

Supplementary Table 1. Characteristics of microbead-based plasma KIM-1 sandwich ELISA in various species.

Parameters	Human	Mouse	Rat
Lower limit of quantitation	4.4 pg/mL	12.1 pg/mL	39 pg/mL
Assay range	0.012–50 ng/mL	0.012–50 ng/mL	0.039–50 ng/mL
Intra assay %CV	<11.45%	<10.15%	<11.4%
Inter assay %CV	<12.3%	<9.8%	<13.7%
Recovery	87-115%	84-110%	85 - 125 %
Linearity	Linear dilutions: 1:8-1:32	Linear dilutions: 1:4-1:32	Linear dilutions: 1:5 - 1:20

CV=coefficient of variation

Supplementary Table 2. Demographics, serum creatinine, urine albumin, and urinary and plasma KIM-1 values in healthy volunteers and patients

Subject	Group	Age / sex / race	Baseline	sCr on day of collection (mg/dL)	Plasma KIM-1 (pg/mL)	Urine KIM-1 (ng/mg uCr)	Urine KIM-1 (ng/ml)	Albuminuria (mg/g uCr)
1	HV	32 / F / A	-	0.79	101.65	0.47	0.058	2.1
2	HV	40 / M / A	-	0.88	16.51	0.49	0.265	3.0
3	HV	20 / M / B	-	1.07	53.29	0.07	0.115	4.0
4	HV	21 / M / A	-	0.97	86.44	0.23	0.073	2.2
5	HV	44 / M / B	-	1.12	65.27	0.07	0.038	10.2
6	HV	21 / M / A	-	0.87	46.37	0.44	0.178	8.1
7	HV	35 / F / B	-	0.76	140.27	0.07	0.005	0.3
8	HV	48 / M / B	-	1.11	18.53	0.11	0.059	3.5
9	HV	45 / F / A	-	0.85	36.43	0.23	0.164	4.1
10	HV	39 / F / A	-	0.85	46.37	0.41	0.396	10.6
11	HV	33 / M / B	-	1.04	49.59	0.13	0.063	4.2
12	HV	37 / M / A	-	0.87	29.53	0.23	0.054	2.1
13	HV	21 / F / A	-	0.83	29.53	0.14	0.112	0.4
14	HV	26 / F / W	-	1.04	59.08	0.22	0.322	0
15	HV	25 / F / W	-	0.9	33.01	0.19	0.064	2.0
16	HV	42 / M / W	-	0.89	240.03	0.24	0.129	1.1
17	HV	33 / M / W	-	1.05	118.21	0.28	0.202	2.0
18	HV	50 / M / W	-	1.11	12.98	0.37	0.317	11.1
19	HV	24 / M / W	-	0.99	106.52	0.10	0.099	0
20	HV	32 / F / B	-	0.76	77.39	0.17	0.019	0
21	HV	29 / M / A	-	0.98	20.48	0.16	0.123	3.28
22	HV	28 / M / B	-	1.01	34.56	0.10	0.119	3.38
23	HV	46 / M / B	-	0.98	123.67	0.14	0.382	5.09
24	HV	28 / F / B	-	0.98	113.12	0.11	0.197	5.24
25	HV	43 / M / B	-	0.99	34.45	0.17	0.175	3.61
26	HV	45 / M / W	-	0.95	67.23	0.56	1.608	22.29
27	HV	46 / M / W	-	1	33.32	0.24	0.191	2.26
28	HV	42 / M / W	-	1	156.76	0.20	0.236	2.22
29	HV	19 / F / W	-	0.56	33.45	0.41	1.138	3.30

30	HV	35 / M / W	-	0.87	29.67	0.10	0.199	17.70
31	HV	31 / F / B	-	0.67	89.65	0.26	0.416	2.65
32	HV	23 / F / W	-	0.73	18.47	0.28	0.009	49.52
33	HV	25 / F / W	-	0.76	88.97	1.52	1.600	1.73
34	HV	25 / F / W	-	0.8	65.78	0.27	0.516	4.33
35	HV	48 / F / W	-	0.9	33.67	0.60	0.675	3.29
36	HV	26 / F / W	-	0.76	98.65	0.12	0.291	2.86
37	HV	30 / F / B	-	0.96	36.89	0.16	0.370	1.72
38	HV	30 / M / W	-	0.72	12.86	0.35	0.683	6.01
39	HV	27 / F / A	-	0.71	11.98	0.43	0.534	4.08
40	HV	36 / M / A	-	0.78	98.34	0.24	0.148	4.52
41	HV	35 / F / M	-	0.86	101.55	0.22	0.520	2.13
42	HV	27 / F / W	-	0.71	47.89	0.35	1.164	2.84
43	HV	20 / M / A	-	0.97	101.23	0.37	0.393	1.71
44	HV	20 / F / W	-	0.69	111.32	0.34	1.256	1.58
45	HV	49 / F / B	-	0.95	78.53	0.27	0.764	9.37
46	HV	43 / M / A	-	0.99	17.87	0.37	0.719	2.46
47	HV	51 / F / B	-	0.98	46.78	0.29	0.880	6.21
48	HV	41 / F / B	-	0.53	16.37	0.48	0.645	3.71
49	CS - no AKI	77 / F / W	0.9	0.73	123.34	1.55	0.540	35.0
50	CS - no AKI	75 / M / W	1.31	1.04	957.70	0.69	0.389	53.8
51	CS - no AKI	79 / M / W	1.4	1.12	243.26	0.47	0.214	45.0
52	CS - no AKI	76 / M / W	1.21	0.84	37.92	0.72	0.530	23.6
53	CS - no AKI	58 / M / W	1.12	1.25	14.64	0.88	0.862	429.94
54	CS - no AKI	83 / M / W	0.94	0.93	26.49	1.38	0.803	0
55	CS - no AKI	83 / F / W	1.27	0.98	108.00	0.52	0.199	3.52
56	CS - no AKI	76 / M / W	1.49	1.55	123.34	0.98	0.323	10.6
57	CS - no AKI	69 / M / W	2.25	1.9	14.64	0.44	0.262	231.13
58	CS - no AKI	78 / M / W	0.98	0.83	339.58	0.47	0.214	20.1
59	CS - no AKI	78 / F / W	1.33	1.07	164.03	0.82	0.433	88.1
60	CS - no AKI	82 / F / W	1.15	0.94	60.06	0.97	0.980	31.0
61	CS - no AKI	57 / F / W	1.03	0.81	253.01	0.88	1.243	59.38
62	CS - no AKI	84 / F / W	2.27	1.8	81.56	0.67	0.671	31.0
63	CS - no AKI	59 / M / W	1.45	1.38	17.12	0.75	0.199	2.0
64	CS - no AKI	67 / M / H	1.15	1.23	727.00	0.16	0.540	82.56
65	CS - AKI	81 / M / W	1	2.23	2831.71	1.69	0.376	30.05

66	CS - AKI	67 / M / W	1.49	3.11	184.07	0.95	0.549	406
67	CS - AKI	64 / M / W	2.2	5	15579.65	7.47	5.429	400
68	CS - AKI	63 / F / W	1.03	2.08	663.37	2.28	2.11	230
69	CS - AKI	56 / M / W	1.82	4.1	6334.09	20.54	14.540	209
70	CS - AKI	71 / M / W	1.08	2.9	971.10	5.31	2.752	202
71	ICU - AKI	41 / M / W	0.9	4.21	922.42	3.42	0.487	120
72	ICU - AKI	62 / M / W	1	4.05	1019.23	6.74	4.671	368
73	ICU - AKI	75 / M / W	1	2.8	663.37	1.20	0.352	100.4
74	ICU - AKI	78 / M / W	0.8	3.05	572.40	1.25	1.275	45.7
75	ICU - AKI	80 / M / W	0.7	2.47	60.06	2.72	1.186	56.4
76	ICU - AKI	74 / M / W	1.3	2.23	771.32	20.32	24.528	368
77	CS - AKI	70 / M / W	1.74	2.7	284.81	7.49	6.444	298.0
78	CS - AKI	85 / F / B	0.95	1.35	311.24	0.87	0.958	35.1
79	CS - AKI	89 / F / W	1.18	2.14	403.11	4.93	1.822	82.8
80	CS - AKI	84 / F / W	0.87	1.6	184.81	0.82	1.571	105.6
81	CS - AKI	82 / M / W	1.32	2.23	544.74	1.68	5.785	20.9
82	CS - AKI	90 / F / W	1.3	2.27	184.81	2.68	2.436	176.0
83	CS - AKI	96 / F / W	1.14	2	403.11	3.12	1.654	115.5
84	CS - AKI	56 / M / HW	2.6	4.01	258.64	9.76	3.416	811.4
85	CS - AKI	80 / M / W	0.66	1.4	1027.26	10.97	2.961	572.0
86	CS - AKI	72 / M / W	1.52	2.5	258.64	5.54	8.535	14.2
87	CS - AKI	60 / F / W	1.22	2.21	331.31	1.94	0.564	110.3
88	CS - AKI	79 / F / W	0.82	1.57	544.74	2.99	1.437	43.1
89	CS - AKI	83 / M / W	2.1	2.52	3291.32	28.96	6.949	169.8
90	CS - AKI	78 / M / W	1.19	2.6	518.15	3.48	1.183	74.5
91	CS - AKI	82 / F / W	0.89	1.68	412.31	1.76	0.810	65.6
92	CS - AKI	77 / F / W	0.7	1.24	1293.48			

Abbreviations: A, Asian; AKI, acute kidney injury; B, Black; CS, cardiac surgery; ICU, intensive care unit; HW, Hispanic White; M, Multi-racial; W, White.

Supplementary Table 3. Biomarker values in patients undergoing cardiac surgery.

	Plasma KIM-1 (pg/mL)			Urinary KIM-1 (ng/mg uCr)			Urinary albumin (mg/g uCr)		
	AKI	No AKI	AUC-ROC	AKI	No AKI	AUC-ROC	AKI	No AKI	AUC-ROC
	Median (IQR) [N]	Median (IQR) [N]		Median (IQR) [N]	Median (IQR) [N]		Median (IQR) [N]	Median (IQR) [N]	
Pre	128.8 (41.9, 167.5) [8]	82.0 (49.8, 154.4) [5]	0.55 (0.26 - 0.82)	505.2 (398.6, 1531.9) [8]	358.4 (150.2, 682.9) [5]	0.73 (0.42 - 0.93)	120.9 (27.8, 137.5) [6]	67.0 (14.0, 128.0) [5]	0.63 (0.31 - 0.89)
	97.5 (41.7, 134.4) [7]	76.9 (42.4, 100.2) [9]	0.51 (0.25 - 0.76)	1499.3 (956.0, 2047.4) [7]	503.1 (341.9, 1041.3) [9]	0.81 (0.54 - 0.96)	85.9 (23.3, 150.3) [5]	27.1 (13.3, 96.8) [9]	0.67 (0.37 - 0.89)
	90.5 (52.3, 133.5) [8]	86.2 (51.5, 107.6) [7]	0.59 (0.31 - 0.83)	444.6 (376.7, 1038.7) [9]	585.7 (313.9, 643.1) [7]	0.52 (0.27 - 0.77)	30.5 (13.5, 127.8) [7]	19.9 (15.6, 33.9) [7]	0.65 (0.36 - 0.88)
4h	-	-		972.9 (511.8, 1511.9) [8]*	1033.6 (871.6, 2050.1) [8]	0.61 (0.34 - 0.84)	44.2 (19.3, 64.9) [6]	32.4 (12.1, 41.8) [8]	0.67 (0.37 - 0.89)
	114.2 (58.1, 167.2) [8]	81.3 (62.3, 120.5) [8]	0.55 (0.29 - 0.79)	1464.0 (1198.3, 2055.8) [9]	1069.6 (608.3, 1646.8) [7]	0.65 (0.38 - 0.87)	52.3 (42.2, 92.0) [7]	48.6 (18.7, 68.5) [7]	0.71 (0.42 - 0.92)
	230.2 (160.7, 365.1) [9]*	103.9 (70.0, 155.1) [9]	0.74 (0.48 - 0.91)	3643.1 (1355.0, 5092.8) [9]	991.2 (532.6, 1487.2) [8]	0.89 (0.64 - 0.99)	72.7 (47.9, 213.2) [7]	46.8 (24.8, 52.4) [8]	0.77 (0.49 - 0.94)
Day 1	241.1 (144.7, 447.5) [8]	125.3 (59.5, 169.6) [9]	0.78 (0.52 - 0.94)	1570.6 (1017.3, 4101.7) [8]	512.4 (323.0, 1083.2) [9]	0.73 (0.42 - 0.93)	52.5 (47.1, 104.9) [7]	45.7 (22.3, 72.8) [9]	0.65 (0.38 - 0.87)
	197.5 (117.5, 458.5) [9]	89.1 (62.5, 137.3) [7]	0.81 (0.54 - 0.96)	1285.1 (847.1, 2170.4) [9]	645.3 (477.7, 686.0) [6]	0.83 (0.56 - 0.97)	142.1 (70.0, 156.7) [7]	45.8 (13.6, 72.2) [6]	0.76 (0.45 - 0.95)
	112.0 (94.3, 244.1) [6]	- (1)	-	785.5 (473.0, 1269.5) [7]	348.7 (231.5, 466.0) [2]	0.86 (0.48 - 0.99)	46.4 (24.8, 85.5) [5]	102.3 (70.7, 133.8) [2]	-

Urine and plasma samples were not available from all patients at all time points. Abbreviations: AUC-ROC, area under the receiver operating characteristics curve; AKI, acute kidney injury; End, end of the surgery. Asterisks mark the time point at which biomarker levels were statistically significantly higher than baseline levels in patients with AKI.

Supplementary Table 4. Characteristics of two study groups of patients with CKD

	CKD of various etiologies (n=46)	Type 1 Diabetes & Proteinuria (n=124)
Age (y)	49 ± 2	42± 10
Male	35 (76%)	72(58%)
Race		
White	30	123
African American	9	1
Asian & Others	7	
sCr (mg/dL)	2.43 ± 0.2	1.39 ± 0.9
eGFR* (mL/min/1.73 m ²)	41.5 ± 30	68 ± 34
Blood KIM-1 (pg/ml)		
CKD stage 1	83 ± 55 (p)	89 ± 70 (s)
CKD stage 2	104 ± 98 (p)	158 ± 173 (s)
CKD stage 3	201 ± 162 (p)	181 ± 178 (s)
CKD stage 4	261 ± 126 (p)	288 ± 336 (s)
CKD stage 5	360 ± 172 (p)	770 ± 770 (s)

Note: Values for continuous variables given as mean ± SD; values for categorical variables given as number or number (percentage).

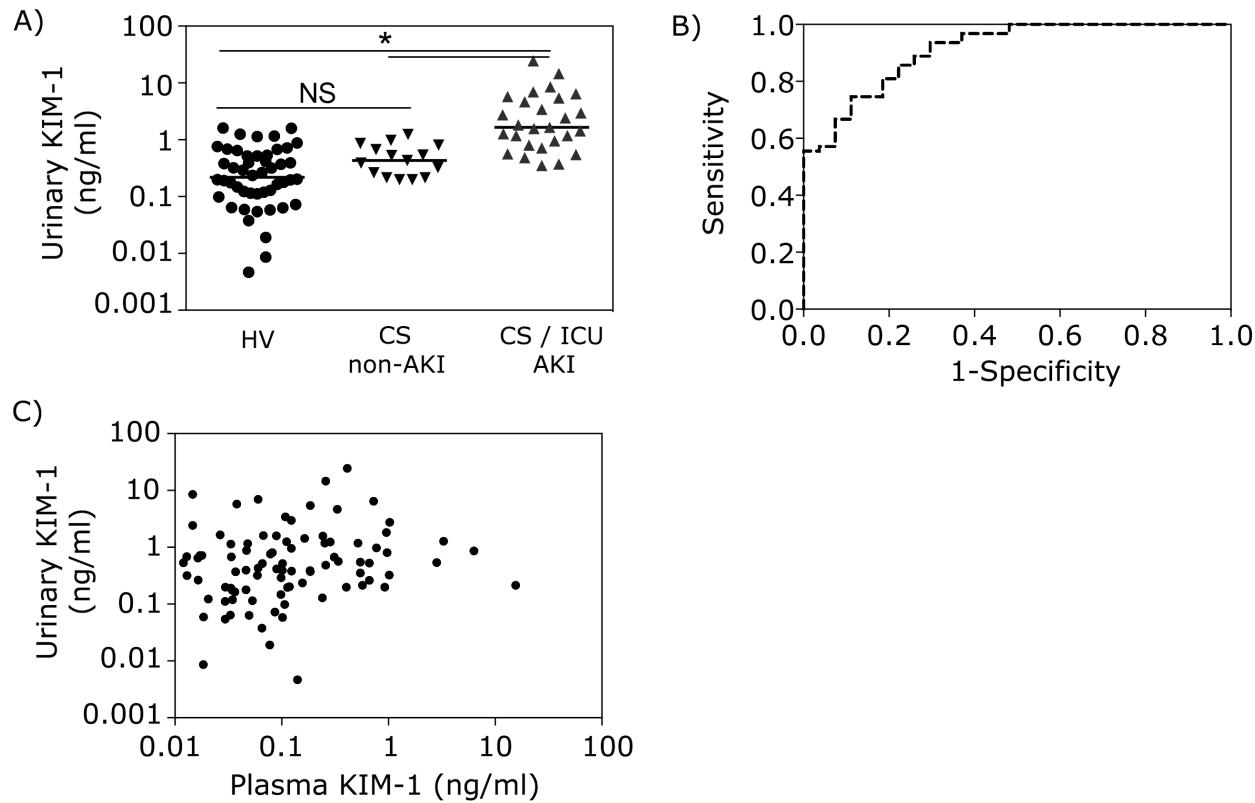
Abbreviations: CKD, chronic kidney injury; eGFR, estimated glomerular filtration rate; sCr, serum creatinine; p, plasma; s, serum.

* Baseline eGFR was calculated using MDRD equation.

Supplementary Table 5. Various etiologies of chronic kidney disease

Pathology
Glomerular
IgA Nephropathy (N=10)
Focal glomerulosclerosis (N=4)
Membranous Glomerulonephritis (N=5)
Lupus (N=2)
Others (N=2)
Tubulointerstitial
Polycystic kidney disease (N=4)
Chronic interstitial toxicity (N=2)
Lithium Toxicity (N=2)
Other
<u>Diabetes/Hypertension/others (N=15)</u>

Supplementary Figure 1.



Supplementary Figure 1. Performance of non-normalized urinary KIM-1. Plasma and urine were collected from healthy volunteers, post cardiac surgery (CS) patients with or without AKI. (A) Dot plot indicates non-normalized urinary KIM-1 for each subject. * $p<0.001$. B) ROC curve analysis comparing performance of non-normalized urinary KIM-1 (AUC-0.91; 95%CI: 0.85-0.97, $p<0.0001$) in patients with and without AKI (HV & CS-ICU non-AKI). C) Scatter plot of non-normalized urinary KIM-1 levels vs. plasma KIM-1 levels in all subjects including healthy volunteers and cardiac surgery ICU patients with or without AKI. ($r = 0.23$, $p= 0.025$).