

OptiPrep™ Mini-Review MS07

Detergent-free strategy for lipid raft isolation

- ◆ The principal aim of this Axis-Shield Mini-Review is to present a bibliography of all of the current papers reporting the use of an iodixanol gradient to purify and analyze lipid rafts from vertebrate cells/tissues prepared in the absence of detergent (see Section 2). Section 1 contains a brief survey of the technique; it has its own short reference list distinct from the comprehensive reference list in Section 2.

1. Background

Five years before McDonald and Pike [1] published their method for the isolation of lipid rafts in the absence of detergent, Kasahara et al [2] used a broadly similar approach in which cerebellar granule cells were disrupted in a Potter-Elvehjem homogenizer in buffered 0.25 M sucrose, 1 mM EDTA and then sonicated before adjusting to 25% iodixanol and fractionated by flotation through a 10-20% iodixanol linear gradient at approx 180,000 g for 18 h. McDonald and Pike [1] performed two rounds of homogenization of CHO cells using multiple passages through a syringe needle. A post-nuclear supernatant was similarly adjusted to 25% (w/v) iodixanol and loaded under a 0-20% iodixanol gradient. The centrifugation was considerably different however – 52,000 g for 90 min; although subsequent papers using the technology have reported the use of much more severe conditions – e.g. 170,000 g for 4 h [3] or 200,000 g for 18 h [4]. The milder centrifugation conditions recall those used by Smart et al [5] in the isolation of caveolae.

A detailed description of the OptiPrep™ methodology see Application Sheet S33 can be found on the OptiPrep™ Applications flash-drive or on the following website: www.axis-shield-density-gradient-media.com (click on “Methodology”, then “Organelles and Subcellular Membranes”) and scroll down the Index.

1. Macdonald, J.L. and Pike, L.J. (2005) *A simplified method for the preparation of detergent-free lipid rafts* J. Lipid Res., **46**, 1061-1067
2. Kasahara, K., Watanabe, K., Takeuchi, K., Kaneko, H., Oohira, A., Yamamoto, T. and Sanai, Y. (2000) *Involvement of gangliosides in GPI-anchored neuronal cell adhesion molecule TAG-1 signaling in lipid rafts* J. Biol. Chem., **275**, 34701-34709
3. Inoue, M., Digman, M.A., Cheng, M., Breusegem, S.Y., Halahiel, N., Sorribas, V., Mantulin, W.W., Gratton, E., Barry, N.P. and Levi, M. (2004) *Partitioning of NAP_i cotransporter in cholesterol-, sphingomyelin-, and glycosphingolipid-enriched membrane domains modulates NAP_i protein diffusion, clustering, and activity* J. Biol. Chem., **279**, 49160-49171
4. Nakagawa, T., Morotomi, A., Tani, M., Sueyoshi, N., Komori, H. and Ito, M. (2005) *C18:3-GM1a induces apoptosis in Neuro2 cells: enzymatic remodeling of fatty acyl chains of glycosphingolipids* J. Lipid Res., **46**, 1103-1112
5. Smart E. J., Ying, Y-S., Mineo, C. and Anderson, R. G. W. (1995) *A detergent-free method for purifying caveolae membrane from tissue culture cells* Proc. Natl. Acad. Sci., USA, **92**, 10104-10108

2. Comprehensive bibliography of papers

Papers reporting the use of the non-detergent method have been divided into **cell type** (or occasionally **tissue**). Within each group, papers are listed alphabetically according to **first author**. To facilitate identification of references of interest **key words in titles are highlighted in light blue**. When a paper reports the study of more than one cell type, reference to that paper will appear under all relevant cell headings. There is also a **Section 18. “Subcellular membranes”** listing papers that report the isolation of rafts from an isolated subcellular membrane fraction rather than whole cells and at the end, a list of **Review articles (19)**.

1. Adipocytes

Han, C.Y., Umemoto, T., Omer, M., Den Hartigh, L.J., et al (2012) *NADPH oxidase-derived reactive oxygen species increases expression of monocyte chemotactic factor genes in cultured adipocytes* J. Biol. Chem., **287**, 10379–10393

Umemoto, T., Han, C.Y., Mitra, P., Averill, M.M., et al (2013) *Apolipoprotein AI and high-density lipoprotein have anti-inflammatory effects on adipocytes via cholesterol transporters ATP-binding cassette A-1, ATP-binding cassette G-1, and scavenger receptor B-1* Circ. Res., **112**, 1345-1354

Brain (see “Neural tissue, neural cells and related cells”)

2. Carcinoma cells (see also “HeLa cells” and “Hepatoma cells”)

- Basiouni, S.**, Stöckel, K., Fuhrmann, H. and Schumann, J. (2012) *Polyunsaturated fatty acid supplements modulate mast cell membrane microdomain composition* Cell. Immunol., **275**, 42–46
- Danza, G.**, Di Serio, C., Ambrosio, M.R., Sturli, N., et al (2013) *Notch3 is activated by chronic hypoxia and contributes to the progression of human prostate cancer* Int. J. Cancer, **133**, 2577–2586
- Dutta, S.**, Bandyopadhyay, C., Bottero, V., Veettil, M.V., et al (2014) *Angiogenin interacts with the plasminogen activation system at the cell surface of breast cancer cells to regulate plasmin formation and cell migration* Mol. Oncol., **8**, 483–507
- Hashimoto, A.**, Oikawa, T., Hashimoto, S., Sugino, H., Yoshikawa, A., Otsuka, Y., Handa, H., Onodera, Y., Nam, J.-M. et al (2016) *P53- and mevalonate pathway-driven malignancies require Arf6 for metastasis and drug resistance* J. Cell Biol., **213**, 81–95
- Irwin, M.E.**, Mueller, K.L., Bohin, N., Ge, Y., et al (2011) *Lipid raft localization of EGFR alters the response of cancer cells to the EGFR tyrosine kinase inhibitor gefitinib* J. Cell. Physiol., **226**, 2316–2328
- Kozyulina, P.Y.**, Loskutov, Y.V., Kozyreva, V.K., Rajulapati, A., Ice, R.J., Jones, B.C. and Pugacheva, E.N. (2015) *Prometastatic NEDD9 regulates individual cell migration via caveolin-1-dependent trafficking of integrins* Mol. Cancer Res., **13**, 423–438
- Kyriakakis, E.**, Maslova, K., Frachet, A., Ferri, N., et al (2013) *Cross-talk between EGFR and T-cadherin: EGFR activation promotes T-cadherin localization to intercellular contacts* Cell. Signal., **25**, 1044–1053
- Lee, C.-Y.**, Lai, T.-Y., Tsai, M.-K., Ou-Yang, P., Tsai, C.-Y., Wu, S.-W., Hsu, L.-C. and Chen, J.-S. (2016) *The influence of a caveolin-1 mutant on the function of P-glycoprotein* Sci. Rep., **6**: 20486
- Lin, H.-C.**, Lai, P.-Y., Lin, Y.-p., Huang, J.-Y. et al (2012) *Fas ligand enhances malignant behavior of tumor cells through interaction with Met, hepatocyte growth factor receptor, in lipid rafts* J. Biol. Chem., **287**, 20664–20673
- Rogers, K.R.**, Kikawa, K.D., Mouradian, M., Hernandez, K., et al (2010) *Docosahexaenoic acid alters epidermal growth factor receptor-related signaling by disrupting its lipid raft association* Carcinogenesis, **31**, 1523–1530
- Rutkowski, R.**, Mertens-Walker I., Lisle, J.E., Herington, A.C., et al (2012) *Evidence for a dual function of EphB4 as tumor promoter and suppressor regulated by the absence or presence of the ephrin-B2 ligand* Int. J. Cancer, **131**, E614–E624
- Soung, Y.H.** and Chung, J. (2011) *Curcumin inhibition of the functional interaction between integrin $\alpha 6 \beta 4$ and the epidermal growth factor receptor* Mol. Cancer Ther., **10**, 883–91
- Tawadros, T.**, Brown, M.D., Hart, C.A. and Clarke, N.W. (2012) *Ligand-independent activation of EphA2 by arachidonic acid induces metastasis-like behaviour in prostate cancer cells* Br. J. Cancer, **107**, 1737–1744

3. CHO cells

- Adak, S.**, DeAndrade, D. and Pike, L.J. (2011) *The tethering arm of the EGF receptor is required for negative cooperativity and signal transduction* J. Biol. Chem., **286**, 1545–1555
- Latif, R.**, Ando, T. and Davies, T.F. (2007) *Lipid rafts are triage centers for multimeric and monomeric thyrotropin receptor regulation* Endocrinology **148**, 3164–3175
- Macdonald, J.L.** and Pike, L.J. (2005) *A simplified method for the preparation of detergent-free lipid rafts* J. Lipid Res., **46**, 1061–1067
- Macdonald, J.**, Li, Z., Su, W. and Pike, L.J. (2006) *The membrane proximal disulfides of the EGF receptor extracellular domain are required for high affinity binding and signal transduction but do not play a role in the localization of the receptor to lipid rafts* Biochim. Biophys. Acta, **1763**, 870–878
- Pike, L.J.**, Han, X. and Gross, R.W. (2005) *Epidermal growth factor receptors are localized to lipid rafts that contain a balance of inner and outer leaflet lipids* J. Biol. Chem., **280**, 26796–26804
- Zhang, X.**, Brovkovycha, V., Zhanga, Y., Tan, F. and Skidgel, R.A. (2015) *Downregulation of kinin B1 receptor function by B2 receptor heterodimerization and signaling* Cell. Signal., **27**, 90–103

4. Endothelial cells (microvascular and progenitor): see also Section 16

- Bandyopadhyay, C.**, Valiya-Veettil, M., Dutta, D., Chakraborty, S., et al (2014) *CIB1 synergizes with ephrinA2 to regulate Kaposi's sarcoma-associated herpesvirus macropinocytic entry in human microvascular dermal endothelial cells* PLoS Pathog., **10**: e1003941
- Bandyopadhyay, C.**, Veettil, M.V., Dutta, S. and Chandran, B. (2014) *p130Cas scaffolds the signalosome to direct adaptor-effector cross talk during Kaposi's sarcoma-associated herpesvirus trafficking in human microvascular dermal endothelial cells* J. Virol., 13858–13878

Chakraborty, S., Veettil, M.V., Sadagopan, S., Paudel, N., et al (2011) *c-Cbl-mediated selective virus-receptor translocations into lipid rafts regulate productive Kaposi's sarcoma-associated herpesvirus infection in endothelial cells* J. Virol., **85**, 12410–12430

Chakraborty, S., Veetti, M.V., Bottero, V. and Chandran, B. (2012) *Kaposi's sarcoma-associated herpesvirus interacts with EphrinA2 receptor to amplify signaling essential for productive infection* Proc. Natl. Acad. Sci. USA, **109**, E1163-E1172

Chi, F., Jong, T.D., Wang, L., Ouyang, Y., et al (2010) *Vimentin-mediated signalling is required for IbeA+ E. coli K1 invasion of human brain microvascular endothelial cells* Biochem. J., **427**, 79–90

Huang, S.-H., Chi, F., Peng, L., Bo, T., Zhang, B., Liu, L.Q., Wu, X., Mor-Vaknin, N., Markovitz, D.M., Cao, H. and Zhou, Y-H. (2016) *Vimentin, a novel NF-KB regulator, is required for meningitic Escherichia coli K1-induced pathogen invasion and PMN transmigration across the blood-brain barrier* PloS One, **11**: e0162641

Margheri, F., Chilla, A., Laurenzana, A., Serrati, S., et al (2011) *Endothelial progenitor cell-dependent angiogenesis requires localization of the full-length form of uPAR in caveolae* Blood, **118**, 3743-3755

Sverdlov, M., Shinin, V., Place, A.T., Castellon, M., et al (2009) *Filamin A regulates caveolae internalization and trafficking in endothelial cells* Mol. Biol. Cell, **20**, 4531-4540

5. Epithelial cells

Han, W.-Q., Chen, W-D., Zhang, K., Liu, J-J., Wu, Y-J. and Gao, P-J. (2016) *Ca²⁺-regulated lysosome fusion mediates angiotensin II-induced lipid raft clustering in mesenteric endothelial cells* Hypertens. Res., **39**, 227–236

Wang, Y., Maciejewski, B.S., Drouillard, D., Santos, M., et al (2010) *A role for caveolin-1 in mechanotransduction of fetal type II epithelial cells* Am. J. Physiol. Lung Cell. Mol. Physiol., **298**, L775–L783

6. Fibroblasts

Dutta, D., Chakraborty, S., Bandyopadhyay, C., Veettil, M.V., et al (2013) *EphrinA2 regulates clathrin mediated KSHV endocytosis in fibroblast cells by coordinating integrin-associated signaling and c-Cbl directed polyubiquitination* PLoS Pathog., **9**: e1003510

Klappe, K., Hummel, I. and Kok, J.W. (2013) *Separation of actin-dependent and actin-independent lipid rafts* Anal. Biochem., **438**, 133–135

Hofman, E.G., Ruonala, M.O., Bader, A.N., van den Heuvel, D., et al (2008) *EGF induces coalescence of different lipid rafts* J. Cell Sci., **121**, 2519-2528

Meszáros, P., Hummel, I., Klappe, K., Draghiciu, O., et al (2013) *The function of the ATP-binding cassette (ABC) transporter ABCB1 is not susceptible to actin disruption* Biochim. Biophys. Acta, **1828**, 340–351

Morris, D.P., B., Lei, Wu, Y-X., Michelotti, G.A., et al (2008) *The α_{1a} -adrenergic receptor occupies membrane rafts with its G protein effectors but internalizes via clathrin-coated pits* J. Biol. Chem., **283**, 2973-2985

7. HeLa cells

Kim, H.Y., Kim, S., Pyun, H.J., Maeng, J. and Lee, K. (2015) *Cellular uptake mechanism of TCTP-PTD in human lung carcinoma cells* Mol. Pharmaceutics, **12**, 194–203

Lee, J.J., Kim, D.G., Kim, D.H., Simborio, H.L., Min, W., Lee, H.J., Her, M., Jung, S.C., Watarai, M. and Kim, S. (2013) *Interplay between clathrin and Rab5 controls the early phagocytic trafficking and intracellular survival of Brucella abortus within HeLa cells* J. Biol. Chem., **288**, 28049–28057

Macdonald, J.L. and Pike, L.J. (2005) *A simplified method for the preparation of detergent-free lipid rafts* J. Lipid Res., **46**, 1061-1067

Milev, M.P., Brown, C.M. and Mouland, A.J. (2010) *Live cell visualization of the interactions between HIV-1 Gag and the cellular RNA-binding protein Staufen1* Retrovirology, **7**: 41

White, A.B., Givogri, M.I., Lopez-Rosas, A., Cao, H., et al (2009) *Psychosine accumulates in membrane microdomains in the brain of Krabbe patients, disrupting the raft architecture* J. Neurosci. **29**, 6068–6077

Zarubica, A., Plazzo, A.P., Stöckl, M., Trombik, T., et al (2009) *Functional implications of the influence of ABCA1 on lipid microenvironment at the plasma membrane: a biophysical study* FASEB J. **23**, 1775–1785

8. Hepatoma cells

Bandyopadhyay, D., Sanchez, J.L., Guerrero, A.M., Chang, F-M., Granados, J.C., Short, J.D. and Banik, B.K. (2015) *Design, synthesis and biological evaluation of novel pyrenyl derivatives as anticancer agents* Eur. J. Medicinal Chem., **89**, 851-862

Carrasco, M.P., Jiménez-López, J.M., Ríos-Marco, P., Segovia, J.L., et al (2010) *Disruption of cellular cholesterol transport and homeostasis as a novel mechanism of action of membrane-targeted alkylphospholipid analogues* Br. J. Pharmacol., **160**, 355–366

Chakraborty, S., Lakshmanan, M., Swa, H.L.F., Chen, J., Zhang, X., Ong, Y.S. et al (2015) *An oncogenic role of Agrin in regulating focal adhesion integrity in hepatocellular carcinoma* Nat. Commun. **6**: 6184
Kim, H.Y., Kim, S., Pyun, H.J., Maeng, J. and Lee, K. (2015) *Cellular uptake mechanism of TCTP-PTD in human lung carcinoma cells* Mol. Pharmaceutics, **12**, 194–203
Li, Y., Masaki, H., Shimakami, T., and Lemon, S.M. (2104) *hnRNP L and NF90 interact with hepatitis C virus 5' terminal untranslated RNA and promote efficient replication* J. Virol., **88**, 7199–7209
Lin, H.-C., Lai, P.-Y., Lin, Y.-p., Huang, J.-Y., et al (2012) *Fas ligand enhances malignant behavior of tumor cells through interaction with Met, hepatocyte growth factor receptor, in lipid rafts* J. Biol. Chem., **287**, 20664–20673

9. Kidney cells

9-1. BHK cells

Hummel, I., Klappe, K., Ercan, C. and Kok, J.W. (2011) *Multidrug resistance-related protein 1 (MRP1) function and localization depend on cortical actin* Mol. Pharmacol., **79**, 229-240
Lund-Katz, S., Lyssenko, N.N., Nickel, M., Nguyen, D., et al (2103) *Mechanisms responsible for the compositional heterogeneity of nascent high density lipoprotein* J. Biol. Chem., **288**, 23150–23160

9-2. Foetal monkey

Ohmine, S., Singh, R.D., Marks, D.L., Meyer, M.A., Pagano, R.E. and Ikeda, Y. (2013) *Viral attachment induces rapid recruitment of an innate immune sensor (TRIM5α) to the plasma membrane* J. Innate Immun., **5**, 414–424

9-3. HEK

Barceló, C., Paco, N., Beckett, A.J., Alvarez-Moya, B., et al (2013) *Oncogenic K-ras segregates at spatially distinct plasma membrane signaling platforms according to its phosphorylation status* J. Cell Sci., **126**, 4553–4559
Fornoni, A., Sageshima, J., Wei, C., Merscher-Gomez, S., et al (2011) *Rituximab targets podocytes in recurrent focal segmental glomerulosclerosis* Sci. Translat Med., **3**: 85ra46
Tao, B., Bu, S., Yang, Z., Siroky, B., et al (2009) *Cystin localizes to primary cilia via membrane microdomains and a targeting motif* J. Am. Soc. Nephrol., **20**, 2570–2580
Zhang, X., Tan, F., Zhang, Y. and Skidgel, R.A. (2008) *Carboxypeptidase M and kinin B1 receptors interact to facilitate efficient B1 signaling from B2 agonists* J. Biol. Chem., **283**, 7994-8004
Zhang, X., Brovkovich, V., Zhanga, Y., Tan, F. and Skidgel, R.A. (2015) *Downregulation of kinin B1 receptor function by B2 receptor heterodimerization and signaling* Cell. Signal., **27**, 90–103

9-4. Human podocytes

Fornoni, A., Sageshima, J., Wei, C., Merscher-Gomez, S., et al (2011) *Rituximab targets podocytes in recurrent focal segmental glomerulosclerosis* Sci. Translat Med., **3**: 85ra46

9-5. LLC-PK₁

Foster, J.D., Adkins, S.D., Lever, J.R. and Vaughan, R.A. (2008) *Phorbol ester induced trafficking-independent regulation and enhanced phosphorylation of the dopamine transporter associated with membrane rafts and cholesterol* J. Neurochem., **105**, 1683-1699

9-6. MDCK

Polymenidou, M., Trusheim, H., Stallmach, L., Moos, R., et al (2008) *Canine MDCK cell lines are refractory to infection with human and mouse prions* Vaccine, **26**, 2601-2614

9-7. Mouse kidney

Follit, J.A., Li, L., Vucica, Y. and Pazour, G.J. (2010) *The cytoplasmic tail of fibrocystin contains a ciliary targeting sequence* J. Cell Biol., **188**, 21–28

9-8. Opossum kidney

Breusegem, S.Y., Halaihel, N., Inoue, M., Zajicek, H., et al (2005) *Acute and chronic changes in cholesterol modulate Na-P_i cotransport activity in OK cells* Am. J. Physiol., **289**, FF154-F165

9-9. Rat glomerular

Boini, K.M., Zhang, C., Xia, M., Han, W-Q., et al (2010) *Visfatin-induced lipid raft redox signaling platforms and dysfunction in glomerular endothelial cells* Biochim. Biophys. Acta, **1801**, 1294–1304

10. Liver cells

Hahn-Obercyger, M., Graeve, L. and Madar, Z. (2009) *A high-cholesterol diet increases the association between caveolae and insulin receptors in rat liver* J. Lipid Res., **50**, 98–107

Morita, S.-y., Tsuda, T., Horikami, M., Teraoka, R., Kitagawa, S. and Terada, T. (2013) *Bile salt-stimulated phospholipid efflux mediated by ABCB4 localized in non-raft membranes* J. Lipid Res., **54**, 1221–1230

11. Lymphocytic cells (incl. Jurkat cells)

Kennedy, C., Nelson, M.D. and Bamezai, A.K. (2011) *Analysis of detergent-free lipid rafts isolated from a CD4+ T cell line: interaction with antigen presenting cells promotes coalescing of lipid rafts* Cell Commun. Signal., **9**: 31

Morales-Garzia, M.G., Fournie, J.-J., Morena-Altamirano, M.M.B., Rodriguez-Luna, G., et al (2008) *A flow-cytometry method for analyzing the composition of membrane rafts* Cytometry Part A, **73A**, 918-925

Mutch, C.M., Sanyal, R., Unruh, T.L., Grigoriou, L., et al (2007) *Activation-induced endocytosis of the raft-associated transmembrane adaptor protein LAB/NTAL in B lymphocytes: evidence for a role in internalization of the B cell receptor* Int. Immunol., **19**, 19-30

Polyak, M.J., Li, H., Shariat, N. and Deans, J.P. (2008) *CD20 Homo-oligomers physically associate with the B cell antigen receptor: dissociation upon receptor engagement and recruitment of phosphoproteins and calmodulin-binding proteins* J. Biol. Chem., **283**, 18545-18552

Quattrocchi, S., Ruprecht, N., Bönsch, C., Bieli, S., et al (2012) *Characterization of the early steps of human parvovirus B19 infection* J. Virol., **86**, 0274-9284

Talaty, P., Emery, A., Holthusen, K. and Everly, Jr, D.N. (2012) *Identification of transmembrane protein 134 as a novel LMP1-binding protein by using bimolecular fluorescence complementation and an enhanced retroviral mutagen* J. Virol., **86**, 11345–11355

12. Macrophages

Morales-Garzia, M.G., Fournie, J.-J., Morena-Altamirano, M.M.B., Rodriguez-Luna, G., et al (2008) *A flow-cytometry method for analyzing the composition of membrane rafts* Cytometry Part A, **73A**, 918-925

Schumann, J., Leichtle, A., Thiery, J. and Fuhrmann, H. (2011) *Fatty acid and peptide profiles in plasma membrane and membrane rafts of PUFA supplemented RAW264.7 macrophages* PLoS One **6**: e24066

Serezani, C.H., Aronoff, D.M., Sitrin, R.G. and Peters-Golden, M. (2009) *FcγRI ligation leads to a complex with BLT1 in lipid rafts that enhances rat lung macrophage antimicrobial functions* Blood, **114**, 3316-3324

Zhu, X., Owen, J.S., Wilson, M.D., Li, H., et al (2010) *Macrophage ABCA1 reduces MyD88-dependent Toll-like receptor trafficking to lipid rafts by reduction of lipid raft cholesterol* J. Lipid Res., **51**, 3196–3206

13. Neural and related cells

13-1. Brain cells, tissue and microvessels

Lochhead, J.J., McCaffrey, G., Sanchez-Covarrubias, L., Finch, J.D., et al. (2012) *Tempol modulates changes in xenobiotic permeability and occludin oligomeric assemblies at the blood-brain barrier during inflammatory pain* Am. J. Physiol. Heart Circ. Physiol., **302**, H582–H593

McCaffrey, G., Staatz, W.D., Quigley, C.A., Nametz, N., et al (2007) *Tight junctions contain oligomeric protein assembly critical for maintaining blood-brain barrier integrity in vivo* J. Neurochem., **103**, 2540-2555

McCaffrey, G., Seelbach, M.J., Staatz, W.D., Nametz, N., et al (2008) *Occludin oligomeric assembly at tight junctions of the blood-brain barrier is disrupted by peripheral inflammatory hyperalgesia* J. Neurochem., **106**, 2395-2409

McCaffrey, G., Willis, C.L., Staatz, W.D., Nametz, N., et al (2009) *Occludin oligomeric assemblies at tight junctions of the blood-brain barrier are altered by hypoxia and reoxygenation stress* J. Neurochem., **110**, 58-71

McCaffrey, G., Staatz, W.D., Sanchez-Covarrubias, L., Finch, J.D., et al (2012) *P-glycoprotein trafficking at the blood-brain barrier altered by peripheral inflammatory hyperalgesia* J. Neurochem., **122**, 962–975

Persaud-Sawin, D.A., Lightcap, S. Harry, G.J. (2009) *Isolation of rafts from mouse brain tissue by a detergent-free method* J. Lipid Res., **50**, 759–767

13-2. Glial/ Microglial cells

Lundgren, T.K., Luebke, M., Stenqvist, A. and Ernfors, P. (2008) *Differential membrane compartmentalization of Ret by PTB-adaptor engagement* FEBS. J., **275**, 2055-2066

Rimmerman, N., Bradshaw, H.B., Kozela, E., Levy, R., et al (2012) *Compartmentalization of endocannabinoids into lipid rafts in a microglial cell line devoid of caveolin-1* Br. J. Pharmacol., **165**, 2436–2449

Rimmerman, N., Ben-Hail, D., Porat, Z., Juknat, A., et al (2013) *Direct modulation of the outer mitochondrial membrane channel, voltage-dependent anion channel 1 (VDAC1) by cannabidiol: a novel mechanism for cannabinoid-induced cell death* Cell Death Dis., **4**: e949

13-3. Hypothalamic cells

Cui, H.L., Guo, B., Scicluna, B., Coleman, B.M., et al (2014) *Prion infection impairs cholesterol metabolism in neuronal cells* J. Biol. Chem., **289**, 789-802

13-4. Neuroblastoma cells

Hummel, I., Klappe, K., Ercan, C. and Kok, J.W. (2011) *Multidrug resistance-related protein 1 (MRP1) function and localization depend on cortical actin* Mol. Pharmacol., **79**, 229-240

Klappe, K., Dijkhuis, A.-J., Hummel, I., van Dam, A., et al (2010) *Extensive sphingolipid depletion does not affect lipid raft integrity or lipid raft localization and efflux function of the ABC transporter MRP1* Biochem. J., **430**, 519–529

Klappe, K., Hummel, I. and Kok, J.W. (2013) *Separation of actin-dependent and actin-independent lipid rafts* Anal. Biochem., **438**, 133–135

Meszaros, P., Klappe, K., Hummel, I., Hoekstra, D. et al (2011) *Function of MRP1/ABCC1 is not dependent on cholesterol or cholesterol-stabilized lipid rafts* Biochem. J., **437**, 483–491

Nakagawa, T., Morotomi, A., Tani, M., Sueyoshi, N., et al (2005) *CI8:3-GM1a induces apoptosis in Neuro2 cells: enzymatic remodeling of fatty acyl chains of glycosphingolipids* J. Lipid Res., **46**, 1103-1112

Qiu, Y., Wang, Y., Law, P.-Y., Chen, H.-Z. et al (2011) *Cholesterol regulates μ -opioid receptor-induced β -arrestin 2 translocation to membrane lipid rafts* Mol. Pharmacol., **80**, 210–218

Sontag, J.-M., Nunbhakdi-Craig, V. and Sontag, E. (2013) *Leucine carboxyl methyltransferase 1 (LCMT1)-dependent methylation regulates the association of protein phosphatase 2A and tau protein with plasma membrane microdomains in neuroblastoma cells* J. Biol. Chem., **288**, 27396–27405

13-5. Neuronal cells

Asimaki, O., Leondaritis, G., Lois, G., Sakellaridis, N. et al (2011) *Cannabinoid 1 receptor-dependent transactivation of fibroblast growth factor receptor 1 emanates from lipid rafts and amplifies extracellular signal-regulated kinase 1/2 activation in embryonic cortical neurons* J. Neurochem., **116**, 866–873

Kasahara, K., Watanabe, K., Takeuchi, K., Kaneko, H., et al (2000) *Involvement of gangliosides in GPI-anchored neuronal cell adhesion molecule TAG-1 signaling in lipid rafts* J. Biol. Chem., **275**, 34701-34709

Salinas, S., Zussy, C., Loustalo, F., Henaff, D., et al (2014) *Disruption of the coxsackievirus and adenovirus receptor-homodimeric interaction triggers lipid microdomain- and dynamin-dependent endocytosis and lysosomal targeting* J. Biol. Chem., **289**, 680-695

Schindler, M., Fabre, C., de Weille, J., Carreau, S., et al (2012) *Disruption of nongenomic testosterone signaling in a model of spinal and bulbar muscular atrophy* Mol. Endocrinol., **26**, 1102–1116

Wang, J. and Yua, R.K. (2013) *Interaction of ganglioside GD3 with an EGF receptor sustains the self-renewal ability of mouse neural stem cells in vitro* Proc. Natl. Acad. Sci. USA, **110**, 19137–19142

14. Polymorphonuclear leukocytes

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Mini-Review MS07: 3rd edition, March 2017-03-08

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