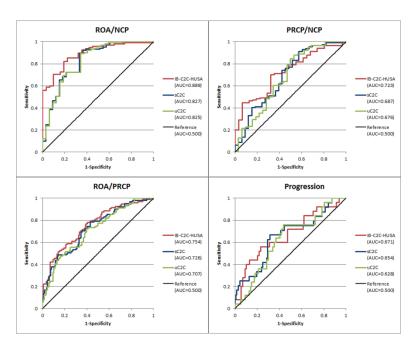
Supplementary Table 1. Baseline descriptive data on biomarkers in cross-sectional and longitudinal cohorts.

Cross-sectional	Whole sample	NCP	PRCP	ROA
cohort	(Weighted N=252.5)	(Weighted N=34.4)	(Weighted N=120.1)	(Weighted N=98.0)
	Mean (SD);	Mean (SD);	Mean (SD);	Mean (SD);
	25 th , median, 75 th			
IB-C2C-HUSA	450.8 (292.2);	276.3 (92.4);	394.4 (241.2);	588.0 (334.9);
	268.1, 383.2, 525.0	221.6, 240.4, 356.0	259.5, 338.5, 461.4	342.0, 478.6, 726.0
sC2C (/100)	248.9 (95.0);	245.4 (84.5);	233.2 (81.8);	268.9 (108.3);
	181.9, 235.4, 282.6	180.3, 227.7, 292.3	178.1, 230.0, 274.0	195.5, 242.7, 301.0
uC2C (/10)	361.9 (265.2);	335.0 (257.4);	349.9 (182.2);	386.2 (338.7);
	217.0, 320.2, 431.0	155.3, 281.5, 464.4	216.5, 334.2, 423.0	234.0, 321.5, 440.3

Longitudinal	Whole sample	Non-progressors	Progressors
cohort	(Weighted N=160.5)	(Weighted N=136.1)	(Weighted N=24.4)
	Mean (SD);	Mean (SD);	Mean (SD);
	25 th , median, 75 th	25 th , median, 75 th	25 th , median, 75 th
IB-C2C-HUSA	466.1 (277.4);	430.9 (215.5);	659.8 (446.5);
	298.6, 409.1, 528.4	295.4, 383.5, 523.3	342.0, 489.5, 941.6
sC2C (/100)	244.7 (84.3);	247.9 (84.6);	226.5 (81.8);
	182.0, 230.9, 281.9	189.3, 232.6, 286.5	167.6, 228.0, 271.3
uC2C (/10)	377.0 (306.0);	386.1 (327.1);	325.4 (144.8);
	227.8, 333.3, 429.1	230.9, 337.8, 439.0	216.5, 303.4, 407.2

[&]quot;/100" and "/10" indicates a change in factor by 100 and 10, respectively, for comparability of the scale of the numbers. Units are pg/ml for serum C2C and ng/mmol creatinine for urine C2C and urine IB-C2C-HUSA. NCP: no cartilage pathology; PRCP: preradiographic cartilage pathology; ROA: radiographic osteoarthritis; IB-C2C-HUSA: human urine sandwich assay; sC2C: serum C2C; uC2C: urine C2C.

Supplementary Figure 1.



Receiver-operating characteristic curves for prediction of ROA vs NCP, PRCP vs NCP, ROA vs PRCP and progression for urine IB-C2C-HUSA, serum C2C, and urine C2C. NCP: no cartilage pathology; PRCP: preradiographic cartilage pathology; ROA: radiographic osteoarthritis; AUC: area under the curve; IB-C2C-HUSA: human urine sandwich assay.

Supplementary Table 2. Pearson correlation coefficients of biomarkers for the whole cohort and subgroups.

		sC2C		uC2C	
		Pearson	p-	Pearson	p-
		correlation	value	correlation	value
		coefficient		coefficient	
Whole cohort					
	IB-C2C-HUSA	0.123	0.059	0.052	0.418
	sC2C	-	-	-0.018	0.776
NCP					
	IB-C2C-HUSA	0.320	0.079	0.160	0.391
	sC2C	-	-	-0.191	0.294
PRCP					
	IB-C2C-HUSA	0.134	0.164	0.091	0.334
	sC2C	-	-	0.058	0.543

able 2 cont.				
IB-C2C-HUSA	0.019	0.858	-0.003	0.974
sC2C	-	-	-0.044	0.669
IB-C2C-HUSA	0.165	0.063	0.034	0.700
sC2C	-	-	-0.070	0.426
IB-C2C-HUSA	0.112	0.611	-0.121	0.563
sC2C	-	-	-0.418	0.047
	IB-C2C-HUSA SC2C IB-C2C-HUSA SC2C	IB-C2C-HUSA 0.019 SC2C - IB-C2C-HUSA 0.165 SC2C - IB-C2C-HUSA 0.112	IB-C2C-HUSA 0.019 0.858 SC2C	IB-C2C-HUSA 0.019 0.858 -0.003 SC2C0.044 IB-C2C-HUSA 0.165 0.063 0.034 SC2C0.070 IB-C2C-HUSA 0.112 0.611 -0.121

NCP: no cartilage pathology; PRCP: preradiographic cartilage pathology; ROA: radiographic osteoarthritis; IB-C2C-HUSA: human urine sandwich assay; sC2C: serum C2C.