Crystal structure analysis of Rab2A

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More than 60 Rab GTPases exist in human cell. Each of them is localized on specific organellar membranes in the cell. Due to its GTP hydrolysis activity, Rab takes two different conformations depending on its bound nucleotide: GTP-bound active form and GDP-bound inactive form. The structures of two regions, switch I and switch II, dynamically change between GTP-bound and GDP-bound forms, so that Rab GTPase works as "molecular switch". GTP-bound Rab can bind its target molecules (effectors) to regulate membrane traffic between organelles. In addition, two conserved cysteines at the C-terminal region of Rab, are lipidated to be anchored to membranes.

Rab2, one of the Rab GTPases, is localized in endoplasmic reticulum (ER) and Golgi apparatus, and regulates membrane traffic from ER to Golgi apparatus. The difference between the structures of GDP- and GTP-bound forms plays important roles in effector binding of Rab GTPases. Although many structures of Rab GTPases have been determined including GDP-bound Rab2A, the structure of GTP-bound Rab2 has not been determined.

We obtained the crystal of GTP-bound form of mouse Rab2A, and performed X-ray diffraction analysis at NW12A (PF-AR, KEK) to determine the structure of GTP-bound Rab2A. The crystal structure of GDP-bound Rab2A (PDB ID: 1Z0A) was used as a search model of molecular replacement (MR). As a search model, we removed switch I region of GDP-bound Rab2A, which is expected to be dramatically altered depending on nucleotide type, to find six molecules in the crystallographic asymmetric unit, so that we could determine the crystal structure GTP-bound Rab2A (Fig. 1).

Comparing this structure and the reported structure of GDP-bound Rab2A revealed that GTP-bound Rab2A has a structured loop with an extra β-sheet in the C-terminal region which was expected to be flexible. We would like to discuss the structural significance of target molecule recognition based on this unique structure.

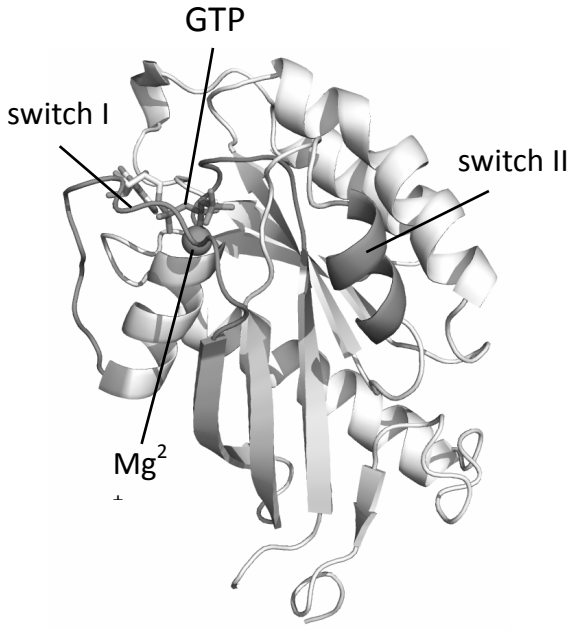

Fig. 1 The structure of Rab2A-GTP