CDB SEMINAR

Speaker: Tadashi Okubo

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Title: **"Wnt signaling and the downstream pathway in lung development"**

Date:	Tuesday, January 18
Time:	16:00 P.M.～ 17:00 P.M.
Place:	1F Auditorium of Building C, CDB

Summary:

In mouse, lung bud arises from foregut ventral region at E9.5 days, then starts branching, and finally forms tree like structure for gas-exchange. Lung development suppose to be regulated by epithelial-mesenchymal interaction, however, the molecular mechanism is not completely understood. Important role of canonical Wnt signaling is well documented in organogenesis such as skin and intestine. In order to figure out the function of Wnt signaling in lung development and identify the downstream pathway, we performed some genetic approaches.

Overexpression of dominant active Lef1 in embryonic lung endoderm driven by human Sftpc-promoter inhibited lung differentiation concomitant with highly proliferative cuboidal epithelium. Unexpectedly, DNA array, RT-PCR and *in situ* showed extensive upregulation of many gastrointestinal genes in the transgenic lungs (*Cdx1*, *Atoh1*, *Tff3*, *cryptdins*). In addition, lung specific β-catenin stabilization by cre-mediated exon3 removal also induced ectopic expression of intestinal genes in the lung. As a result, prolonged hyperactive Wnt signaling in lung endoderm changed the cell fate into stomach or small intestine which are also derived from definitive foregut endoderm. In conclusion, Wnt signaling in lung development is precisely regulated, and the threshold and timing of activated Wnt signaling is important for cell proliferation and maintenance of the identity as lung progenitor cells.

Lastly, I would also like to talk about my recent data.

Reference: T. Okubo and B.L. Hogan (2004) Journal of Biology. 3. 11

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