

OptiPrep™ Reference List RC08

Hepatic non-parenchymal cells: Kupffer cells, sinusoidal endothelial cells (and other liver cell types)

- ◆ **This Reference List** provides a complete list of publications that report the use of OptiPrep™ for the purification of hepatic non-parenchymal cells (NPC) **other than stellate cells**.
- ◆ The only NPCs that can be isolated at sufficiently high purity, using solely density gradient centrifugation, are **stellate cells** (see **Application Sheet C27 and Reference List RC07**).
- ◆ Very often a total NPC fraction is prepared using an iodixanol barrier or discontinuous gradient (see **Application Sheet C26**) and the NPCs analyzed by flow cytometry alone. Kupffer cells and sinusoidal endothelial cells may be analyzed in this manner.
- ◆ **Kupffer or sinusoidal endothelial cells** may also be resolved using a secondary technique involving (1) the use of an antibody (usually bound to magnetic beads), (2) elutriation or (3) selective adherence of Kupffer cells to a collagen-coated plastic substratum.
- ◆ **Kupffer cells** have also been isolated using only an iodixanol density gradient (see **Section 4 and Application Sheet C28**).
- ◆ Epithelial cells, leukocytes, macrophages, NK cells and oval (progenitor) cells are also listed
- ◆ **RC09** provides a reference list of all **stellate cell** papers

Important notes

- ◆ To avoid excessive duplication, references on both **endothelial and Kupffer cells** are listed under **Non-parenchymal cells** (Section 7) and are divided alphabetically according to **Research Topic**.
- ◆ **Langerhans cells** are included in **Reference List RC05**

1. Dendritic and leukocytic cells

- Connolly, M.K.**, Ayo, D., Malhotra, A., Hackman, M., Bedrosian, A.S., Ibrahim, J., Cieza-Rubio, N.E., Nguyen, A.H., Henning, J.R., et al (2011) *Dendritic cell depletion exacerbates acetaminophen hepatotoxicity* Hepatology, **54**, 959-968
- Cremer, I.**, Dieu-Nosjean, M-C., Maréchal, S., Dezutter-Dambuyant, C., Goddard, S., Adams, D., Winter, N., Menetrier-Caux, C., Sautès-Fridman, C., Fridman, W.H. and Mueller, C.G. (2002) *Long-lived immature dendritic cells mediated by TRANCE-RANK interaction* Blood, **100**, 3646-3655
- Eksteen, B.**, Mora, J.R., Haughton, E.L., Henderson, N.C., Lee-Turner, L., Villablanca E.J., Curbishley, S.M., Aspinall, A.I., Von Andrian, U.H. and Adams, D.H. (2009) *Gut homing receptors on CD8 T cells are retinoic acid dependent and not maintained by liver dendritic or stellate cells* Gastroenterology, **137**, 320–329
- Goddard, S.**, Youster, J., Morgan, E. and Adams, D.H. (2004) *Interleukin-10 secretion differentiates dendritic cells from human liver and skin* Am. J. Pathol., **164**, 511-519
- Henning, J.R.**, Graffeo, C.S., Rehman, A., Fallon, N.C., Zambirinis, C.P., Ochi, A., Barilla, R., Jamal, M., Deutsch, M., et al (2013) *Dendritic cells limit fibroinflammatory injury in nonalcoholic steatohepatitis in mice* Hepatology, **58**, 589-602
- Kim, J-W.**, Roh, Y-S., Jeong, H., Yi, H-K., Lee, M-H., Lim, C-W. and Kim, B. (2018) *Spliceosome-associated protein 130 exacerbates alcohol-induced liver injury by inducing NLRP3 inflammasome-mediated IL-1b in mice* Am. J. Pathol., **188**, 967-980
- Kingham, T.P.**, Chaudhry, U.I., Plitas, G., Katz, S.C., Raab, J. and DeMatteo, R.P. (2007) *Murine liver plasmacytoid dendritic cells become potent immunostimulatory cells after Flt-3 ligand expansion* Hepatology, **45**, 445-454
- Lalor, P.F.**, Curbishley, S.M. and Adams, D.H. (2010) *Identifying homing interactions in T-cell traffic in human disease* In, T-Cell Trafficking (eds. Marelli-Berg, F.M. and Nourshargh, S.), Methods Mol. Biol., **616**, Springer Science+Business Media, pp. 231-252
- Oo, Y.H.**, Weston, C.J., Lalor, P.F., Curbishley, S.M., Withers, D.R., Reynolds, G.M., Shetty, S., Harki, J., Shaw, J.C. et al (2010) *Distinct roles for CCR4 and CXCR3 in the recruitment and positioning of regulatory T cells in the inflamed human liver* J. Immunol., **184**, 2886–2898

Plitas, G., Burt, B.M., Stableford, J.A., Nguyen, H.M., Welles, A.P. and DeMatteo, R.P. (2008) *Dendritic cells are required for effective cross-presentation in the murine liver* Hepatology, **47**, 1343-1351

Rehman, A., Hemmert, K.C., Ochi, A., Jamal, M., Henning, J.R., Barilla, R., Quesada, J.P., Zambirinis, C.P., Tang, K. et al (2013) *Role of fatty-acid synthesis in dendritic cell generation and function* J. Immunol., **190**, 4640–4649

Ueta, H., Shi, C., Miyanari, N., Xu, X-D., Zhou, S., Yamashita, M., Ezaki, T. and Matsuno, K. (2008) *Systemic transmigration of allosensitizing donor dendritic cells to host secondary lymphoid organs after rat liver transplantation* Hepatology, **47**, 1352-1362

Wiegard, C., Wolint, P., Frenzel, C., Cheruti, U., Schmitt, E., Oxenius, A., Lohse, A.W. and Herkel, J. (2007) *Defective T helper response of hepatocyte-stimulated CD4 T cells impairs antiviral CD8 response and viral clearance* Gastroenterology **133**, 2010-2018

2. Epithelial cells

Gerbal-Chaloin, S., Duret, C., Raulet, E., Navarro, F., Blanc, P., Ramos, J., Maurel, P. and Daujat-Chavanieu, M. (2010) *Isolation and culture of adult human liver progenitor cells: in vitro differentiation to hepatocyte-like cells* In, Hepatocytes, (ed. Maurel, P. ed.) Methods Mol. Biol., **640**, Springer Science+Business Media, pp.247-260

3. Hepatocytes

Pepe-Mooney, B.J., Dill, M.T., Alemany, A., Ordovas-Montanes, J., Matsushita, Y., Rao, A., Sen, A., Miyazaki, M., Anakk, S. (2019) *Single-cell analysis of the liver epithelium reveals dynamic heterogeneity and an essential role for YAP in homeostasis and regeneration* Cell Stem Cell, **25**, 23–38

Seong, H-A., Manoharan, R. and Ha, H. (2017) *Zinc finger protein ZPR9 functions as an activator of AMPK-related serine/threonine kinase MPK38/MELK involved in ASK1/TGF- β /p53 signaling pathways* Sci. Rep., **7**: 42502

4. Kupffer cells

Mukhopadhyay, P., Horváth, B., Rajesh, M., Varga, .V., Gariani, K., Ryu, D., Cao, Z., E. Holovac et al (2017) *PARP inhibition protects against alcoholic and non-alcoholic steatohepatitis* J. Hepatol., **66**, 589–600

5. Leukocytes

Kuniyasu, Y., Qamar, A., Sheikh, S.Z., Jhandier, M.N., Hakim, W. and Mehal, W.Z. (2005) *Blocking intrahepatic deletion of activated CD8⁺ T cells by an altered peptide ligand* Cell. Immunol., **238**, 31-37

6. Macrophages

Docan Dragomir, A-C., Sun, R., Choi, H., Laskin, J.D. and Laskin, D.L. (2012) *Role of galectin-3 in classical and alternative macrophage activation in the liver following acetaminophen intoxication* J. Immunol., **189**, 5934–5941

Eguchi, A., Lazaro, R.G., Wang, J., Kim, J., Povero, D., Williams, B., Ho, S.B., Stearkel, P., Schnabl, B. et al (2017) *Extracellular vesicles released by hepatocytes from gastric infusion model of alcoholic liver disease contain a microRNA barcode that can be detected in blood* Hepatology, **65**, 475-490

Samaniego, S. and Marcu, K.B. (2013) *IKK β in myeloid cells controls the host response to lethal and sublethal Francisella tularensis LVS infection* PLoS One, **8**: e54124

7. Non-parenchymal cells

Acetaminophen hepatotoxin

Hoque, R., Sohail, M.A., Salhanick, S., Malik, A.F., Ghani, A., Robson, S.C. and Mehal, W.Z (2012) *P2x7 receptor-mediated purinergic signaling promotes liver injury in acetaminophen hepatotoxicity in mice* Am. J. Physiol. Gastrointest. Liver Physiol., **302**, G1171–G1179

Acute liver injury

Chan, C-C., Cheng, L-Y., Lu, J., Huang, Y-H., Chiou, S-H., Tsai, P-H., Huo, T-I., Lin, H-C., Lee, F-Y. (2012) *The role of interferon-c inducible protein-10 in a mouse model of acute liver injury post induced pluripotent stem cells transplantation* PLoS One, **7**: e50577

Deutsch, M., Graffeo, C.S., Rokosh, R., Pansari, M., Ochi, A., Levie, E.M., Van Heerden, E., Tipples, D.M. et al. (2015) *Divergent effects of RIP1 or RIP3 blockade in murine models of acute liver injury* Cell Death Dis., **6**: e1759

Schwinge, D., Carambia, A., Quaas, A., Krech, T., Wegscheid, C., Tiegs, G., Prinz, I., Lohse, A.W., Herkel, J. and Schramm, C. (2015) *Testosterone suppresses hepatic inflammation by the downregulation of IL-17, CXCL-9, and CXCL-10 in a mouse model of experimental acute cholangitis* J. Immunol., **194**, 2522–2530

Adipose tissue lipolysis

Ma, W., Zhao, D., He, F. and Tang, L. (2019) *The role of Kupffer cells as mediators of adipose tissue lipolysis* J. Immunol., **203**, 2689–2700

Alcoholic injury

Banerjee, A., Abdelmegeed, M.A., Jang, S. and Song, B-J. (2015) *Increased sensitivity to binge alcohol-induced gut leakiness and inflammatory liver disease in HIV transgenic rats* PLoS One, **10**: e0140498

Byun, J-S., Suh, Y-G., Yi, H-S., Lee, Y-S. and Jeong, W-I. (2013) *Activation of toll-like receptor 3 attenuates alcoholic liver injury by stimulating Kupffer cells and stellate cells to produce interleukin-10 in mice* J. Hepatol., **58**, 342–349

Choi, W-M., Kim, H-H., Kim, M-H., Cinar, R., Yi, H-S., Eun, H.S., Kim, S-H., Choi, Y.J., Lee, Y-S et al (2019) *Glutamate signaling in hepatic stellate cells drives alcoholic steatosis* Cell Metab., **30**, 877–889

Chung, H.K., Kim, J.T., Kim, H-W., Kwon, M., Kim, S.Y., Shong, M., Kim, K.S. and Yi, H-S. (2017) *GDF15 deficiency exacerbates chronic alcohol- and carbon tetrachloride-induced liver injury* Sci. Rep. **7**: 17238

Hu, S., Yin, S., Jiang, X., Huang, D. and Shen, G. (2009) *Melatonin protects against alcoholic liver injury by attenuating oxidative stress, inflammatory response, and apoptosis* Eur. J. Pharmacol., **616**, 287–292

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Antisense oligonucleotides

Prakash, T.P., Graham, M.J., Yu, J., Carty, R., Low, A., Chappell, A., Schmidt, K., Zhao, C., Aghajan, M., Murray, H.F., et al (2013) *Targeted delivery of antisense oligonucleotides to hepatocytes using triantennary N-acetylgalactosamine improves potency 10-fold in mice* Nucleic Acids Res., **42**, 8796–8807

Autophagy

Cassidy, L.D., Young, A.R.J., Pérez-Mancera, P.A., Nimmervoll, B., Jaulim, A., Chen, H-C., McIntyre, D.J.O., Brais, R., Ricketts, T. et al (2018) *A novel Atg5-shRNA mouse model enables temporal control of autophagy in vivo* Autophagy, **14**, 1256-1266

Bone loss

Schmidt, T., Schwinge, D., Rolvien, T., Jeschke, A., Schmidt, C., Neven, M., Butscheidt, S., Kriz, M., Kunzmann, L. et al (2019) *Th17 cell frequency is associated with low bone mass in primary sclerosing cholangitis* J. Hepatol., **70**, 941–953

Cannabinoid CB2 receptor

Horváth, B., Magid, L., Mukhopadhyay, P., Bátkai, S., Rajesh, M., Park, O., Tanchian, G., Gao, R.Y., Goodfellow, C.E., Glass, M., Mechoulam, R. and Pacher, P. (2012) *A new cannabinoid CB2 receptor agonist HU-910 attenuates oxidative stress, inflammation and cell death associated with hepatic ischaemia/reperfusion injury* Br. J. Pharmacol., **165**, 2462-2478

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Yang, H., Tong, C., Fu, C., Xu, Y., Liu, X., Chen, Q., Zhang, Y., Lü, S., Li, N. and Long, M. (2016) *Analyses of movement and contact of two nucleated cells using a gas-driven micropipette aspiration technique* J. Immunol. Meth., **428**, 20–29

Chemokine production

Valatas, V., Kolios, G., Manousou, P., Notas, G., Xidakis, C., Diamantis, I. and Kouroumalis, E. (2004) *Octreotide regulates CC but not CXC LPS-induced chemokine secretion in rat Kupffer cells* Br. J. Pharm., **141**, 477-487

Xidakis, C., Ljumovic, D., Manousou, P., Notas, G., Valatas, V., Kolios, G., and Kouroumalis, E. (2005) *Production of pro- and anti-fibrotic agents by rat kupffer cells; the effect of octreotide* Digest. Dis. Sci., **50**, 935-941

Dietary fructose

Ferrere, G., Leroux, A., Wrzosek, L., Puchois, V., Gaudin, F., Ciocan, D., Renoud, M-L., Naveauet, S. et al (2016) *Activation of Kupffer cells is associated with a specific dysbiosis induced by fructose or high fat diet in mice* PLoS One, **11**: e0146177

Differentiation

Xie, G., Wang, X., Wang, L., Wang, L., Atkinson, R.D., Kanel, G.C., Gaarde, W.A. and Deleve, L.D. (2012) *Role of differentiation of liver sinusoidal endothelial cells in progression and regression of hepatic fibrosis in rats* Gastroenterology, **142**, 918–927

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Kim, S.Y., Jeong, J-M., Kim, S.J., Seo, W., Kim, M-H., Choi, W-M., Yoo, W., Lee, J-H. et al (2017) *Pro-inflammatory hepatic macrophages generate ROS through NADPH oxidase 2 via endocytosis of monomeric TLR4–MD2 complex* Nat. Comm., **8**: 2247

Lao, Y., Li, Y., Hou, Y., Chen, H., Qiu, B., Lin, W. et al (2017) *Proteomic analysis reveals Dab2 mediated receptor endocytosis promotes liver sinusoidal endothelial cell dedifferentiation* Sci. Rep., **7**: 13456

Exosomes

Tamura, R., Uemoto, S. and Tabata, Y. (2017) *Augmented liver targeting of exosomes by surface modification with cationized pullulan* Acta Biomaterialia, **57**, 274–284

Factor VIII Fc fusion protein

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Fatty acids

Etienne-Mesmin, L., Vijay-Kumar, M., Gewirtz, A.T. and Chassaing, B. (2016) *Hepatocyte toll-like receptor 5 promotes bacterial clearance and protects mice against high-fat diet–induced liver disease* Cell. Mol. Gastroenterol. Hepatol., **2**, 584–604

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McMahan, R.H., Porsche, C.E., Edwards, M.G. and Rosen, H.R. (2016) *Free fatty acids differentially downregulate chemokines in liver sinusoidal endothelial cells: insights into non-alcoholic fatty liver disease* PLoS One, **11**: e0159217

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Fibrosis

Cong, M., Liu, T., Wang, P., Fan, X., Yang, A., Bai, Y., Peng, Z., Wu, P., Tong, X., Chen, J., Li, H., Cong, R., Tang, S., Wang, B., Jia, J. and You, H. (2013) *Antifibrotic effects of a recombinant adeno-associated virus carrying small interfering RNA targeting TIMP-1 in rat liver fibrosis* Am. J. Pathol., **182**, 1607-1616

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Francisella tularensis LVS infection

Samaniego, S. and Marcu, K.B. (2013) *IKK β in myeloid cells controls the host response to lethal and sublethal Francisella tularensis LVS infection* PLoS One, **8**: e54124

Hedgehog ligands

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Xie, G., Choi, S.S., Syn, W-K., Michelotti, G.A., Swiderska, M., Karaca, G., Chan, I.S., Chen, Y. and Diehl, A.M. (2013) *Hedgehog signalling regulates liver sinusoidal endothelial cell capillarisation* Gut, **62**, 299–309

Hepatitis

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Hepatocarcinogenesis

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Hepato-pulmonary syndrome

Chen, L., Han, Y., Li, Y., Chen, B., Bai, X., Belguise, K., Wang, X., Chen, Y., Yi, B. and Lu, K. (2019) *Hepatocyte-derived exosomal MiR-194 activates PMVECs and promotes angiogenesis in hepato-pulmonary syndrome* Cell Death Dis., **10**: 853

Hepatotoxicity

Rose, K.A., Holman, N.S., Green, A.M., Andersen, M.E. and LeCluyse, E.L. (2016) *Co-culture of hepatocytes and Kupffer cells as an in vitro model of inflammation and drug-induced hepatotoxicity* J. Pharmaceut. Sci., **105**, 950-964

High-density lipoprotein uptake

Brundert, M., Heeren, J., Merkel, M., Carambia, A., Herkel, J., Groitl, P., Dobner, T., Ramakrishnan, R., Moore, K.J. and Rinninger, F. (2011) *Scavenger receptor CD36 mediates uptake of high density lipoproteins in mice and by cultured cells* J. Lipid Res., **52**, 745–758

Immunity/Immune responses

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Inflammasomes/Inflammatory responses

Banerjee, A., Abdelmegeed, M.A., Jang, S. and Song, B-J. (2015) *Increased sensitivity to binge alcohol-induced gut leakiness and inflammatory liver disease in HIV transgenic rats* PLoS One, **10**: e0140498

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