

Supplemental Material for

Biomarkers of gut barrier dysfunction and risk of hepatocellular carcinoma in the REVEAL-HBV and REVEAL-HCV Cohort Studies

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Supplemental Tables S1 and S2

Supplemental Table S1. Spearman correlation coefficients for markers of gut bacterial translocation among controls in the REVEAL-HBV and REVEAL-HCV studies.

	anti-Flagellin			anti-LPS			sCD14	LBP	ALT
	IgA	IgG	IgM	IgA	IgG	IgM			
anti-flagellin IgA	1.000	0.813*	0.485*	0.803*	0.694*	0.116	-0.062	0.171*	-0.018
anti-flagellin IgG		1.000	0.587*	0.615*	0.776*	0.100	0.016	0.227*	0.043
anti-flagellin IgM			1.000	0.403*	0.422*	0.569*	0.038	0.068	0.094
anti-LPS IgA				1.000	0.747*	0.162*	0.011	0.141*	0.016
anti-LPS IgG					1.000	0.102	-0.021	0.136*	-0.002
anti-LPS IgM						1.000	0.070	-0.091	0.075
Soluble CD14							1.000	0.456*	0.165*
LPS Binding Protein								1.000	0.159*
ALT									1.000

*P<0.05.

Supplemental Table S2. Multivariate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between markers of gut bacterial translocation and hepatocellular carcinoma (HCC) among participants of the REVEAL-HBV and REVEAL-HCV cohorts, excluding cases diagnosed within 5 years of baseline.

	REVEAL-HBV				REVEAL-HCV			
	Controls	Cases	OR ¹	95% CI	Controls	Cases	OR ²	95% CI
anti-Flagellin IgA								
Quartile 1	41	30	1.00	(referent)	24	28	1.00	(referent)
Quartile 2	41	37	1.43	(0.63, 3.23)	24	23	0.82	(0.29, 2.34)
Quartile 3	40	51	1.35	(0.61, 3.00)	24	16	0.66	(0.23, 1.94)
Quartile 4	39	57	1.85	(0.84, 4.09)	24	26	1.12	(0.44, 2.82)
<i>P-value for trend</i> ³				0.17				0.96
Continuous (log ₂)	161	175	1.70	(1.01, 2.84)	96	93	1.23	(0.50, 2.99)
anti-Flagellin IgG								
Quartile 1	42	30	1.00	(referent)	24	25	1.00	(referent)
Quartile 2	40	40	1.45	(0.64, 3.30)	24	17	0.56	(0.17, 1.82)
Quartile 3	39	46	1.84	(0.82, 4.13)	24	26	1.19	(0.46, 3.10)
Quartile 4	40	59	1.81	(0.82, 4.00)	24	25	0.98	(0.36, 2.65)
<i>P-value for trend</i> ³				0.18				0.76
Continuous (log ₂)	161	175	1.60	(0.81, 3.15)	96	93	1.09	(0.32, 3.69)
anti-Flagellin IgM								
Quartile 1	40	36	1.00	(referent)	24	22	1.00	(referent)
Quartile 2	40	49	1.11	(0.52, 2.37)	24	25	1.12	(0.40, 3.13)
Quartile 3	41	47	0.83	(0.38, 1.81)	24	18	0.58	(0.19, 1.76)
Quartile 4	40	43	0.81	(0.37, 1.75)	24	28	1.11	(0.41, 2.99)
<i>P-value for trend</i> ³				0.45				0.90
Continuous (log ₂)	161	175	0.97	(0.58, 1.62)	96	93	1.10	(0.37, 3.32)
anti-LPS IgA								
Quartile 1	40	20	1.00	(referent)	24	28	1.00	(referent)
Quartile 2	40	54	2.65	(1.13, 6.23)	24	25	0.82	(0.33, 2.01)
Quartile 3	41	42	1.56	(0.66, 3.72)	24	17	0.44	(0.16, 1.22)
Quartile 4	40	59	2.17	(0.93, 5.06)	24	23	0.93	(0.35, 2.52)
<i>P-value for trend</i> ³				0.52				0.70
Continuous (log ₂)	161	175	1.22	(0.80, 1.85)	96	93	0.75	(0.33, 1.72)
anti-LPS IgG								
Quartile 1	41	31	1.00	(referent)	24	22	1.00	(referent)
Quartile 2	41	35	0.80	(0.35, 1.84)	24	22	0.84	(0.28, 2.48)
Quartile 3	39	58	1.75	(0.79, 3.84)	24	23	1.21	(0.39, 3.71)
Quartile 4	40	51	1.05	(0.47, 2.34)	24	26	1.34	(0.44, 4.06)
<i>P-value for trend</i> ³				0.46				0.46
Continuous (log ₂)	161	175	1.29	(0.65, 2.59)	96	93	1.93	(0.40, 9.36)
anti-LPS IgM								
Quartile 1	41	33	1.00	(referent)	24	21	1.00	(referent)
Quartile 2	39	46	1.30	(0.59, 2.83)	24	31	1.38	(0.56, 3.38)
Quartile 3	41	41	0.88	(0.39, 1.96)	24	16	0.68	(0.25, 1.86)
Quartile 4	40	55	1.44	(0.67, 3.10)	24	25	0.98	(0.36, 2.61)
<i>P-value for trend</i> ³				0.58				0.64
Continuous (log ₂)	161	175	1.22	(0.67, 2.22)	96	93	0.89	(0.33, 2.40)
sCD14								
Quartile 1	40	33	1.00	(referent)	24	36	1.00	(referent)
Quartile 2	41	37	1.30	(0.57, 2.94)	24	24	0.40	(0.14, 1.15)
Quartile 3	40	44	1.14	(0.51, 2.55)	24	16	0.34	(0.13, 0.94)
Quartile 4	40	61	1.61	(0.73, 3.53)	24	17	0.38	(0.13, 1.09)
<i>P-value for trend</i> ³				0.28				0.030
Continuous (log ₂)	161	175	1.33	(0.70, 2.52)	96	93	0.31	(0.13, 0.74)
LPS Binding Protein								
Quartile 1	42	29	1.00	(referent)	24	38	1.00	(referent)
Quartile 2	39	27	1.15	(0.49, 2.66)	24	11	0.08	(0.02, 0.36)

Quartile 3	40	48	1.45	(0.66, 3.15)	24	31	0.79	(0.31, 2.01)
Quartile 4	40	71	2.21	(1.02, 4.80)	24	13	0.14	(0.04, 0.48)
<i>P-value for trend</i> ³				0.030				0.078
Continuous (log ₂)	161	175	1.95	(1.11, 3.44)	96	93	0.54	(0.28, 1.05)

¹Unconditional logistic regression adjusted for age, sex, HBV DNA copies at baseline, smoking status, alcohol consumption, BMI, education status, baseline cirrhosis status, ALT, and HbeAG.

²Conditional logistic regression adjusted for matching factors (age, sex, and HCV-RNA-positive rate), smoking status, alcohol consumption, BMI, education status, baseline cirrhosis status, baseline diabetes status, ALT, and HCV genotype.

³P-value for trend calculated using the Wald test.