

OptiPrep™ Reference List RC07

Hepatic and pancreatic stellate cells

- ◆ This **Reference List RC07** provides a complete list of publications that report the use of OptiPrep™ for the purification of hepatic and pancreatic stellate cells. It complements **Application Sheet C25** which provides a brief overview of the separation technology and **Reference List RC08**: a complete list of published papers primarily reporting the analysis of hepatic Kupffer and sinusoidal endothelial cells; it 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 – p11**
 - ◆ **Rat liver – p11**
 - ◆ **Rat pancreas – p 17**
- ◆ **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 can be accessed from the usual website: www.Optiprep.com. Select “Cells” then scroll down to “Hepatic cells – stellate cells” or “Pancreatic stellate cells” to open the appropriate Application Sheet.

Human liver

Activation

Hong, Y., Li, S., Wang, J. and Li, Y. (2018) *In vitro inhibition of hepatic stellate cell activation by the autophagy-related lipid droplet protein ATG2A* Sci. Rep., **8**: 9232

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., Peppas, 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

Casas-Grajales, S., Alvarez-Suarez, D., Ramos-Tovar, E., Buendía-Montaña, L.D., Reyes-Gordillo, K., Camacho, J., Tsutsumi, V., Lakshman, M.R. and Muriel, P. (2019) *Stevioside inhibits experimental fibrosis by down-regulating profibrotic Smad pathways and blocking hepatic stellate cell activation* Basic Clin. Pharmacol. Toxicol. 2019, **124**, 670–6800

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

Casas-Grajales, S., Alvarez-Suarez, D., Ramos-Tovar, E., Buendía-Montaña, L.D., Reyes-Gordillo, K., Camacho, J., Tsutsumi, V., Lakshman, M.R. and Muriel, P. (2019) *Stevioside inhibits experimental fibrosis by down-regulating profibrotic Smad pathways and blocking hepatic stellate cell activation* Basic Clin. Pharmacol. Toxicol. 2019, **124**, 670–6800

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 transdifferentiation* 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- β_4 (T β_4) 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

Hepatitis (T-cell mediated)

Chen, L., Gu, J., Qian, Y., Li, M., Qian, Y., Xu, M., Li, J., Wen, Y., Xia, L. et al (2019) *Deletion of C-C motif chemokine ligand 5 worsens invariant natural killer T-cell mediated hepatitis via compensatory up-regulation of CXCR2-related chemokine activity* Cell. Mol. Gastroenterol. Hepatol., **7**, 623–639

Hypertension

Jalan, R., De Chiara, F., Balasubramanian, 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

Memory T-cells

Swadling, L., Pallett, L.J., Diniz, M.O., Baker, J.M., Amin, O.E., Stegmann, K.A., Burton, A.R., Schmidt, N.M., Jeffery-Smith, A. et al (2020) *Human liver memory CD8+ T cells use autophagy for tissue residence* Cell Rep., **30**, 687–698

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 transdifferentiation* 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 transdifferentiation* 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 achieve matrix-metalloprotease-activated infectivity of oncolytic adenovirus* Journal of Control. Release, **192**, 148–156

Mouse liver

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

Autophagy

Chen, M., Liu, J., Yang, W. and Ling, W. (2017) *Lipopolysaccharide mediates hepatic stellate cell activation by regulating autophagy and retinoic acid signalling* *Autophagy*, **13**, 813–1827

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

Cell-cell communication

Xiong, X., Kuang, H., Ansari, S., Liu, T., Gong, J., Wang, S., Zhao, X-Y., Ji, Y., Li, C., Guo, L. et al (2019) *Landscape of intercellular crosstalk in healthy and NASH liver revealed by single-cell secretome gene analysis* *Mol. Cell*, **75**, 644–660

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

Chronic liver injury

Kim, J-W., Yang, D., Jeong, H., Park, S., Lee, M-H., Lim, C.W. and Kim, B. (2019) *Dietary zerumbone, a sesquiterpene, ameliorates hepatotoxin-mediated acute and chronic liver injury in mice* *Phytother. Res.*, **33**, 1538–1550

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

Li, P., Li, Y., Zhu, L., Yang, Z., He, J., Wang, L., Shang, Q., Pan, H., Wang, H., Ma, X. et al (2018) *Targeting secreted cytokine BMP9 gates the attenuation of hepatic fibrosis* *BBA – Mol. Basis Dis.*, **1864**, 709–720

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 CCl₄-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-Sánchez, 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

EphB2 receptor tyrosine kinase

Mimche, P.N., Lee, C.M., Mimche, S.M., Thapa, M., Grakoui, A., Henkemeyer, M. and Lamb, T.J. (2018) *EphB2 receptor tyrosine kinase promotes hepatic fibrogenesis in mice via activation of hepatic stellate cells* Sci. Rep., **8**: 2532

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

Fatty liver disease

Zhong, L., Huang, L., Xue, Q., Liu, C., Xu, K., Shen, W. and Deng, L. (2019) *Cell-specific elevation of Runx2 promotes hepatic infiltration of macrophages by upregulating MCP-1 in high-fat diet-induced mice NAFLD* J. Cell. Biochem. **120**, 11761-11774

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

Casas-Grajales, S., Alvarez-Suarez, D., Ramos-Tovar, E., Buendía-Montaña, L.D., Reyes-Gordillo, K., Camacho, J., Tsutsumi, V., Lakshman, M.R. and Muriel, P. (2019) *Stevioside inhibits experimental fibrosis by down-regulating profibrotic Smad pathways and blocking hepatic stellate cell activation* Basic Clin. Pharmacol. Toxicol. **2019**, **124**, 670–6800

Chen, L., Li, J., Zhang, J., Dai, C., Liu, X., Wang, J. et al (2015) *SI00A4 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

Chen, W., Wu, X., Yan, Z., Xu, A., Yang, A. and You, H. (2019) *Multitranscriptome analyses reveal prioritized genes specifically associated with liver fibrosis progression independent of etiology* Am. J. Physiol. Gastrointest. Liver Physiol., **316**, G744–G754

Chen, X., Li, X.-F., Chen, Y., Zhu, S., Li, H.-D., Chen, S.-Y., Wang, J.-N., Pan, X.-Y., Bu, F.-T., Huang, C. and Li, J. (2019) *Hesperetin derivative attenuates CCl4-induced hepatic fibrosis and inflammation by Gli-1-dependent mechanisms* Int. Immunopharm., **76**: 105838

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

Jiang, Y., Zhao, Y., He, F. and Wang, H. (2019) *Artificial microRNA-mediated Tgfb2 and Pdgfrb co-silencing ameliorates carbon tetrachloride-induced hepatic fibrosis in mice* Hum. Gene Ther., **30**, 179-196

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

Kong, De-L., Kong, F.-Y., Liu, X.-Y., Yan, C., Cui, J., Tang, R.-X. and Zheng, K.-Y. (2019) *Soluble egg antigen of Schistosoma japonicum induces pyroptosis in hepatic stellate cells by modulating ROS production* Parasites Vectors, **12**: 475

- Lao, Y.**, Li, Y., Zhang, P., Shao, Q., Lin, W., Qiu, B., Lv, Y., Tang, L., Su, S et al (2018) *Targeting endothelial Erk1/2-Akt axis as a regeneration strategy to bypass fibrosis during chronic liver injury in mice* Mol. Ther., **26**, 2779-2797
- Li, P.**, Li, Y., Zhu, L., Yang, Z., He, J., Wang, L., Shang, Q., Pan, H., Wang, H., Ma, X. et al (2018) *Targeting secreted cytokine BMP9 gates the attenuation of hepatic fibrosis* BBA – Mol. Basis Dis., **1864**, 709–720
- Li, Y.**, Pu, S., Liu, Q., Li, R., Zhang, J., Wu, T., Chen, L., Li, H. et al (2019) *An integrin-based nanoparticle that targets activated hepatic stellate cells and alleviates liver fibrosis* J. Control. Release, **303**, 77–90
- Mimche, P.N.**, Lee, C.M., Mimche, S.M., Thapa, M., Grakoui, A., Henkemeyer, M. and Lamb, T.J. (2018) *EphB2 receptor tyrosine kinase promotes hepatic fibrogenesis in mice via activation of hepatic stellate cells* Sci. Rep., **8**: 2532
- Strowitzki, M.J.**, Kirchberg, J., Tuffs, C., Schiedeck, M., Ritter, A.S., Biller, M., Harnoss, J.M., Lasitschka F. et al (2018) *Loss of prolyl-hydroxylase 1 protects against biliary fibrosis via attenuated activation of hepatic stellate cells* Am. J. Pathol., **188**, 2826-2838
- You, K.**, Li, S-Y., Gong, J., Fang, J-H., Zhang, M., Yuan, Y., Yang, J. and Zhuang, S-M. (2018) *Micro RNA-125b promotes hepatic stellate cell activation and liver fibrosis by activating RhoA signaling* Mol. Ther. Nucl. Acids, **12**, 57-66
- Yu, F.**, Dong, B., Dong, P., He, Y., Zheng, J. and Xu, P. (2020) *Hypoxia induces the activation of hepatic stellate cells through the PVT1-miR-152-ATG14 signaling pathway* Mol. Cell. Biochem., **465**, 115–123
- Zhan, T.**, Ma, H., Jiang, S., Zhong, Z., Wang, X., Li, C., Yu, D., Liu, L., Xu, J. and Xia, C. (2019) *Interleukin-9 blockage reduces early hepatic granuloma formation and fibrosis during Schistosoma japonicum infection in mice* Immunology, **158**, 296–303
- 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
- Zhu, J.**, Luo, Z., Pan, Y., Zheng, W., Li, W., Zhang, Z., Xiong, P., Xu, D. et al (2019) *H19/miR-148a/USP4 axis facilitates liver fibrosis by enhancing TGF- β signaling in both hepatic stellate cells and hepatocytes* J. Cell. Physiol. **234**, 9698–9710
- Zou, X.**, Ramachandran, P., Kendall, T.J., Pellicoro, A., Dora, E., Aucott, R.L., Manwani, K., Man, T.Y. et al (2018) *11Beta-hydroxysteroid dehydrogenase-1 deficiency or inhibition enhances hepatic myofibroblast activation in murine liver fibrosis* Hepatology, **67**, 2167-2181

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 transdifferentiation* Hepatology, **56**, 1129-1139

Growth factors and growth factor receptors/signalling

- Bahrani, 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

Hepatitis (T-cell mediated)

Chen, L., Gu, J., Qian, Y., Li, M., Qian, Y., Xu, M., Li, J., Wen, Y., Xia, L. et al (2019) *Deletion of C-C motif chemokine ligand 5 worsens invariant natural killer T-cell mediated hepatitis via compensatory up-regulation of CXCR2-related chemokine activity* Cell. Mol. Gastroenterol. Hepatol., **7**, 623–639

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

Hypoxia

Yu, F., Dong, B., Dong, P., He, Y., Zheng, J. and Xu, P. (2020) *Hypoxia induces the activation of hepatic stellate cells through the PVT1-miR-152-ATG14 signaling pathway* Mol. Cell. Biochem., **465**, 115–123

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 CCl₄-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

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Interferon signalling

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Interleukin expression

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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

Intrahepatic signaling

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Leishmania

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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 CB₁ receptors by stellate cell-derived endocannabinoids mediates alcoholic fatty liver* Cell Metab., **7**, 227-235

Lipopolysaccharide

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Macrophage-mediated liver injury

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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

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Methodology

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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

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MHC

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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

NF κ B 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 NF κ B 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 J κ ameliorates hepatic fibrosis by attenuating inflammation through cylindromatosis in mice* Hepatology, **61**, 303-314

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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

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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 J κ 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

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Zhang, X., Tan, Z., Wang, Y., Tang, J., Jiang, R., Hou, J., Zhuo, H., Wang, X., Ji, J., Qin, X. and Sun, B. (2015) *PTPRO-associated hepatic stellate cell activation plays a critical role in liver fibrosis* Cell. Physiol. Biochem., **35**, 885-898

Proteoglycans

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Proteomics

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

Retinoic acid/ester

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- Leask, A.**, Chen, S., Pala, D., Brigstock, D.R. (2008) *Regulation of CCN2 mRNA expression and promoter activity in activated hepatic stellate cells* J. Cell. Commun. Signal., **2**, 49-56
- You, K.**, Li, S-Y., Gong, J., Fang, J-H., Zhang, C., Zhang, M., Yuan, Y., Yang, J. and Zhuang, S-M. (2018) *Micro RNA-125b promotes hepatic stellate cell activation and liver fibrosis by activating RhoA signaling* Mol. Ther. Nucl. Acids, **12**, 57-66
- Yu, F.**, Zheng, J., Mao, Y., Dong, P., Lu, Z., Li, G., Guo, C., Liu, Z. and Fan, X. (2015) *Long non-coding RNA growth arrest-specific transcript 5 (GAS5) inhibits liver fibrogenesis through a mechanism of competing endogenous RNA* J. Biol. Chem., **290**, 28286–28298
- Zheng, J.**, Dong, P., Mao, Y., Chen, S., Wu, X., Li, G., Lu, Z. and Yu, F. (2015) *lincRNA-p21 inhibits hepatic stellate cell activation and liver fibrogenesis via p21* FEBS J., **282**, 4810–4821

Schistosome infection

- 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
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- Wang, Y.**, Lin, C., Cao, Y., Duan, Z., Guan, Z., Xu, J., Zhu, X-Q. and Xia, C. (2017) *Up-regulation of Interleukin-21 contributes to liver pathology of schistosomiasis by driving GC immune responses and activating HSCs in mice* Sci. Rep., **7**: 16682
- Zhan, T.**, Ma, H., Jiang, S., Zhong, Z., Wang, X., Li, C., Yu, D., Liu, L., Xu, J. and Xia, C. (2019) *Interleukin-9 blockage reduces early hepatic granuloma formation and fibrosis during Schistosoma japonicum infection in mice* Immunology, **158**, 296–303
- 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

Steatohepatitis

- Asakawa, M.**, Itoh, M., Suganami, T., Sakai, T., Kanai, S., Shirakawa, I., Yuan, X., Hatayama, T., Shimada, S. et al (2019) *Upregulation of cancer-associated gene expression in activated fibroblasts in a mouse model of non-alcoholic steatohepatitis* Sci. Rep., **9**: 19601
- Kim, K.H.**, Kim, S.H., Han, D.H., Jo, J.S., Lee, Y-h. and Lee, M-S, (2018) *Growth differentiation factor 15 ameliorates non-alcoholic steatohepatitis and related metabolic disorders in mice* Sci. Rep., **8**: 6789
- 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

Pulli, B., Ali, M., Iwamoto, Y., Zeller, M.W.G., Schob, S., Linnoila, J.J. and Chen, J.W. (2015) *Myeloperoxidase–hepatocyte–stellate cell cross talk promotes hepatocyte injury and fibrosis in experimental nonalcoholic steatohepatitis* *Antioxid. Redox Signal.*, **23**, 1255–1269

T-cells

Chinnadurai, R. and Grakoui, A. (2010) *B7-H4 mediates inhibition of T cell responses by activated murine hepatic stellate cells* *Hepatology*, **52**, 2177-2185

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

Feng, M., Wang, Q., Jiang, Z., Ding, J., Wang, H., Wang, M., Lu, L. and Guan, W. (2016) *Adoptive transferred hepatic stellate cells attenuated drug-induced liver injury by modulating the rate of regulatory T cells/T helper 17 cells* *Clin. Immunol.*, **165**, 12–18

Feng, M., Wang, Q., Jiang, Z., Ding, J., Wang, H., Wang, M., Lu, L. and Guan, W. (2016) *Adoptive transferred hepatic stellate cells attenuated drug-induced liver injury by modulating the rate of regulatory T cells/T helper 17 cells* *Clin. Immunol.*, **165**, 12–18

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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 P110 δ -dependent induction and expansion of regulatory T cells in mice* *Hepatology*, **63**, 620-632

TGF- β signalling

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

Toll-like receptor signalling

Seifert, L., Deutsch, M., Allothman, 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

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 $\gamma\delta$ T cells in liver fibrosis* *Hepatology* **64**, 616-631

Transcription

Inflammatory response

Elsharkawy, A.M., Oakley, F., Lin, F., Packham, G., Mann, D.A, and Mann, J. (2010) *The NF- κ B p50:p50:HDAC-1 repressor complex orchestrates transcriptional inhibition of multiple pro-inflammatory genes* *J. Hepatol.*, **53**, 519-527

Oakley, F., Mann, J., Nailard, S., Smart, D.E., Mungalasingh, N., Constandinou, C., Ali, S., Wilson, S.J. et al (2005) *Nuclear factor- κ B1 (p50) limits the inflammatory and fibrogenic responses to chronic injury* *Am. J. Pathol.*, **166**, 695-708

Metalloproteinases

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

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 transdifferentiation* *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 transdifferentiation* *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

Erkan, M., Adler, G., Apte, M.V., Bachem, M.G., Buchholz, M., Detlefsen, S., Esposito, I., Friess, H. et al (2012) *StellaTUM: current consensus and discussion on pancreatic stellate cell research* Gut, **61**, 172-178

Charrier, A., Chen, R., Chen, L., Kemper, S., Hattori, T., Takigawa, M. and Brigstock, D.R. (2014) *Connective tissue growth factor (CCN2) and microRNA-21 are components of a positive feedback loop in pancreatic stellate cells (PSC) during chronic pancreatitis and are exported in PSC-derived exosomes* J. Cell Commun. Signal., **8**, 147–156

Lawrencia, C., Charrier, A., Huang, G. and Brigstock, D.R. (2009) *Ethanol-mediated expression of connective tissue growth factor (CCN2) in mouse pancreatic stellate cells* Growth Factors, **27**, 91–99

Liu, J., Gao, M., Nipper, M., Deng, J., Sharkey, F.E., Johnson, R.L., Crawford, H.C., Chen, Y. and Wang, P. (2019) *Activation of the intrinsic fibroinflammatory program in adult pancreatic acinar cells triggered by Hippo signaling disruption* PLoS Biol., **17**: e3000418

Ulmasov, B., Xu, Z., Tetri, L.H., Inagami, T. and Neuschwander-Tetri, B.A. (2009) *Protective role of angiotensin II type 2 receptor signaling in a mouse model of pancreatic fibrosis* Am. J. Physiol. Gastrointest. Liver Physiol., **296**, G284–G294

Rat liver (majority of papers relate to fibrosis)

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

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

Oakley, F., Meso, M., Iredale, J.P., Green, K., Marek, C.J., Zhou, X., May, M.J. et al (2005) *Inhibition of inhibitor of κ B kinases stimulates hepatic stellate cell apoptosis and accelerated recovery from rat liver fibrosis* Gastroenterology, **128**, 108-120

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

Bile duct ligation

Kageyama, Y., Ikeda, H., Watanabe, N., Nagamine, M., Kusumoto, Y., Yashiro, M., Satoh, Y., Shimosawa, T., Shinozaki, K., et al (2012) *Antagonism of sphingosine 1-phosphate receptor 2 causes a selective reduction of portal vein pressure in bile duct-ligated rodents* Hepatology, **56**, 1427-1438

Chemotaxis

Gong, J., Han, J., He, J., Liu, J., Han, P., Wang, Y., Li, M., Li, D., Ding, X. et al (2017) *Paired related homeobox protein 1 regulates PDGF-induced chemotaxis of hepatic stellate cells in liver fibrosis* Lab. Invest., **97**, 1020–1032

Cirrhosis

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NF-κB

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