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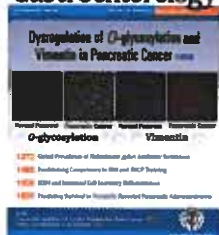
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*D. Leddin, D. A. Lieberman, F. Tse, A. N. Barkun, A. M. Abou-Setta, J. K. Marshall, N. J. Samadder, H. Singh, J. J. Telford, J. Tinmouth, A. N. Wilkinson, and G. I. Leontiadis*

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*C. Liu, M. L. Bettington, N. I. Walker, J. Dwine, G. F. Hartel, B. A. Leggett, and V. L. J. Whitehall*

High-level methylation in sessile serrated adenomas is an advanced molecular alteration that develops prior to development of dysplasia and cancer. It is strongly associated with patient age and proximal colonic site.

**1366 Interactions Between KIR3DS1 and HLA-F Activate Natural Killer Cells to Control HCV Replication in Cell Culture**

*S. Lunemann, A. Schöbel, J. Kah, P. Fittje, A. Hölzemer, A. E. Langeneckert, L. U. Hess, T. Poch, G. Martrus, W. F. Garcia-Beltran, C. Körner, A. E. Ziegler, L. Richert, K. J. Oldhafer, J. Schulze zur Wiesch, C. Schramm, M. Dandri, E. Herker, and M. Altfeld*

The activating Natural Killer cell receptor KIR3DS1 interacts with its ligand HLA-F on the surface of infected hepatocytes and contributes to the control of Hepatitis C virus infection.

**Full Reports****Clinical—Alimentary Tract****1372 Prevalence of Antibiotic Resistance in *Helicobacter pylori*: A Systematic Review and Meta-analysis in World Health Organization Regions**

*A. Savoldi, E. Carrara, D. Y. Graham, M. Conti, and E. Tacconelli*

See editorial on page 1300.

Primary resistance rates to clarithromycin, metronidazole, and levofloxacin were  $\geq 15\%$  in the majority of WHO regions while secondary resistance rates were  $\geq 15\%$  in all WHO regions.

**1383 Effects of Organized Colorectal Cancer Screening on Cancer Incidence and Mortality in a Large Community-Based Population**

*T. R. Levin, D. A. Corley, C. D. Jensen, J. E. Schottinger, V. P. Quinn, A. G. Zauber, J. K. Lee, W. K. Zhao, N. Udaltsova, N. R. Ghai, A. T. Lee, C. P. Quesenberry, B. H. Fireman, and C. A. Doubeni*

See editorial on page 1302.

Organized colorectal cancer (CRC) screening based on annual fecal immunochemical testing and colonoscopy rapidly increased screening participation to the  $\geq 80\%$  target set by national organizations and was associated with substantial decreases in CRC incidence and mortality.

**1392** **Equivalent Accuracy of 2 Quantitative Fecal Immunochemical Tests in Detecting Advanced Neoplasia in an Organized Colorectal Cancer Screening Program**

www

*E. Wieten, C. M. de Klerk, A. van der Steen, C. R. Ramakers, E. J. Kuipers, B. E. Hansen, I. Lansdorp-Vogelaar, P. M. Bossuyt, E. Dekker, and M. C. W. Spaander*

The two most commonly used fecal immunochemical tests in colorectal cancer (CRC) screening, FOB-Gold and OC-Sensor, have similar accuracy in detecting advanced neoplasia in an organized CRC screening program.

**1400** **No Difference in Colorectal Cancer Incidence or Stage at Detection by Colonoscopy Among 3 Countries With Different Lynch Syndrome Surveillance Policies**

www

*C. Engel, H. F. Vasen, T. Seppälä, S. Aretz, M. Bigirwamungu-Bargeman, S. Y. de Boer, K. Bucksch, R. Büttner, E. Holinski-Feder, S. Holzapfel, R. Hüneburg, M. A. J. M. Jacobs, H. Järvinen, M. Kloor, M. von Knebel Doeberitz, J. J. Koornstra, M. van Kouwen, A. M. Langers, P. C. van de Meeberg, M. Morak, G. Möslein, F. M. Nagengast, K. Pylvänäinen, N. Rahner, L. Renkonen-Sinisalo, S. Sanduleanu, H. K. Schackert, W. Schmigel, K. Schulmann, V. Steinke-Lange, C. P. Strassburg, J. Vecht, M.-L. Verhulst, W. de Vos tot Nederveen Cappel, S. Zachariae, J.-P. Mecklin, and M. Loeffler, on behalf of the German HNPCC Consortium, the Dutch Lynch Syndrome Collaborative Group, and the Finnish Lynch Syndrome Registry*

We compared colonoscopic surveillance data from three countries, each having different surveillance policies (annually, 1–2-yearly, 2–3-yearly), and found that strict annual colonoscopies were not associated with lower CRC incidence or earlier stages.

**1410** **Routine Molecular Analysis for Lynch Syndrome Among Adenomas or Colorectal Cancer Within a National Screening Program***A. Goverde, A. Wagner, M. J. Bruno, R. M. W. Hofstra, M. Doukas, M. M. van der Weiden, H. J. Dubbink, W. N. M. Dinjens, and M. C. W. Spaander*

Lynch syndrome is the most common hereditary colorectal cancer syndrome. These results indicate that routine screening for Lynch syndrome in adenoma patients within a population-based CRC screening program is not an effective strategy.

**1416** **Incidence, Risk Factors, and Clinical Effects of Recurrent Diverticular Hemorrhage: A Large Cohort Study**

www

*R. K. Vajravelu, R. Mamtani, F. I. Scott, A. Waxman, and J. D. Lewis*

The incidence rate of recurrent diverticular hemorrhage is more than 300 times that of an initial episode. Platelet aggregation inhibitors, but not anticoagulants, are risk factors for recurrent hemorrhage.

**Clinical—Liver****1428** **Association Between Magnetic Resonance Imaging–Proton Density Fat Fraction and Liver Histology Features in Patients With Nonalcoholic Fatty Liver Disease or Nonalcoholic Steatohepatitis**

CME www

*B. Wildman-Tobriner, M. M. Middleton, C. A. Moylan, S. Rossi, O. Flores, Z. A. Chang, M. F. Abdelmalek, C. B. Sirlin, and M. R. Bashir*

MRI proton density fat fraction (PDFF) values correlate with several liver histology features. However, liver biopsy should remain the gold standard for assessing those features.

**1436** **Incidence of Hepatocellular Carcinoma After Direct Antiviral Therapy for HCV in Patients With Cirrhosis Included in Surveillance Programs**

www

*P. Nahon, R. Layese, V. Bourcier, C. Cagnot, P. Marcellin, D. Guyader, S. Pol, D. Larrey, V. De Ledinghen, D. Ouzan, F. Zoulim, D. Roulot, A. Tran, J.-P. Bronowicki, J.-P. Zarski, G. Riachi, P. Calès, J.-M. Péron, L. Alric, M. Bourlière, P. Mathurin, J.-F. Blanc, A. Abergel, L. Serfaty, A. Mallat, J.-D. Grangé, P. Attali, Y. Bacq, C. Wartelle, T. Dao, D. Thabut, C. Pilette, C. Silvain, C. Christidis, E. Nguyen-Khac, B. Bernard-Chabert, D. Zucman, V. Di Martino, A. Sutton, F. Roudot-Thoraval, and E. Audureau, for the ANRS CO12 CirVir Group*

The apparent increase in HCC following DAAs can be explained by confounders favoring the development of liver cancer. These findings also suggest limited prior HCC surveillance programs in these patients, suggesting under-diagnosed cancerous focal lesions before DAA implementation.

**1451 Effects of Allocating Livers for Transplantation Based on Model for End-Stage Liver****(V) (www) Disease-Sodium Scores on Patient Outcomes**

*S. Nagai, L. C. Chau, R. E. Schilke, M. Safwan, M. Rizzari, K. Collins, A. Yoshida, M. S. Abouljoud, and D. Moonka*

The MELD-Na score-based liver allocation successfully improved waitlist outcomes. Given the discrepancy in transplant survival benefit, the current allocation rules may require revisiting; "Share 21" instead of "Share 15".

**1463 GS-0976 Reduces Hepatic Steatosis and Fibrosis Markers in Patients With Nonalcoholic Fatty Liver Disease**

*R. Loomba, Z. Kayali, M. Nouredin, P. Ruane, E. J. Lawitz, M. Bennett, L. Wang, E. Harting, J. M. Tarrant, B. J. McColgan, C. Chung, A. S. Ray, G. M. Subramanian, R. P. Myers, M. S. Middleton, M. Lai, M. Charlton, and S. A. Harrison*

**See editorial on page 1304.**

Patients with NAFLD treated with an inhibitor of acetyl-CoA carboxylase for 12 weeks had a meaningful decrease in liver fat that was accompanied by decreased markers of liver injury.

**Clinical—Pancreas****1474 Increased Levels of Branched-Chain Amino Acid Associated With Increased Risk of Pancreatic Cancer in a Prospective Case-Control Study of a Large Cohort**

*R. Katagiri, A. Goto, T. Nakagawa, S. Nishiumi, T. Kobayashi, A. Hidaka, S. Budhathoki, T. Yamaji, N. Sawada, T. Shimazu, M. Inoue, M. Iwasaki, M. Yoshida, and S. Tsugane*

In a large prospective study, increased plasma levels of branched-chain amino acids (BCAA) were associated with an increased risk of pancreatic cancer, particularly when the increase was observed 10 years or more prior to diagnosis.

**Clinical—Biliary****1483 Competence in Endoscopic Ultrasound and Endoscopic Retrograde Cholangiopancreatography, From Training Through Independent Practice**

*S. Wani, R. N. Keswani, S. Han, E. M. Aagaard, M. Hall, V. Simon, W. M. Abidi, S. Banerjee, T. H. Baron, M. Bartel, E. Bowman, B. C. Brauer, J. M. Buscaglia, L. Carlin, A. Chak, H. Chatrath, A. Choudhary, B. Confer, G. A. Coté, K. K. Das, C. J. DiMaio, A. M. Dries, S. A. Edmundowicz, A. H. El Chafic, I. El Hajj, S. Ellert, J. Ferreira, A. Gamboa, I. S. Gan, L. M. Gangarosa, B. Gannavarapu, S. R. Gordon, N. M. Guda, H. T. Hammad, C. Harris, S. Jalaj, P. S. Jowell, S. Kenshil, J. Klapman, M. L. Kochman, S. Komanduri, G. Lang, L. S. Lee, D. E. Loren, F. J. Lukens, D. Mullady, V. R. Muthusamy, A. S. Nett, M. S. Olyaei, K. Pakseresht, P. Perera, P. Pfau, C. Piraka, J. M. Poneris, A. Rastogi, A. Razzak, B. Riff, S. Saligram, J. M. Scheiman, I. Schuster, R. J. Shah, R. Sharma, J. P. Spaete, A. Singh, M. Sohail, J. Sreenarasimhaiah, T. Stevens, J. H. Tabibian, D. Tzimas, D. S. Uppal, S. Urayama, D. Vitterbo, A. Y. Wang, W. Wassef, P. Yachimski, S. Zepeda-Gomez, T. Zuchelli, and D. Early*

**See editorial on page 1307.**

Most advanced endoscopy trainees participating in a competency-based training program achieve competence in EUS and ERCP and meet quality indicator thresholds for these procedures at the end of their 1<sup>st</sup> year of independent practice.

**Basic and Translational—Alimentary Tract****1495 Inhibiting Growth of *Clostridioides difficile* by Restoring Valerate, Produced by the Intestinal Microbiota**

*J. A. K. McDonald, B. H. Mullish, A. Pechlivanis, Z. Liu, J. Brignardello, D. Kao, E. Holmes, J. V. Li, T. B. Clarke, M. R. Thursz, and J. R. Marchesi*

The short chain fatty acid valerate is depleted from the gut following antibiotic treatment and restored with FMT. Valerate significantly decreased *C difficile* growth in an interventional mouse model of infection.

**1508 Sox4 Promotes Atoh1-Independent Intestinal Secretory Differentiation Toward Tuft and Enteroendocrine Fates**

www

A. D. Gracz, L. A. Samsa, M. J. Fordham, D. C. Trotier, B. Zwarycz, Y.-H. Lo, K. Bao, J. Starmer, J. R. Raab, N. F. Shroyer, R. L. Reinhardt, and S. T. Magness

SOX4 is required for normal stem cell function and secretory differentiation in the intestinal epithelium and is sufficient for enteroendocrine and tuft cell lineage specification.

**1524 Deletion of Stearoyl-CoA Desaturase-1 From the Intestinal Epithelium Promotes Inflammation and Tumorigenesis, Reversed by Dietary Oleate**

www

S. Ducheix, C. Peres, J. Härdfeldt, C. Frau, G. Mocciaro, E. Piccinin, J.-M. Lobaccaro, S. De Santis, M. Chieppa, J. Bertrand-Michel, M. Plateroti, J. L. Griffin, C. Sabbà, J. M. Ntambi, and A. Moschetta

Using multidisciplinary gain and loss of function approaches, the authors identified a direct role for oleic acid in the prevention of intestinal inflammation and tumorigenesis.

**1539 Activated ATF6 Induces Intestinal Dysbiosis and Innate Immune Response to Promote Colorectal Tumorigenesis**

E www

O. I. Coleman, E. M. Lobner, S. Bierwirth, A. Sorbie, N. Waldschmitt, E. Rath, E. Berger, I. Lagkouravdos, T. Clavel, K. D. McCoy, A. Weber, M. Heikenwalder, K.-P. Janssen, and D. Haller

See editorial on page 1309.

A transcription factor (ATF6) of the misfolded-protein stress response is associated with poor prognosis in CRC patients. ATF6 has a causal role in tumorigenesis and is linked to innate bacterial sensing.

**1553 Tropheryma whipplei Increases Expression of Human Leukocyte Antigen-G on Monocytes to Reduce Tumor Necrosis Factor and Promote Bacterial Replication**

www

E. Ben Azzouz, A. Boumaza, S. Mezouar, M. Bardou, F. Carlini, C. Picard, D. Raoult, J.-L. Mège, and B. Desnues

The immunomodulatory molecule HLA-G is increased in patients with *Tropheryma whipplei* infections. *T. whipplei* induces the expression of HLA-G to reduce TNF expression, which may favor bacterial replication.

**Basic and Translational—Liver****1564 Simvastatin Prevents Progression of Acute on Chronic Liver Failure in Rats With Cirrhosis and Portal Hypertension**

www

D. M. Tripathi, M. Vilaseca, E. Lafoz, H. Garcia-Calderó, G. Viegas Haute, A. Fernández-Iglesias, J. Rodrigues de Oliveira, J. C. García-Pagán, J. Bosch, and J. Gracia-Sancho

Acute-on-chronic liver failure due to bacterial infection exacerbates hepatic and systemic inflammation, leading to aggravation in hepatic microvascular dysfunction and decreased survival. Simvastatin prevents these detrimental de-regulations.

**1578 Solute Carrier Organic Anion Transporter Family Member 3A1 Is a Bile Acid Efflux Transporter in Cholestasis**

www

Q. Pan, X. Zhang, L. Zhang, Y. Cheng, N. Zhao, F. Li, X. Zhou, S. Chen, J. Li, S. Xu, D. Huang, Y. Chen, L. Li, H. Wang, W. Chen, S.-y. Cai, J. L. Boyer, and J. Chai

OATP3A1 acts as a novel bile acid efflux transporter, facilitating removal of excessive bile acids in the liver. Thus, enhancement of OATP3A1 function may protect the liver from cholestasis-induced injury.

**Basic and Translational—Pancreas****1593 GNAS<sup>R201C</sup> Induces Pancreatic Cystic Neoplasms in Mice That Express Activated KRAS by Inhibiting YAP1 Signaling**

www

N. Ideno, H. Yamaguchi, B. Ghosh, S. Gupta, T. Okumura, D. J. Steffen, C. G. Fisher, L. D. Wood, A. D. Singhi, M. Nakamura, J. S. Gutkind, and A. Maitra

Expression of mutant GNAS caused a shift from phosphorylated YAP1-altering KRAS-mediated tumor progression to development of more differentiated cancer associated with cystic precursor lesions resembling human IPMN in mice.

**1608 Disruption of *C1galt1* Gene Promotes Development and Metastasis of Pancreatic Adenocarcinomas in Mice**

www COV

*S. Chugh, S. Barkeer, S. Rachagani, R. K. Nimmakayala, N. Perumal, R. Pothuraju, P. Atri, S. Mahapatra, I. Thapa, G. A. Talmon, L. M. Smith, X. Yu, S. Neelamegham, J. Fu, L. Xia, M. P. Ponnusamy, and S. K. Batra*

Genomic disruption of *C1galt1* along with *Kras* and *p53* mutations accelerates PDAC progression and metastasis. Loss of *C1galt1* results in truncation of MUC16 O-glycosylation that could promote PDAC aggressiveness.

**1625 Immune Cell and Stromal Signature Associated With Progression-Free Survival of Patients With Resected Pancreatic Ductal Adenocarcinoma**

E www

*U. M. Mahajan, E. Langhoff, E. Goni, E. Costello, W. Greenhalf, C. Halloran, S. Ormanns, S. Kruger, S. Boeck, S. Ribback, G. Beyer, F. Dombrowski, F.-U. Weiss, J. P. Neoptolemos, J. Werner, J. G. D'Haese, A. Bazhin, J. Peterhansl, S. Pichlmeier, M. W. Büchler, J. Kleeff, P. Ganesh, M. Sendler, D. H. Palmer, T. Kohlmann, R. Rad, I. Regel, M. M. Lerch, and J. Mayerle*

See editorial on page 1312.

The authors developed a histological signature to understand the influence of tissue composition in poor outcomes of pancreatic cancer. Immune infiltrate, not stromal cells, appears to determine tissue composition.

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