CDB SEMINAR

Speaker: Takayoshi Sakai

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Title: **"Fibronectin Requirement in Branching Morphogenesis"**

Date: **Monday, September 29**

Time: **16:00 P.M.～17:00 P.M.**

Place: **7th floor Conference Room of Building A, CDB**

Summary

Many organs including salivary gland, lung, and kidney are formed during embryonic development by epithelial branching. In branching morphogenesis, repetitive epithelial cleft and bud formation create the complex, three-dimensional branching structures characteristic of many organs. Although the mechanisms are poorly understood, one might involve site- specific accumulation of some regulatory protein. Here we show that the extracellular matrix protein fibronectin is essential for cleft formation during initiation of epithelial branching. Fibronectin (FN) mRNA and fibrils appeared transiently and focally in forming cleft regions of submandibular salivary gland epithelia, accompanied by adjacent loss of cadherin localization. FN reduction using small interfering RNA (siRNA) andinhibition by FN or integrin antibodies blocked cleft formation and branching. Exogenous FN accelerated cleft formation and branching. Similar effects of FN suppression and augmentation were observed in developing lung and kidney. Mechanistic studies revealed that fibrillar FN can induce cell-matrix adhesions on cultured human salivary epithelial cells with local loss of cadherins at cell-cell junctions. We conclude that FN expression is required for cleft formation in branching morphogenesis associated with conversion of cell- cell adhesions to cell-matrix adhesions.

Reference:

1. **Sakai, T., Larsen M., and Yamada K.M. Essential Role for Fibronectin in Branching Morphogenesis. Nature 423, 876-881,2003**
2. **Bussell, K., Extracellular Matrix, A new branch, Nat. Rev. Mol. Cell Biol. 4, 597, 2003**
3. **LeBrasseur, N. Research Rounup; Fibronectin for branching. J Cell Biol. 162, 12, 2003,**
4. **NIDCR Press Releases, July 17, 2003 http://www.nidr.nih.gov/news/07162003.asp**

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