Laboratory Investigation (2016) 96, 1144–1146

EDITORIAL

Laboratory Investigation web focus on China

Catherine M Ketcham[1], Akihiro Umezawa[2], Hejian Zou[3] and Gene P Siegal[4]

The vast growth of China's publishing output is a reflection of the increasing strength of Chinese science. The editors of *Laboratory Investigation* (*LI*) present a collection of papers that showcases research by authors from institutions across China, highlighting the significant contributions of Chinese scientists to the journal.

Laboratory Investigation (2016) **96,** 1144–1146; doi:10.1038/labinvest.2016.110

The editors of *Laboratory Investigation* (LI) are proud to present a Web Focus that features research by authors from institutions across China. We selected 20 recent papers to highlight the significant contributions of Chinese scientists to LI and to introduce the journal to an even wider audience.

Why did we select China?

From 2005 to 2015, submissions from Chinese institutions to *Laboratory Investigation* (*LI*) increased tenfold, and in 2015, 31% of the papers published in the journal had corresponding authors from China. This was no surprise to the editors. The increasing strength of Chinese science is abundantly clear in the Nature Index, a database of author affiliations from research articles published in a group of 68 high-quality journals. In 2015, China ranked second in publishing output in the Nature Global Index. In addition, from 2012–2014, the growth of China's publishing output in the index vastly surpassed that of any other nation. (Note: *LI* is not a part of the Nature Index.)

The scope of *LI*

LI is the basic and translational pathology research journal owned by the United States and Canadian Academy of Pathology and published by Springer Nature. *LI* is among the most highly cited general experimental pathology journals in the English language, with an impact factor of 4.202. We publish original research in all biomedical disciplines relating to the understanding of human disease and reports of new methods for the diagnosis of disease. Both human and experimental studies are welcome. The focus of LI is mechanistic, with a need for rigorous functional data. The broad scope of the journal is demonstrated below by the brief summaries of the papers in the Web Focus.

Review articles

Review articles in *LI* summarize timely topics and contain both in-depth analyses and unique insights. The review article by Yang *et al*[1] describes recent progress in the understanding WNT/β-catenin signaling in physiology, stem cell differentiation, and several types of cancer. The authors also discuss therapeutic opportunities for targeting Wnt/β-catenin. In the second review article, Zhang *et al*[2] apply multifactorial theory to study the causal relationship between Parkinson's disease and paraquat exposure.

Technical reports

LI publishes substantive technical reports (TR) that describe novel technical advances or new model systems for the investigation and diagnosis of human disease. The first TR in this Web Focus, by Chen *et al*,[3] outlines the establishment of an animal model to examine the role of the gasotransmitter SO_2 in the pathogenesis of acute lung injury. In the second, Xue *et al*[4] describe a robust protocol for cell-of-origin classification of diffuse large B-cell lymphoma using RNA samples from formalin-fixed paraffin-embedded tissues and massive parallel quantitative reverse transcription polymerase chain reaction. The final TR in this collection, by Liang *et al*,[5] defines a murine model of systemic sclerosis that will be useful to investigate immunological mechanisms and test therapeutic interventions for the human disease.

[1]United States and Canadian Academy of Pathology, Evans, GA, USA; [2]Department of Reproductive Biology, National Institute for Child Health and Development, Tokyo, Japan; [3]Division of Rheumatology, Huashan Hospital, Fudan University, Shanghai, China and [4]Department of Pathology, The University of Alabama at Birmingham, Birmingham, AL, USA
Correspondence:
E-mail: labinvest@comcast.net

Research articles

Most papers in *LI* fall into the category of research articles. The papers described below emphasize the fact that the journal has a broad focus which covers all organ systems and a wide range of topics such as cancer, inflammation and/or fibrosis, autoimmunity, and infectious disease.

Lung

We include two papers that address the mechanisms of pulmonary fibrosis. In the first, Zhang *et al*[6] reveal the role of cathepsin B in the interstitial lung disease associated with polymyositis and dermatomyositis, and show that an inhibitor of the enzyme decreases inflammation, fibrosis, and apoptosis in the lung through downregulation of TGF-β1. The paper by Xing *et al*[7] shows that binding of lipopolysaccharide to toll-like receptor 4 results in activation of histone deacetylases that promote the deacetylation of histones H3 and H4 at the Thy-1 gene promoter region, leading to Thy-1 gene silencing and lung fibroblast proliferation.

The majority of diagnosed lung cancer cases are non-small cell lung cancers, and the paper by Nie *et al*[8] shows that stathmin 1 may be a much-needed new prognostic marker. Stathmin 1 is a microtubule-depolymerizing protein that correlates with poor tumor differentiation, large tumor size and advanced stage, and its knockdown in lung cancer cells decreases proliferation and invasion.

Heart

In an intriguing study, Qiang *et al*[9] demonstrated the capacity of human amniotic mesenchymal stem cells to ameliorate lung injury in an animal model of cardiopulmonary bypass. Transplantation of stem cells inhibited the pathological immune processes contributing to ischemia/reperfusion injury by regulating inflammatory molecules.

Kidney

Diabetic nephropathy is a leading cause of end-stage renal disease. In the paper by Cao *et al*,[10] two endoplasmic reticulum stress inhibitors are shown to prevent hyperglycemia-induced podocyte apoptosis, decrease urinary albuminuria, and attenuate mesangial expansion. Another study, by Xiao *et al*,[11] may offer a new therapeutic intervention for the ultrafiltration failure seen after long-term use of peritoneal dialysis for renal replacement therapy. Overexpression of microRNA-129-5p can protect against the development of fibrosis by prevention of mesothelial/epithelial–mesenchymal transition via the SIP1 and SOX4 pathways.

Liver

There are no effective drugs to inhibit the fibrosis that develops in chronic liver disease, which may result in cirrhosis, liver failure, and portal hypertension. Zhang *et al*[12] used a rat model of cholestatic liver fibrosis to show that Notch signaling is required for differentiation of hepatic progenitor cells into cholangiocytes, indicating that Notch inhibition may offer a new approach for treatment of biliary liver fibrosis. Another paper, by Yu *et al*,[13] shows that miRNA-17-5p expression is increased during liver fibrosis and that Smad7 is its direct target, revealing a new therapeutic target for liver fibrosis.

Hepatocellular carcinoma, the most common primary malignancy of the liver, is highly aggressive and resistant to chemotherapy and radiotherapy. The study presented by Wei *et al*[14] shows that treatment with 17β-estradiol inhibits the malignant behavior of hepatocellular carcinoma cells through MAPK pathway-mediated upregulation of the NLRP3 inflammasome. A separate paper, by Tang *et al*,[15] shows that the anti-aging enzyme Klotho inhibits the Wnt/β-catenin pathway in hepatocellular carcinoma and may function as a tumor suppressor. Furthermore, serum Klotho levels appear to be a prognostic biomarker.

Gastrointestinal system

Though miRNAs have many functions, they can play crucial roles in carcinogenesis and cancer progression. The first digestive tract paper in this series, by He *et al*,[16] shows that expression of miR-186 is downregulated in esophageal squamous cell carcinoma, and is associated with differentiation, stage, and metastasis. They also determine that miR-186 has a suppressive role in this disease via the SKP2 ubiquitination/proteasomal degradation pathway and is therefore a potential therapeutic target. In a separate work, Shi *et al*[17] show that miR-518a-5p is downregulated in imatinib-resistant gastrointestinal stromal tumors, and that PIK3C2A is its gene-specific target. Mechanistically, miR-518a-5p reduces proliferation and promotes apoptosis, so that low expression of miR-518a-5p up-regulates PIK3C2A and affects the cellular response to the drug, causing imatinib resistance.

Ovary

The zinc finger protein TRIM27 is identified as a new molecular target for diagnosis and treatment of ovarian cancer in the study by Ma *et al.*[18] TRIM27 expression correlates with metastasis and stage in ovarian serous carcinoma patients, induces cell cycle arrest and apoptosis in ovarian cancer cells, and its knockdown in an animal model suppresses proliferation.

Immune system

Notch signaling is a critical factor in the imbalance of the Th17/Treg ratio seen in immune thrombocytopenia. Yu *et al*[19] show that inactivation of Notch signaling might be a potential immunoregulatory strategy for immune thrombocytopenia. Mechanistically, inactivation of Notch signaling downregulates interleukin17 and the transcription factor RORγt, reducing Th17 levels.

Bone and soft tissue

The final paper in this Web Focus describes the role of the nucleus pulposus in intervertebral disc degeneration and low back pain. Chen *et al*[20] show that carbonic anhydrase 12 is downregulated in degenerated nuclei pulposi by the prolyl hydroxylase /HIF-1 axis, and may lead to decreased extracellular matrix synthesis.

DISCLOSURE/CONFLICT OF INTEREST

The authors declare no conflict of interest.

1. Yang K, Wang X, Zhang H, *et al.* The evolving roles of canonical WNT signaling in stem cells and tumorigenesis: implications in targeted cancer therapies. Lab Invest 2016;96:116–136.
2. Zhang XF, Thompson M, Xu YH. Multifactorial theory applied to the neurotoxicity of paraquat and paraquat-induced mechanisms of developing Parkinson's disease. Lab Invest 2016;96:496–507.
3. Chen S, Zheng S, Liu Z, *et al.* Endogeous sulfur dioxide protects against oleic acid-induced acute lung injury in association with inhibition of oxidative stress in rats. Lab Invest 2015;95:142–156.
4. Xue X, Zeng N, Gao Z, *et al.* Diffuse large B-cell lymphoma: sub-classification by massive parallel quantitative RT-PCR. Lab Invest 2015;95:113–120.
5. Liang M, Lv J, Zou L, *et al.* A modified murine model of systemic sclerosis: bleomycin given by pump infusion induced skin and pulmonary inflammation and fibrosis. Lab Invest 2015;95:342–350.
6. Zhang L, Fu XH, Yu Y, *et al.* Treatment with CA-074Me, a Cathepsin B inhibitor, reduces lung interstitial inflammation and fibrosis in a rat model of polymyositis. Lab Invest 2015;95:65–77.
7. Xing S, Nie F, Xu Q, *et al.* HDAC is essential for epigenetic regulation of Thy-1 gene expression during LPS/TLR4-mediated proliferation of lung fibroblasts. Lab Invest 2015;95:1105–1116.
8. Nie W, Xu MD, Gan L, *et al.* Overexpression of stathmin 1 is a poor prognostic biomarker in non-small cell lung cancer. Lab Invest 2015;95:56–64.
9. Qiang Y, Liang G, Yu L. Human amniotic mesenchymal stem cells alleviate lung injury induced by ischemia and reperfusion after cardiopulmonary bypass in dogs. Lab Invest 2016;96:537–546.
10. Cao AL, Wang L, Chen X, *et al.* Ursodeoxycholic acid and 4-phenylbutyrate prevent endoplasmic reticulum stress-induced podocyte apoptosis in diabetic nephropathy. Lab Invest 2016;96:610–622.
11. Xiao L, Zhou X, Liu F, *et al.* MicroRNA-129-5p modulates epithelial-to-mesenchymal transition by targeting SIP1 and SOX4 during peritoneal dialysis. Lab Invest 2015;95:817–832.
12. Zhang X, Du G, Xu Y, *et al.* Inhibition of notch signaling pathway prevents cholestatic liver fibrosis by decreasing the differentiation of hepatic progenitor cells into cholangiocytes. Lab Invest 2016;96:350–360.
13. Yu F, Guo Y, Chen B, *et al.* MicroRNA-17-5p activates hepatic stellate cells through targeting of Smad7. Lab Invest 2015;95:781–789.
14. Wei Q, Guo P, Mu K, *et al.* Estrogen suppresses hepatocellular carcinoma cells through ERbeta-mediated upregulation of the NLRP3 inflammasome. Lab Invest 2015;95:804–816.
15. Tang X, Wang Y, Fan Z, *et al.* Klotho: a tumor suppressor and modulator of the Wnt/beta-catenin pathway in human hepatocellular carcinoma. Lab Invest 2016;96:197–205.
16. He W, Feng J, Zhang Y, *et al.* microRNA-186 inhibits cell proliferation and induces apoptosis in human esophageal squamous cell carcinoma by targeting SKP2. Lab Invest 2016;96:317–324.
17. Shi Y, Gao X, Hu Q, *et al.* PIK3C2A is a gene-specific target of microRNA-518a-5p in imatinib mesylate-resistant gastrointestinal stromal tumor. Lab Invest 2016;96:652–660.
18. Ma Y, Wei Z, Bast Jr. RC , *et al.* Downregulation of TRIM27 expression inhibits the proliferation of ovarian cancer cells *in vitro* and *in vivo*. Lab Invest 2016;96:37–48.
19. Yu S, Liu C, Li L, *et al.* Inactivation of Notch signaling reverses the Th17/Treg imbalance in cells from patients with immune thrombocytopenia. Lab Invest 2015;95:157–167.
20. Chen S, Fang XQ, Wang Q, *et al.* PHD/HIF-1 upregulates CA12 to protect against degenerative disc disease: a human sample, *in vitro* and *ex vivo* study. Lab Invest 2016;96:561–569.