

# The American Journal of Pathology

Official Journal of the American Society for Investigative Pathology

May 2012 • Volume 180, Number 5

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**On the Cover:** A novel system is presented for 3D histological reconstruction that integrates whole-slide imaging (virtual slides), image serving, registration, and 3D visualization into a single package. The system can be used to reconstruct entire tissue blocks at a microscopic level. Examples are illustrated for 3D volume rendering (left) and 3D visualization (right) of anatomical features of a mouse embryo. (See page 1835.)

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## 1761 This Month in *AJP*

### ASIP Centennial Review

1762 Alzheimer's Disease 2012: The Great Amyloid Gamble

*Vincent T. Marchesi*

### Commentary

1768 Nature versus Nurture in Glioblastoma: Microenvironment and Genetics Can Both Drive Mesenchymal Transcriptional Signature

*Brent A. Orr and Charles G. Eberhart*

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### Short Communications

1772 MicroRNA 96 Is a Post-Transcriptional Suppressor of Anaplastic Lymphoma Kinase Expression

*Deeksha Vishwamitra, Yong Li, Desiree Wilson, Roxsan Manshouri, Choladda V. Curry, Bin Shi, Xi Ming Tang, Andrea M. Sheehan, Ignacio I. Wistuba, Ping Shi, and Hesham M. Amin*

1781 Genetic Polymorphisms of *DNMT3L* Involved in Hypermethylation of Chromosomal Ends Are Associated with Greater Risk of Developing Ovarian Endometriosis

*Bruno Borghese, Pietro Santulli, Delphine Héquet, Guillaume Pierre, Dominique de Ziegler, Daniel Vaiman, and Charles Chapron*

### Regular Articles

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

1787 MicroRNA 15a, Inversely Correlated to PKC $\alpha$ , Is a Potential Marker to Differentiate between Benign and Malignant Renal Tumors in Biopsy and Urine Samples

*Melanie von Brandenstein, Jency J. Pandarakalam, Lukas Kroon, Heike Loeser, Jan Herden, Gabriele Braun, Katherina Wendland, Hans P. Dienes, Ulrich Engelmann, and Jochen W.U. Fries*

1798 Co-Expression of XIAP and Cyclin D1 Complex Correlates with a Poor Prognosis in Patients with Hepatocellular Carcinoma

*Yufang Che, Fei Ye, Ruliang Xu, Haitao Qing, Xinying Wang, Fei Yin, Miao Cui, David Burstein, Bo Jiang, and David Y. Zhang*

1808 miR-143, miR-222, and miR-452 Are Useful as Tumor Stratification and Noninvasive Diagnostic Biomarkers for Bladder Cancer

*Patricia Puerta-Gil, Rodrigo García-Baquero, Angela Y. Jia, Sara Ocaña, Miguel Alvarez-Múgica, Jose L. Alvarez-Ossorio, Carlos Cordon-Cardo, Fernando Cava, and Marta Sánchez-Carbayo*

1816 Amplification of the *STOML3*, *FREM2*, and *LHFP* Genes Is Associated with Mesenchymal Differentiation in Gliosarcoma

*Masaya Nagaishi, Young-Ho Kim, Michel Mittelbronn, Felice Giangaspero, Werner Paulus, Benjamin Brokinkel, Anne Vital, Yuko Tanaka, Yoichi Nakazato, Catherine Legras-Lachuer, Joel Lachuer, and Hiroko Ohgaki*

Continued

- 1824 Cathepsin E, Maspin, Plk1, and Survivin Are Promising Prognostic Protein Markers for Progression in Non-Muscle Invasive Bladder Cancer  
*Niels Frstrup, Benedicte P. Ulbøi, Karin Birkenkamp-Demtröder, Francisco Mansilla, Marta Sanchez-Carbayo, Ulrika Segersten, Per-Uno Malmström, Arndt Hartmann, Joan Palou, Miguel Alvarez-Múgica, Karsten Zieger, Michael Borre, Torben F. Ørntoft, and Lars Dyrskjøt*
- Biophysical Imaging and Computational Biology*
- 1835 Toward Routine Use of 3D Histopathology as a Research Tool  
*Nicholas Roberts, Derek Magee, Yi Song, Keeran Brabazon, Mike Shires, Doreen Crellin, Nicolas M. Orsi, Richard Quirke, Philip Quirke, and Darren Treanor*
- Cardiovascular, Pulmonary, and Renal Pathology*
- 1843 Genetic Susceptibility to Experimental Autoimmune Glomerulonephritis in the Wistar Kyoto Rat  
*John Reynolds, Paul R. Cook, Jacques Behmoaras, Jennifer Smith, Gurjeet Bhangal, Susan Tadros, Jonathan Tee, Alan D. Salama, David J. Evans, Timothy J. Aitman, H. Terence Cook, and Charles D. Pusey*
- 1852 Arteriolar Lesions in Renal Transplant Biopsies: Prevalence, Progression, and Clinical Significance  
*Verena Bröcker, Victoria Schubert, Irina Scheffner, Anke Schwarz, Marcus Hiss, Jan Ulrich Becker, Ralph Scherer, Hermann Haller, Hans Heinrich Kreipe, Michael Mengel, and Wilfried Gwinner*
- 1863 MT1-MMP-Dependent Remodeling of Cardiac Extracellular Matrix Structure and Function Following Myocardial Infarction  
*Gerald C. Koenig, R. Grant Rowe, Sharlene M. Day, Farideh Sabeh, Jeffrey J. Atkinson, Kenneth R. Cooke, and Stephen J. Weiss*
- Cell Injury, Repair, Aging, and Apoptosis*
- 1879 Age-Related Dysfunction of the Lacrimal Gland and Oxidative Stress: Evidence from the Cu,Zn-Superoxide Dismutase-1 (*Sod1*) Knockout Mice  
*Takashi Kojima, Tais H. Wakamatsu, Murat Dogru, Yoko Ogawa, Ayako Igarashi, Osama M.A. Ibrahim, Takaaki Inaba, Takahiko Shimizu, Setsuko Noda, Hiroto Obata, Shigeru Nakamura, Alda Wakamatsu, Takuji Shirasawa, Jun Shimazaki, Kazuno Negishi, and Kazuo Tsubota*
- 1897 Focal Immune-Mediated White Matter Demyelination Reveals an Age-Associated Increase in Axonal Vulnerability and Decreased Remyelination Efficiency  
*David W. Hampton, Neill Innes, Doron Merkler, Chao Zhao, Robin J.M. Franklin, and Siddharthan Chandran*
- Epithelial and Mesenchymal Cell Biology*
- 1906 PI3 Kinase  $\delta$  Is a Key Regulator of Synoviocyte Function in Rheumatoid Arthritis  
*Beatrix Bartok, David L. Boyle, Yi Liu, Pingda Ren, Scott T. Ball, William D. Bugbee, Christian Rommel, and Gary S. Firestein*
- 1917 Evidence for Baseline Retinal Pigment Epithelium Pathology in the Trp1-Cre Mouse  
*Aristomenis Thanos, Yuki Morizane, Yusuke Murakami, Andrea Gianti, Dimosthenis Mantopoulos, Maki Kayama, Mi In Rob, Norman Michaud, Basil Pawlyk, Michael Sandberg, Lucy H. Young, Joan W. Miller, and Demetrios G. Vavvas*
- Gastrointestinal, Hepatobiliary, and Pancreatic Pathology*
- 1928 Enhanced Expression of Fibroblast Growth Factor Receptor 2 IIIc Promotes Human Pancreatic Cancer Cell Proliferation  
*Toshiyuki Ishiwata, Yoko Matsuda, Tetsushi Yamamoto, Eiji Uchida, Murray Korc, and Zenya Naito*
- 1942 Phosphorylation of sst2 Receptors in Neuroendocrine Tumors after Octreotide Treatment of Patients  
*Beatrice Waser, Renzo Cescato, Qisbeng Liu, Yachu J. Kao, Meike Körner, Emanuel Christ, Agnes Schonbrunn, and Jean Claude Reubi*
- Growth Factors, Cytokines, and Cell Cycle Molecules*
- 1950 Altered Expression of CX3CL1 in Patients with Epilepsy and in a Rat Model  
*Yali Xu, Kebin Zeng, Yanbing Han, Liang Wang, Dan Chen, Zhiqin Xi, Heng Wang, Xuefeng Wang, and Guojun Chen*

*Continued*

1963 Cytokine-Like Factor 1 Gene Expression Is Enriched in Idiopathic Pulmonary Fibrosis and Drives the Accumulation of CD4<sup>+</sup> T Cells in Murine Lungs: Evidence for an Antifibrotic Role in Bleomycin Injury  
*Daniel J. Kass, Guoying Yu, Katrina S. Lob, Asaf Savir, Alain Borczuk, Reban Kabloon, Brenda Juan-Guardela, Giuseppe DeLuca, John Tedrow, Jiin Choi, Thomas Richards, Najtali Kaminski, and Steven M. Greenberg*

1979 A Novel, Dual Role of CCN3 in Experimental Glomerulonephritis: Pro-Angiogenic and Antimesangioproliferative Effects  
*Claudia R.C. van Roeyen, Peter Boor, Erawan Borkham-Kamphorst, Song Rong, Uta Kunter, Ina V. Martin, Ana Kaitovic, Stefan Fleckenstein, Bernard Perbal, Christian Trautwein, Ralf Weiskirchen, Tammo Ostendorf, and Jürgen Floege*

Immunopathology and Infectious Diseases

1991 Phenotypic Changes to the Endogenous Antigen-Specific CD8<sup>+</sup> T Cell Response Correlates with the Development and Resolution of Allergic Airway Disease  
*Jeffrey T. McNamara, Craig M. Schramm, Anurag Singh, Eric R. Secor, Jr., Linda A. Guernsey, Leo Lefrançois, and Roger S. Thrall*

2001 IFN- $\gamma$ -Driven IDO Production from Macrophages Protects IL-4R $\alpha$ -Deficient Mice against Lethality during *Schistosoma mansoni* Infection  
*Reena Rani, Michael B. Jordan, Senad Divanovic, and De'Broski R. Herbert*

2009 Promotion of a Functional B Cell Germinal Center Response after Leishmania Species Co-Infection Is Associated with Lesion Resolution  
*Katherine N. Gibson-Corley, Paola M. Boggiatto, Marie M. Bockenstedt, Christine A. Petersen, Thomas J. Waldschmidt, and Douglas E. Jones*

2018 Resolvin D1 Receptor Stereoselectivity and Regulation of Inflammation and Proresolving MicroRNAs  
*Sriram Krishnamoorthy, Antonio Recchiuti, Nan Chiang, Gabrielle Fredman, and Charles N. Serhan*

Matrix Pathobiology

2028 Interaction of Clusterin and Matrix Metalloproteinase-9 and Its Implication for Epithelial Homeostasis and Inflammation  
*Shinwu Jeong, Dolena R. Ledee, Gabriel M. Gordon, Tatsuo Itakura, Nitin Patel, Aaron Martin, and M. Elizabeth Fini*

2040 A Mouse Model of Schwartz-Jampel Syndrome Reveals Myelinating Schwann Cell Dysfunction with Persistent Axonal Depolarization *in Vitro* and Distal Peripheral Nerve Hyperexcitability When Perlecan Is Lacking  
*Marie Bangratz, Nadège Sarrazin, Jérôme Devaux, Désirée Zambroni, Andoni Echaniz-Laguna, Frédérique René, Delphine Boério, Claire-Sophie Davoine, Bertrand Fontaine, Maria Laura Feltri, Evelyne Benoit, and Sophie Nicole*

2056 Heparan Sulfate Subdomains that are Degraded by Sulf Accumulate in Cerebral Amyloid  $\beta$  Plaques of Alzheimer's Disease: Evidence from Mouse Models and Patients  
*Tomomi Hosono-Fukao, Shiori Ohtake-Niimi, Hitomi Hoshino, Markus Britschgi, Hiroyasu Akatsu, Md. Motarab Hossain, Kazuchika Nishitsuji, Toin H. van Kuppevelt, Koji Kimata, Makoto Michikawa, Tony Wyss-Coray, and Kenji Uchimura*

Musculoskeletal Pathology

2068 The F508del Mutation in Cystic Fibrosis Transmembrane Conductance Regulator Gene Impacts Bone Formation  
*Carole Le Henaff, Annelise Gimenez, Eric Haÿ, Caroline Marty, Pierre Marie, and Jacky Jacquot*

2076 Aberrant Calreticulin Expression Is Involved in the Dedifferentiation of Dedifferentiated Liposarcoma  
*Masanori Hisaoka, Atsuji Matsuyama, and Mitsubiro Nakamoto*

Stem Cells, Tissue Engineering, and Hematopoietic Elements

2084 Malignant Germ Cell-Like Tumors, Expressing Ki-1 Antigen (CD30), Are Revealed during *in Vivo* Differentiation of Partially Reprogrammed Human-Induced Pluripotent Stem Cells  
*Frank Griscelli, Olivier Féraud, Noufissa Oudbiri, Emilie Gobbo, Ibrahim Casal, Jean-Claude Chomel, Ivan Bièche, Pierre Duwillard, Paule Opolon, Ali G. Turban, and Annelise Bennaceur-Griscelli*

Tumorigenesis and Neoplastic Progression

2097 PIAS1 Is Increased in Human Prostate Cancer and Enhances Proliferation through Inhibition of p21  
*Julia Hoefler, Georg Schäfer, Helmut Klocker, Holger H. H. Erb, Ian G. Mills, Ludger Hengst, Martin Pubr, and Zoran Culig*

2108 The Tumor Microenvironment Strongly Impacts Master Transcriptional Regulators and Gene Expression Class of Glioblastoma

*Lee A.D. Cooper, David A. Gutman, Candace Chisolm, Christina Appin, Jun Kong, Yuan Rong, Tahsin Kurc, Erwin G. Van Meir, Joel H. Saltz, Carlos S. Moreno, and Daniel J. Brat*

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2120 Yin Yang 1 Plays an Essential Role in Breast Cancer and Negatively Regulates p27

*Meimei Wan, Weiwei Huang, Timothy E. Kute, Lance D. Miller, Qiang Zhang, Heather Hatcher, Jingxuan Wang, Daniel B. Stovall, Gregory B. Russell, Paul D. Cao, Zhiyong Deng, Wei Wang, Qingyuan Zhang, Ming Lei, Suzy V. Torti, Steven A. Akman, and Guangchao Sui*

Vascular Biology, Atherosclerosis, and Endothelium Biology

2134 Immune Modulation of Vascular Resident Cells by Axl Orchestrates Carotid Intima-Media Thickening  
*Janice Gerloff and Vyacheslav A. Korsbunov*

2144 Cartilage Destruction in Granulomatosis with Polyangiitis (Wegener's Granulomatosis) Is Mediated by Human Fibroblasts after Transplantation into Immunodeficient Mice

*Nina Kesel, Dorothee Köhler, Lena Herich, Martin Laudien, Konstanze Holl-Ulrich, Astrid Jüngel, Michel Neidhart, Steffen Gay, Renate E. Gay, Elena Csernok, Peter Lamprecht, Wolfgang L. Gross, Udo Schumacher, and Sebastian Ulrich*

2156 Skeletal Muscle-Specific Genetic Determinants Contribute to the Differential Strain-Dependent Effects of Hindlimb Ischemia in Mice

*Joseph M. McClung, Timothy J. McCord, Seboon Keum, Soraya Johnson, Brian H. Annex, Douglas A. Marchuk, and Christopher D. Kontos*

2170 Lysophosphatidic Acid Induces Lymphangiogenesis and IL-8 Production *in Vitro* in Human Lymphatic Endothelial Cells

*Hong Mu, Tiffany L. Calderone, Michael A. Davies, Victor Prieto, Hua Wang, Gordon B. Mills, Menashe Bar-Eli, and Jeffrey E. Gershenwald*

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▀ denotes participating articles in this issue

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