

Supplementary material

A nested case-control study of untargeted circulatory albumin adductomics and acute myeloid leukemia.

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Supplementary Table 1: Characteristics of AML cases (n = 52) by study cohort

Characteristics	CLUE I (n = 12)	CLUE II (n = 5)	CLUE I and II (n = 7)	All CLUE (n = 24)	PLCO (n = 28)
Year of study recruitment	1974	1989	1974	1974-1989	1994-2001
Year of AML diagnosis	1978-2004	1992-2004	1995-2004	1978-2004	1996-2004
Median (range) of follow-up after study enrollment to AML diagnosis in years ^a	13.3 (4.0-26.6)	7.9 (3.1-14.9)	27.5 (20.7-29.9)	14.9 (3.1-29.9)	3.2 (1.0-9.6)

CLUE: Campaign Against Cancer and Stroke (CLUE I, 1974; CLUE II, 1989)

PLCO: Prostate, Lung, Colorectal and Ovarian cancer screening trial.

^aOne AML case in CLUE I was missing follow-up information.

Supplementary Table 2. Median (25th, 75th percentiles) of albumin adducts (relative log abundance) by AML case-control status and study

Adduct	Annotation	Elemental composition of added mass	% CV	AML cases (n=52)	Controls (n=103)	p-value*	CLUE (n = 72)	PLCO (n = 83)	p-value*
805.76	Cys34 → oxoalanine	- SH2, + O	1.24	12.6 (12.4, 12.7)	12.5 (12.4, 12.7)	0.79	12.5 (12.4 12.7)	12.5 (12.4 12.7)	0.39
808.72	Unknown		3.98	12.3 (11.9, 12.6)	12.5 (12.0, 12.8)	0.25	12.4 (11.9 12.7)	12.5 (11.9 12.8)	0.75
816.41	Unknown		1.67	12.8 (12.7, 13.0)	12.8 (12.6, 13.0)	0.73	12.8 (12.7 13)	12.8 (12.7 13)	0.88
816.43	methylation (not Cys34)	CH3	2.74	11.9 (11.7, 12.2)	12.0 (11.8, 12.4)	0.37	11.9 (11.7 12.3)	12.1 (11.8 12.3)	0.77
821.74	Unknown		1.51	11.8 (11.7, 12.0)	11.8 (11.6, 11.9)	0.80	11.8 (11.7 12)	11.8 (11.6 11.9)	0.86
822.42	Cys34 sulfinic acid	HO2	0.92	15.9 (15.8, 16.0)	15.9 (15.8, 16.0)	0.76	15.9 (15.8 16)	15.9 (15.8 16)	0.80
826.43	ethylene oxide adduct	C2H5O	8.43	13.4 (12.8, 14.2)	13.4 (12.7, 14.0)	0.68	13.6 (12.6 14.6)	13.3 (12.9 13.5)	0.09
827.09	S-(O)-O-CH3	CH3O2	5.29	12.4 (11.9, 12.6)	12.2 (11.9, 12.6)	0.67	12.3 (11.8 12.6)	12.3 (12 12.6)	0.55
827.75	Cys34 sulfonic acid	HO3	1.08	14.6 (14.4, 14.7)	14.6 (14.4, 14.8)	0.53	14.6 (14.4 14.8)	14.5 (14.4 14.7)	0.27
829.12	Unknown		2.13	11.9 (11.7, 12.0)	11.9 (11.7, 12.1)	0.72	11.9 (11.7 12)	11.9 (11.7 12.1)	0.34
829.75	Unknown		1.56	12.2 (12.0, 12.3)	12.2 (12.0, 12.4)	0.61	12.2 (12 12.4)	12.2 (12 12.3)	0.95
830.43	Acrolein addition +56	C3H5O	1.64	12.7 (12.6, 12.9)	12.7 (12.6, 12.8)	0.91	12.8 (12.6 12.9)	12.7 (12.6 12.8)	0.60
831.1	Reduced acrolein addition +58	C3H7O	2.14	12.8 (12.7, 13.0)	12.8 (12.7, 13.0)	0.80	12.8 (12.7 13)	12.8 (12.7 13)	0.50
833.08	SulfurDioxide	SO2H	2.43	11.8 (11.6, 11.9)	11.8 (11.7, 12.0)	0.29	11.8 (11.6 11.9)	11.8 (11.7 12)	0.30
835.1	methylvinylketone adduct/crotonaldehyde	C4H7O	1.49	13.2 (13.1, 13.4)	13.3 (13.1, 13.4)	0.77	13.2 (13.1 13.4)	13.3 (13.2 13.4)	0.65
838.41	SulfurTrioxid	SO3H	1.81	13.9 (13.7, 14.2)	13.9 (13.7, 14.1)	0.40	14 (13.7 14.2)	13.9 (13.7 14.1)	0.46
841.09	Unknown	C3H5O3	7.25	9.2 (8.8, 9.7)	9.3 (8.8, 9.7)	0.94	9.5 (8.8 10.1)	9.1 (8.8 9.6)	0.23
841.75	S-mercaptoacetic acid	C2H3O2S	0.83	12.5 (12.5, 12.7)	12.6 (12.5, 12.9)	0.04	12.6 (12.5 12.8)	12.6 (12.4 12.8)	0.75
845.1	Glutaraldehyde	C5H9O2	2.47	11.7 (11.4, 11.8)	11.7 (11.5, 11.9)	0.53	11.7 (11.5 11.8)	11.7 (11.4 11.9)	0.79
845.42	S-Cys (– H2O)	C3H4NOS	1.18	12.9 (12.7, 13.1)	13.0 (12.8, 13.1)	0.18	12.9 (12.8 13.1)	12.9 (12.7 13.1)	0.85
849.06	Unknown	HO3S2	2.12	14.4 (14.1, 14.6)	14.4 (14.1, 14.7)	0.97	14.4 (14.2 14.6)	14.4 (14 14.6)	0.35
851.08	Unknown		2.09	11.7 (11.4, 11.9)	11.7 (11.5, 12.0)	0.24	11.7 (11.5 11.9)	11.7 (11.5 12)	0.80
851.42	S-Cys	C3H6NO2S	0.78	18.1 (18.0, 18.3)	18.2 (18.0, 18.3)	0.49	18.2 (18 18.3)	18.1 (18 18.3)	0.74
851.75	S-Cys(NH2 → OH)	C3H5O3S	3.16	14.4 (14.2, 14.7)	14.5 (14.3, 14.7)	0.16	14.5 (14.2 14.7)	14.5 (14.3 14.7)	0.42
857.09	Unknown	C4H9O3S	2.64	12.5 (12.2, 12.7)	12.4 (12.3, 12.7)	0.89	12.4 (12.3 12.6)	12.5 (12.3 12.8)	0.28
858.75	Na adduct of S-Cys	C5H4NO2S	1.24	14.0 (13.9, 14.2)	14.0 (13.8, 14.2)	0.17	14 (13.9 14.2)	14 (13.9 14.3)	0.88
860.77	S-hCys, plus methylation	C5H1NO2S	2.62	12.6 (12.3, 12.8)	12.5 (12.3, 12.8)	0.80	12.5 (12.3 12.7)	12.5 (12.3 12.8)	0.98

864.07	Unknown		1.7	14.3 (14.1, 14.5)	14.2 (14.0, 14.5)	0.16	14.3 (14 14.5)	14.2 (14 14.5)	0.86
864.43	Unknown	C5H7N2O2S	2.91	11.6 (11.4, 11.8)	11.7 (11.5, 11.8)	0.07	11.6 (11.5 11.8)	11.6 (11.4 11.8)	0.68
869.06	Unknown		1.6	13.3 (13.1, 13.4)	13.2 (13.0, 13.5)	0.22	13.2 (13 13.4)	13.2 (13 13.5)	0.83
870.43	S-Cys-Gly	C5H9N2O3S	0.9	15.8 (15.7, 15.9)	15.8 (15.7, 15.9)	0.74	15.8 (15.7 16)	15.8 (15.7 15.9)	0.83
877.76	Unknown		2.73	11.9 (11.6, 12.2)	11.9 (11.5, 12.1)	0.17	11.9 (11.5 12.1)	11.8 (11.6 12.2)	0.82
883.08	Unknown		3.15	12.0 (11.7, 12.4)	12.1 (11.7, 12.3)	0.75	12 (11.7 12.3)	12.1 (11.7 12.3)	0.84
888.07	Unknown		4.62	11.3 (10.9, 11.6)	11.2 (10.8, 11.6)	0.21	11.2 (10.9 11.5)	11.3 (10.8 11.6)	0.66
894.44	S-γ-Glu-Cys	C8H13N2O5S	1.53	12.6 (12.5, 12.8)	12.8 (12.6, 12.9)	0.04	12.7 (12.5 12.8)	12.7 (12.6 12.8)	0.75
913.44	S-glutathione	C1H16N3O6S	1.99	12.7 (12.6, 13.0)	12.8 (12.6, 12.9)	0.28	12.8 (12.6 13)	12.8 (12.6 12.9)	0.83
965.49	Unknown	C23H32N3O5S	3.22	12.7 (12.4, 13.0)	12.6 (12.3, 12.9)	0.84	12.6 (12.3 12.9)	12.7 (12.3 13)	0.87
976.81	Unknown		3.47	11.6 (11.5, 11.9)	11.7 (11.4, 11.9)	0.42	11.6 (11.4 11.9)	11.7 (11.5 11.9)	0.41
811.75_1	T3 labile adduct		1.62	14.4 (14.3, 14.7)	14.5 (14.3, 14.7)	0.61	14.5 (14.3 14.8)	14.5 (14.3 14.7)	0.58
811.75_2	unmodified T3		2.86	15.1 (14.8, 15.3)	15.1 (14.9, 15.3)	0.73	15.1 (14.9 15.3)	15.1 (14.9 15.4)	0.52
811.75_3	T3 dimer		2.19	17.7 (17.4, 18.0)	17.7 (17.4, 18.0)	0.77	17.7 (17.4 17.9)	17.7 (17.4 18)	0.90
856.09_1	Unknown		1.08	15.9 (15.9, 16.1)	16.0 (15.9, 16.1)	0.34	16 (15.9 16.2)	16 (15.9 16.1)	0.64

*p-values were calculated using linear mixed effect model, where case-control match ID was modeled as random intercept to account for correlation within matched pair.

Supplemental Table 3. Associations of albumin adducts and incident AML risk in the CLUE and PLCO studies (52 cases and 102 matched controls).

Adduct	Annotation	Elemental composition of added mass	Continuous		tertile 2 vs tertile 1		tertile 3 vs tertile 1		<i>p</i> -trend
			OR (95% CI)*	<i>p</i> -value	OR (95% CI)*	<i>p</i> -value	OR (95% CI)*	<i>p</i> -value	
805.76	Cys34 → oxoalanine	- SH2, + O	1.21 (0.32 - 4.6)	0.78	1.07 (0.41 - 2.82)	0.89	2.16 (0.88 - 5.27)	0.09	0.06
808.72	Unknown		0.69 (0.37 - 1.31)	0.26	1.08 (0.49 - 2.42)	0.84	0.63 (0.25 - 1.57)	0.32	0.31
816.41	Unknown		1.18 (0.32 - 4.37)	0.80	0.91 (0.4 - 2.09)	0.83	1.00 (0.45 - 2.26)	0.99	1.00
816.43	methylation (not Cys34)	CH3	0.69 (0.32 - 1.49)	0.34	0.45 (0.2 - 1.01)	0.05	0.32 (0.13 - 0.83)	0.02	0.01
821.74	Unknown		1.15 (0.37 - 3.59)	0.81	1.42 (0.57 - 3.53)	0.45	1.39 (0.55 - 3.54)	0.48	0.51
822.42	Cys34 sulfinic acid	HO2	0.75 (0.14 - 4.06)	0.73	1.46 (0.66 - 3.21)	0.35	1.01 (0.44 - 2.34)	0.98	0.97
826.43	ethylene oxide adduct	C2H5O	0.92 (0.64 - 1.32)	0.66	1.06 (0.44 - 2.54)	0.90	0.95 (0.41 - 2.23)	0.91	0.91
827.09	S-(O)-O-CH3	CH3O2	1.17 (0.55 - 2.48)	0.68	0.55 (0.22 - 1.38)	0.21	1.14 (0.48 - 2.7)	0.76	0.68
827.75	Cys34 sulfonic acid	HO3	0.63 (0.15 - 2.63)	0.53	1.48 (0.64 - 3.4)	0.36	1.04 (0.42 - 2.56)	0.94	0.94
829.12	Unknown		0.86 (0.41 - 1.8)	0.69	1.12 (0.54 - 2.33)	0.76	0.68 (0.29 - 1.61)	0.39	0.44
829.75	Unknown		0.7 (0.2 - 2.52)	0.59	1.07 (0.47 - 2.44)	0.87	0.78 (0.33 - 1.82)	0.57	0.60
830.43	Acrolein addition +56	C3H5O	1.08 (0.19 - 6.34)	0.93	1.01 (0.42 - 2.41)	0.99	1.41 (0.57 - 3.5)	0.45	0.44
831.1	Reduced acrolein addition +58	C3H7O	1.2 (0.26 - 5.51)	0.81	1.01 (0.4 - 2.59)	0.98	1.55 (0.57 - 4.23)	0.39	0.37
833.08	SulfurDioxide	SO2H	0.51 (0.14 - 1.87)	0.31	0.75 (0.35 - 1.61)	0.45	0.47 (0.21 - 1.09)	0.08	0.08
835.1	methylvinylketone adduct/crotonaldehyde	C4H7O	1.24 (0.21 - 7.43)	0.82	0.59 (0.24 - 1.42)	0.24	0.86 (0.4 - 1.87)	0.71	0.74
838.41	SulfurTrioxid	SO3H	1.56 (0.58 - 4.2)	0.38	1.22 (0.53 - 2.79)	0.64	1.36 (0.6 - 3.11)	0.46	0.47
841.09	Unknown	C3H5O3	0.99 (0.65 - 1.51)	0.95	1.13 (0.5 - 2.55)	0.77	0.84 (0.34 - 2.07)	0.70	0.71
841.75	S-mercaptoacetic acid	C2H3O2S	0.24 (0.06 - 1.02)	0.05	0.79 (0.37 - 1.67)	0.53	0.21 (0.07 - 0.63)	0.006	0.01
845.1	Glutaraldehyde	C5H9O2	0.65 (0.18 - 2.3)	0.50	1.07 (0.48 - 2.38)	0.87	0.72 (0.29 - 1.78)	0.48	0.50
845.42	S-Cys (– H2O)	C3H4NOS	0.33 (0.07 - 1.66)	0.18	0.52 (0.23 - 1.18)	0.12	0.55 (0.24 - 1.28)	0.17	0.13
849.06	Unknown	HO3S2	1.02 (0.43 - 2.39)	0.97	0.87 (0.38 - 1.99)	0.74	1.11 (0.48 - 2.53)	0.81	0.80
851.08	Unknown		0.65 (0.31 - 1.37)	0.26	0.91 (0.42 - 1.96)	0.80	0.63 (0.29 - 1.39)	0.26	0.27
851.42	S-Cys	C3H6NO2S	0.62 (0.15 - 2.6)	0.51	0.77 (0.37 - 1.6)	0.48	0.58 (0.24 - 1.38)	0.22	0.21
851.75	S-Cys(NH2 → OH)	C3H5O3S	0.48 (0.17 - 1.32)	0.15	0.61 (0.28 - 1.35)	0.22	0.59 (0.25 - 1.41)	0.24	0.20
857.09	Unknown	C4H9O3S	1.04 (0.42 - 2.58)	0.93	1.11 (0.49 - 2.52)	0.80	0.98 (0.44 - 2.22)	0.97	0.97
858.75	Na adduct of S-Cys	C5H4NO2S	2.33 (0.68 - 8.02)	0.18	3.63 (1.38 - 9.56)	0.01	2.13 (0.75 - 6.02)	0.15	0.28
860.77	S-hCys, plus methylation	C5H1NO2S	1.11 (0.45 - 2.73)	0.82	1.01 (0.43 - 2.39)	0.98	1.22 (0.54 - 2.79)	0.63	0.63
864.07	Unknown		2.37 (0.73 - 7.7)	0.15	2.98 (1.22 - 7.27)	0.02	1.53 (0.58 - 4.03)	0.39	0.53
864.43	Unknown	C5H7N2O2S	0.41 (0.14 - 1.17)	0.10	0.58 (0.26 - 1.29)	0.18	0.62 (0.28 - 1.34)	0.22	0.20
869.06	Unknown		2.2 (0.67 - 7.19)	0.19	2.80 (1.17 - 6.71)	0.02	1.54 (0.59 - 3.99)	0.37	0.37

870.43	S-Cys-Gly	C5H9N2O3S	1.26 (0.31 - 5.16)	0.75	0.92 (0.42 - 2.02)	0.84	1.04 (0.48 - 2.27)	0.92	0.92
877.76	Unknown		1.74 (0.79 - 3.82)	0.17	0.86 (0.39 - 1.91)	0.71	1.23 (0.55 - 2.74)	0.61	0.61
883.08	Unknown		1.11 (0.55 - 2.22)	0.77	0.67 (0.29 - 1.56)	0.35	0.96 (0.41 - 2.27)	0.93	0.91
888.07	Unknown		1.51 (0.79 - 2.91)	0.21	1.56 (0.66 - 3.71)	0.31	1.68 (0.73 - 3.85)	0.22	0.24
894.44	S-γ-Glu-Cys	C8H13N2O5S	0.18 (0.04 - 0.92)	0.04	0.61 (0.29 - 1.30)	0.20	0.40 (0.16 - 0.96)	0.04	0.04
913.44	S-glutathione	C1H16N3O6S	0.56 (0.18 - 1.75)	0.32	0.78 (0.33 - 1.81)	0.56	0.99 (0.47 - 2.09)	0.98	0.97
965.49	Unknown	C23H32N3O5S	0.94 (0.52 - 1.68)	0.83	1.81 (0.76 - 4.31)	0.18	1.27 (0.55 - 2.93)	0.58	0.55
976.81	Unknown		0.7 (0.31 - 1.58)	0.39	0.72 (0.3 - 1.74)	0.47	0.71 (0.3 - 1.66)	0.43	0.42
811.75_1	T3 labile adduct		1.28 (0.51 - 3.22)	0.60	0.75 (0.34 - 1.64)	0.47	0.84 (0.38 - 1.84)	0.66	0.64
811.75_2	unmodified T3		0.79 (0.26 - 2.45)	0.69	0.42 (0.18 - 1.02)	0.05	0.82 (0.34 - 1.94)	0.64	0.55
811.75_3	T3 dimer		0.89 (0.42 - 1.91)	0.77	0.55 (0.22 - 1.37)	0.20	1.18 (0.56 - 2.47)	0.67	0.50
856.09_1	Unknown		0.52 (0.12 - 2.21)	0.37	0.78 (0.35 - 1.75)	0.54	0.57 (0.24 - 1.36)	0.20	0.20

Unadjusted conditional logistic regression models. AML cases and controls were matched on age at blood collection, sex, race, study assignment

Supplementary Table 4. Associations of albumin adducts and incident AML risk in the CLUE and PLCO studies with and without adjusting for age at blood collection and current smoking.

Adduct	Annotation	Conditional logistic regression, unadjusted					Conditional logistic regression, adjusted for age and current smoking				
		Continuous exposure		Tertile 2 vs Tertile 1		<i>p</i> -trend	Continuous		tertile 2 vs tertile 1		<i>p</i> -trend
		OR (95% CI)*	<i>p</i> -value	OR (95% CI)*	OR (95% CI)*		OR (95% CI)*	<i>p</i> -value	OR (95% CI)*	OR (95% CI)*	
816.43	methylation (not Cys34)	0.69 (0.32 - 1.49)	0.34	0.45 (0.20 - 1.01)	0.32 (0.13 - 0.83)	0.01	0.58 (0.24 - 1.38)	0.22	0.39 (0.17 - 0.92)	0.25 (0.09 - 0.73)	0.01
841.75	S-mercaptoacetic acid	0.24 (0.06 - 1.02)	0.05	0.79 (0.37 - 1.67)	0.21 (0.07 - 0.63)	0.01	0.23 (0.05 - 0.97)	0.049	0.81 (0.38 - 1.71)	0.20 (0.07 - 0.60)	0.01
894.44	S-γ-Glu-Cys	0.18 (0.04 - 0.92)	0.04	0.61 (0.29 - 1.30)	0.40 (0.16 - 0.96)	0.04	0.16 (0.03 - 0.86)	0.03	0.62 (0.28 - 1.36)	0.39 (0.16 - 0.95)	0.04

Supplementary Table 5. Associations of selected albumin adducts and incident AML risk in the CLUE and PLCO studies, with and without adjusting for BMI. A total of 119 participants (40 cases and 79 controls) with available BMI data were included in the analysis.

Without adjusting for BMI							With adjusting for BMI				
Adduct	Annotation	Continuous		Tertile 2 vs Tertile 1	Tertile 3 vs Tertile 1	<i>p</i> -trend	Continuous		Tertile 2 vs Tertile 1	Tertile 3 vs Tertile 1	<i>p</i> -trend
		OR (95% CI)	<i>P</i> -value	OR (95% CI) ^a	OR (95% CI) ^a		OR (95% CI)	<i>P</i> -value	OR (95% CI) ^a	OR (95% CI) ^a	
816.43	methylation (not Cys34)	1.09 (0.44 - 2.71)	0.85	0.54 (0.22 - 1.29)	0.46 (0.16 - 1.32)	0.12	0.92 (0.35 - 2.41)	0.87	0.55 (0.22 - 1.34)	0.45 (0.15 - 1.34)	0.12
841.75	S-mercaptoacetic acid	0.36 (0.07 - 1.88)	0.23	0.87 (0.35 - 2.17)	0.37 (0.11 - 1.2)	0.12	0.35 (0.07 - 1.82)	0.21	0.97 (0.38 - 2.47)	0.35 (0.1 - 1.16)	0.11
894.44	S-γ-Glu-Cys	0.19 (0.03 - 1.17)	0.07	0.55 (0.24 - 1.3)	0.43 (0.16 - 1.14)	0.08	0.17 (0.03 - 1.10)	0.06	0.55 (0.23 - 1.31)	0.51 (0.19 - 1.35)	0.15

^a Conditional logistic regression models with exact method were used to estimate effects for tertiles of adduct levels

Supplemental Table 6. Spearman's correlation coefficient (*p*-value) among selected covariates and albumin adducts in the overall study population, AML cases, and matched controls (from top to bottom within a cell, respectively)

	Methylation (not Cys34) (816.43)	S-mercaptoacetic acid (841.75)	S-γ-Glu-Cys (894.44)
Age	-0.012 (0.88) 0.048 (0.74) -0.035 (0.72)	0.088 (0.28) 0.33 (0.016) -0.002 (0.98)	0.07 (0.39) 0.13 (0.37) 0.036 (0.72)
BMI ^a	-0.036 (0.7) 0.23 (0.15) -0.12 (0.29)	0.012 (0.9) -0.19 (0.25) 0.13 (0.25)	0.015 (0.88) -0.091 (0.58) 0.11 (0.32)
Current smoking ^b	0.30 (0.00016) 0.17 (0.24) 0.37 (0.00013)	-0.11 (0.17) 0.006 (0.97) -0.16 (0.1)	-0.22 (0.0068) -0.16 (0.25) -0.26 (0.0085)
Ever smoking ^b	0.13 (0.11) 0.046 (0.75) 0.19 (0.06)	-0.22 (0.006) -0.14 (0.31) -0.24 (0.014)	-0.14 (0.095) 0.14 (0.31) -0.25 (0.012)
Methylation (not Cys34) (816.43)	1 1 1	-0.19 (0.018) -0.015 (0.92) -0.29 (0.003)	-0.13 (0.10) -0.09 (0.55) -0.18 (0.065)
S-mercaptoacetic acid (841.75)		1 1 1	0.21 (0.008) 0.061 (0.67) 0.25 (0.0096)
S-γ-Glu-Cys (894.44)			1 1 1

^aBMI data were missing for all CLUE I participants (n= 36).

^bSmoking data were missing for one PLCO participant.

Supplemental Table 7. Spearman's correlation coefficients among selected Cys34 albumin adducts in the overall study population, CLUE, and PLCO studies (from top to bottom within a cell, respectively)

Adduct	methylation (not Cys34)	S-mercaptoacetic acid	S- γ -Glu-Cys
	1	-0.19	-0.13
methylation (not Cys34)	1	-0.22	-0.14
	1	-0.17	-0.05
	-0.19	1	0.21
S-mercaptoacetic acid	-0.22	1	0.33
	-0.17	1	0.12
	-0.13	0.21	1
S- γ -Glu-Cys	-0.14	0.33	1
	-0.05	0.12	1

Supplemental Table 8. Multi-adduct model showing associations of circulatory human albumin adducts and incident AML risk in the CLUE and PLCO studies.

Adduct	Annotation	Elemental composition of added mass	Continuous		Tertile 2 vs Tertile 1		Tertile 3 vs Tertile 1		<i>p</i> -trend
			OR (95% CI)*	<i>p</i> -value	OR (95% CI)*	<i>p</i> -value	OR (95% CI)*	<i>p</i> -value	
816.43	methylation (not Cys34)	CH3	0.52 (0.22 – 1.21)	0.13	0.27 (0.10 – 0.75)	0.01	0.21 (0.07 – 0.63)	0.005	0.004
841.75	S-mercaptoacetic acid	C2H3O2S	0.24 (0.05 – 1.10)	0.07	0.87 (0.37 – 2.06)	0.75	0.26 (0.08 – 0.85)	0.03	0.03
894.44	S-γ-Glu-Cys	C8H13N2O5S	0.17 (0.03 – 0.94)	0.04	0.55 (0.23 – 1.31)	0.18	0.30 (0.11 – 0.82)	0.02	0.02

Conditional logistic regression models. AML cases and controls were matched on age at blood collection, sex, race, study cohort
All three adducts were simultaneously included in the same model

Supplementary Table 9. Associations of albumin adducts and AML risk separately in the CLUE and PLCO studies.

Adduct	Annotation	CLUE (24 cases, 48 controls) ^a					PLCO (28 cases, 55 controls) ^b				
		Continuous		Tertile 2 vs Tertile 1	Tertile 3 vs Tertile 1	<i>p</i> - trend	Continuous		Tertile 2 vs Tertile 1	Tertile 3 vs Tertile 1	<i>p</i> - trend
		OR (95% CI)	<i>P</i> - value	OR (95% CI)	OR (95% CI)		OR (95% CI)	<i>P</i> - value	OR (95% CI)	OR (95% CI)	
816.43	methylation (not Cys34)	0.39 (0.13 - 1.15)	0.09	0.33 (0.09 - 1.24)	0.19 (0.05 - 0.81)	0.02	1.67 (0.49 - 5.65)	0.41	0.62 (0.21 - 1.85)	0.63 (0.20 - 2.01)	0.42
841.75	S-mercaptoacetic acid	0.02 (0.00 - 0.29)	0.005	0.41 (0.13 - 1.26)	----- ^c	0.0003	0.87 (0.16 - 4.83)	0.87	1.45 (0.50 - 4.16)	0.78 (0.24 - 2.56)	0.78
894.44	S-γ-Glu-Cys	0.08 (0.01 - 0.69)	0.02	0.52 (0.15 - 1.83)	0.29 (0.08 - 1.05)	0.06	0.60 (0.05 - 6.71)	0.68	0.70 (0.25 - 1.97)	0.48 (0.14 - 1.67)	0.24

Matching was broken within each stratum and unconditional logistic regression models, adjusted for age at blood collection, and sex were used

^a For the CLUE studies, the number of controls (cases) for the 1st, 2nd, and 3rd tertiles were 19(17), 13(4), 16(3) for adduct 816.43; 11(14), 19(10), 18(0) for adduct 841.75; and 16(13), 13(6), 19(5) for adduct 894.44, respectively

^b For the PLCO Trial, the number of controls (cases) for the 1st, 2nd, and 3rd tertiles were 16(11), 21(9), 18(8) for adduct 816.43; 23(11), 16(11), 16(6) for adduct 841.75; and 19(13), 21(10), 15(5) for adduct 894.44, respectively

^c Model did not converge, as there were no AML cases in the highest tertile group

Supplementary Table 10: Associations of albumin adducts and incident AML risk among cases diagnosed ≥ 5.5 years of follow-up after phlebotomy at study enrollment in the CLUE alone vs CLUE and PLCO combined.

Adduct	Annotation	CLUE alone (20 cases, 40 controls) ^a								CLUE + PLCO (27 cases, 54 controls) ^b							
		Continuous		Tertile 2 vs Tertile 1 ^c		Tertile 3 vs Tertile 1 ^c		<i>p</i> -trend		Continuous		Tertile 2 vs Tertile 1 ^c		Tertile 3 vs Tertile 1 ^c		<i>p</i> -trend	
		OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value			OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value		
816.43	methylation (not Cys34) adduct	0.49 (0.17-1.46)	0.20	0.48 (0.12-1.98)	0.31	0.25 (0.06-1.09)	0.06	0.055		0.72 (0.28-1.85)	0.50	0.39 (0.11-1.34)	0.14	0.45 (0.14-1.44)	0.18	0.13	
841.75	S-mercaptoacetic acid	0.03 (0.00-0.51)	0.02	0.50 (0.15-1.66)	0.26	----- ^d	-----	0.003		0.07 (0.01-0.61)	0.02	0.73 (0.26-2.08)	0.56	0.04 (0-0.38)	0.01	0.002	
894.44	S-γ-Glu-Cys	0.10 (0.01-0.97)	0.047	0.50 (0.12-2.02)	0.33	0.32 (0.08-1.25)	0.10	0.100		0.08 (0.01-0.63)	0.02	0.31 (0.09-1.02)	0.05	0.26 (0.08-0.86)	0.03	0.02	

^aFor CLUE alone with a follow-up ≥ 5.5 years category, the number of controls (cases) for the 1st, 2nd, and 3rd tertiles were 16 (13), 10 (4), 14 (3) for adduct 816.43; 11 (10), 15 (9), 14 (0) for adduct 841.75; and 12 (10), 11 (5), 17 (5) for adduct 894.44, respectively

^bFor CLUE + PLCO with a follow-up ≥ 5.5 years category, the number of controls (cases) for the 1st, 2nd, and 3rd tertiles were 16 (11), 16 (6), 22 (9) for adduct 816.43; 15 (12), 18 (13), 21 (1) for adduct 841.75; and 15 (15), 18 (6), 21 (6) for adduct 894.44, respectively.

Estimates for continuous adduct models represent odds ratios for each unit (log relative abundance) change in circulatory albumin adduct levels

Abbreviations: CLUE: Campaign Against Cancer and Stroke (CLUE I, 1974; CLUE II, 1989); PLCO: Prostate, Lung, Colorectal and Ovarian cancer screening trial.

Follow-up information was missing for one AML case in CLUE I study