Supplementary Information (SI) for Environmental Science: Processes & Impacts.

Supplementary Materials

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Supplementary Table 1 | Baseline data of the included and excluded participants (N = 9756).

Variables	**Overall**
Participants	N=9756
Continuous variables, Median (Q1-Q3)	
AAMA(ng/mL)	46.500 (24.500-86.675)
AMCC(ng/mL)	116.000 (59.975-239.750)
ATCA(ng/mL)	138.000 (64.675-273.000)
BPMA(ng/mL)	4.070 (1.290-11.325)
CEMA(ng/mL)	96.800 (49.200-184.000)
CYMA(ng/mL)	1.825 (0.979-4.757)
DHBMA(ng/mL)	297.000 (167.000-476.000)
2HPMA(ng/mL)	31.050 (16.200-56.900)
3HPMA(ng/mL)	235.000 (120.000-457.000)
MHBMA3(ng/mL)	5.640 (2.810-10.875)
Low-frequency PTA(db)	8.750 (4.583-14.583)
Speech-frequency PTA(db)	10.312 (5.625-17.188)
High-frequency PTA(db)	18.333 (10.833-31.667)
BMI (kg/m^2)	24.500 (19.300-29.800)
Age(year)	26.000 (9.000-52.000)
Creatinine (mg/dL)	0.820 (0.690-0.980)
Categorical variables, %	
Gender	
Male	4856 (49.774%)
Female	4900 (50.226%)
Race/Ethnicity	
Mexican American	1355 (13.889%)
Non-Hispanic White	1076 (11.029%)
Non-Hispanic Black	2973 (30.474%)
Other races	4352 (44.608%)
Education level	
Below high school	1332 (23.978%)
High school	1169 (21.044%)
Above high school	3054 (54.977%)
Hypertension	2031 (32.944%)
Diabetes	708 (7.567%)
Cigarette smoking	2369 (42.662%)
Alcohol drinking	3577 (71.871%)
Noise Exposure	540 (13.818%)

SD, Standard Deviation; BMI, Body Mass Index. VOCs, Volatile Organic Compounds: AAMA, Urinary N-Acetyl-S-(2-carbamoylethyl)-L-cysteine; AMCC, Urinary N-Acetyl-S-(N-methylcarbamoyl)-L-cysteine; ATCA, Urinary 2-Aminothiazoline-4-carboxylic acid; BPMA, Urinary N-Acetyl-S-(n-propyl)-L-cysteine; CEMA, Urinary N-Acetyl-S-(2-carboxyethyl)-L-cysteine; CYMA, Urinary N-Acetyl-S-(2-cyanoethyl)-L-cysteine; DHBMA, Urinary N-Acetyl-S-(3,4-dihydroxybutyl)-L-cysteine; 2HPMA, Urinary N-Acetyl-S-(2-hydroxypropyl)-L-cysteine; 3HPMA, Urinary N-Acetyl-S-(3-hydroxypropyl)-L-cysteine; MA, Urinary Mandelic acid; MHBMA3, Urinary N-Acetyl-S-(4-hydroxy-2-butenyl)-L-cysteine.

Supplementary Table 2 | Distribution of the urinary VOCs metabolites levels in NHANES 2011-2012 (n = 9756).

Variable	LLOD	10th percentile	25th percentile	50th percentile	75th percentile	90th percentile
URXAAM	2.200	13.150	24.500	46.500	86.675	167.000
URXAMC	6.260	30.100	59.975	116.000	239.750	481.000
URXATC	15.00	31.850	64.675	138.000	273.000	486.500
URXBPM	1.200	0.850	1.290	4.070	11.325	28.700
URXCEM	6.960	24.600	49.200	96.800	184.000	325.500
URXCYM	0.500	0.550	0.979	1.825	4.757	106.000
URXDHB	5.250	89.550	167.000	297.000	476.000	683.000
URXGAM	9.400	6.650	6.650	6.650	14.000	24.800
URXHEM	0.791	0.559	0.559	0.970	1.850	3.735
URXHP2	5.300	8.645	16.200	31.050	56.900	113.500
URXHPM	13.000	61.050	120.000	235.000	457.000	920.000
URXMB1	0.700	0.495	0.495	0.495	0.495	0.495
URXMB2	0.700	0.495	0.495	0.495	0.495	0.732
URXMB3	0.700	1.370	2.810	5.640	10.875	25.850

VOCs, Volatile Organic Compounds. The variable names are detailed in the attached table

Supplementary Table 3 |Sensitive analysis for the association between urinary ATCA concentrations and hearing threshold shift (N = 9756).

β (95% CI), P value of urinary ATCA concentrations, (ng/mL)						
ATCA	Crude Model		Model I		Model II	
Low-frequency PTA						
Q1	Reference	P Value	Reference	P Value	Reference	P Value
Q2	1.056 (-1.020, 3.132)	0.319	0.495 (-1.584, 2.575)	0.641	0.394 (-1.679, 2.468)	0.709
Q3	4.632 (2.558, 6.706)	<0.001	3.434 (1.326, 5.541)	0.001	3.102 (0.992, 5.211)	0.004
Q4	5.452 (3.377, 7.527)	<0.001	3.636 (1.481, 5.791)	<0.001	3.241(1.074, 5.408)	0.003
Speech-frequency PTA						
Q1	Reference	P Value	Reference	P Value	Reference	P Value
Q2	-0.015 (-2.051, 2.021)	0.988	0.213 (-1.833, 2.258)	0.839	0.103 (-1.941, 2.146)	0.922
Q3	2.429 (0.395, 4.462)	0.019	2.834 (0.761, 4.908)	0.007	2.504 (0.426, 4.583)	0.018
Q4	2.759 (0.724, 4.793)	0.008	3.321 (1.201, 5.441)	0.002	**2.859 (0.725, 4.994)**	**0.009**
High-frequency PTA						
Q1	Reference	P Value	Reference	P Value	Reference	P Value
Q2	-4.461 (-7.106, -1.817)	<0.001	-1.599 (-4.174, 0.976)	0.224	-1.414 (-3.986, 1.158)	0.281
Q3	-6.115 (-8.757, -3.474)	<0.001	-0.265 (-2.875, 2.345)	0.842	0.075 (-2.541, 2.691)	0.955
Q4	-9.141 (-11.784, -6.498)	<0.001	-0.445 (-3.114, 2.224)	0.744	-0.094 (-2.781, 2.593)	0.945

Crude Model = unadjusted. Model I = Crude Model + Gender, Age. Model II = Model I + Race/Ethnicity, BMI, Education level, Hypertension, Diabetes, Cigarette smoking, Alcohol drinking, Creatinine and Noise Exposure. CI, Confidence Interval; BMI, Body Mass Index.

Supplementary Table 4 | Smoking-related stratified analysis for the association between ATCA concentrations and hearing threshold shift (N = 1048).

ATCA	N	Low-frequency PTA		Speech-frequency PTA		High-frequency PTA	
Non-smoking		β (95% CI), P value of urinary ATCA concentrations, (ng/mL)					
Q1	146	Reference	P Value	Reference	P Value	Reference	P Value
Q2	169	0.911 (-0.911, 2.733)	0.328	0.950 (-0.874, 2.773)	0.308	0.346 (-2.351, 3.043)	0.802
Q3	167	1.320 (-0.544, 3.184)	0.166	1.339 (-0.527, 3.205)	0.160	0.753 (-2.006, 3.513)	0.593
Q4	153	1.683 (-0.266, 3.632)	0.091	**1.970 (0.019, 3.921)**	**0.048**	1.992 (-0.893, 4.877)	0.176
Smoking		β (95% CI), P value of ATCA concentrations, (ng/mL)					
Q1	114	Reference	P Value	Reference	P Value	Reference	P Value
Q2	95	1.775 (-0.452, 4.002)	0.119	2.014 (-0.311, 4.338)	0.090	2.153 (-1.605, 5.912)	0.262
Q3	95	0.787 (-1.449, 3.023)	0.491	1.015 (-1.320, 3.349)	0.395	1.710 (-2.064, 5.484)	0.375
Q4	109	1.084 (-1.130, 3.297)	0.338	1.518 (-0.793, 3.829)	0.199	2.590 (-1.147, 6.326)	0.175

Adjusted for gender, Race/Ethnicity, BMI, Education level, Hypertension, Diabetes, Alcohol drinking, Creatinine, and Noise exposure.

CI, Confidence Interval; PTA, Pure tone audiometry. ATCA, Urinary 2-Aminothiazoline-4-carboxylic acid

Supplementary Table 5| Transcription factor prediction of hepatocyte growth factor (HGF) gene.

Matrix ID	Name	Score	Relative score	Sequence ID	Start	End	Strand	Predicted sequence
MA0465.3	MA0465.3.CDX2	14.592027	1.000000006	NC_000007.14:c81774047-81772047	751	758	+	GCAATAAA
MA1473.2	MA1473.2.CDX4	15.482717	1.000000003	NC_000007.14:c81774047-81772047	751	759	+	GCAATAAAA
MA0913.3	MA0913.3.HOXD9	15.327005	1.000000001	NC_000007.14:c81774047-81772047	751	759	+	GCAATAAAA
MA0442.3	MA0442.3.SOX10	11.610084	1	NC_000007.14:c81774047-81772047	636	641	+	ACAAAG
MA0442.3	MA0442.3.SOX10	11.610084	1	NC_000007.14:c81774047-81772047	825	830	+	ACAAAG
MA0442.3	MA0442.3.SOX10	11.610084	1	NC_000007.14:c81774047-81772047	1721	1726	+	ACAAAG
MA0442.3	MA0442.3.SOX10	11.610084	1	NC_000007.14:c81774047-81772047	1772	1777	+	ACAAAG
MA1125.2	MA1125.2.ZNF384	14.630931	0.999999998	NC_000007.14:c81774047-81772047	1469	1476	-	AAAAAAAA
MA1125.2	MA1125.2.ZNF384	14.630931	0.999999998	NC_000007.14:c81774047-81772047	1470	1477	-	AAAAAAAA
MA1125.2	MA1125.2.ZNF384	14.630931	0.999999998	NC_000007.14:c81774047-81772047	1628	1635	+	AAAAAAAA
MA1125.2	MA1125.2.ZNF384	14.630931	0.999999998	NC_000007.14:c81774047-81772047	1629	1636	+	AAAAAAAA
MA1125.2	MA1125.2.ZNF384	14.630931	0.999999998	NC_000007.14:c81774047-81772047	1630	1637	+	AAAAAAAA
MA0878.3	MA0878.3.CDX1	16.87225	0.999999991	NC_000007.14:c81774047-81772047	750	759	+	GGCAATAAAA
MA0899.2	MA0899.2.HOXA10	13.389124	0.995139121	NC_000007.14:c81774047-81772047	751	759	+	GCAATAAAA
MA1125.2	MA1125.2.ZNF384	12.618615	0.9665189	NC_000007.14:c81774047-81772047	1022	1029	+	AAAAAAAT
MA1125.2	MA1125.2.ZNF384	12.618615	0.9665189	NC_000007.14:c81774047-81772047	1485	1492	+	AAAAAAAT
MA1125.2	MA1125.2.ZNF384	12.618615	0.9665189	NC_000007.14:c81774047-81772047	1631	1638	+	AAAAAAAT
MA1125.2	MA1125.2.ZNF384	12.446241	0.963650929	NC_000007.14:c81774047-81772047	1486	1493	+	AAAAAATA
MA1125.2	MA1125.2.ZNF384	12.388456	0.962689497	NC_000007.14:c81774047-81772047	798	805	+	AAAAAAAC
MA1125.2	MA1125.2.ZNF384	12.388456	0.962689497	NC_000007.14:c81774047-81772047	1468	1475	-	AAAAAAAC
MA1125.2	MA1125.2.ZNF384	11.94268	0.955272634	NC_000007.14:c81774047-81772047	1348	1355	+	AAAAAAAG
MA1125.2	MA1125.2.ZNF384	11.844371	0.953636951	NC_000007.14:c81774047-81772047	799	806	+	AAAAAACA

MA1125.2	MA1125.2.ZNF384	11.844371	0.953636951	NC_000007.14:c81774047-81772047	820	827	+	AAAAAACA
MA1473.2	MA1473.2.CDX4	11.901981	0.951378084	NC_000007.14:c81774047-81772047	1974	1982	-	GCCATAAAG
MA0878.3	MA0878.3.CDX1	13.313726	0.948176068	NC_000007.14:c81774047-81772047	1974	1983	-	GGCCATAAAG
MA0465.3	MA0465.3.CDX2	11.670449	0.935950885	NC_000007.14:c81774047-81772047	736	743	+	ACAATAAA
MA0465.3	MA0465.3.CDX2	11.596826	0.934336849	NC_000007.14:c81774047-81772047	1975	1982	-	GCCATAAA
MA1125.2	MA1125.2.ZNF384	10.433926	0.930169832	NC_000007.14:c81774047-81772047	1023	1030	+	AAAAAATT
MA1125.2	MA1125.2.ZNF384	10.433926	0.930169832	NC_000007.14:c81774047-81772047	1632	1639	+	AAAAAATT
MA0913.3	MA0913.3.HOXD9	10.696103	0.929022654	NC_000007.14:c81774047-81772047	1974	1982	-	GCCATAAAG
MA0899.2	MA0899.2.HOXA10	10.09461	0.923045298	NC_000007.14:c81774047-81772047	1974	1982	-	GCCATAAAG
MA1125.2	MA1125.2.ZNF384	9.832055	0.920155853	NC_000007.14:c81774047-81772047	1467	1474	-	AAAAAACT
MA1125.2	MA1125.2.ZNF384	9.761436	0.918980894	NC_000007.14:c81774047-81772047	1349	1356	+	AAAAAAGT
MA1473.2	MA1473.2.CDX4	8.8909025	0.910491388	NC_000007.14:c81774047-81772047	736	744	+	ACAATAAAG
MA0465.3	MA0465.3.CDX2	10.20262	0.903771967	NC_000007.14:c81774047-81772047	301	308	-	GAAATAAA
MA0899.2	MA0899.2.HOXA10	9.204637	0.90357001	NC_000007.14:c81774047-81772047	736	744	+	ACAATAAAG
MA0899.2	MA0899.2.HOXA10	9.192059	0.903294766	NC_000007.14:c81774047-81772047	1346	1354	+	GTAAAAAAA

Supplementary Table 6 | Transcription factor prediction of cellular-mesenchymal epithelial transition factor (MET) gene.

Matrix ID	Name	Score	Relative score	Sequence ID	Start	End	Strand	Predicted sequence
MA0510.3	MA0510.3.RFX5	14.912289	0.893220772	NC_000007.14:116670196-116672196	370	383	+	ATTGCTATGGAAAC
MA0510.3	MA0510.3.RFX5	14.73566	0.891282239	NC_000007.14:116670196-116672196	370	383	-	GTTTCCATAGCAAT

Supplementary Table 7 | Transcription factor prediction of Superoxide Dismutase 1 (SOD1) gene.

Matrix ID	Name	Score	Relative score	Sequence ID	Start	End	Strand	Predicted sequence
MA1564.2	MA1564.2.SP9	15.800247	1.000000006	NC_000021.9:31657693-31659693	1750	1759	+	CCACGCCCCC
MA1513.2	MA1513.2.KLF15	14.972673	1.000000005	NC_000021.9:31657693-31659693	1816	1823	-	CCCCGCCC
MA1513.2	MA1513.2.KLF15	14.972673	1.000000005	NC_000021.9:31657693-31659693	1852	1859	+	CCCCGCCC
MA0741.1	MA0741.1.KLF16	17.682444	0.999999994	NC_000021.9:31657693-31659693	1749	1759	+	GCCACGCCCCC
MA0746.3	MA0746.3.SP3	18.364372	0.998402324	NC_000021.9:31657693-31659693	1749	1759	+	GCCACGCCCCC
MA1512.2	MA1512.2.KLF11	16.631697	0.997776223	NC_000021.9:31657693-31659693	1750	1759	+	CCACGCCCCC
MA1516.2	MA1516.2.KLF3	16.752602	0.994217284	NC_000021.9:31657693-31659693	1748	1757	+	GGCCACGCCC
MA1517.2	MA1517.2.KLF6	14.075645	0.990143904	NC_000021.9:31657693-31659693	1750	1758	+	CCACGCCCC
MA0741.1	MA0741.1.KLF16	16.384356	0.978779943	NC_000021.9:31657693-31659693	1851	1861	+	GCCCCGCCCCC
MA1564.2	MA1564.2.SP9	14.688722	0.978726103	NC_000021.9:31657693-31659693	1852	1861	+	CCCCGCCCCC
MA1513.2	MA1513.2.KLF15	13.365077	0.974446424	NC_000021.9:31657693-31659693	1901	1908	-	GCCCGCCC
MA0746.3	MA0746.3.SP3	16.40809	0.97180914	NC_000021.9:31657693-31659693	1851	1861	+	GCCCCGCCCCC
MA1512.2	MA1512.2.KLF11	13.907747	0.957164874	NC_000021.9:31657693-31659693	1852	1861	+	CCCCGCCCCC
MA1517.2	MA1517.2.KLF6	11.182343	0.934651331	NC_000021.9:31657693-31659693	1815	1823	-	CCCCGCCCC
MA1517.2	MA1517.2.KLF6	11.182343	0.934651331	NC_000021.9:31657693-31659693	1852	1860	+	CCCCGCCCC
MA1516.2	MA1516.2.KLF3	11.612109	0.923598609	NC_000021.9:31657693-31659693	1850	1859	+	GGCCCCGCCC
MA1564.2	MA1564.2.SP9	11.755391	0.922583993	NC_000021.9:31657693-31659693	1899	1908	-	GCCCGCCCCC
MA1564.2	MA1564.2.SP9	11.49181	0.917539212	NC_000021.9:31657693-31659693	1814	1823	-	CCCCGCCCCG
MA1564.2	MA1564.2.SP9	11.231851	0.912563755	NC_000021.9:31657693-31659693	1943	1952	-	CCTCGCCCAC
MA0757.2	MA0757.2.ONECUT3	14.176346	0.910616216	NC_000021.9:31657693-31659693	769	780	+	ATAAATCGATAG
MA1517.2	MA1517.2.KLF6	9.667968	0.905606135	NC_000021.9:31657693-31659693	1944	1952	-	CCTCGCCCA
MA1512.2	MA1512.2.KLF11	10.197224	0.901844696	NC_000021.9:31657693-31659693	1899	1908	-	GCCCGCCCCC

Supplementary Table 8 | Transcription factor prediction of Toll-like receptor 4 (TLR4) gene.

Matrix ID	Name	Score	Relative score	Sequence ID	Start	End	Strand	Predicted sequence
MA0143.5	MA0143.5.SOX2	12.655396	1.000000002	NC_000009.12:117702403-117704403	758	764	+	ACAATGG
MA0492.2	MA0492.2.JUND	16.849583	0.988585599	NC_000009.12:117702403-117704403	1433	1443	+	AATGAGGTCAT
MA0497.2	MA0497.2.MEF2C	15.5764065	0.969150017	NC_000009.12:117702403-117704403	566	576	+	TTAAAAATAGA
MA0052.5	MA0052.5.MEF2A	14.926926	0.957565372	NC_000009.12:117702403-117704403	566	575	+	TTAAAAATAG
MA0492.2	MA0492.2.JUND	13.339054	0.950673139	NC_000009.12:117702403-117704403	1434	1444	-	AATGACCTCAT
MA0489.1	MA0489.1.JUN	13.702142	0.941255552	NC_000009.12:117702403-117704403	1182	1195	-	GCTGGGTGACTCAT
MA1126.2	MA1126.2.FOS::JUN	13.134733	0.938508571	NC_000009.12:117702403-117704403	1434	1443	-	ATGACCTCAT
MA0143.5	MA0143.5.SOX2	9.778614	0.932261762	NC_000009.12:117702403-117704403	683	689	+	ACAATAG
MA0497.2	MA0497.2.MEF2C	12.965759	0.929464789	NC_000009.12:117702403-117704403	1690	1700	-	ATTAAAATAGC
MA0143.5	MA0143.5.SOX2	9.551398	0.926911619	NC_000009.12:117702403-117704403	703	709	+	ACAATGC
MA0080.5	MA0080.5.SPI1	19.592257	0.918632908	NC_000009.12:117702403-117704403	1894	1913	-	GGGTGAGAGGAAGTGAAAGC
MA0489.1	MA0489.1.JUN	11.89915	0.918054449	NC_000009.12:117702403-117704403	1177	1190	+	AAGCCATGAGTCAC
MA0489.1	MA0489.1.JUN	10.868551	0.904792589	NC_000009.12:117702403-117704403	1743	1756	+	GTCAGATGACTAAT
MA0497.2	MA0497.2.MEF2C	11.289192	0.903978792	NC_000009.12:117702403-117704403	1283	1293	-	CTGAAAATAAA
MA1126.2	MA1126.2.FOS::JUN	11.604256	0.902058819	NC_000009.12:117702403-117704403	1434	1443	+	ATGAGGTCAT
MA0497.2	MA0497.2.MEF2C	11.114759	0.901327188	NC_000009.12:117702403-117704403	378	388	-	ATTAAAATAAA
MA0492.2	MA0492.2.JUND	8.659078	0.900131057	NC_000009.12:117702403-117704403	1073	1083	-	CATGACATAAC

Supplementary Table 9 | Gene associated miRNAs.

Mirnaid	Refseqid	Genesymbol	Duplex	Start	End	Bindingp	Energy	Seed	Accessibility	Au	Phylopstem	Phylopflank	Me	Number_of pairings	Binding region length	Longest consecutive pairings	Position	Validated	Targetscan	Mirdb
Hsa-mir-148a-3p	Nm_001127500	Met	Tcagtgcactacagaactttgt#acaggatctcactctgttgccagggctgtagtgcagtggt	5155	5195	1	-24	0	4.99e-06	0.456	-0.4221774	0.422178296	-7.938095362	15	20	10	3utr	Mirt054388	1	1
Hsa-mir-216a-3p	Nm_001127500	Met	Tcacagtggtctctgggattat#cccagaacaggccactc	5013	5030	1	-20.3	0	0.01040498	0.515	0.171171148	0.309159427	-9.546562469	13	17	7	3utr		1	1
Hsa-mir-130b-3p	Nm_001127500	Met	Cagtgcaatgatgaaagggcat#tgctcttgccaaaattgcacta	4708	4730	1	-20.8	1	0.02524403	0.691	2.1345205	1.045275195	-8.717445699	17	22	8	3utr		1	1
Hsa-mir-148a-3p	Nm_000245	Met	Tcagtgcactacagaactttgt	5101	5141	1	-24	0	4.99e-	0.	-0.422	0.4221	-7.9	15	20	10	3utr	Mirt05438	1	1

			#acaggatctcactctgttgccagggctgtagtgcagtggt						06	456	1774	78296	38095362					8		
Hsa-mir-216a-3p	Nm_000245	Met	Tcacagtggtctctgggattat#cccagaacaggccactc	4959	4976	1	-20.3	0	0.01040498	0.515	0.171171148	0.309159427	-9.546562469	13	17	7	3utr		1	1
Hsa-mir-130b-3p	Nm_000245	Met	Cagtgcaatgatgaaagggcat#tgctcttgccaaaattgcacta	4654	4676	1	-20.8	1	0.02524403	0.691	2.1345205	1.045275195	-8.717445699	17	22	8	3utr		1	1
Hsa-mir-204-5p	Nm_000601	Hgf	Ttccctttgtcatcctatgcct#aggtatatttgctggatgataaagatttcatgggaaa	2529	2566	1	-22.3	1	0.008075223	0.691	0	0	-3.937574446	22	37	10	3utr		1	1
Hsa-mir-204-5p	Nm_001010932	Hgf	Ttccctttgtcatcctatgcct#aggtatatttgctggatgataaag	2514	2551	1	-22.3	1	0.008075223	0.69	0	0	-3.93757	22	37	10	3utr		1	1

			atttcatgggaaa							1			4446						
Hsa-mir-211-5p	Nm_001010934	Hgf	Ttccctttgtcatccttcgcct#ggggaggggggactactggaat	1582	1603	1	-20.4	0	7.81e-05	0.6031	0	0	-17.16169516	15	21	9	3utr	1	1
Hsa-mir-448	Nm_138554	Tlr4	Ttgcatatgtaggatgtcccat#gggaagtgctacataaatgcaag	11500	11523	1	-22.6	1	0.01595048	0.676	-0.45106212	-0.024340349	-5.459754139	18	23	7	3utr	1	1