

Supplementary Table 1: Geometric means of biomarkers by smoking status in total control subjects

(n=5364), The Lung Cancer Cohort Consortium (LC3) Study

Biomarkers	Current smokers	Former smokers	Never smokers	P value^a
Tryptophan (μmol/L)	67.55	66.45	62.15	< 0.0001
Kynurenine (μmol/L)	1.49	1.64	1.43	< 0.0001
KTRb	22.09	24.73	23.08	< 0.0001
Quinolinic acid (nmol/L)	331.7	416.2	365.7	< 0.0001
Neopterin (nmol/L)	10.54	11.94	10.87	< 0.0001

^a for difference in geometric means among three smoking groups.

^aKTR: Kynurenine: tryptophan ratio (x 1000).

Supplementary Table 2 Median (20th-80th percentiles) of circulating biomarker concentrations among control subjects from different cohorts, The Lung Cancer Cohort Consortium (LC3) Study

Cohorts by Region	N	Tryptophan, (μmol/L)	Kynurenine, (μmol/L)	Kynurenine/ Tryptophan Ratio	Quinolinic acid (nmol/L)	Neopterin (nmol/L)
US cohorts						
CLUE I & II	191	68.3 (57.2-80.7)	1.58 (1.29-1.88)	22.9 (19.3-27.6)	353 (278-468)	13.6 (10.3-19.5)
CPS-II	182	71.6 (60.4-86.8)	1.81 (1.47-2.16)	24.5 (20.7-30.6)	454 (340-614)	9.71 (7.60-12.9)
HPFS	155	67.4 (60.0-77.3)	1.64 (1.37-1.92)	23.9 (20.3-29.9)	362 (273-497)	9.34 (6.87-12.2)
MEC	174	67.6 (57.9-79.2)	1.63 (1.40-1.92)	24.2 (20.6-28.7)	383 (283-534)	17.3 (13.3-22.3)
NHS	345	69.3 (58.7-81.0)	1.52 (1.29-1.80)	21.7 (18.4-27.5)	349 (261-475)	13.6 (10.5-18.1)
NYUWHS	171	66.0 (57.8-77.5)	1.44 (1.23-1.84)	22.3 (19.2-26.3)	331 (250-430)	14.0 (11.0-18.4)
PHS	81	64.2 (57.2-71.3)	1.60 (1.37-1.83)	25.0 (21.8-29.1)	397 (324-521)	7.16 (5.85-9.86)
PLCO	450	64.7 (53.2-78.8)	1.68 (1.35-2.05)	25.1 (21.1-31.3)	433 (317-598)	12.4 (8.84-17.2)
SCCS	226	54.6 (45.6-65.5)	1.24 (1.05-1.46)	22.5 (18.2-27.3)	325 (232-473)	8.83 (7.03-13.2)
WHI	241	51.3 (45.7-57.7)	1.28 (1.07-1.55)	24.8 (20.9-29.9)	308 (244-412)	13.4 (9.33-17.7)
WHS	184	68.7 (59.4-79.3)	1.50 (1.24-1.83)	22.0 (18.7-26.0)	363 (280-494)	6.66 (4.72-8.82)
EU/AU cohorts						
ATBC	200	76.1 (65.7-86.8)	1.62 (1.37-1.93)	21.5 (19.0-24.2)	367 (291-453)	12.9 (10.3-16.6)
HUNT	193	73.7 (63.1-84.0)	1.59 (1.38-1.92)	22.0 (18.8-27.2)	319 (244-449)	9.51 (6.29-13.7)
MCCS	354	68.6 (59.7-78.1)	1.54 (1.28-1.81)	22.2 (18.8-26.4)	345 (274-451)	11.2 (8.81-14.1)
MDCS	198	63.2 (55.9-74.1)	1.40 (1.16-1.71)	21.8 (18.5-27.0)	324 (245-422)	10.7 (7.51-14.3)
NSHDS	244	61.9 (58.7-81.0)	1.41 (1.19-1.69)	22.7 (19.4-27.1)	306 (241-407)	5.89 (4.42-8.05)
Asian cohorts						
SCHS	422	66.9 (56.9-77.7)	1.58 (1.34-1.89)	24.0 (20.1-28.0)	365 (285-472)	16.9 (13.2-21.9)
SCS	513	75.4 (64.8-86.2)	1.53 (1.30-1.81)	20.3 (17.7-23.7)	331 (263-422)	10.8 (8.36-14.3)
SMHS	421	64.4 (56.6-73.6)	1.43 (1.24-1.68)	22.1 (19.1-26.8)	343 (267-455)	8.53 (6.13-11.9)
SWHS	419	64.2 (56.3-73.1)	1.38 (1.18-1.64)	21.7 (18.5-25.5)	363 (296-460)	8.28 (6.37-11.8)

US: United States; WHI: The Women's Health Initiative; SCCS: The Southern Community Cohort Study; NYUWHS: The New York University Women's Health Study; CPS-II: The American Cancer Society Cancer Prevention Study-II Nutrition Cohort; CLUE I: The Campaign Against Cancer and Stroke; CLUE II: The Campaign Against Cancer Heart Disease; MEC: The Multiethnic Cohort; WHS: Women's Health Study; PHS: Physician's Health Study; NHS: The Nurses' Health Study; HPFS: Health Professional's Follow-up Study; EU: European; AU: Australian; MCCS: The Melbourne Collaborative Cohort Study; MDCS: The Malmö Diet and Cancer Study; NSHDS: The Northern Sweden Health and Disease Study; ATBC: The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study; HUNT: The Nørd-Trøndelag Health Study; SMHS: The Shanghai Men's Health Study; SWHS: The Shanghai Women's Health Study; SCHS: The Singapore Chinese Health Study; SCS: The Shanghai Cohort Study.

Supplemental Table 3: Age-sex-adjusted pairwise Spearman correlation coefficients^a between two circulating biomarkers among all control subjects (n=5364),
The Lung Cancer Cohort Consortium (LC3) Study

Biomarkers	Kynurenine	KTR ^a	Neopterin	Quinolinic acid
Tryptophan	0.45	-0.43	-0.01 ^b	0.13
Kynurenine		0.55	0.34	0.66
KTR ^a			0.35	0.53
Neopterin				0.34

^c KTR, Kynurenine to tryptophan ratio (x 1000).

^a P > 0.05 for this and P < 0.001 for all other correlation coefficients.