**Photoactivatable substrates for dissecting biology and physics of collective cell behavior**

**Jun Nakanishi**

WPI Center for Materials Nanoarchitectonics (MANA), National Institute for Materials Science (NIMS)

Collective cell migration plays critical roles in both physiological and pathological processes. Basically, epithelial cells migrate collectively, whereas mesenchymal cells prefer to migrate as individuals. However, in some spatiotemporally limited situations of life, cells aggressively ignore this rule. For example, the change in the collective characteristics via epithelial-mesenchymal transition (EMT) or vice versa (MET) is essential in embryonic development and morphogenesis. Also, cancer metastasis can be considered as a loss of collectivity upon escaping from the original tissue and its retrieval on settling down and forming new colonies in distant tissues. Therefore, comprehensive understanding of the mechanisms regulating collective cell behaviors is important not only for fundamental biological interests, but also for tissue engineering and drug discovery.

Various internal and external factors have been shown to modulate collective characteristics in vitro and in vivo. In contrast to well-studied single cell migration, however, proximity effects make the things complex in collective cell migration; not only juxtacrine and paracrine factors, but also physical forces need to be considered. To rationally tackle this issue, our group is studying collective cell migration under conditions with well-controlled cell-cell and cell-ECM interactions by using originally-developed photoactivatable substrates (1-3). The common feature of these substrates is that the surface changes from a state that preventing cell adhesion to that promoting cell adhesion in response to photoirradiation. In this presentation, I will present some of our interesting findings in biological as well as mechanical responses of cell clusters upon migrating under such defined microenvironments.

[References]

1. . J. Nakanishi,\* Y. Kikuchi, S. Inoue, K. Yamaguchi, T. Takarada,\* M. Maeda, "Spatiotemporal Control of Migration of Single Cells on a Photoactivatable Cell-Microarray", Journal of the American Chemical Society, 129, 6694-6695 (2007).
2. C. Rolli, H. Nakayama, K. Yamaguchi, J. P Spatz, R. Kemkemer, and J. Nakanishi   
   "Switchable adhesive substrates: Revealing geometry dependence in collective cell behavior", Biomaterials, 33, 2409-2418, (2012).
3. Y. Shimizu, H. Boehm, K. Yamaguchi, J. P. Spatz, and J. Nakanishi,\*   
   "A Photoactivatable nanopatterned substrate for analyzing collective cell migration with precisely tuned cell extracellular matrix ligand interactions", PLoS One, 9(3) e91875 (2014).