. He has served as a professor in Korea University since 2001. He got a Medical Doctor license from Korean Government in 1995 and a Doctor of Philosophy degree in Biomedical Engineering at the Seoul National University in 1998. He is an expert in chemical surface modification and nanopatterning. He has interests in nanobiotechnologies, especially in nano-bio-interfaces between nanopatterned surfaces and stem cells for the improvement of cell-material interaction and the modulation of cellular responses to biomaterials.

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