CDB SEMINAR

Michael M. Shen

Departments of Medicine and Genetics & Development,
Herbert Irving Comprehensive Cancer Center,
Columbia University Medical Center, USA

Thursday, June 9, 2011
15:00~16:00 A7F Seminar Room

Stem cells and the origin of prostate cancer

Summary

Understanding the lineage relationship between normal progenitor cells and cell type(s) of origin for cancer may yield important molecular insights into prostate cancer prognosis and treatment response [1]. In our work, we have shown that a known regulator of prostate epithelial differentiation, the homeobox gene *Nkx3.1*, marks a luminal stem cell population that functions during prostate regeneration and is an efficient target for oncogenic transformation in prostate cancer [2]. Genetic lineagetracing studies demonstrate that rare cells which express Nkx3.1 in the absence of testicular androgens (castration-resistant Nkx3.1-expressing cells, CARNs) are bipotential and can self-renew *in vivo*, while single-cell transplantation assays show that CARNs can reconstitute prostate ducts in renal grafts. Targeted deletion of the *Pten* tumor suppressor gene in CARNs results in rapid formation of carcinoma following androgen-mediated regeneration. In our ongoing studies, we are investigating the properties of CARNs as well as other epithelial cell types during prostate regeneration and as cells of origin for cancer *in vivo.* In particular, we have utilized *CK5-Cre^{ERT2}* transgenic mice for lineage-tracing of basal cells during androgen-mediated prostate regeneration and oncogenic transformation. I will discuss our recent findings with respect to elucidating the prostate epithelial lineage hierarchy and its relationship to cancer initiation.

[1] Shen, M. M., and Abate-Shen, C. (2010). Molecular genetics of prostate cancer: new prospects for old challenges. *Genes Dev.* 24: 1967-2000.
[2] Wang, X., Kruithof-de Julio, M., Economides, K. D., Walker, D., Yu, H., Halili, M. V., Hu, Y.-P., Price, S. M., Abate-Shen, C., and Shen, M. M. (2009). A luminal epithelial stem cell that is a cell of origin for prostate cancer. *Nature* 461: 495-500.

Host:
Shinichi Nishikawa
Stem Cell Biology, CDB
nishikawa@cdb.riken.jp
Tel:078-306-1893
(ext : 5301)