IZUMI laboratory

(Laboratory of Molecular Endocrinology and Metabolism,
Institute for Molecular and Cellular Regulation, Gunma University)

Our goal is to understand the molecular pathogenesis of metabolic diseases such as obesity and diabetes. If you are interested in our research and/or want to join our lab, please contact Prof. Izumi.

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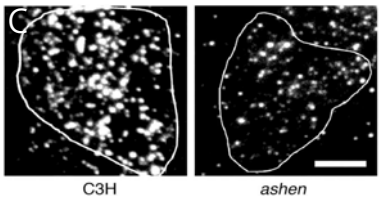
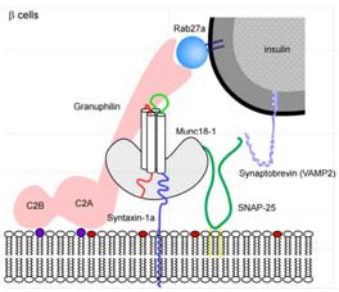
Molecular mechanism of insulin secretion in β cells

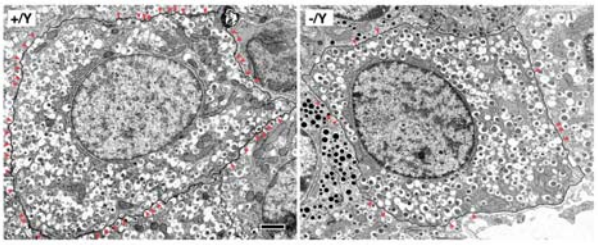
The logistics system in the human community is the management of the flow of foods and goods between the producers and the retailers in order to provide these goods to the consumers. Eukaryotic cells also possess "Intracellular logistics (membrane traffic)," which is involved in protein, lipid and nutrient transport to different organelles or other cells. Impairment of these processes can cause diseases such as cancer, neurodegradative disease, and diabetes. For example, insulin granule exocytosis is finely regulated in pancreatic β-cells, and its dysfunction causes diabetes. We investigate molecular mechanism of insulin secretion in terms of "logistics" using mouse models and cultured cell.



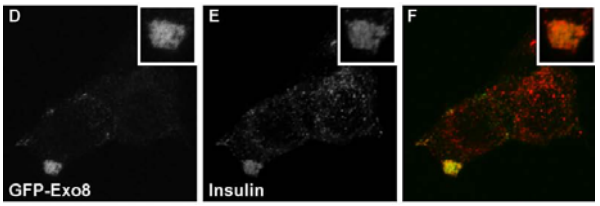
A left: Rab27a-knockout mice (ashen mice), **right**: Wild-type mice (C3H mice). Rab27a-knockout mice show impaired insulin secretion and a pigmentation disorder (ash color of body hair). Kasai K, et.al (2005) J. Clin. Invest., 115, 388-396.
B: TIRF(Total Internal Reflection Fluorescence) microscope. Insulin granules observed by TIRF microscopy. **C**: Insulin secretion events are dramatically reduced in β-cells of ashen mouse (right panel).

The Rab27a effector, Granuphilin, inhibits insulin secretion. Its knockout mouse exhibits a defect in insulin granule docking to the plasma membrane. **right figure**: electron micrographs of wild-type (left panel) and Granuphilin-knockout mouse islets (right panel). Red arrowheads indicate docked insulin granules. Gomi H et.al (2005) J. Cell. Biol., 171, 99–109. **right model** : The model of insulin granule docking to the plasma membrane.

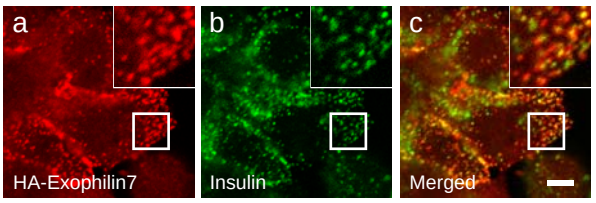




right upper figure: Overexpression of GFP-Exophilin8, a Rab27 effector (binding protein), in a β-cell line causes accumulation of insulin granules in the actin-rich cell cortex. left panel: GFP-Exophilin8 (green), center panel: insulin granules (red), right panal: merged figure. Mizuno K et al. (2011) Mol. Biol. Cell., 22, 1716-1726.



right bellow figure: Localization of Exophilin7 in a β-cell line. Exophilin7 localizes to the insulin granules and functions in undocked guranule exocytosis. left panel: HA-Exophilin7 (red), center panel: insulin granules (green), right panal: merged figure.Wang H et al. (2013) Mol. Biol. Cell. in press



Genetic analysis of diabetes and obesity in the TSOD mouse

The TSOD mouse is a polygenic model of obesity and type 2 diabetes. We have identified several loci affecting body weight and blood glucose levels. One of congenic strains (a part of TSOD mouse chromosome is replaced by wild-type mouse chromosome) generated in our laboratory shows dramatically reduced body weight and adipose size. We have recently identified ALK7 gene mutation that is responsible for the obesity and elucidated the mechanism of ALK7-mediated regulation of fat mass.

(This work (Yogosawa S et al. (2013) Diabetes) receives newspaper coverage!! Please see our web site for more detail.)

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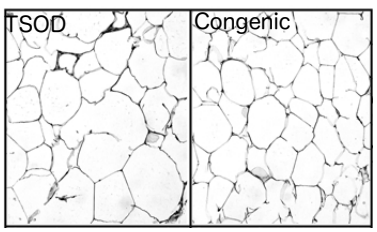

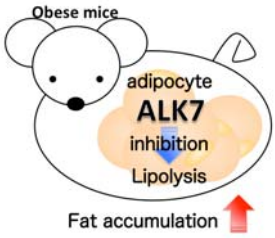

left: The TSOD mouse (left) and Wild-type BALB mouse (right). TSOD mouse shows obesity and hyperglycemia. **center**: Adipocytes of the congenic mice are smaller than those of the TSOD mice. Mizutani S et. al (2006). Mammalian Genome, 17, 375-384. **right**: The model of fat accumulation by ALK7. Yogosawa S et al. (2013) Diabetes, 62, 115-123.

Member's photo
(curry party in an Indian restaurant)