演講題目(Topic)

Roles of Rabs for apical transport, ciliogenesis, and diseases: lessons from knockout mice.

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摘要(Abstract)

The molecular mechanism of apical transport in epithelial cells are less well understood compared to basolateral transport. Recently, a number of Rabs have been known to be involved in apical transport. We have previously demonstrated that Rab8a is required for localizing apical markers in various organisms. Given that Rab8a has a closely related isoform, Rab8b, we generated Rab8ab double knockout mice. Rab8ab double knockout mice exhibited mislocalisation of apical markers earlier than Rab8a knockout mice, showing apparent redundancy between Rab8a and Rab8b. In addition, the intestine-specific Rab11a knockout mice, apical proteins in the intestines of knockout mice also mislocalized. Ultrastructurally, a shortening of apical microvilli, an increased number of enlarged lysosomes, and microvillus inclusions, which are hallmarks of microvillus inclusion disease in human, in the enterocytes were observed in Rab8a single knockout, Rab8ab double knockout, and Rab11a intestine-specific knockout mice.

Recently, Rab8 is also thought to be involved in ciliogenesis. However, the morphology and the length of primary and motile cilia, and the frequency of ciliated cells appeared to be unaffected in Rab8ab double knockout mice. An additional knockdown of Rab10 in double knockout MEF greatly reduced the percentage of ciliated cells.

Our results indicated that Rab8a, Rab8b, and Rab11a are required for apical transport. On the other hand, Rab8a, Rab8b, and Rab10 are required for ciliogenesis, suggesting that different combinations of Rabs are required for apical transport and ciliogenesis.

To know the molecular mechanism of apical transport further, we have detected and analyzed binding proteins of Rab8 and the results will be also presented.

References

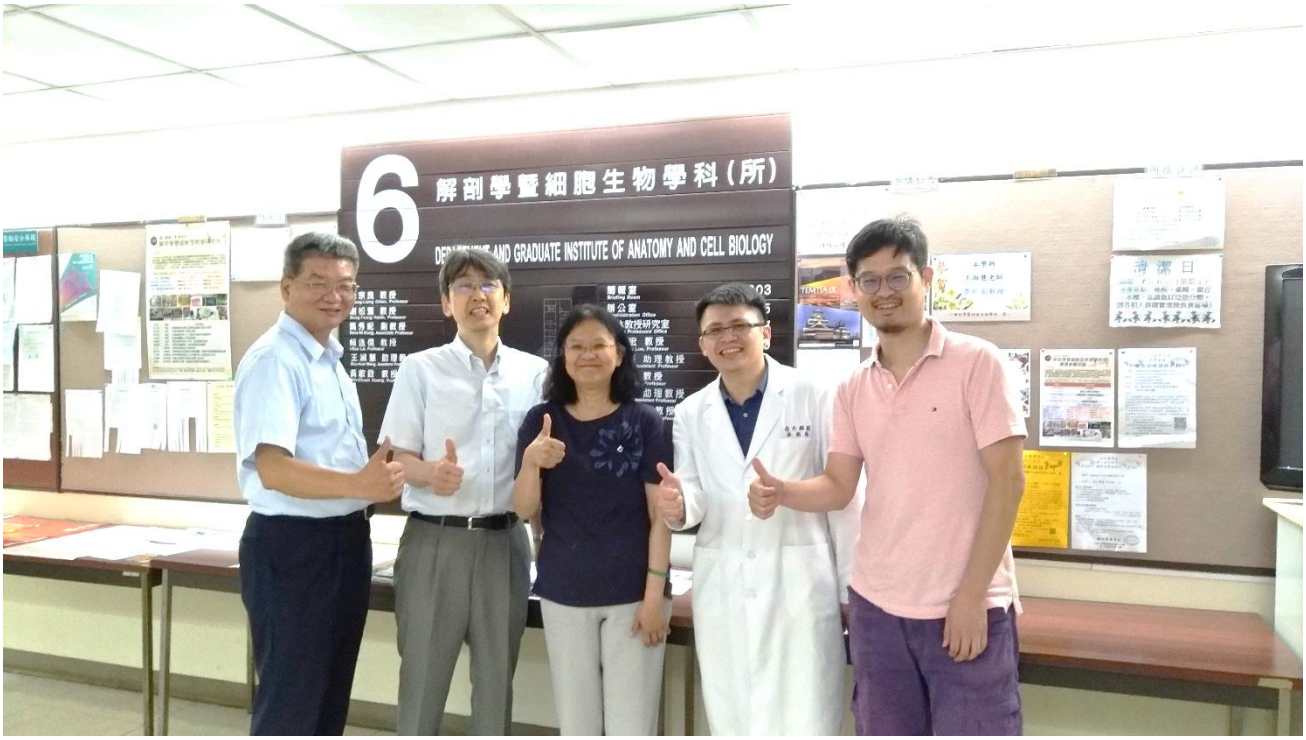
The Rab8 GTPase regulates apical protein localization in intestinal cells. Sato T et al. ***Nature*** 448: 366-369 (2007)

Rab8a and Rab8b are essential for several apical transport pathways but insufficient for ciliogenesis. Sato T et al. ***J Cell Sci*** 127: 422-31 (2014)

Rab11a is required for apical protein localisation in the intestine. Sobajima T et al. ***Biol Open*** 4: 86-94 (2014)

EHBP1L1 coordinates Rab8 and Bin1 to regulate apical-directed transport in polarized epithelial cells. Nakajo A et al. ***J Cell Biol*** 212: 297-306 (2016)

活動剪影一 Harada 教授至解剖學科暨細胞研究所演講



活動剪影二 演講結束後與所長及師長合照