輸送小胞形成・積み荷蛋白質選別の分子機構とその高次機能における役割

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Principal Investigator	**大野 博司** The Institute of Physical and Chemical Research, 免疫系構築研究チーム, チームリーダー (50233226)
Co-Investigator(Kenkyū-buntansha)	長谷 耕二 独立行政法人理化学研究所, 免疫系構築研究チーム, 研究員 (20359714) 中津 史 独立行政法人理化学研究所, 免疫系構築研究チーム, 研究員 (50360607)
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Research Abstract

上皮細胞特異的に発現し、側基底面細胞膜への膜蛋白質の極性輸送を担うクラスリンアダプター複合体,AP-1B複合体の個体レベルでの役割を明らかにする目的で、AP-1Bのサブユニットμ1Bの遺伝子欠損マウスの解析を行った。μ1B欠損マウスは成長障害が認められ、ほとんどは3ヶ月以内に死亡した。組織学的検討の結果、腸管上皮の過形成が認められた。免疫組織染色の結果、μ1B依存的に側基底面細胞膜に局在するLDL受容体がμ1B欠損マウスでは管腔側細胞膜にも存在しており、また本来管腔側細胞膜のみに局在するsucraseやvillinが側基底面細胞膜にも局在していた。電顕による観察でも本来管腔側のみに見られる微絨毛が側基底面細胞膜に異所性に認められた。これらの結果は、AP-1Bが個体レベルでも上皮細胞における極性輸送制御に重要であることを示唆している。
μ1B欠損マウスでは腸管粘膜上皮の過形成が見られたことからKi67陽性の増殖細胞の分布を調べたところ、野生型では幹細胞が存在するクリプト底部にのみ見られるのに対し、μ1B欠損マウスではクリプトから絨毛部にかけて広く分布していた。EGF受容体ファミリーのErbB2/ErbB3ヘテロ2量体はEGF増殖シグナルを伝達するが、分化した上皮細胞では、ErbB3は管腔側に、ErbB2はAP-1Bにより側基底面細胞膜に分かれて局在するため増殖シグナルは伝達されない。しかしμ1B欠損マウスにおいてはErbB2が管腔側にも局在するため異常な増殖シグナル伝達が起こることが示唆された。さらに、μ1B欠損マウスではβ-cateninの核移行も亢進していた。β-cateninは上皮細胞のクリプトー絨毛軸における移動を制御するEphB2の転写も制御することから、β-cateninの核移行亢進がμ1B欠損マウスにおける増殖細胞の異常分布に寄与している可能性が示唆された。

Report (5 results)

2007 Annual Research Report

2006 Annual Research Report

2005 Annual Research Report

2004 Annual Research Report

2003 Annual Research Report

Research Products (36 results)

All | 2007 | 2006 | 2005 | 2004 | Other

All | Journal Article | Presentation | Remarks | Publications

[Journal Article] Psg18 is specifically expressed in follicle-associated epithelium. 2007

[Journal Article] Construction of an open-access database that integrates cross-reference information from the transcriptome anda proteome of immune cells. 2007

[Journal Article] CD19-CD35+B220+cells function as an inducer of the follicular dendritic cell-network formation. 2007

[Journal Article] Mutation screening of AP3M2 in Japanese epilepsy patients. 2007

[Journal Article] Visualization of the post-Golgi trafficking of multi-photon photoactivated transferrin receptors. 2006

[Journal Article] CMRF-35-like molecule-5 constitutes novel paired receptors, with CMRF-35-like molecule-1, to transduce activation signal upon association with FcRγ. 2006

[Journal Article] CD300 Antigen Like Family Member G : A Novel Ig Receptor Like Protein Exclusively Expressed on Capillary Endothelium. 2006

[Journal Article] Fukamachi, H., Kato, Y., Koseki, H., Ohno, H. : Foxl1-deficient mice exhibit aberrant epithelial cell positioning due to dysregulated EphB/EphrinB in the small intestine. 2006

[Journal Article] The membrane-bound chemokine CXCL16 expressed on follicle-associated epithelium and M cells mediates lympho-epithelial interaction in GALT. 2006

[Journal Article] Clathrin adaptor AP-2 is essential for early embryonal development. 2005

[Journal Article] Distinct gene expression profiles characterize cellular phenotypes of follicle-associated epithelium and M cells. 2005

[Journal Article] Defective function of GABA-containing synaptic vesicles in mice lacking the AP-3B clathrin adatptor 2004

[Journal Article] Reduction of SNAP25 in acid secretion defect of Foxl1-/- gastric parietal cells 2004

[Presentation] ニュートリメタボノミクスにおける安定同位体標識技術の適用 2007

[Presentation] 腸内細菌群のニュートリメタボノミクス基盤技術の構築 2007

[Presentation] 非ストレス状態におけるJNKによる翻訳調節 2007

[Presentation] Identification of molecules expressed in FAE and M cells to be involved in mucosal immunity. 2007

[Presentation] Identification of a CDllc^+CD19^+ unique cell population in the mucosa-associated lymphoid tissues: A potential role in M cell development 2007

[Presentation] Epithelial-specific adaptor complex, AP-1B is essential for maintenance of immunological tolerance in the colon 2007

[Presentation] Bacterial adhesin is a ligand for endocytic receptor glycoprotein 2 expressedon M cells 2007

[Presentation] Psg18 is specifically expressed in follicle-associated epithelium 2007

[Presentation] Gene expression profiles of follicle-associated epithelium covering murine intestinal Peyer's patches in response to host-bacterial cross-talk 2007

[Presentation] Endogenous prion protein expressed on M cells: A potential antigen uptake receptor 2007

[Presentation] M-Sec: the M cell-specific Sec family molecule that regulates tunneling nanotubule (TNT) formation 2007

[Presentation] Activation-induced cytidine deaminase deficiency causes severe gastritis with mucosal hyperplasia 2007

[Presentation] Identification of CD11c^+CD19^+ cells in the mucosa-associated lymphoid tissues: A potential role in M cell development 2007

[Presentation] Differential gene expression profiles of follicle-associated epithelium covering murine intestinal Peyer's patches in response to host-bacterial cross-talks. 2007

[Presentation] Identification of a new endocytic receptor expressed in the apical plasma membrane of M cells. 2007

[Presentation] Endogenous prion protein expressed on the apical plasma membrane in M cells could function as a potential antigen uptake receptor 2007

[Presentation] 宿主-腸内フローラ間相互作用の解析とその評価系の構築 2007

[Presentation] Analysis of epithelial-specific AP-1B-deficient mice 2007

[Presentation] CD300 antigen like family member G: A novel Ig receptor like Protein exclusively expressed on capillary endothelium 2007

[Remarks]

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