CDB SEMINAR

Thursday, March 16
15:00~16:45
A7F CDB Conference Room

1. 15:00~16:00

George Cotsarelis

University of Pennsylvania School of Medicine

Hair follicle stem cells

Over 15 years ago, we proposed that quiescent keratinocytes in the hair follicle bulge were epithelial stem cells important for hair follicle cycling, epidermal renewal, wound healing and carcinogenesis. Since that time, we identified cytokeratin 15 (K15) expression as a marker for these cells and developed several transgenic mouse models using the K15 promoter to further study the bulge cells. Using K15-EGFP mice, we isolated bulge cells and demonstrated that they possessed an epithelial stem cell phenotype of quiescence, high proliferative potential and multipotency. We also characterized the cells at the molecular level using microarrays and identified approximately 150 differentially expressed genes in these cells. Through genetic lineage analysis using an inducible K15-CrePR;R26R bigenic mouse, we showed that bulge cells generate all of the epithelial lineages within the lower anagen hair follicle. However, ablation of bulge cells using K15-thymidine kinase mice resulted in permanent hair loss but survival of the epidermis. Over a prolonged period, bulge cells did not contribute to epidermal homeostasis, but in response to wounding bulge cell progeny rapidly moved into the wound area to assist in reepithelialization. Bulge derived cells did not persist in the epidermis indicating that epidermal stem cells and hair follicle stem cells are distinct populations each with self renewing capabilities.

2. 16:15~16:45

Manabu Ohyama

Keio University School of Medicine

Characterization and isolation of stem cell enriched human hair follicle bulge cells

The human hair follicle bulge provides an important niche for keratinocyte stem cells (KSC). Analysis of global gene expression profiles and identification of unique cell surface markers could enable the elucidation of human bulge cell biology. The lack of distinctive bulge morphology in human anagen hair follicles has hampered studies of bulge cells and KSC. In this study, we determined the distribution of label-retaining cells to define the human anagen hair follicle bulge. Using navigated-laser capture microdissection, bulge cells and outer root sheath cells from other follicle regions were obtained and analyzed with Affymetrix Genechip microarrays. Gene transcripts encoding inhibitors of *WNT* and *Activin/BMP* signaling were over-represented in the bulge, while genes responsible for cell proliferation were under-represented, consistent with quiescent non-cycling KSC in anagen follicles. Positive markers for bulge cells included CD59 and CD200, while CD24, 34, 71 and 146 were preferentially expressedby non-bulgen keratinocytes. Importantly, CD200+ cells ($CD200^{hi}24^{lo}34^{lo}71^{lo}146^{lo}$) obtained from hair follicle cell suspensions demonstrated high colony forming efficiency in clonogenic assays, indicating successful enrichment of living human bulge stem cells. Now, the stem cell behavior of enriched bulge cells and their utility for hair regeneration are ready to be assessed by in vivo assays.

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