OptiPrep™ Mini-Review MC09

Hepatic and pancreatic stellate cells – a bibliography

- This Mini-Review provides a complete bibliography of publications that report the use of OptiPrep™ for the purification of hepatic and pancreatic stellate cells. It complements **Mini-Review MC08** which provides a brief overview of the separation technology. **Mini-Review MC10** is a bibliography of published papers primarily reporting the analysis of hepatic Kupffer and sinusoidal endothelial cells; this also lists papers on non-parenchymal epithelial cells, NK cells, oval cells and progenitor cells.

- References are divided into following sections based on cell source:
- **Human liver – p1**
- **Human pancreas – p3**
- **Mouse liver – p3**
- **Mouse pancreas – p9**
- **Rat liver – p9**
- **Rat pancreas – p 14**

- **Sections on human, mouse and rat liver are further sorted into sub-sections alphabetically according research topic**.

- Within each section or sub-section references are listed alphabetically according to **first author** (multiple examples are listed chronologically).
- Important note: the number of published papers on rodent liver stellate cells that refer to fibrosis, fibrogenesis and liver injury is so huge that they are listed only under the analytical study.

Important note
Detailed protocols are available either on the flash drive or at the usual website: **www.axis-shield-density-gradient-media.com** Select "Cells" then scroll down to "Hepartic cells – stellate cells" or "Pancreatic stellate cells" to open the appropriate Application Sheet.

Human liver

Activators

Longato, L., Andreola, F., Davies, S.S., Roberts, J.L., Fusai, G., Pinzani, M., Moore, K., Rombouts, K. (2017) *Reactive gamma-ketoaldehydes as novel activators of hepatic stellate cells in vitro* Radic. Biol. Med., **102**, 162-173

Apoptosis

Singh, H.D., Otano, I., Rombouts, K., Singh, K.P., Peppa, D., Gill, U.S., Böttcher, K., Kennedy, P.T.F., Oben, J. et al (2017) *TRAIL regulatory receptors constrain human hepatic stellate cell apoptosis* Sci. Rep., **7**: 5514

Cirrhosis

De Mesquita, F.C., Guixé-Muntet, S., Fernández-Iglesias, A., Maeso-Díaz, R., Vila, S., Hide, D., Ortega-Ribera, M., Rosa, J.L. et al (2017) *Liraglutide improves liver microvascular dysfunction in cirrhosis: Evidence from translational studies* Sci. Rep., **7**: 3255

Cryopreservation

Nakamura, A., Ueno, T., Yagi, Y., Okuda, K., Ogata, T., Nakamura, T., Torimura, T., Iwamoto, H., Ramadoss, S., Sata, M., Tsutsumi, V., et al (2010) *Human primary cultured hepatic stellate cells can be cryopreserved* Med. Mol. Morphol., **43**, 107–115

Fibrosis

Chen, J.Y., Newcomb, B., Zhou, C., Pondick, J.V., Ghoshal, S., York, S.R., Motola, D.L., Coant, N., Yi, J.K., Mao, C. et al (2017) *Tricyclic antidepressants promote ceramide accumulation to regulate collagen production in human hepatic stellate cells* Sci. Rep., **7**: 44867

Gene transfer

Perugorria, M.J., Wilson, C.L., Zeybel, M., Walsh, M., Amin, S., Robinson, S., White, S.A., Burt, A.D., Oakley, F., Tsukamoto, H., Mann, D.A. and Mann, J. (2012) *Histone methyltransferase ASH1 orchestrates fibrogenic gene transcription during myofibroblast tansdifferentiation* Hepatology, **56**, 1129-1139

Growth factors and growth factor receptors/signalling

Barnaeva, E., Nadezhda, A., Hannappel, E., Sjogren, M.H. and Rojkind, M. (2007) *Thymosin β_4 upregulates the expression of hepatocyte growth factor and downregulates the expression of PDGF-β receptor in human hepatic stellate cells* Ann. N.Y. Acad. Sci., **1112**, 154-160

Reyes-Gordillo, K., Shah, R., Popratiloff, A., Fu, S., Hindle, A., Brody, F. and Rojkind, M. (2011) *Thymosin-β4 (Tβ4) blunts PDGF-dependent phosphorylation and binding of AKT to actin in hepatic stellate cells* Am. J. Pathol., **178**, 2100–2108

Hepatitis B

Pallett, L.J., Gill, U.S., Quaglia, A., Sinclair, L.V., Jover-Cobos, M., Schurich, A., Singh, K.P., Thomas, N. et al. (2015) *Metabolic regulation of hepatitis B immunopathology by myeloid-derived suppressor cells* Nat. Med., 21, 591-600

Hypertension

Jalan, R., De Chiara, F., Balasubramaniyan, V., Andreola, F., Khetan, V., Malago, M., Pinzani, M., Mookerjee, R.P. and Rombouts, K. (2016) *Ammonia produces pathological changes in human hepatic stellate cells and is a target for therapy of portal hypertension* J. Hepatol., **64**, 823–833

Phosphoinositides

Rombouts, K. and Carloni, V. (2016) *Determination and characterization of tetraspanin-associated phosphoinositide-4 kinases in primary and neoplastic liver cells* In Methods Mol. Biol., **1376**, Astrocytes: Methods and Protocols (ed. Waugh, M.G.) Springer Science+Business Media, LLC pp 203-212

RNA

Zhou, C., York, S.R., Chen, J.Y., Pondick, J.V., Motola, D.L., Chung, R.T. and Mullen, A.C. (2016) *Long noncoding RNAs expressed in human hepatic stellate cells form networks with extracellular matrix proteins* Genome Med., **8**: 31

Zhou, C., York, S.R., Chen, J.Y., Pondick, J.V., Motola, D.L., Chung, R.T. and Mullen, A.C. (2016) *Long noncoding RNAs expressed in human hepatic stellate cells form networks with extracellular matrix proteins* Genome Med., **8**: 31

Transcription factors

E-box DNA

Vincent, K.J., Jones, E., Arthur, M.J.P., Smart, D.E., Trim, J., Wright, M.C. and Mann, D.A. (2001) *Regulation of E-box DNA binding during in vivo and in vitro activation of rat and human hepatic stellate cells* Gut, **49**, 713-719

Metalloproteinases

Bertrand-Philippe, M., Ruddell, R.G., Arthur, M.J.P., Thomas, J., Mungalsingh, N. and Mann, D.A. (2004) *Regulation of tissue inhibitor of metalloproteinase 1 gene transcription by RUNX1 and RUNX2* J. Biol. Chem., **279**, 24530-24539

Perugorria, M.J., Wilson, C.L., Zeybel, M., Walsh, M., Amin, S., Robinson, S., White, S.A. et al (2012) *Histone methyltransferase ASH1 orchestrates fibrogenic gene transcription during myofibroblast tansdifferentiation* Hepatology, **56**, 1129-1139

Methylation

Perugorria, M.J., Wilson, C.L., Zeybel, M., Walsh, M., Amin, S., Robinson, S., White, S.A. et al (2012) *Histone methyltransferase ASH1 orchestrates fibrogenic gene transcription during myofibroblast tansdifferentiation* Hepatology, **56**, 1129-1139

Vitamin D

Beilfuss, A., Sowa, J-P., Sydor, S., Beste, M., Bechmann, L.P., Schlattjan, M., Syn, W-K., Wedemeyer, I. et al (2015) *Vitamin D counteracts fibrogenic TGF-β signalling in human hepatic stellate cells both receptor-dependently and independently* Gut, **64**, 791–799

Human pancreas

Armstrong, T., Packham, G., Murphy, L.B., Bateman, A.C., Conti, J.A., Fine, D.R., Johnson, C.D., Benyon, R.C. and Iredale, J.P. (2004) *Type 1 collagen promotes the malignant phenotype of pancreatic ductal adenocarcinoma* Clin. Cancer Res., **10**, 7427-7437

José, A., Rovira-Rigau, M., Luna, J., Giménez-Alejandre, M., Vaquero, E., García de la Torre, B., Andreu, D., Alemany, R. and Fillat, C. (2014) *A genetic fiber modification to achievematrix-metalloprotease-activated infectivity of oncolytic adenovirus* Journal of Control. Release, **192**, 148–156

Mouse liver

Activation (of fibrosis)

Ben-Shoshan, S.O., Kagan, P., Sultan, M., Barabash, Z., Dor, C., Jacob-Hirsch, J., Harmelin, A., Pappo, O. et al (2017) *ADAR1 deletion induces NFκB and interferon signaling dependent liver inflammation and fibrosis RNA* Biol., **14**, 587–602

Chen, L., Li, J., Zhang, J., Dai, C., Liu, X., Wang, J. et al (2015) *S100A4 promotes liver fibrosis via activation of hepatic stellate cells* J. Hepatol., **62**, 156-164

Chen, L. and Brigstock, D.R. (2017) *Cellular or exosomal microRNAs associated with CCN gene expression in liver fibrosis* In CCN Proteins: Methods and Protocols, Methods Mol. Biol., 1489, (ed. Takigawa, M.) Springer Science+Business Media, LLC, pp 465-480

Chen, L. and Brigstock, D.R. (2017) *Analysis of pathological activities of CCN proteins in fibrotic diseases: liver fibrosis* In CCN Proteins: Methods and Protocols, Methods Mol. Biol., **1489**, (ed. Takigawa, M.) Springer Science+Business Media, LLC, pp 445-463

Jiang, X., Shen, T., Tang, X., Yang, W., Guo, H. and Ling, W. (2017) *Cyanidin-3-O-β-glucoside combined with its metabolite protocatechuic acid attenuated the activation of mice hepatic stellate cells* Food Funct., 2017, 8, 2945–2957

Kagan, P., Sultan, M., Tachlytski, I., Safran, M. and Ben-Ari, Z. (2017) *Both MAPK and STAT3 signal transduction pathways are necessary for IL-6-dependent hepatic stellate cells activation* PLoS One, **12**: e0176173

Kim, J., Hyun, J., Wang, S., Lee, C., Lee, J-W., Moon, E-Y., Cha, H., Diehl, A.M. and Jung, Y. (2017) *Thymosin beta-4 regulates activation of hepatic stellate cells via hedgehog signalling* Sci. Rep., **7**: 3815

Zhao, X-K., Yu, L., Cheng, M-L., Che, P., Lu, Y-Y., Zhang, Q., Mu, M., Li, H. et al (2017) *Focal adhesion kinase regulates hepatic stellate cell activation and liver fibrosis* Sci. Rep., **7**: 4032

Anthocyanins

Jiang, X., Shen, T., Tang, X., Yang, W., Guo, H. and Ling, W. (2017) *Cyanidin-3-O-β-glucoside combined with its metabolite protocatechuic acid attenuated the activation of mice hepatic stellate cells* Food Funct., 2017, 8, 2945–2957

Antigenic targeting

Wu, F., Wuensch, S.A., Azadniv, M., Ebrahimkhani, M.R. and Crispe, I.N. (2009) *Galactosylated LDL nanoparticles: a novel targeting delivery system to deliver antigen to macrophages and enhance antigen specific T cell responses* Mol. Pharmaceut., **6**, 1506-1517

Apoptosis

Duan, Y., Gu, X., Zhu, D., Sun, W., Chen, J., Feng, J., Song, K., Xu, F., He, X. and He, X. (2014) *Schistosoma japonicum soluble egg antigens induce apoptosis and inhibit activation of hepatic stellate cells: a possible molecular mechanism* Int. J. Parasitol., **44**, 217–224

Tao, Y-y., Yan, X-c., Zhou, T., Shen, L., Liu, Z-l. and Liu, C-h., (2014) *Fuzheng Huayu recipe alleviates hepatic fibrosis via inhibiting TNF-α induced hepatocyte apoptosis* BMC Complement. Altern. Med., **14**: 449

Autoimmune hepatitis

Murthy, A., Shao, Y.W., Defamie, V., Wedeles, C., Smookler, D. and Khokha, R. (2012) *Stromal TIMP3 regulates liver lymphocyte populations and provides protection against Th1 T cell-driven autoimmune hepatitis* J. Immunol., **188**, 2876–2883

B cell activity

Thapa, M., Chinnadurai, R., Velazquez, V.M., Tedesco, D., Elrod, E., Han, J-H., Sharma, P., et al (2015) *Liver fibrosis occurs through dysregulation of MyD88-dependent innate B-cell activity* Hepatology, **61**, 2067-2079

Bile duct ligation

Cui, W., Matsuno, K., Iwata, K., Ibi, M., Matsumoto, M., Zhang, J., Zhu, K., Katsuyama, M., Torok, N.J. and Yabe-Nishimura, C. (2011) *NOX1/Nicotinamide adenine dinucleotide phosphate, reduced form (NADPH) oxidase promotes proliferation of stellate cells and aggravates liver fibrosis induced by bile duct ligation* Hepatology, **54**, 949-958

Carcinogenesis

Seifert, L., Deutsch, M., Alothman, S., Alqunaibit, D., Werba, G., Pansari, M., Pergamo, M., Ochi, A. (2015) *Dectin-1 regulates hepatic fibrosis and hepatocarcinogenesis by suppressing TLR4 signalling pathways* Cell Rep., **13**, 1–13

Wright, J.H., Johnson, M.M., Shimizu-Albergine, M., Bauer, R.L., Hayes, B.J., Surapisitchat, J., Hudkins, K.L., Riehle, K.J., Johnson, S.C., et al (2014) *Paracrine activation of hepatic stellate cells in platelet-derived growth factor C transgenic mice: Evidence for stromal induction of hepatocellular carcinoma* Int. J. Cancer, **134**, 778–788

Wright, J.H., Johnson, M.M., Shimizu-Albergine, M., Bauer, R.L., Hayes, B.J., Surapisitchat, J., Hudkins et al (2014) *Paracrine activation of hepatic stellate cells in platelet-derived growth factor C transgenic mice: Evidence for stromal induction of hepatocellular carcinoma* Int. J. Cancer, **134**, 778–788

Chemokine receptor

Lee, Y-S., Eun, H.S., Kim, S.Y., Jeong, J-M., Seo, W., Byun, J-S., Jeong, W-I. and Yi, H-S. (2106) *Hepatic immunophenotyping for streptozotocin-induced hyperglycemia in mice* Sci. Rep., **6**: 30656

Connective tissue/collagen

Huang, G. and Brigstock, D.R. (2011) *Integrin expression and function in the response of primary culture hepatic stellate cells to connective tissue growth factor (CCN2)* J. Cell. Mol. Med., **15**, 1087-1095

Oben, J.A., Yang, S., Lin, H., Ono, M. and Diehl. A.M. (2003) *Acetylcholine promotes the proliferation and collagen gene expression of myofibroblastic hepatic stellate cells* Biochem. Biophys. Res. Commun., **300**, 172-177

Oben, J.A., Yang, S., Lin, H., Ono, M. and Diehl, A.M. (2003) *Norepinephrine and neuropeptide Y promote proliferation and collagen gene expression of hepatic myofibroblastic stellate cells* Biochem. Biophys. Res. Commun., **302**, 685-690

Cytokines

Kandhi. R., Bobbala, D., Yeganeh. M., Mayhue, M., Menendez, A. and Ilangumaran, S. (2016) *Negative regulation of the hepatic fibrogenic response by suppressor of cytokine signalling 1* Cytokine, **82**, 58–69

Ogiso, H., Ito, H., Ando, T., Arioka, Y., Kanbe, A., Ando, K., Ishikawa, T. et al (2016) *The deficiency of indoleamine 2,3-dioxygenase aggravates the CCl_4-induced liver fibrosis in mice* PLoS One, **11**: e0162183

Drug effects

Liang, Y-J., Luo, J., Yuan, Q., Zheng, D., Liu, Y-P., Shi, L., Zhou, Y., Chen, A-L. et al (2011) *New insight into the antifibrotic effects of praziquantel on mice in infection with Schistosoma japonicum* PLoS One **6**: e20247

Dystroglycan

Kastanis, G.J., Hernandez-Nazara, Z., Nieto, N,, Rincón-Sanchez, A.R., Popratiloff, A., Dominguez-Rosales, J.A., Lechuga, C.G., Rojkind, M. (2011) *The role of dystroglycan in PDGF-BB-dependent migration of activated hepatic stellate cells/myofibroblasts* Am. J. Physiol. Gastrointest. Liver Physiol., **301**, G464–G474

Epigenetic therapy

Zeybel, M., Luli, S., Sabater, L., Hardy, T., Oakley, F., Leslie, J., Page, A., Salvador, E.M., Sharkey, V., Tsukamoto, H., Chu, D.C.K. et al (2017) *A proof-of-concept for epigenetic therapy of tissue fibrosis: inhibition of liver fibrosis progression by 3-deazaneplanocin A* Mol. Ther., **25**, 218-231

Gene transfer

Perugorria, M.J., Wilson, C.L., Zeybel, M., Walsh, M., Amin, S., Robinson, S., White, S.A., Burt, A.D., Oakley, F., Tsukamoto, H., Mann, D.A. and Mann, J. (2012) *Histone methyltransferase ASH1 orchestrates fibrogenic gene transcription during myofibroblast tansdifferentiation* Hepatology, **56**, 1129-1139

Growth factors and growth factor receptors/signalling

Bahrami, A.J., Gunaje, J.J., Hayes, J., Riehle, K.J., Kenerson, H.L., Yeung, R.S., Stempien-Otero, A.S., Campbell, J.S. and Mahoney Jr, W.M. (2014) *Regulator of G-protein signalling-5 is a marker of hepatic stellate cells and expression mediates response to liver injury* PLoS One, **9**: e108505

Huang, G., Besner, G.E. and Brigstock, D.R. (2012) *Heparin-binding epidermal growth factor-like growth factor suppresses experimental liver fibrosis in mice* Lab. Invest., **92**, 703–712

Kastanis, G.J., Hernandez-Nazara, Z., Nieto, N,, Rincón-Sanchez, A.R., Popratiloff, A., Dominguez-Rosales, J.A., Lechuga, C.G., Rojkind, M. (2011) *The role of dystroglycan in PDGF-BB-dependent migration of activated hepatic stellate cells/myofibroblasts* Am. J. Physiol. Gastrointest. Liver Physiol., **301**, G464–G474

Tsai, S-M. and Wang, W-P. (2011) *Expression and function of fibroblast growth factor (FGF) 7 during liver regeneration* Cell. Physiol. Biochem., **27**, 641-652

Gut microbiota

Bigorgne, A.E., John, B., Ebrahimkhani, M.R., Shimizu-Albergine, M., Campbell, J.S. and Crispe, I.N. (2016) *TLR4-dependent secretion by hepatic stellate cells of the neutrophil-chemoattractant CXCL1 mediates liver response to gut microbiota* PLoS One, **11**: e0151063

Hedgehog signalling

Hyun, J., Wang, S., Kim, J., Rao, K.M., Park, S.Y., 2, Chung, I., Ha, C-S. et al (2016) *MicroRNA-378 limits activation of hepatic stellate cells and liver fibrosis by suppressing Gli3 expression* Nat. Comm., **7**: 10993

Kim, J., Hyun, J., Wang, S., Lee, C., Lee, J-W., Moon, E-Y., Cha, H., Diehl, A.M. and Jung, Y. (2017) *Thymosin beta-4 regulates activation of hepatic stellate cells via hedgehog signalling* Sci. Rep., **7**: 3815

Hyperglycaemia

Lee, Y-S., Eun, H.S., Kim, S.Y., Jeong, J-M., Seo, W., Byun, J-S., Jeong, W-I. and Yi, H-S. (2106) *Hepatic immunophenotyping for streptozotocin-induced hyperglycemia in mice* Sci. Rep., **6**: 30656

Indoleamine 2,3-dioxygenase

Ogiso, H., Ito, H., Ando, T., Arioka, Y., Kanbe, A., Ando, K., Ishikawa, T., Saito, K., Hara, A., Moriwaki, H., Shimizu, M. and Seishima, M. (2016) *The deficiency of indoleamine 2,3-dioxygenase aggravates the CCl_4-induced liver fibrosis in mice* PLoS One, **11**: e0162183

Integrin expression

Huang, G. and Brigstock, D.R. (2011) *Integrin expression and function in the response of primary culture hepatic stellate cells to connective tissue growth factor (CCN2)* J. Cell. Mol. Med., **15**, 1087-1095

Martin, K., Pritchett, J., Llewellyn, J., Mullan, A.F., Athwal, V.S., Dobie, R., Harvey, E., Zeef, L. et al (2016) *PAK proteins and YAP-1 signalling downstream of integrin beta-1 in myofibroblasts promote liver fibrosis* Nat. Comm., **7**: 12502

Interferon signalling

Ben-Shoshan, S.O., Kagan, P., Sultan, M., Barabash, Z., Dor, C., Jacob-Hirsch, J., Harmelin, A., Pappo, O. et al (2017) *ADAR1 deletion induces NFκB and interferon signalling dependent liver inflammation and fibrosis RNA* Biol., **14**, 587–602

Interleukin expression

Kagan, P., Sultan, M., Tachlytski, I., Safran, M. and Ben-Ari, Z. (2017) *Both MAPK and STAT3 signal transduction pathways are necessary for IL-6-dependent hepatic stellate cells activation* PLoS One, **12**: e0176173

Mchedlidze, T., Waldner, M., Zopf, S., Walker, J., Rankin, A.L., Schuchmann, M., Voehringer, D. et al (2013) *Interleukin-33-dependent innate lymphoid cells mediate hepatic fibrosis* Immunity, **39**, 357–371

Seo, W., Eun, H.S., Kim, S.Y., Yi, H-S., Lee, Y-S., Park, S-H., Jang, M-J., Jo, E., Kim, S.C. et al (2016) *Exosome-mediated activation of toll-like receptor 3 in stellate cells stimulates interleukin-17 production by γδ T cells in liver fibrosis* Hepatology **64**, 616-631

Tan, Z., Qian, X., Jiang, R., Liu, Q., Wang, Y., Chen, C., Wang, X., Ryffe, B. and Sun, B. (2013) *IL-17A plays a critical role in the pathogenesis of liver fibrosis through hepatic stellate cell activation* J. Immunol., **191**, 1835–1844

Leishmania

Khadem, F., Gao, X., Mou, Z., Jia, P., Movassagh, H., Onyilagha, C., Gounni, A.S., Wright, M.C. and Uzonna, J.E. (2016) *Hepatic stellate cells regulate liver immunity to visceral Leishmaniasis through P110δ-dependent induction and expansion of regulatory T cells in mice* Hepatology, **63**, 620-632

Lipid metabolism

Jeong, W-I., Osei-Hyiaman, D., Park, O., Liu, J., Batkai, S., Mukhopadhyay, P., Horiguchi, N., Harvey-White, J. et al (2008) *Paracrine activation of hepatic CB_1 receptors by stellate cell-derived endocannabinoids mediates alcoholic fatty liver* Cell Metab., **7**, 227-235

Mesenchymal/mesothelial cells

Li, Y., Wang, J. and Asahina, K. (2013) *Mesothelial cells give rise to hepatic stellate cells and myofibroblasts via mesothelial–mesenchymal transition in liver injury* Proc. Natl. Acad. Sci. USA, **110**, 2324-2329

Li, Y., Lua, I., French, S.W. and Asahina, K. (2016) *Role of TGF-β signalling in differentiation of mesothelial cells to vitamin A-poor hepatic stellate cells in liver fibrosis* Am. J. Physiol. Gastrointest. Liver Physiol., **310**, G262–G272

Lua, I., James, D., Wang, J., Wang, K.S. and Asahina, K. (2014) *Mesodermal mesenchymal cells give rise to myofibroblasts, but not epithelial cells, in mouse liver injury* Hepatology, **60**, 311-322

Sicklick, J.K., Choi, S.S., Bustamente, M., McCall, S.J., Hernández-Pérez, E., Huang, J., Li, Y-X., Rojkind, M. and Diehl, A.M. (2006) *Evidence for epithelial-mesenchymal transitions in adult liver cells* Am. J. Physiol. Liver Physiol., **291**, G575-G583

Methodology

Liu, W., Hou, Y., Chen, H., Wei, H., Lin, W., Li, J., Zhang, M., He, F. and Jiang, Y. (2011) *Sample preparation method for isolation of single-cell types from mouse liver for proteomic studies* Proteomics **11**, 3556–3564

Chang, W., Yang, M., Song, L., Shen, K., Wang, H., Gao, X., Li, M., Niu, W. and Qin, X. (2014) *Isolation and culture of hepatic stellate cells from mouse liver*Acta Biochim. Biophys. Sin., **46**, 291–298

Weiskirchen, S., Tag, C.G., Sauer-Lehnen, S., Tacke, F. and Weiskirchen, R. (2017) *Isolation and culture of primary murine hepatic stellate cells* In Fibrosis: Methods and Protocols, Methods in Molecular Biology, **1627**, Rittié, L. (ed.), Springer Science+Business Media LLC pp165-191

MHC

Zhou, C-L., Kong, D-L., Liu, J-F., Lu, Z-K., Guo, H-F., Wang, W., Qiu, J-F., Liu, X-J. and Wang, Y. (2017) *MHC II^-, but not MHC II^+, hepatic stellate cells contribute to liver fibrosis of mice in infection with Shistosoma japonicum* BBA – Mol. Basis Disease, **1863**, 1848–1857

Microfluidic chip mimicking

Du, Y., Li, N., Yang, H., Luo, C., Gong, Y., Tong, C., Gao, Y., Lü, S. and Long, M. (2017) *Mimicking liver sinusoidal structures and functions using a 3D-configured microfluidic chip* Lab. Chip, **17**, 782-794

NADPH oxidase – NOX1 isoform

Cui, W., Matsuno, K., Iwata, K., Ibi, M., Matsumoto, M., Zhang, J., Zhu, K., Katsuyama, M., Torok, N.J. and Yabe-Nishimura, C. (2011) *NOX1/Nicotinamide adenine dinucleotide phosphate, reduced form (NADPH) oxidase promotes proliferation of stellate cells and aggravates liver fibrosis induced by bile duct ligation* Hepatology, **54**, 949-958

NFκB signalling

Ben-Shoshan, S.O., Kagan, P., Sultan, M., Barabash, Z., Dor, C., Jacob-Hirsch, J., Harmelin, A., Pappo, O. et al (2017) *ADAR1 deletion induces NFκB and interferon signalling dependent liver inflammation and fibrosis RNA* Biol., **14**, 587–602

He, F., Guo, F-C., Li, Z., Yu, H-C., Ma, P-F., Zhao, J-L., Feng, L., Li, W-N. et al (2015) *Myeloid-specific disruption of recombination signal binding protein Jj ameliorates hepatic fibrosis by attenuating inflammation through cylindromatosis in mice* Hepatology, **61**, 303-314

He, X., Pu, G., Tang, R., Zhang, D. and Pan, W. (2014) *Activation of nuclear factor kappa B in the hepatic stellate cells of mice with Schistosomiasis japonica* PloS One **9**: e104323

NK cell killing

Jeong, W-I., Park, O. and Gao, B. (2008) *Abrogation of the antifibrotic effect of natural killer cells/interferon-γ contributes to alcohol acceleration of liver fibrosis* Gastroenterology **134**, 248-258

Radaeva, S., Sun, R., Jaruga, B., Nguyen, V.T., Tian, Z. and Gao, B. (2006) *Natural killer cells ameliorate liver fibrosis by killing activated stellate cells in NKG2D-dependent and tumor necrosis factor-related apoptosis-inducing ligand-dependent manners* Gastroenterology, **130**, 434-452

Radaeva. S., Wang, L., Radaeva, S., Jeong, W-I., Park, O. and Gao, B. (2007) *Retinoic acid signalling sensitizes hepatic stellate cells to NK cell killing via upregulation of NK cell activating ligand RAE1* Am. J. Physiol. Gastrointest. Liver Physiol., **293**, G809-G816

Notch signalling

He, F., Guo, F-C., Li, Z., Yu, H-C., Ma, P-F., Zhao, J-L., Feng, L., Li, W-N. et al (2015) *Myeloid-specific disruption of recombination signal binding protein Jj ameliorates hepatic fibrosis by attenuating inflammation through cylindromatosis in mice* Hepatology, **61**, 303-314

Paracrine stimulation

Corbett, L., Mann, J. and Mann, D.A. (2015) *Non-canonical Wnt predominates in activated rat hepatic stellate cells, influencing HSC survival and paracrine stimulation of Kupffer cells* PLoS One, **10**: e0142794

Wright, J.H., Johnson, M.M., Shimizu-Albergine, M., Bauer, R.L., Hayes, B.J., Surapisitchat, J., Hudkins et al (2014) *Paracrine activation of hepatic stellate cells in platelet-derived growth factor C transgenic mice: Evidence for stromal induction of hepatocellular carcinoma* Int. J. Cancer, **134**, 778–788

PDGF signalling

Wright, J.H., Johnson, M.M., Shimizu-Albergine, M., Bauer, R.L., Hayes, B.J., Surapisitchat, J., Hudkins, K.L., Riehle, K.J., Johnson, S.C., et al (2014) *Paracrine activation of hepatic stellate cells in platelet-derived growth factor C transgenic mice: Evidence for stromal induction of hepatocellular carcinoma* Int. J. Cancer, **134**, 778–788

Wright, J.H., Johnson, M.M., Shimizu-Albergine, M., Bauer, R.L., Hayes, B.J., Surapisitchat, J., Hudkins, K.L. et al (2014) *Paracrine activation of hepatic stellate cells in platelet-derived growth factor C transgenic mice: Evidence for stromal induction of hepatocellular carcinoma* Int. J. Cancer, **134**, 778–788

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Retinoic acid/ester

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RNA (various types)

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Schistosome infection

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Steatohepatitis

McCommis, K.S., Hodges, W.T., Brunt, E.M., Nalbantoglu, I., McDonald, W.G., Holley, C., Fujiwara, H. et al (2017) *Targeting the mitochondrial pyruvate carrier attenuates fibrosis in a mouse model of nonalcoholic steatohepatitis* Hepatology, 65, 1543-1556
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T-cells

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Dunham, R.M., Thapa, M., Velazquez, V.M., Elrod, E.J., Denning, T.L., Pulendran, B. and Grakoui, A. (2013) *Hepatic stellate cells preferentially induce Foxp3$^+$ regulatory T cells by production of retinoic acid* J. Immunol., **190**, 2009–2016
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TGF-β signalling

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Toll-like receptor signalling

Seifert, L., Deutsch, M., Alothman, S., Alqunaibit, D., Werba, G., Pansari, M., Pergamo, M., Ochi, A. (2015) *Dectin-1 regulates hepatic fibrosis and hepatocarcinogenesis by suppressing TLR4 signalling pathways* Cell Rep., **13**, 1–13

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Transcription

Inflammatory response

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Metalloproteinases

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Methylation

Perugorria, M.J., Wilson, C.L., Zeybel, M., Walsh, M., Amin, S., Robinson, S., White, S.A. et al (2012) *Histone methyltransferase ASH1 orchestrates fibrogenic gene transcription during myofibroblast tansdifferentiation* Hepatology, **56**, 1129-1139

Viral hepatitis

Jie, Z., Liang, Y., Yi, P., Tang, H., Soong, L., Cong, Y., Zhang, K. and Sun, J. (2017) *Retinoic acid regulates immune responses by promoting IL-22 and modulating S100 proteins in viral hepatitis* J. Immunol., **198**, 3448–3460

Wnt system

Corbett, L., Mann, J. and Mann, D.A. (2015) *Non-canonical Wnt predominates in activated rat hepatic stellate cells, influencing HSC survival and paracrine stimulation of Kupffer cells* PLoS One, **10**: e0142794

Mouse pancreas

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Rat liver

Adipogenesis

Jiang, Y., Wang, S., Zhao, Y., Lin, C., Zhong, F., Jin, L., He, F. and Wang, H. (2015) *Histone H3K9 demethylase JMJD1A modulates hepatic stellate cells activation and liver fibrosis by epigenetically regulating peroxisome proliferator-activated receptor γ* FASEB J. **29**, 1830–1841

Alcoholic liver injury

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

Apoptosis

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Atorvastatin effects

Klein, S., Klösel, J., Schierwagen, R., Körner, C., Granzow, M., Huss, S., Reza Mazar, I.G. et al (2012) *Atorvastatin inhibits proliferation and apoptosis, but induces senescence in hepatic myofibroblasts and thereby attenuates hepatic fibrosis in rats* Lab. Invest., **92**, 1440–1450

Autophagic cell death

Shaker, M.E., Ghani, A., Shiha, G.E., Ibrahim, T.M., Mehal, W.Z.(2013) *Nilotinib induces apoptosis and autophagic cell death of activated hepatic stellate cells via inhibition of histone deacetylases* Biochim. Biophys. Acta, **1833**, 1992–2003

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Cirrhosis

De Mesquita, F.C., Guixé-Muntet, S., Fernández-Iglesias, A., Maeso-Díaz, R., Vila, S., Hide, D., Ortega-Ribera, M., Rosa, J.L. et al (2017) *Liraglutide improves liver microvascular dysfunction in cirrhosis: Evidence from translational studies* Sci. Rep., **7**: 3255
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Tang, W-P., Akahoshi, T., Piao, J-S., Narahara, S., Murata, M., Kawano, T., Hamano, N., Ikeda, T. and Hashizume, M. (2016) *Splenectomy enhances the therapeutic effect of adipose tissue-derived mesenchymal stem cell infusion on cirrhosis rats* Liver Int.,**36**, 1151–1159

Connective tissue/collagen

Jiroutova, A., Slavkovsky, R., Cermakova, M., Majdiakova, L., Hanovcova, I., Bolehovska, R., Hadjzlerova, M., Radilova, H., Ruszova, E. and Kanta, J. (2007) *Expression of mRNAs related to connective tissue metabolism in rat hepatic stellate cells and myofibroblasts* Exp. Toxicol. Pathol., **58**, 263-273
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Contractile properties

Laleman W., Van Landeghem L, Severi T, Vander Elst I, Zeegers M, Bisschops R, Van Pelt J, Roskams T, Cassiman D, Fevery J, Nevens F. (2007) *Both Ca^{2+}-dependent and -independent pathways are involved in rat hepatic stellate cell contraction and intrahepatic hyperresponsiveness to methoxamine* Am. J. Physiol. Gastrointest. Liver Physiol., **292,** G556–G564

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3D-Assembly

Weng, Y-S., Chang, S-F., Shih, M-C., Tseng, S-H. and Lai, C-H. (2017) *Scaffold-free liver-on-a-chip with multiscale organotypic cultures* Adv. Mater., **29**: 1701545

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Drug effects

Habens, F., Srinivasan, N., Oakley, F., Mann, D.A., Ganesan, A. and Packham, G. (2005) *Novel sulfasalazine analogues with enhanced NF-kB inhibitory and apoptosis promoting activity* Apoptosis, **10**, 481-491

Khan, F., Peltekian, K.M. and Peterson, T.C. (2008) *Effect of interferon-alpha, Ribavirin, pentoxifylline, and interleukin-18 antibody on hepatitis C sera-stimulated hepatic stellate cell proliferation* J. Interferon Cytokine Res., **28**, 643-652

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Oakley, F., Meso, M., Iredale, J.P., Green, K., Marek, C.J., Zhou, X., May, M.J., Millward-Sadler, H., Wright, M.C. and Mann, D.A. (2005) *Inhibition of inhibitor of κB kinases stimulates hepatic stellate cell apoptosis and accelerated recovery from rat liver fibrosis* Gastroenterology, **128**, 108-120

Peterson, T.C. and Rowden, G. (1998) *Drug-metabolizing enzymes in rat liver myofibroblasts* Biochem. Pharmacol., **55**, 703-708

Epigallocatechin

Fu, Y. and Chen, A. (2006) *The phyto-chemical (−)-epigallocatechin gallate suppresses gene expression of epidermal growth factor receptor in rat hepatic stellate cells in vitro by reducing the activity of Egr-1* Biochem. Pharmacol., **72**, 227-238

Fu, Y., Zheng, S., Lu, S.C. and Chen, A. (2008) *Epigallocatechin-3-gallate inhibits growth of activated hepatic stellate cells by enhancing the capacity of glutathione synthesis* Mol. Pharmacol., **73**, 1465-1473

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Fatty liver disease

Li, B-H., He, F-P., Yang, X, Chen, Y-W. and Fan, J-G. (2017) *Steatosis induced CCL5 contributes to early-stage liver fibrosis in nonalcoholic fatty liver disease progress* Translat. Res., **180**, 103–117

Gene transfer

Gao, R., McCormick, C.J., Arthur, M.J.P., Ruddell, R., Oakley, F., Smart, D.E., Murphy, F.R., Garris, M.P.G. and Mann, D.A. (2002) *High efficiency gene transfer into cultured primary rat and human hepatic stellate cells using baculovirus vectors* Liver **22**, 15-22

Smith, P.G., Oakley, F., Fernandez, M., Mann, D.A., Lemoine, N.R. and Whitehouse, A. (2005) *Herpesvirus saimiri-based vector biodistribution using noninvasive optical imaging* Gene Ther., **12**, 1465-1476

Growth factors and growth factor receptors/signalling

Cassiman, D., Denef, C., Desmet, V.J. and Roskams, T. (2001) *Human and rat hepatic stellate cells express neurotrophins and neurotrophin receptors* Hepatology, **33**, 148-158
De Leve, L.D., Wang, X. and Wang, L. (2016) *VEGF-sdf1 recruitment of CXCR7$^+$ bone marrow progenitors of liver sinusoidal endothelial cells promotes rat liver regeneration* Am. J. Physiol. Gastrointest Liver Physiol., **310**, G739–G746
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Zhang, Z., Zha, Y., Hu, W., Huang, Z., Gao, Z., Zang, Y., Chen, J., Dong, L. and Zhang, J. (2013) The *Autoregulatory feedback loopof microRNA-21/programmed cell death protein 4/activation protein-1 (MiR-21/PDCD4/AP-1) as a driving force for hepatic fibrosis development* J. Biol. Chem., **288**, 37082-37093

Hedgehog signalling

Hyun, J., Wang, S., Kim, J., Kim, G.J. and Jung, Y. (2015) *MicroRNA125b-mediated Hedgehog signalling influences liver regeneration by chorionic plate-derived mesenchymal stem cells* Sci. Rep., **5**: 14135

Interleukin expression

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

Mesenchymal/mesothelial cells

Hyun, J., Wang, S., Kim, J., Kim, G.J. and Jung, Y. (2015) *MicroRNA125b-mediated Hedgehog signalling influences liver regeneration by chorionic plate-derived mesenchymal stem cells* Sci. Rep., **5**: 14135
Tang, W-P., Akahoshi, T., Piao, J-S., Narahara, S., Murata, M., Kawano, T., Hamano, N. et al (2015) *Basic fibroblast growth factor-treated adipose tissue-derived mesenchymal stem cell infusion to ameliorate liver cirrhosis via paracrine hepatocyte growth factor* J. Gastroenterol. Hepatol., **20**, 1065–1074
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Myofibroblast (proliferation/migration/senescence)

Klein, S., Klösel, J., Schierwagen, R., Körner, C., Granzow, M., Huss, S., Reza Mazar, I.G., Weber, S., van den Ven, P.F.M., Pieper-Fürst, U., et al (2012) *Atorvastatin inhibits proliferation and apoptosis, but induces senescence in hepatic myofibroblasts and thereby attenuates hepatic fibrosis in rats* Lab. Invest., **92**, 1440–1450

Myofibroblast transdifferentiation – see "Transcription factors - Methylation"

Neurotransmitters

Cassiman, D., van Pelt, J., de Vos, R., van Lommel, F., Desmet, V., Yap, S-H. and Roskams, T. (1999) *Synaptophysin: a novel marker for human and rat hepatic stellate cells* Am. J. Pathol., **155**, 1831-1839

Opioid system

Ebrahimkhani, M.R., Kiani, S., Oakley, F., Kendall, T., Shariftabrizi, A., Tavangar, S.M., Moezi, L. et al (2006) *Naltrexone, an opioid receptor antagonist, attentuates liver fibrosis in bile duct ligated rats* Gut, **55**, 1606-1616

Oxidases/oxygen species

Ping, J., Li, J-T., Liao, Z-X., Shang, L. and Wang, H. (2011) *Indole-3-carbinol inhibits hepatic stellate cells proliferation by blocking NADPH oxidase/reactive oxygen species/p38 MAPK pathway* Eur. J. Pharmacol., **650**, 656–662

Peroxisome proliferators-activated receptor-γ

Jiang, Y., Wang, S., Zhao, Y., Lin, C., Zhong, F., Jin, L., He, F. and Wang, H. (2015) *Histone H3K9 demethylase JMJD1A modulates hepatic stellate cells activation and liver fibrosis by epigenetically regulating peroxisome proliferator-activated receptor γ* FASEB J. **29**, 1830–1841

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Portal hypertension

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