

renal tubular injury  
biomarker

lipid peroxidation  
hypoxic tissue injury

sepsis

renal transplantation

ischemia

nephrotoxins

cardiac surgery

acute tubular necrosis

apheresis

radiocontrast agents

microcirculation

predicting dialysis-free survival

hypertension

diabetes nephropathy

FOR EARLY DETECTION OF ISCHEMIC EVENTS ON **ACUTE KIDNEY INJURY**  
FOR DISEASE MANAGEMENT OF **CHRONIC KIDNEY DISEASES**

# RENISCHEM<sup>®</sup> L-FABP ELISA Kit

Urinary L-FABP ELISA kit

L-FABP BIOMARKER WEBSITE OPENED!

search

CMIC HOLDINGS Co., Ltd.

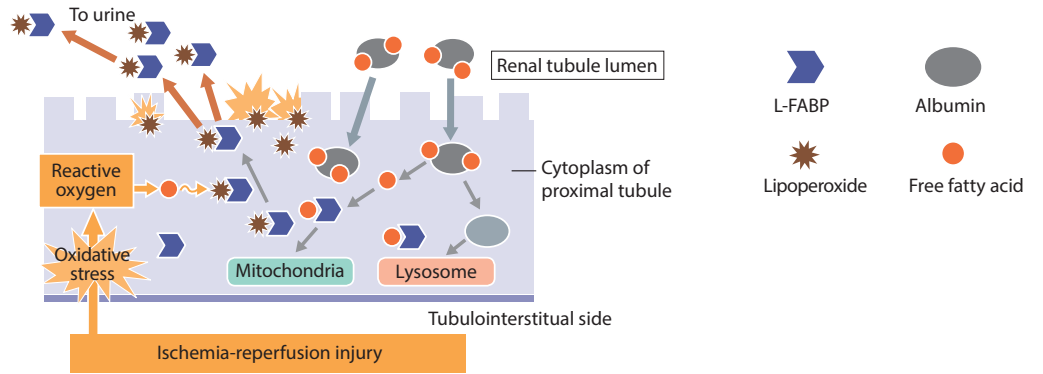
# Mechanism of L-FABP excretion

## L-FABP urinary excretion within proximal tubule cytoplasm

Free Fatty Acids (FFAs) are bound to serum albumin filtered through glomeruli and reabsorbed into the proximal tubule along with albumin. FFAs up-regulate of L-FABP gene expression. L-FABP, a carrier protein or 14kDa expressed in the proximal tubule plays a role in the intracellular transport of FFAs to mitochondria and/or peroxisomes for metabolism.

Lipoperoxides are accumulated in proximal tubules during renal ischemia/reperfusion. L-FABP is excreted from the proximal tubules into urine by binding these cytotoxic lipids.

Reactive oxygen generated due to peritubular ischemia/reperfusion injury change free fatty acids to fatty acid peroxides (lipoperoxides), which are highly toxic to cells. L-FABP binds with these lipoperoxides, and is excreted outside of cells. Thus, it is thought that L-FABP is "renoprotective"—it works to protect the kidneys.

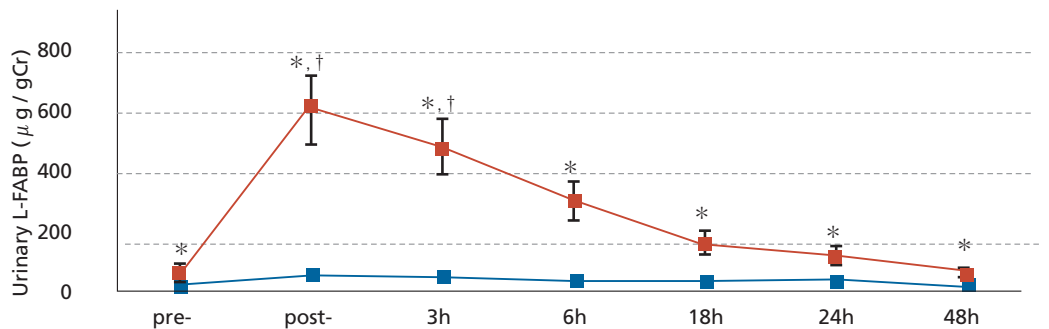
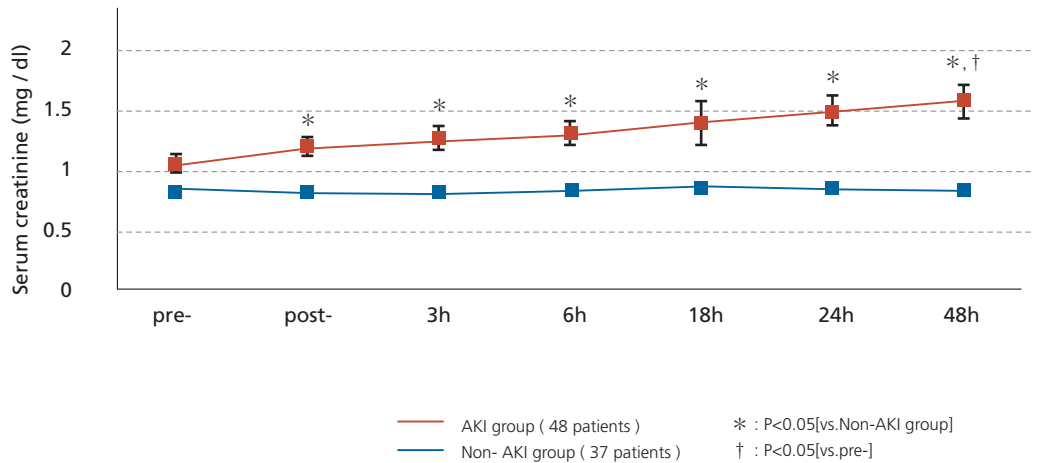


## Clinical Evidence

### Urinary L-FABP is a useful biomarker for early detection of Acute Kidney Injury (AKI) and is a good predictor of the onset of AKI

The conventional diagnostic method for AKI, uses serum creatinine as an indicator of detected AKI development 24 hours after cardiac surgery. In contrast, urinary L-FABP showed a significant increase immediately after the operation which demonstrated that urinary L-FABP can be used for earlier detection of AKI development.

A total of 85 patients who underwent cardiac surgery were classified into AKI group and non-AKI group according to AKIN criteria. Serum creatinine and urinary L-FABP were measured both pre- and post- operation.

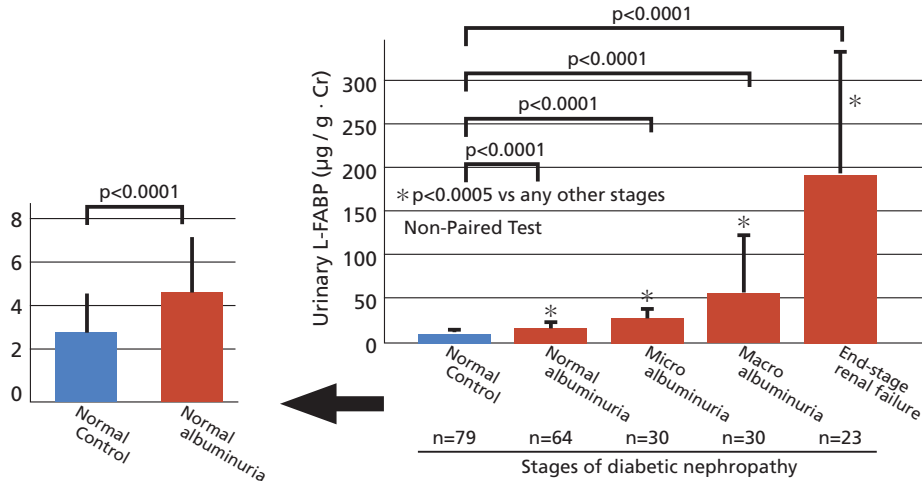


# Clinical Evidence

## For early diagnosis of diabetic nephropathy

The level of urinary L-FABP increased significantly according to the severity of diabetic nephropathy. Urinary L-FABP in the patients with normal albuminuria was significantly higher than in normal control subjects. Thus, urinary L-FABP is a useful biomarker for early diagnosis of diabetic nephropathy.

### Relationship between urinary L-FABP levels and progression of diabetic nephropathy

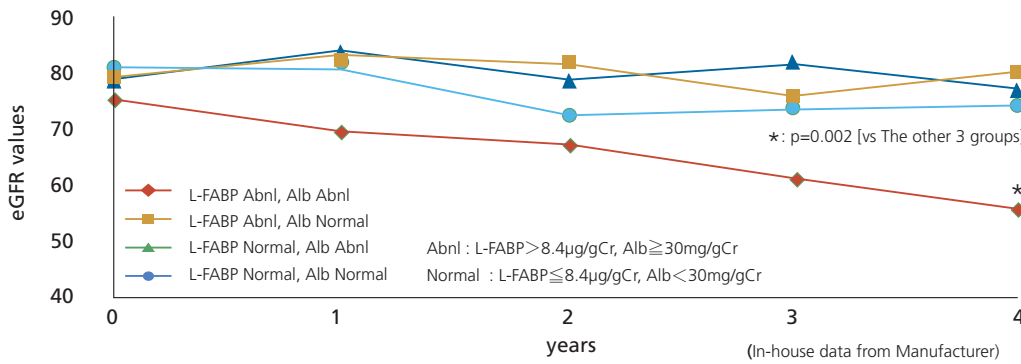


Urinary L-FABP was measured in 147 patients who had diabetic nephropathy and was divided according to the disease stage. The average value and standard variation of each disease stage were calculated and shown in the graph to the right, together with the urinary L-FABP value of healthy volunteers.

Modified from Kamijyo-Ikemori.A.et al.Diabetes Care 34: 691-696,2011

## Urinary L-FABP is useful to detect the risk of renal function deterioration

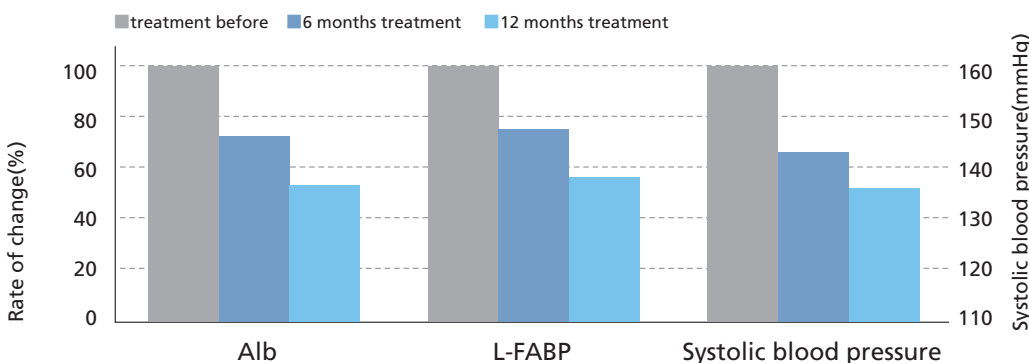
Renal function decreased significantly in the following 4 years in the group that showed abnormal values in both urinary L-FABP and urinary albumin. Early stage risk of renal function deterioration resulting in diabetic nephropathy can be detected with high accuracy by measuring urinary L-FABP, which reflects tubular function, together with simultaneous measurement of urinary albumin, which is an indicator of glomerular injury.



A total of 86 cases with eGFR 60 were taken from the 147 diabetic patients and classified into 4 groups according to urinary L-FABP levels (Normal: 8.4µg/gCr or less) and urinary albumin levels (Normal: under 30mg/gCr) collected during the first year following diagnosis. The changes in eGFR were tracked in the 4 groups.

## For monitoring effectiveness of kidney disease treatment

Urinary albumin, urinary L-FABP, and systolic blood pressure after 6 months of treatment and 12 months treatment were significantly decreased compared to the baseline values. Urinary L-FABP, similarly to urinary albumin is useful, for monitoring antihypertensive therapy for early-stage diabetic nephropathy.



Patients who have microalbuminuria were randomly assigned to receive ARB for 12 months. Urinary albumin, urinary L-FABP, and systolic blood pressure were then monitored to observe the course of treatment.

# L-FABP ELISA TMB Kit, High Sensitivity Kit

Urinary L-FABP ELISA kit

## Assay specifications

Size:	96 Wells
Intended User:	Lab professionals
Store Temperature:	2-8°C
Method:	Enzyme-Linked-Immuno-Sorbent Assay of 2-step sandwich method
Sample:	Human urine
Assay time:	120min.
Shelf life:	24 months (TMB) 12 months (High Sensitivity)
Measurable range:	1.5 – 200ng/mL (TMB) 0.3 – 60ng/mL (High Sensitivity)

## Kit component

L-FABP Antibody Coated Microplate	96 Well x 1
Pretreatment Solution	12mL x 1
Assay Buffer	12mL x 1
The 2nd Ab-POD Conjugate	12mL x 1
Substrate Solution	12mL x 1
Wash Agent (x 40 concentrate)	50mL x 1
Stop Solution	12mL x 1
Standard Diluent (0ng/mL)	2.5mL x 1
L-FABP Standard (400ng/mL)	0.5mL x 1
Pretreatment Microplate	96Well x 1
Plate Seal	x 2 sheets



## L-FABP-Related Articles

### CKD

- [1] Urinary fatty acid-binding protein as a new clinical marker of the progression of chronic renal disease. *J Lab Clin Med.* 143(1): 23-30, 2004.
- [2] Clinical evaluation of urinary excretion of liver-type fatty acid-binding protein as a marker for the monitoring of chronic kidney disease: A multicenter trial. *J Lab Clin Med.* 145(3): 125-133, 2005.
- [3] Clinical significance of urinary liver-type fatty acid-binding protein in patients with diabetic nephropathy. *Diabetes Care.* 28(8): 2038-2039, 2005.
- [4] Urinary liver-type fatty acid-binding protein: discrimination between IgA nephropathy and thin basement membrane nephropathy. *Am J Nephrol.* 25(5): 447-450, 2005.
- [5] Urinary liver-type fatty acid-binding protein predicts progression to nephropathy in type 1 diabetic patients. *Diabetes Care.* 33(6): 1320-1324, 2010.
- [6] Urinary L-FABP and anaemia: distinct roles of urinary markers in type 2 diabetes. *Eur J Clin Invest.* 40(2): 95-102, 2010.
- [7] Clinical significance of urinary liver-type fatty acid-binding protein in diabetic nephropathy of type 2 diabetic patients. *Diabetes Care.* 34(3): 691-696, 2011.
- [8] Predictive effects of urinary liver-type fatty acid-binding protein for deteriorating renal function and incidence of cardiovascular disease in type 2 diabetic patients without advanced nephropathy. *Diabetes Care.* 36(5): 1248-1253, 2013.
- [9] Urinary liver-type fatty acid-binding protein and progression of diabetic nephropathy in type 1 diabetes. *Diabetes Care.* 36(7): 2077-2083, 2013.
- [10] Clinical significance of urinary liver-type fatty acid-binding protein as a predictor of ESRD and CVD in patients with CKD. *Clin Exp Nephrol.* 20(2): 195-203, 2016.

### AKI

- [11] Quantification of L-type fatty acid binding protein in the urine of preterm neonates. *Early Hum Dev.* 81(7): 643-646, 2005.
- [12] Renal L-type fatty acid-binding protein in acute ischemic injury. *J Am Soc Nephrol.* 18(11): 2894-2902, 2007.
- [13] Liver fatty acid-binding protein as a biomarker of acute kidney injury after cardiac surgery. *Kidney Int.* 73(4): 465-472, 2008.
- [14] Urinary liver-type fatty acid-binding protein in septic shock: effect of polymyxin B-immobilized fiber hemoperfusion. *Shock.* 31(5): 454-459, 2009.
- [15] Evaluation of new acute kidney injury biomarkers in a mixed intensive care unit. *Crit Care Med.* 39(11): 2464-2469, 2011.
- [16] Usefulness of urinary biomarkers in early detection of acute kidney injury after cardiac surgery in adults. *Circulation Journal.* 76(1): 213-220, 2012.
- [17] Mild elevation of urinary biomarkers in prerenal acute kidney injury. *Kidney Int.* 82(10): 1114-1120, 2012.
- [18] Urinary liver-type fatty acid-binding protein linked with increased risk of acute kidney injury after allogeneic stem cell transplantation. *Biol Blood Marrow Transplant.* 20(12): 2010-2014, 2014.
- [19] Elevation of urinary liver-type fatty acid binding protein after cardiac catheterization related to cardiovascular events. *Int J Nephrol Renovasc Dis.* 8: 91-99, 2015.
- [20] Clinical usefulness of urinary liver-type fatty acid-binding protein as a perioperative marker of acute kidney injury in patients undergoing endovascular or open-abdominal aortic aneurysm repair. *J Anesth.* 30(1):89-99, 2015.
- [21] Impact of clinical context on acute kidney injury biomarker performances: differences

between neutrophil gelatinase-associated lipocalin and L-type fatty acid-binding protein. *Sci Rep.* 6:33077, 2016.

### Pharmacology

- [22] Effect of pitavastatin on urinary liver-type fatty acid-binding protein levels in patients with early diabetic nephropathy. *Diabetes Care.* 28(11): 2728-2732, 2005.
- [23] Angiotensin II receptor antagonist reduces urinary liver-type fatty acid-binding protein levels in patients with diabetic nephropathy and chronic renal failure. *Diabetologia.* 50(2): 490-492, 2007.
- [24] Tubular and glomerular injury in diabetes and the impact of ACE inhibition. *Diabetes Care.* 32(9): 1684-1688, 2009.
- [25] Effect of pioglitazone on urinary liver-type fatty acid-binding protein concentrations in diabetes patients with microalbuminuria. *Diabetes Metab Res Rev.* 22(5): 385-389, 2006.
- [26] Renal L-type fatty acid-binding protein mediates the bezafibrate reduction of cisplatin-induced acute kidney injury. *Kidney Int.* 73(12): 1374-1384, 2008.
- [27] Renoprotective effects of various angiotensin II receptor blockers in patients with early-stage diabetic nephropathy. *Kidney Blood Press Res.* 33(3): 213-220, 2010.
- [28] Additive antioxidative effects of azelnidipine on angiotensin receptor blocker olmesartan treatment for type 2 diabetic patients with albuminuria. *Hypertens Res* 34: 935-941, 2011.
- [29] Renoprotective and antioxidant effects of cilnidipine in hypertensive patients. *Hypertens Res.* 35(11): 1058-1062, 2012.
- [30] Renoprotective effect of the xanthine oxidoreductase inhibitor, Topiroxostat, on Adenine-Induced Renal Injury. *Am J Physiol Renal Physiol.* 310(11):F1366-1376, 2016.

### Toxicology

- [31] Urinary excretion of liver-type fatty acid-binding protein in contrast medium-induced nephropathy. *Am J Kidney Dis.* 47(3): 439-444, 2006.
- [32] A role of liver fatty acid-binding protein in cisplatin-induced acute renal failure. *Kidney Int.* 72(3): 348-358, 2007.
- [33] L-type fatty acid binding protein transgenic mouse as a novel tool to explore cytotoxicity to renal proximal tubules. *Drug Metab Pharmacokin.* 23(4): 271-278, 2008.
- [34] Renal liver-type fatty acid binding protein (L-FABP) attenuates acute kidney injury in aristolochic acid nephrotoxicity. *Am J Pathol.* 178(3): 1021-1032, 2011.
- [35] Urinary liver-type fatty acid-binding protein level as a predictive biomarker of contrast-induced acute kidney injury. *Eur J Clin Invest.* 42(5): 557-563, 2012.
- [36] Remote ischemic pre-conditioning alleviates contrast-induced acute kidney injury in patients with moderate chronic kidney disease. *Circulation Journal.* 77(12): 3037-3044, 2013.
- [37] Human liver-type fatty acid-binding protein protects against tubulointerstitial injury in aldosterone-induced renal injury. *Am J Physiol Renal Physiol.* 308(2): F114-121, 2014.
- [38] Response of urinary liver-type fatty acid-binding protein to contrast media administration has a potential to predict one-year renal outcome in patients with ischemic heart disease. *Heart Vessels.* 30(3): 296-303, 2015.

## [Contact]

[Manufacturer]

**CMIC HOLDINGS Co., Ltd.**

Address: Hamamatsucho Bldg., 1-1-1 Shibaura, Minato-ku, Tokyo 105-0023, JAPAN

URL: <http://www.cmic-holdings.co.jp/e/index.shtml>

E-mail: [l-fabp@cmic.co.jp](mailto:l-fabp@cmic.co.jp)