Electronic Supplementary Material (ESI) for Metallomics.

Urine metallomics signature as an indicator of pancreatic cancer

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This file includes:

Figure S1

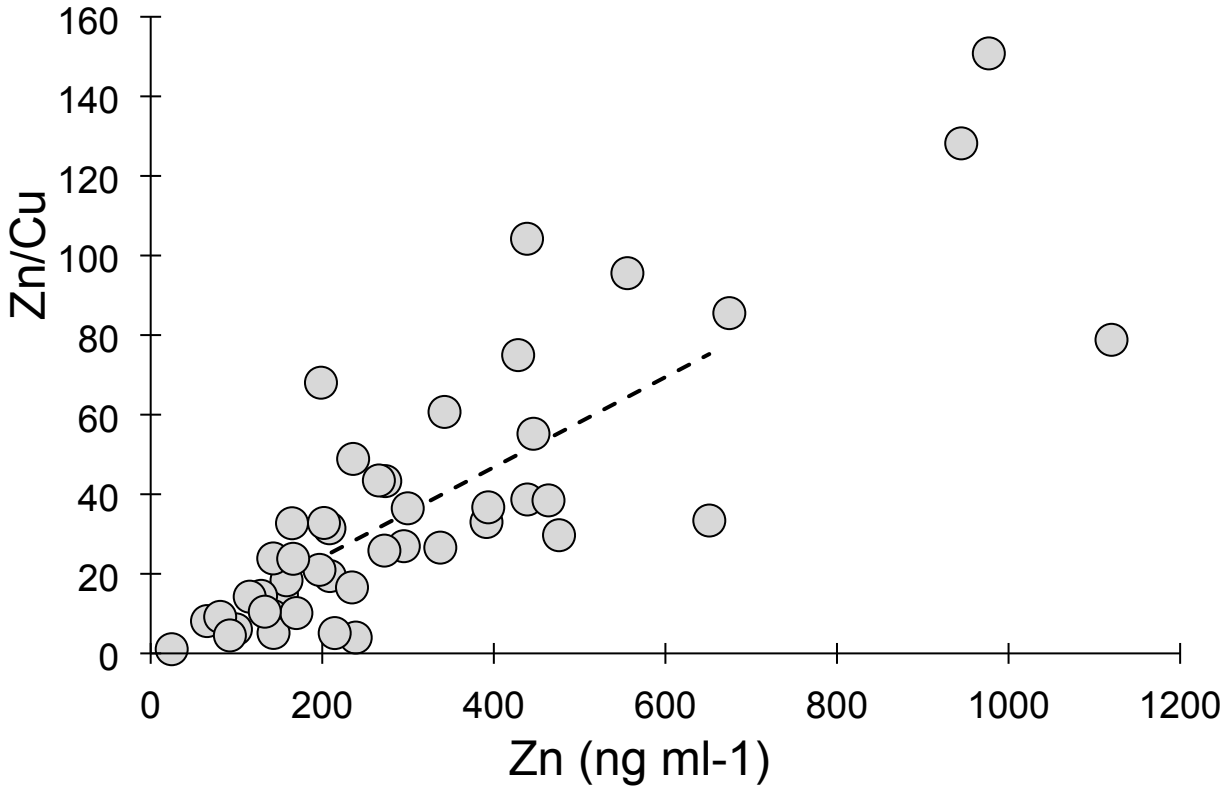

Figure S1. Correlation of urinary Zn with Zn/Cu ratio for the healthy controls. The dashed line represents the linear regression [$y = 0.113\ x + 1.49$, $R^2 = 0.70$].

Table S1. Summary of demographic information (gender, age) for the healthy controls (a) and gender, age and cancer stage for PDAC urine samples (b). NA = no additional data.

a)

Sample ID	Gender	Age
HC-01	M	87
HC-02	F	66
HC-03	M	59
HC-04	M	59
HC-05	F	36
HC-06	F	70
HC-07	F	63
HC-08	F	63
HC-09	M	59
HC-10	F	67
HC-11	M	49
HC-12	M	47
HC-13	F	73
HC-14	F	83
HC-15	F	60
HC-16	F	44
HC-17	F	55
HC-18	F	51
HC-19	F	56
HC-20	F	65
HC-21	M	45
HC-22	F	64
HC-23	F	26
HC-24	F	67
HC-25	F	64
HC-26	F	50
HC-27	F	81
HC-28	M	71
HC-29	F	71
HC-30	F	35
HC-31	F	57
HC-32	M	46
HC-33	F	71
HC-34	F	38
HC-35	M	50
HC-36	F	84
HC-37	F	64
HC-38	F	55
HC-39	M	55
HC-40	M	55
HC-41	M	50
HC-42	F	50
HC-43	F	59
HC-44	F	61
HC-45	F	47
HC-46	NA	24

b)

Sample ID	Gender	Age	Stage
PDAC-01	F	63	T3 N1 M1 (IV)
PDAC-02	M	44	T3 NX M1 (IV)
PDAC-03	M	65	T4 N1 M0 (III)
PDAC-04	F	62	T3 N1 M0 (IIB)
PDAC-05	F	51	T3 N1 M0 (IIB)
PDAC-06	M	58	T4 N1 M0 (III)
PDAC-07	F	83	T3 N0 M0 (IIA)
PDAC-08	M	75	T4 N0 M1 (IV)
PDAC-09	F	72	NA
PDAC-10	F	70	T2 N1 pM0 (IIB)
PDAC-11	F	76	T3 N2 M0 (III)
PDAC-12	F	80	T3 N2 M0 (III)
PDAC-13	F	68	T2 N1 M1 (IV)
PDAC-14	M	73	T2 N1 M0 (IIB)
PDAC-15	M	79	T2 N1 M0 (IIB)
PDAC-16	M	69	T2 N0 M0 (IB)
PDAC-17	F	64	T4 N0 M1 (IV)
PDAC-18	F	77	T4 N1 M1 (IV)
PDAC-19	M	70	T3 N0 M0 (IIA)
PDAC-20	NA	NA	NA
PDAC-21	NA	NA	NA

Table S2. Data quality assessment including mean procedural blank, limits of detection (LOD), limits of quantification (LOQ), 75th percentile and % sample <LOD or <LOQ.

Element	Mean procedural blanks	LOD	LOQ	75th Percentile	%<LOD PDAC	%<LOD Healthy
	ng/ml					
Mg	0.00	0	0	0	0	0
Zn	1.07	5.15	10.72	2.56	0	0
Li	0.00	0.00	0.02	0.00	0	0
Al	3.24	9.73	46.24	8.06	0	0
Ca	0.06	0.17	166.42	11.77	0	0
Rb	0.00	0.00	0.00	0.00	0	0
Fe	1.65	4.94	89.85	4.82	19	0
Co	0.01	0.02	0.12	0.02	10	0
Ni	0.06	0.17	7.50	0.17	5	0
Cu	0.03	0.09	3.66	0.23	0	0
Cr	0.26	0.79	17.31	0.81	38	41
As	0.00	0.00	0.44	0.00	0	0
Sr	0.08	0.25	1.57	0.26	0	0
Mo	0.04	0.11	2.72	0.09	0	0
Cd	0.00	0.00	0.06	0.00	0	0
Ba	0.02	0.06	1.26	0.05	5	0
Pb	0.01	0.04	0.14	0.03	10	0

Table S3. Major and trace element concentrations and the mean values in healthy urine samples (n = 46).
LOD = limit of detection

	Major (µg/ml)				Trace (ng/ml)													
Sample ID	**Na**	**K**	**Mg**	**Ca**	**Li**	**Al**	**Rb**	**Fe**	**Zn**	**Co**	**Ni**	**Cu**	**Cr**	**As**	**Sr**	**Mo**	**Cd**	**Ba**	**Pb**
HC-01	3398	3887	104.8	154.7	48.5	71.8	2604	45.29	152.99	0.43	3.81	10.32	2.65	43.29	165.09	28.13	0.35	3.73	1.31
HC-02	1035	6240	56	122.1	20.6	45.5	2437	30.02	142.31	0.33	2.36	15.12	<LOD	112.83	112.53	45.06	0.31	2.88	0.94
HC-03	1120	4988	118	234.9	13.7	<LOD	2495	26.37	391.43	0.24	1.17	11.85	<LOD	19.51	222.23	68.49	0.23	3.36	0.54
HC-04	1537	3317	109.6	155.4	15.3	9.8	2337	21.07	977	0.3	3.03	6.48	<LOD	1791.14	258.81	81.7	1.06	3.16	1.23
HC-05	2083	2449	59.4	225.1	17	9.8	1567	27.16	65.65	0.19	1.91	8.08	<LOD	6.25	193.7	145.5	0.31	2.05	0.35
HC-06	1609	2163	49.7	168.7	14.6	10.9	1785	25.37	158.35	0.18	1.29	8.62	3.46	491.24	181.31	15.03	0.33	3.69	0.7
HC-07	2801	3113	56.1	75.1	27.7	12.5	2027	12	236	0.21	0.93	4.83	<LOD	16.27	96.97	19.04	0.16	1.54	0.54
HC-08	2860	2640	89.5	338.4	25.4	28.9	1933	30.4	208.86	0.35	3.39	10.74	1.35	60.43	393.22	12.09	0.28	4.82	1.11
HC-09	2501	2800	65.1	162	18.3	<LOD	2060	17.2	555.69	0.3	2.9	5.81	<LOD	8.73	189.66	109.86	0.39	1.6	0.85
HC-10	1920	3521	115.1	84.8	18.5	14.3	3366	13.06	446.2	0.54	2.73	8.08	0.86	7.9	128.01	34.34	0.19	1.49	0.81
HC-11	3195	4928	102.1	239	29.3	16.9	2614	27.21	674.5	0.33	2.62	7.89	<LOD	8.47	268.23	294.67	0.56	15.07	0.82
HC-12	2764	2151	34.3	163.9	7.4	<LOD	1483	27.29	208.38	0.21	0.98	6.63	<LOD	8.62	147.05	16.37	0.33	4.23	0.9
HC-13	12251	29395	250.5	575.5	191.2	277.7	13036	95.19	239	4.46	9.33	60.06	5.74	68.18	1072.34	288.14	2.25	13.04	7.15
HC-14	1190	3935	67.5	164.3	14.1	57.7	3750	29.84	476	0.61	2.98	16.03	1.36	49.09	105.83	35.18	0.54	1.41	1.92
HC-15	8826	18543	624	1222.4	76.9	724.1	8228	187.2	214.5	1.85	14.88	42	5.43	36.61	698.29	78.3	0.4	15.24	5.01
HC-16	6194	2871	173.6	355.5	41.8	283.2	1841	41.43	99.38	1.84	8.92	16.47	2.78	194.4	233.31	31.85	0.22	2.66	0.83
HC-17	1196	1873	53.3	117.4	19.8	10.7	1794	35.54	128.67	0.46	2.45	8.9	2.34	47.52	215.55	73.32	0.31	4.12	0.92
HC-18	4193	4113	85.7	144.5	54	30	2711	21.79	81	0.4	3.92	8.82	1.42	13.82	169.07	54.85	0.48	10.01	1.16
HC-19	2428	12405	153.1	393.6	80.1	133.2	8725	65.41	143.2	1.06	7.03	27.85	3.57	55.41	628.38	99.94	0.53	67.04	5.16
HC-20	1221	2350	92.7	81.6	16.7	26.7	1356	13.67	428.35	0.42	4.36	5.71	<LOD	115.14	98.3	12.1	0.24	4.08	0.52
HC-21	2600	4468	39.3	40.6	15.6	11.9	2694	10.62	164.73	0.26	1.09	5.04	1.73	5.75	49.52	45.47	0.11	0.77	0.33
HC-22	6639	8580	191.7	326	36.6	112	4056	77.43	92.33	0.66	10.49	20.46	2.93	34.67	238.55	41.02	0.29	6.29	2.93

HC-23	4640	2881	57.7	140.9	27.8	84.1	1314	24.09	393.5	0.22	2.55	10.72	1.17	5.24	236.78	44.94	0.05	2.84	0.89
HC-24	1244	1972	178.2	161.8	31.7	16.7	1754	19.67	944.83	2.47	4.24	7.37	<LOD	802.72	205.91	51.11	0.81	14.08	1.15
HC-25	2703	3529	105.8	131.8	17.9	<LOD	2127	18.84	342.53	0.26	1.24	5.64	<LOD	39.25	125.71	42.64	0.27	3.32	1.17
HC-26	707	902	66.6	114.2	34.6	<LOD	1022	5.11	273.45	1.61	2.41	6.32	<LOD	16.76	147.62	26.97	0.1	3.84	0.52
HC-27	544	2942	68.6	59.2	23.5	39.8	1829	30.99	295.07	0.32	9.1	10.95	<LOD	131.62	75.68	12.94	1.18	1.29	1
HC-28	2197	1799	41.1	67.2	14.2	<LOD	906	12.85	115.43	0.18	1.48	8.1	2.02	24.16	117.66	26.58	0.14	1.25	0.31
HC-29	3681	3016	302.1	609	43.7	39.4	1906	64.17	234.67	0.62	3.94	14.15	1.65	209.89	684.61	45.18	0.61	11.16	3.8
HC-30	6981	4236	44.2	209.3	15.3	10.2	1894	17.78	142.86	0.26	1.32	5.99	<LOD	35.69	127.14	65.46	0.19	2.84	0.37
HC-31	1662	3068	153.9	268.1	31.8	13.4	1493	33.48	196.75	2.03	4	9.37	0.91	144.83	335.75	39.87	0.23	6.91	1.36
HC-32	312	903	37.4	71.5	16.4	<LOD	1720	17.4	438.69	0.16	1.46	4.21	<LOD	29.94	109.9	43.43	0.15	1.36	0.34
HC-33	5224	6516	146.2	191.6	46.5	22.6	3530	32.68	337.6	1.26	2.57	12.7	1.37	73.52	329.9	35.23	0.46	7.97	1.48
HC-34	2969	4421	171.6	704	76	41.3	4809	100.68	24.5	0.57	4.9	23.34	2.41	140.25	747.44	199.65	0.31	9.49	1.32
HC-35	572	1943	30.3	6.2	12.2	<LOD	2701	9.45	198.5	0.18	1.14	2.92	<LOD	78.79	48.22	19.57	0.14	0.27	1
HC-36	583	3811	83.7	191.9	28.4	21	2306	30.2	1120	0.26	1.98	14.21	<LOD	13.62	158.74	20.74	0.19	1.45	1.5
HC-37	1859	840	175.6	123.6	45.5	46.4	631	23.77	439	0.27	4.41	11.35	0.84	23.84	220.89	23.04	0.35	2.2	2.34
HC-38	3054	888	90.1	212.6	12.2	22.9	489	35.61	272.42	0.11	4.52	10.54	1.76	10.92	183.3	48.93	0.61	3.89	0.94
HC-39	2863	1956	67.5	77.5	10.8	28.4	1071	19.63	166.11	0.23	2.98	6.99	2.42	13.39	73.86	14.56	0.3	1.3	0.49
HC-40	4234	1770	89.5	49.2	13.9	53.3	1411	39.28	169.85	0.27	3.87	16.76	1.67	19.53	69.16	39.1	0.33	2.35	1.89
HC-41	1982	1970	54	56.1	13	18.7	1276	19.83	463.71	0.08	2.74	12.06	2.69	37.17	170.7	116.99	0.39	2.15	0.81
HC-42	2998	2947	65.3	216.5	14.9	12.5	1735	34.72	202	0.1	1.41	6.16	<LOD	6.89	205.43	14.64	0.31	2.08	1.35
HC-43	4432	1423	135.2	145.7	251.8	51.7	719	28.91	133	0.38	2.69	12.69	2.55	21.19	120.55	46.34	0.29	1.76	0.55
HC-44	3316	1290	52.4	199.1	36.7	<LOD	932	33.89	299.64	0.19	2.41	8.22	0.79	9.6	193.82	10.19	0.34	5.24	0.72
HC-45	3943	1675	105.1	139.7	10.9	16.2	974	25.09	266	0.51	1.97	6.12	2.08	7.82	189.89	26.6	0.26	2.75	0.54
HC-46	3052	2045	71	2	16.8	19.6	1094	8.26	651.16	0.57	3.04	19.5	<LOD	10.04	44.22	29.66	0.31	0.4	0.54
Mean	**3029**	**4119**	**110.53**	**210.7**	**35.9**	**66.1**	**2490.04**	**34.06**	**313.17**	**0.62**	**3.59**	**12.22**	**2.22**	**110.91**	**234.54**	**58.15**	**0.40**	**5.75**	**1.36**

Table S4. Major and trace element concentrations and the mean values in PDAC urine samples (n= 21).
LOD = limit of detection

	Major (µg/ml)				Trace (ng/ml)														
Sample ID	**Na**	**K**	**Mg**	**Ca**	**Li**	**Al**	**Rb**	**Fe**	**Zn**	**Co**	**Ni**	**Cu**	**Cr**	**As**	**Sr**	**Mo**	**Cd**	**Ba**	**Pb**
PDAC-01	219	206	4.9	10.9	2.71	10.07	126.3	10.7	218.6	0.03	0.61	3.3	<LOD	3.43	27.86	6.77	6.77	1.06	0.2
PDAC-02	762	236	10.5	13.1	2.51	<LOD	126.6	<LOD	761.8	0.03	0.48	1.92	<LOD	1.77	24.6	4.17	4.17	0.13	0.07
PDAC-03	1571	2692	143.8	330.4	23.65	11.94	1797.4	79.7	4221.9	0.7	3.45	75.84	1.35	41.48	302.9	76.73	2.15	5.57	2.92
PDAC-04	6724	2026	87.1	68.2	30.52	129.12	2157.2	98.8	6512.8	0.76	9.78	140.74	4.79	35.77	146.49	45.61	9.32	2.46	0.95
PDAC-05	3380	6848	80	218.3	38.61	15.88	4955.3	107	2774.8	0.64	4.14	53.33	2.5	797.94	312.52	61.17	3.54	1.2	1.64
PDAC-06	295	2458	12.7	13.8	9.65	23.34	2222.1	117.3	295.5	1.23	3.33	31.79	0.86	35.12	44.01	28.42	1	0.74	2.28
PDAC-07	396	998	16.1	52.9	9.92	38.89	922.7	24.3	395.9	0.2	5.26	71.01	1.68	1.47	64.06	53.25	2.81	0.29	0.39
PDAC-08	251	4924	104.2	6.3	49.35	10.37	3229.5	208.3	49.5	3.6	61.5	39.4	120.5	25.8	99.5	163.7	0.3	15.9	2.73
PDAC-09	694	506	14.4	1.6	34.85	29.39	387.8	<LOD	136.9	<LOD	0.94	4.43	<LOD	2.99	24.4	7.36	0.16	0.3	0.37
PDAC-10	148	504	1.6	7	1.58	<LOD	437.4	<LOD	65.2	<LOD	0.22	1.36	<LOD	1.96	6.24	3.95	0.08	<LOD	<LOD
PDAC-11	1941	4121	72.4	163.2	20.38	8.64	2729.3	26.1	1058.6	0.24	1.55	28.21	<LOD	125.77	139.2	59.23	2.03	4.37	0.67
PDAC-12	1066	2874	43.5	115.6	10.62	25.08	1704.7	17.9	482.7	0.33	2.63	9.41	<LOD	59.32	115.29	21.69	0.24	7.54	0.36
PDAC-13	411	707	32.2	46.7	6.92	29.98	651.3	8.4	1326.7	0.38	1.54	33.81	1.05	5.69	84.85	24.77	0.36	3.56	0.33
PDAC-14	551	2455	39.6	45.3	10.54	32.91	1733.1	15.7	890.5	1.34	3.79	21.51	1.41	14.63	46.2	31.48	0.35	0.43	0.51
PDAC-15	50	580	10.1	18.3	2.89	<LOD	294.9	5.5	324.7	0.12	0.22	45.58	<LOD	35.06	22.44	3.39	0.37	0.06	0.13
PDAC-16	133	157	5.4	10.7	1.13	<LOD	90.6	<LOD	56.6	0.02	<LOD	0.88	<LOD	4.78	19.18	2.16	0.01	0.2	0.04
PDAC-17	3721	980	83.9	44.81	51.46	50.31	3606.9	13.68	2113.5	0.45	6.34	16.52	4.98	31.17	75.18	246.8	0.97	0.37	1.9
PDAC-18	2107	1946	36.4	62.79	16.06	14.7	1692.1	56.75	475.6	0.45	2.46	19.12	2.27	7.56	138.97	90.58	0.18	2.32	0.24
PDAC-19	1716	1618	41.7	46.2	20.73	<LOD	916.8	6.34	98.9	0.04	0.52	5.08	0.66	34.97	81.11	45.23	0.23	0.43	0.37
PDAC-20	156	1083	85.7	74.3	10.74	34.57	1348.9	36.5	3143.1	1.06	3.46	88.34	1.63	36.69	118.57	20.57	1.71	0.26	0.91
PDAC-21	134	907	79.1	232.9	33.89	16.56	587.9	57.6	1933	0.16	1.79	79.32	0.8	15.67	171.21	16.76	1.11	1.26	2.04
Mean	**1258**	**1849**	**47.9**	**75.4**	**18.5**	**30.1**	**1510.4**	**52.4**	**1301.8**	**0.62**	**5.70**	**36.71**	**11.11**	**62.81**	**98.32**	**48.28**	**1.80**	**2.42**	**0.95**

Table S5: Zinc concentrations and zinc isotope compositions ($\delta^{66/64}$Zn) associated 2SD and number of replicates for healthy controsl and PDAC urine samples.

Sample ID	Zn (ng ml^{-1})	$\delta^{66/64}$Zn (‰)	RMS (SD) (‰)	n
Healthy controls				
HC-03	391.4	0.27	0.13 (0.09)	2
HC-04	977	-0.09	0.13 (0.00)	2
HC-05	65.7	0.67	0.13 (0.00)	2
HC-06	158.4	-0.05	0.13	1
HC-07	236	0.21	0.13 (0.12)	2
HC-08	208.9	0.16	0.13	1
HC-09	555.7	0	0.13 (0.01)	2
HC-10	446.2	0.03	0.13 (0.03)	2
HC-11	674.5	-0.04	0.13 (0.08)	3
HC-12	208.4	0.1	0.13 (0.10)	2
HC-14	476	-0.04	0.13	1
HC-17	128.7	-0.16	0.13 (0.01)	2
HC-20	428.4	-0.03	0.1 (0.08)	2
HC-21	164.7	0.03	0.1 (0.06)	2
HC-23	393.5	-0.02	0.13	1
HC-24	944.8	-0.26	0.05 (0.06)	4
HC-25	342.5	0.1	0.13 (0.03)	2
HC-26	273.5	0.19	0.13 (0.14)	2
HC-27	295.1	0.02	0.13 (0.13)	2
HC-28	115.4	-0.17	0.13	1
HC-31	196.8	0.25	0.13	1
HC-32	438.7	-0.11	0.13 (0.21)	2
HC-33	337.6	-0.16	0.13	1
HC-36	1120	-0.24	0.13 (0.09)	3
HC-37	439	0.06	0.13 (0.18)	4
HC-38	272.4	0.16	0.13 (0.07)	3
HC-39	166.1	-0.18	0.13	1
HC-41	463.7	-0.19	0.13 (0.10)	2
HC-42	202	0.09	0.13 (0.10)	2
HC-43	133	0.3	0.13	1
HC-44	299.6	0.29	0.13 (0.15)	2
HC-45	266	0.01	0.13 (0.21)	2
HC-46	651.2	0.07	0.13	1

PDAC				
PDAC-01	218.6	0.09	0.13 (0.07)	4
PDAC-02	761.8	0.05	0.13	1
PDAC-03	4221.9	-0.22	0.13 (0.08)	3
PDAC-04	6512.8	-0.06	0.13 (0.11)	3
PDAC-05	2774.8	-0.32	0.13 (0.06)	4
PDAC-06	295.5	-0.09	0.13 (0.08)	4
PDAC-07	395.9	0.15	0.13 (0.09)	4
PDAC-08	49.5	-0.15	0.13 (0.10)	2
PDAC-10	65.2	-0.32	0.13 (0.19)	2
PDAC-11	1058.6	-0.27	0.13 (0.08)	2
PDAC-12	482.7	-0.14	0.13 (0.12)	3
PDAC-13	1326.7	-0.22	0.13	1
PDAC-14	890.5	-0.18	0.13 (0.12)	2
PDAC-15	324.7	-0.18	0.13 (0.04)	2
PDAC-16	56.6	-0.33	0.13	1
PDAC-17	2113	0.02	0.13	1
PDAC-21	1933	-0.13	0.13 (0.09)	4