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### ORIGINAL RESEARCH

- 1 [Macrophage SCAP Contributes to Metaflammation and Lean NAFLD by Activating STING–NF- \$\kappa\$ B Signaling Pathway](#)

*X. Huang, Y. Yao, X. Hou, L. Wei, Y. Rao, Y. Su, G. Zheng, X. Z. Ruan, D. Li, and Y. Chen*

[See editorial, Kennedy L et al, on page 236](#)

*In the mouse model of lean NAFLD induced by Paigen diet, macrophage SCAP was abnormally increased and led to severe metaflammation through activating STING–NF- $\kappa$ B signaling pathway. The metaflammation increased lipolysis in the adipose and enhanced hepatic lipid uptake and synthesis, consequently resulting in ectopic lipid deposition in the liver and hepatic injury.*

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**27 Myenteric Neurons Do Not Replicate in Small Intestine Under Normal Physiological Conditions in Adult Mouse**

H. Virtanen, D. R. Garton, and J.-O. Andressoo

See editorial, Goldstein AM, on page 239

*A controversial study by Kulkarni and colleagues has claimed that about 70% of myenteric neurons in the adult small intestine replicate in 1 week. Using the same and alternative methods, we find no evidence of neuronal replication.*

**35 The Host-Microbiome Response to Hyperbaric Oxygen Therapy in Ulcerative Colitis Patients**

C. G. Gonzalez, R. H. Mills, M. C. Kordahi, M. Carrillo-Terrazas, H. Secaira-Morocho, C. E. Widjaja, M. S. Tsai, Y. Mittal, B. A. Yee, F. Vargas, K. Weldon, J. M. Gauglitz, C. Delaroque, C. Saucedo, L.-A. Rossitto, G. Ackermann, G. Humphrey, A. D. Swafford, C. A. Siegel, J. C. Buckley Jr., L. E. Raffals, C. Sadler, P. Lindholm, K. M. Fisch, M. Valasek, A. Suriawinata, G. W. Yeo, P. Ghosh, J. T. Chang, H. Chu, P. Dorrestein, Q. Zhu, B. Chassaing, R. Knight, D. J. Gonzalez, and P. S. Dulai

*Hyperbaric oxygen therapy improves disease activity in ulcerative colitis through a reduction in STAT3 mediated neutrophil degranulation and shifts in microbial composition and metabolism. Treatment resistance is mediated by microbial adaptations to oxygen exposure, particularly for Akkermansia muciniphila.*

**55 The CEL-HYB1 Hybrid Allele Promotes Digestive Enzyme Misfolding and Pancreatitis in Mice**

X.-T. Mao, W.-B. Zou, Y. Cao, Y.-C. Wang, S.-J. Deng, D. N. Cooper, C. Férec, Z.-S. Li, J.-M. Chen, and Z. Liao

*The hybrid allele of the carboxyl ester lipase gene (CEL-HYB1) increases the risk of chronic pancreatitis. Here, we report that expression of a humanized form of CEL-HYB1 in mice promotes pancreatitis through protein misfolding, endoplasmic reticulum stress, and impaired autophagy.*

**75 Mannan-Binding Lectin via Interaction With Cell Surface Calreticulin Promotes Senescence of Activated Hepatic Stellate Cells to Limit Liver Fibrosis Progression**

J. Luo, L. Li, B. Chang, Z. Zhu, F. Deng, M. Hu, Y. Yu, X. Lu, Z. Chen, D. Zuo, and J. Zhou

*Mannan-binding lectin is a crucial component in the liver microenvironment. Here, we discovered that mannan-binding lectin–hepatic stellate cell interaction via cell surface calreticulin promotes senescence of activated hepatic stellate cells, contributing to the control of hepatic fibrosis progression.*

**101 Targeting USP9X–AMPK Axis in ARID1A-Deficient Hepatocellular Carcinoma**

F.-K. Zhang, Q.-Z. Ni, K. Wang, H.-J. Cao, D.-X. Guan, E.-B. Zhang, N. Ma, Y.-K. Wang, Q.-W. Zheng, S. Xu, B. Zhu, T.-W. Chen, J. Xia, X.-S. Qiu, X.-F. Ding, H. Jiang, L. Qiu, X. Wang, W. Chen, S.-Q. Cheng, D. Xie, and J.-J. Li

See editorial, Chan F-F and Wong C-M on page 241

*AT-rich interaction domain 1A loss renders hepatocellular carcinoma cells resistant to glucose deprivation via the ubiquitin-specific peptidase 9 X-linked–adenosine 5′-monophosphate-activated protein kinase axis, providing a synthetic lethal therapeutic strategy for AT-rich interaction domain 1A-deficient hepatocellular carcinoma.*

**129 Survival of Stem Cells and Progenitors in the Intestine Is Regulated by LPA<sub>5</sub>-Dependent Signaling**

Z. Liang, P. He, Y. Han, and C. C. Yun

*Lysophosphatidic acid, a bioactive phospholipid, mediates multiple cellular effects. Using a conditional knockout mouse, we show that lysophosphatidic acid receptor 5 is necessary for the survival of stem cells and progenitors in the intestine.*

**151 Interleukin 1 $\beta$  Blockade Reduces Intestinal Inflammation in a Murine Model of Tumor Necrosis Factor–Independent Ulcerative Colitis**

M. Liso, G. Verna, E. Cavalcanti, S. De Santis, R. Armentano, A. Tafaro, A. Lippolis, P. Campiglia, A. Gasbarrini, M. Mastronardi, T. T. Pizarro, F. Cominelli, L. R. Lopetuso, and M. Chieppa

*Anakinra administration represents a therapeutic option for tumor necrosis factor–independent ulcerative colitis subjects. Circulating interleukin 1 $\beta$  can predict the candidate subpopulation of ulcerative colitis patients non responder to the anti-tumor necrosis factor therapy, who may benefit from anakinra administration.*

**173 Single-Cell Analysis of Refractory Celiac Disease Demonstrates Inter- and Intra-Patient Aberrant Cell Heterogeneity**

T. Dieckman, M. Schreurs, A. Mahfouz, Y. Kooy-Winkelaar, A. Neefjes-Borst, G. Bouma, and F. Koning

*Using high-dimensional single-cell and spatial technologies, we demonstrate substantial intertumoral and intratumoral heterogeneity of the aberrant cell population in patients with refractory celiac disease type II (RCDII). These findings may have implications for future diagnostics and treatment of RCDII.*

**193 STIM1 Deficiency In Intestinal Epithelium Attenuates Colonic Inflammation and Tumorigenesis by Reducing ER Stress of Goblet Cells**

X. Liang, J. Xie, H. Liu, R. Zhao, W. Zhang, H. Wang, H. Pan, Y. Zhou, and W. Han  
[See editorial, Glauben R et al, on page 243](#)

*Stromal interaction molecule 1 deficiency in intestinal epithelium reduces goblet cell endoplasmic reticulum stress and subsequent cell loss induced by stressors through attenuating Ca<sup>2+</sup> overload, maintaining the mucus layer, and decreasing microbial exposure, therefore, rendering intestinal epithelium-specific stromal interaction molecule 1 conditional knockout mice less susceptible to colitis and colitis-associated colorectal cancer.*