Analysis of cell-type specific adaptor protein (AP) complexes in cells and organisms

2005 Fiscal Year Final Research Report Summary

Analysis of cell-type specific adaptor protein (AP) complexes in cells and organisms

Research Project

Project/Area Number

15370042

Research Category

Grant-in-Aid for Scientific Research (B)

Allocation Type

Single-year Grants

Section

一般

Research Field

Structural biochemistry

Research Institution

RIKEN (2004-2005)
Kanazawa University (2003)

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Project Period (FY)

2003 – 2005

Keywords

vesicular transport / neurons / epithelial cells / gastric acid secretion / SNAP25 / AP complexes / KO mice / sorting signal

Research Abstract

We investigated the roles of membrane traffic, especially AP complexes, in neurons and epithelial cells. The following has bee elucidated during the term of this grant. 1.Foxl1 is a transcription factor expressed in mesenchymes of gastrointestinal tract. Foxl1-KO mice suffer from hardly detectable gastric acid secretion. Upon stimulation, proton pump, H,K-ATPase, translocates from internal tubulovesicles to the plasma membrane in gastric parietal cells, which leads to gastric acid secretion. In foxl1-KO mice, however, this translocation does not occur. We found that the expression SNAP25, a SNARE involved in the fusion of tubulovesicules and the plasma membrane, was

significantly reduced, which likely is a major problem involved in acid secretion insufficiency in these mice.
2.We established and analyzed KO mice for AP-3B, the neuron-specific AP complex. AP-3B-KO mice suffered from epileptic seizure. Structural abnormalities of synaptic terminals and synaptic vesicles were seen in AP-3B-KO mice. Consistent with the observation, release of the inhibitory neurotransmitter, GABA, was impaired, and abnormal excitability was observed in electrophysiological examinations, in these KO mice. Taken together, these observations suggest that insufficient release of GABA causes imbalance in neuroexcitability in AP-3B-KO mice, which ultimately leads to epileptic seizure in these mice.
3.Previous studies on cultured cells have suggested that the AP-2 complex, involved in endocytosis, is not essential for cell survival. However, there should still be a small, residual amount of AP-2 in these experimental conditions, which may be sufficient for cells to survive. To test this possibility, we have tried to establish AP-2-KO mice. To our surprise, no homozygous embryo has been recovered at embryonic day 3.5 or later, suggesting that AP-2 is essential for cell survival or embryonic development at very early stages.

Research Products (6 results)

All | 2005 | 2004

All | Journal Article

- [Journal Article] Clathrin adaptor AP-2 is essential for early embryonal development — 2005
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- [Journal Article] Reduction of SNAP25 in acid secretion defect of Foxl1-/-gastric parietal cells — 2004
- [Journal Article] Defective function of GABA-containing synaptic vesicles in mice lacking the AP-3B clathrin adaptor — 2004
- [Journal Article] Reduction of SNAP25 in acid secretion defect of Foxl1-/-gastric parietal cells. — 2004
- [Journal Article] Defective function of GABA-containing synaptic vesicles in mice lacking the AP-3B clathrin adaptor. — 2004

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