

# The American Journal of Pathology

*Official Journal of the American Society for Investigative Pathology*

August 2012 • Volume 181, Number 2

---

**On the Cover:** In the pig model of cystic fibrosis (CF), mucous cell metaplasia and duct cell proliferation do not have a primary role in the pathogenesis of pancreatic disease but are a late response to fetal inflammation and tissue destruction. As shown in newborn pigs, obstructed ducts are often distended with mucus (magenta area), and the mucous cells are prominent in the epithelium. Cells were treated with PAS stain. (See page 504.)

---

## 375 This Month in AJP

### ASIP Centennial Commentary

376 A Brief History of Anti-VEGF for the Treatment of Ocular Angiogenesis

*Leo A. Kim and Patricia A. D'Amore*

### Mini-Review

380 Decorin: A Guardian from the Matrix

*Thomas Neill, Liliana Schaefer, and Renato V. Iozzo*

### Commentary

388 Calpain Inhibition as a Potential Treatment of Alzheimer's Disease

*Godfrey S. Getz*

★ Related article appears on page 616

## Regular Articles

### Biomarkers, Genomics, Proteomics, and Gene Regulation

392 Long-Term Rescue of Dystrophin Expression and Improvement in Muscle Pathology and Function in Dystrophic *mdx* Mice by Peptide-Conjugated Morpholino

*Bo Wu, Peijuan Lu, Caryn Cloer, Mona Shaban, Snimar Grewal, Stephanie Milazi, Sapana N. Shab, Hong M. Moulton, and Qi Long Lu*

401 Genomic Deletion of *PTEN* Is Associated with Tumor Progression and Early PSA Recurrence in ERG Fusion-Positive and Fusion-Negative Prostate Cancer

*Antje Krohn, Tobias Diedler, Lia Burkhardt, Pascale-Sophie Mayer, Colin De Silva, Marie Meyer-Kornblum, Darja Kötschau, Pierre Tennstedt, Joseph Huang, Clarissa Gerhäuser, Malte Mader, Stefan Kurtz, Hüseyin Sirma, Fred Saad, Thomas Steuber, Markus Graefen, Christoph Plass, Guido Sauter, Ronald Simon, Sarah Minner, and Thorsten Schlomm*

413 CDKN1C/P57 Is Regulated by the Notch Target Gene *Hes1* and Induces Senescence in Human Hepatocellular Carcinoma

*Catia Giovannini, Laura Gramantieri, Manuela Minguzzi, Francesca Fornari, Pasquale Chieco, Gian Luca Grazi, and Luigi Bolondi*

423 Krüppel-Like Factor 10 Expression as a Prognostic Indicator for Pancreatic Adenocarcinoma

*Vincent H.S. Chang, Pei-Yi Chu, Shu-Ling Peng, Tsui-Lien Mao, Yan-Shen Shan, Ching-Fang Hsu, Chun-Yu Lin, Kelvin K.C. Tsai, Winston C.Y. Yu, and Hui-Ju Ch'ang*

Cardiovascular, Pulmonary, and Renal Pathology

- 431 Co-Exposure to Cigarette Smoke and Alcohol Decreases Airway Epithelial Cell Cilia Beating in a Protein Kinase C $\epsilon$ -Dependent Manner  
*Todd A. Wyatt, Joseph H. Sisson, Diane S. Allen-Gipson, Michael L. McCaskill, Jessica A. Boten, Jane M. DeVasure, Kristina L. Bailey, and Jill A. Poole*
- 441 Neonatal Oxygen Increases Sensitivity to Influenza A Virus Infection in Adult Mice by Suppressing Epithelial Expression of Ear1  
*Michael A. O'Reilly, Min Yee, Bradley W. Buczynski, Peter F. Vitiello, Peter C. Keng, Stephen L. Welle, Jacob N. Finkelstein, David A. Dean, and B. Paige Lawrence*

Cell Injury, Repair, Aging, and Apoptosis

- 452 NK Cells Modulate the Inflammatory Response to Corneal Epithelial Abrasion and Thereby Support Wound Healing  
*Qiong Liu, C. Wayne Smith, Wanyu Zhang, Alan R. Burns, and Zhibjie Li*
- 463 Interaction of CSR1 with XIAP Reverses Inhibition of Caspases and Accelerates Cell Death  
*Zhong-Liang Zheng, Lang-Zhu Tan, Yan P. Yu, George Michalopoulos, and Jian-Hua Luo*
- 472 Prevention of Age-Related Macular Degeneration-Like Retinopathy by Rapamycin in Rats  
*Nataliya G. Kolosova, Natalia A. Muraleva, Anna A. Zhdankina, Natalia A. Stefanova, Anzhela Z. Fursova, and Mikhail V. Blagosklonny*

Gastrointestinal, Hepatobiliary, and Pancreatic Pathology

- 478 Targeting  $\alpha$ -7 Nicotinic Acetylcholine Receptor in the Enteric Nervous System: A Cholinergic Agonist Prevents Gut Barrier Failure after Severe Burn Injury  
*Todd W. Costantini, Michael Krzyzaniak, Gerald A. Cheadle, James G. Putnam, Ann-Marie Hageny, Nicole Lopez, Brian P. Eliceiri, Vishal Bansal, and Raul Coimbra*
- 487 Methylation-Dependent Activation of CDX1 through NF- $\kappa$ B: A Link from Inflammation to Intestinal Metaplasia in the Human Stomach  
*Tilman T. Rau, Anja Rogler, Myrjam Frischauf, Andreas Jung, Peter C. Konturek, Arno Dimmler, Gerhard Fallner, Bettina Sebnert, Wael El-Rifai, Arndt Hartmann, Reinhard E. Voll, and Regine Schneider-Stock*
- 499 Pancreatic Damage in Fetal and Newborn Cystic Fibrosis Pigs Involves the Activation of Inflammatory and Remodeling Pathways  
*Maisam Abu-El-Hajja, Shyam Ramachandran, David K. Meyerbolz, Marwa Abu-El-Hajja, Michelle Griffin, Radhama L. Giriyyappa, David A. Stoltz, Michael J. Welsh, Paul B. McCray Jr., and Aliye Uc*

Immunopathology and Infectious Diseases

- 508 Activated B Cells in the Granulomas of Nonhuman Primates Infected with *Mycobacterium tuberculosis*  
*Jia Yao Phuab, Joshua T. Mattila, Philana L. Lin, and JoAnne L. Flynn*
- 515 Spread of Classic BSE Prions from the Gut via the Peripheral Nervous System to the Brain  
*Martin Kaatz, Christine Fast, Ute Ziegler, Anne Balkema-Buschmann, Bärbel Hammerschmidt, Markus Keller, Anja Oelschlegel, Leila McIntyre, and Martin H. Groschup*
- 525 Role of miR-132 in Angiogenesis after Ocular Infection with Herpes Simplex Virus  
*Sachin Mulik, John Xu, Pradeep B.J. Reddy, Naveen K. Rajasagi, Fernanda Gimenez, Shalini Sharma, Patrick Y. Lu, and Barry T. Rouse*
- 535 Toward Homeostasis: Regulatory Dendritic Cells from the Bone Marrow of Mice with Inflammation of the Airways and Peritoneal Cavity  
*Naomi M. Scott, Royce L.X. Ng, Deborah H. Strickland, Jacqueline L. Bisley, Scott A. Bazely, Shelley Gorman, Mary Norval, and Prue H. Hart*

Metabolic, Endocrine, and Genitourinary Pathobiology

- 548 Increased Smooth Muscle Contractility in Mice Deficient for Neuropilin 2  
*Diane R. Bielenberg, Abbisbek Seth, Akio Sbimizu, Kristine Pelton, Vivian Cristofaro, Aruna Ramachandran, Bernadette M.M. Zwaans, Cheng Chen, Ramaswamy Krishnan, Meetu Seth, Lin Huang, Seiji Takashima, Michael Klagsbrun, Maryrose P. Sullivan, and Rosalyn M. Adam*

- 560 Global Levels of H3K27me3 Track with Differentiation *in Vivo* and Are Deregulated by MYC in Prostate Cancer  
*Laxmi G. Pellakuru, Tsuyoshi Iwata, Bora Gurel, Denise Schultz, Jessica Hicks, Carlise Bethel, Srinivasan Yegnasubramanian, and Angelo M. De Marzo*

- 570 Thrombospondin-1 Mimetic Peptide ABT-898 Affects Neovascularization and Survival of Human Endometriotic Lesions in a Mouse Model  
*Diane S. Nakamura, Andrew K. Edwards, Sobia Virani, Richard Thomas, and Chandrakant Tayade*

Molecular Pathogenesis of Genetic and Inherited Diseases

- 583 AMPK Activation Stimulates Autophagy and Ameliorates Muscular Dystrophy in the *mdx* Mouse Diaphragm  
*Marion Pauly, Frederic Daussin, Yan Burelle, Tong Li, Richard Godin, Jeremy Fauconnier, Christelle Koechlin-Ramonatxo, Gerald Hugon, Alain Lacampagne, Marjorie Coisy-Quivy, Feng Liang, Sabah Hussain, Stefan Matecki, and Basil J. Petrof*

- 593 Defective T-Lymphocyte Migration to Muscles in Dystrophin-Deficient Mice  
*Cynthia M. Cascabulho, Cristiane Bani Corrêa, Vinicius Cotta-de-Almeida, and Andrea Henriques-Pons*

- 605 Mutations of the Serine Protease *CAP1/Prss8* Lead to Reduced Embryonic Viability, Skin Defects, and Decreased ENaC Activity  
*Simona Frateschi, Anna Keppner, Samedba Malsure, Justyna Iwaszkiewicz, Chloé Sergi, Anne-Marie Merillat, Nicole Fowler-Jaeger, Nadia Randrianarison, Carole Planès, and Edith Hummler*

Neurobiology

- 616 Calpain Inhibitor A-705253 Mitigates Alzheimer's Disease-Like Pathology and Cognitive Decline in Aged 3xTgAD Mice  
*Rodrigo Medeiros, Masashi Kitazawa, Meredith A. Chabrier, David Cheng, David Baglietto-Vargas, Andreas Kling, Achim Moeller, Kim N. Green, and Frank M. LaFerla*

★ Related Commentary appears on page 387

- 626 The Mutation in *Chd7* Causes Misexpression of *Bmp4* and Developmental Defects in Telencephalic Midline  
*Xuan Jiang, Yue Zhou, Li Xian, Weiqian Chen, Hanwei Wu, and Xiang Gao*

- 642 Kinetics of Proinflammatory Monocytes in a Model of Multiple Sclerosis and Its Perturbation by Laquinimod  
*Manoj K. Mishra, Janet Wang, Claudia Silva, Mathias Mack, and V. Wee Yong*

Tumorigenesis and Neoplastic Progression

- 652 Cytoplasmic NANOG-Positive Stromal Cells Promote Human Cervical Cancer Progression  
*Ting-Ting Gu, Shu-Yan Liu, and Peng-Sheng Zheng*

- 662 ECT2 and RASAL2 Mediate Mesenchymal-Amoeboid Transition In Human Astrocytoma Cells  
*Adrienne Weeks, Nadia Okolowsky, Brian Golbourn, Stacey Ivanchuk, Christian Smith, and James T. Rutka*

- 675 Nuclear Exclusion of TET1 Is Associated with Loss of 5-Hydroxymethylcytosine in *IDH1* Wild-Type Gliomas  
*Tim Müller, Marco Gessi, Anke Waba, Lukas Jan Isselstein, Daniel Luxen, Dorothee Freiboff, Johannes Freiboff, Albert Becker, Matthias Simon, Jennifer Hammes, Dorota Denkhaus, Anja zur Mühlen, Torsten Pietsch, and Andreas Waba*

- 684 Transcriptional Up-Regulation of Sox9 by NF- $\kappa$ B in Endometrial Carcinoma Cells, Modulating Cell Proliferation Through Alteration in the p14<sup>ARF</sup>/p53/p21<sup>WAF1</sup> Pathway  
*Makoto Saegusa, Miki Hashimura, Erina Suzuki, Tsutomu Yoshida, and Takeshi Kuwata*

Vascular Biology, Atherosclerosis, and Endothelium Biology

- 693 Highly Invasive Melanoma Cells Activate the Vascular Endothelium via an MMP-2/Integrin  $\alpha$ v $\beta$ 5-Induced Secretion of VEGF-A  
*Anna Desch, Elwira A. Strozyk, Alexander T. Bauer, Volker Huck, Verena Niemeyer, Thomas Wieland, and Stefan W. Schneider*

706 Fenofibrate Increases High-Density Lipoprotein and Sphingosine 1 Phosphate Concentrations Limiting Abdominal Aortic Aneurysm Progression in a Mouse Model  
*Smriti M. Krishna, Sai Wang Seto, Joseph V. Moxon, Catherine Rush, Philip J. Walker, Paul E. Norman, and Jonathan Golledge*

719 CD11b<sup>+</sup> Bone Marrow-Derived Monocytes Are the Major Leukocyte Subset Responsible for Retinal Capillary Leukostasis in Experimental Diabetes in Mouse and Express High Levels of CCR5 in the Circulation  
*Andreia M. Serra, Jennifer Waddell, Ayyakkannu Manivannan, Heping Xu, Mary Cotter, and John V. Forrester*

**ASIP Semiannual 2012/2 AJP CME Program in Pathogenesis** appears online. See <http://www.asip.org/CME/journalCME.htm> for educational goals, registration, and examination details. The planning committee members and staff have no relevant financial relationships with commercial interest to disclose. Relevant financial relationships of the authors of selected articles in this journal-based CME activity will be disclosed in a footnote to the published article and in each journal CME examination. See below for CME accreditation statement.

▼ denotes participating articles in this issue

---

**CME Accreditation Statement:** This activity ("ASIP Semiannual 2012/2 AJP CME Program in Pathogenesis") has been planned and implemented in accordance with the Essential Areas and policies of the Accrediation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the American Society for Clinical Pathology (ASCP) and the American Society for Investigative Pathology (ASIP). ASCP is accredited by the ACCME to provide continuing medical education for physicians.

The ASCP designates this journal-based CME activity ("ASIP Semiannual 2012/2 AJP CME Program in Pathogenesis") for a maximum of 24 AMA PRA Category 1 Credit(s)<sup>™</sup>. Physicians should only claim credit commensurate with the extent of their participation in the activity.