

## **SUPPLEMENTAL MATERIAL**

**Table S1.** Histologic classifications of malignant and benign tumors in FH and RP cohorts.

**Table S2.** Lipid species retained for analysis in both patient cohorts.

**Table S3.** Plasma concentrations ( $\mu\text{M}$ ) for representative lipid species by class.

**Table S4.** Selected top differential metabolites by case status.

**Table S5.** Selected top differential metabolites by case status in stage-stratified analyses.

**Table S6.** Performance characteristics for selected lipid species (Table 2) using data from FH cohort.

**Table S7.** Patient and tumor characteristics (GEO samples).

**Table S8.** Lipid transport-related GO gene sets selected and individual genes available for analysis.

**Figure S1.** Lipid class assignments for 546 analyzed lipid species.

**Figure S2.** Distributions of coefficients of variation (CV) calculated for 546 analyzed lipid species.

**Figure S3.** Lipid class differences in cases versus controls.

**Figure S4.** Plasma CA125 values (U / mL) for cases and controls.

**Figure S5.** ROC curves and performance metrics for base models comprised of CA125, age, and BMI.

**Figure S6.** Spearman correlation analysis of lipid concentrations in paired ascites and plasma.

**Figure S7.** Schematic summary.

**Table S1. Histologic classifications of malignant and benign tumors in FH and RP cohorts.**

FRED HUTCH					
Cases [50]			Controls [50]		
	n	%		n	%
<b>SEROUS [50]</b>			<b>SEROUS [50]</b>		
Serous carcinoma	47	94.0	Serous cystadenofibroma	19	38.0
STIC lesion	1	2.0	Serous cystadenoma	14	28.0
Other	2	4.0	Serous adenofibroma	4	8.0
			Other	13	26.0
ROSWELL PARK					
Cases [60]			Controls [58]		
	n	%		n	%
<b>SEROUS [32]</b>			<b>SEROUS [19]</b>		
Cystadenofibroma, malignant serous	1	3.1	Serous adenoma	1	5.3
Papillary serous adenocarcinoma	4	12.5	Serous cyst	3	15.8
Papillary serous cystadenocarcinoma	1	3.1	Serous cystadenofibroma	4	21.1
Serous adenocarcinoma, NOS	4	12.5	Serous cystadenoma	11	57.9
Serous carcinoma, NOS	13	40.6			
Serous cystadenocarcinoma, NOS	7	21.9			
Serous surface papillary carcinoma	2	6.3			
<b>NON-SEROUS [28]</b>			<b>NON-SEROUS [39]</b>		
Carcinosarcoma, NOS	2	7.1	Benign Teratoma	1	2.6
Clear cell adenocarcinoma, NOS	1	3.6	Brenner Tumor	1	2.6
Clear cell carcinoma	1	3.6	Complex Cyst	1	2.6
Endometrioid adenocarcinoma, NOS	3	10.7	Corpus Luteum Cyst	1	2.6
Leiomyosarcoma, NOS	1	3.6	Cyst	2	5.1
Lymphoma, malig, large B-cell, diffuse, NOS	1	3.6	Cystadenoma	5	12.8
Malignant melanoma, NOS	1	3.6	Endometriosis of Ovary	1	2.6
Mixed cell adenocarcinoma	5	17.9	Endometrioid cystadenofibroma	1	2.6
Mucinous adenocarcinoma	6	21.4	Endosalpingiosis	1	2.6
Mucinous carcinoma	1	3.6	Epithelial inclusion cyst	1	2.6
Mucinous cystadenocarcinoma, NOS	3	10.7	Fibroma	2	5.1
Mullerian mixed tumor	1	3.6	Fibrothecoma	1	2.6
Papillary adenocarcinoma, NOS	1	3.6	Follicular Cyst	2	5.1
Yolk sac tumor	1	3.6	Hemorrhagic Corpus Luteal Cyst	2	5.1
			Hemorrhagic Cyst	1	2.6
			Hydrosalpinx	1	2.6
			Mature Cystic Teratoma	2	5.1
			Mesothelial Inclusion Cyst	1	2.6
			Mucinous Adenoma	2	5.1
			Mucinous Cystadenoma	7	18.0
			Simple Cyst	2	5.1
			Struma Ovarii	1	2.6

**Table S2. Lipid species retained for analysis in both patient cohorts.**

	<u>Metabolite</u>	<u>Class</u>		<u>Metabolite</u>	<u>Class</u>		<u>Metabolite</u>	<u>Class</u>
1	CE(12:0)	CE	76	PC(16:0/20:5)	PC	151	TAG46:1-FA16:1	TAG
2	CE(14:0)	CE	77	PC(16:0/22:4)	PC	152	TAG46:1-FA18:1	TAG
3	CE(14:1)	CE	78	PC(16:0/22:5)	PC	153	TAG46:2-FA12:0	TAG
4	CE(15:0)	CE	79	PC(16:0/22:6)	PC	154	TAG46:2-FA14:0	TAG
5	CE(16:1)	CE	80	PC(17:0/18:1)	PC	155	TAG46:2-FA14:1	TAG
6	CE(17:0)	CE	81	PC(17:0/18:2)	PC	156	TAG46:2-FA16:0	TAG
7	CE(18:0)	CE	82	PC(17:0/20:4)	PC	157	TAG46:2-FA16:1	TAG
8	CE(18:1)	CE	83	PC(18:0/16:1)	PC	158	TAG46:2-FA18:1	TAG
9	CE(18:2)	CE	84	PC(18:0/18:0)	PC	159	TAG46:2-FA18:2	TAG
10	CE(18:3)	CE	85	PC(18:0/18:1)	PC	160	TAG46:3-FA16:0	TAG
11	CE(18:4)	CE	86	PC(18:0/18:2)	PC	161	TAG46:3-FA16:1	TAG
12	CE(20:0)	CE	87	PC(18:0/18:3)	PC	162	TAG46:3-FA18:1	TAG
13	CE(20:1)	CE	88	PC(18:0/20:3)	PC	163	TAG46:3-FA18:2	TAG
14	CE(20:2)	CE	89	PC(18:0/20:4)	PC	164	TAG46:4-FA18:2	TAG
15	CE(20:3)	CE	90	PC(18:0/20:5)	PC	165	TAG47:0-FA15:0	TAG
16	CE(20:5)	CE	91	PC(18:0/22:4)	PC	166	TAG47:0-FA16:0	TAG
17	CE(22:2)	CE	92	PC(18:0/22:5)	PC	167	TAG47:1-FA15:0	TAG
18	CE(22:4)	CE	93	PC(18:0/22:6)	PC	168	TAG47:1-FA16:0	TAG
19	CE(22:5)	CE	94	PC(18:1/16:1)	PC	169	TAG47:1-FA16:1	TAG
20	CE(22:6)	CE	95	PC(18:1/18:1)	PC	170	TAG47:1-FA18:1	TAG
21	CER(18:0)	CER	96	PC(18:1/18:2)	PC	171	TAG47:2-FA18:1	TAG
22	CER(24:0)	CER	97	PC(18:1/18:3)	PC	172	TAG47:2-FA18:2	TAG
23	CER(24:1)	CER	98	PC(18:1/20:2)	PC	173	TAG48:0-FA14:0	TAG
24	HCER(22:0)	CER	99	PC(18:1/20:3)	PC	174	TAG48:0-FA16:0	TAG
25	HCER(24:0)	CER	100	PC(18:1/20:4)	PC	175	TAG48:0-FA18:0	TAG
26	LCER(24:1)	CER	101	PC(18:1/20:5)	PC	176	TAG48:1-FA12:0	TAG
27	DAG(14:0/18:1)	DAG	102	PC(18:1/22:5)	PC	177	TAG48:1-FA14:0	TAG
28	DAG(14:1/18:1)	DAG	103	PC(18:1/22:6)	PC	178	TAG48:1-FA14:1	TAG
29	DAG(16:0/16:0)	DAG	104	PC(18:2/16:1)	PC	179	TAG48:1-FA16:0	TAG
30	DAG(16:0/16:1)	DAG	105	PC(18:2/18:2)	PC	180	TAG48:1-FA16:1	TAG
31	DAG(16:0/18:1)	DAG	106	PC(18:2/20:3)	PC	181	TAG48:1-FA18:0	TAG
32	DAG(16:0/18:2)	DAG	107	PC(18:2/20:4)	PC	182	TAG48:1-FA18:1	TAG
33	DAG(16:1/18:1)	DAG	108	PE(16:0/18:1)	PE	183	TAG48:2-FA12:0	TAG
34	DAG(16:1/18:2)	DAG	109	PE(16:0/18:2)	PE	184	TAG48:2-FA14:0	TAG
35	DAG(18:0/18:1)	DAG	110	PE(16:0/20:4)	PE	185	TAG48:2-FA14:1	TAG
36	DAG(18:0/18:2)	DAG	111	PE(16:0/22:6)	PE	186	TAG48:2-FA16:0	TAG
37	DAG(18:1/18:1)	DAG	112	PE(18:0/18:0)	PE	187	TAG48:2-FA16:1	TAG
38	DAG(18:1/18:2)	DAG	113	PE(18:1/18:1)	PE	188	TAG48:2-FA18:0	TAG
39	DAG(18:1/20:3)	DAG	114	PE(18:1/18:2)	PE	189	TAG48:2-FA18:1	TAG
40	DAG(18:1/20:4)	DAG	115	PE(18:1/20:4)	PE	190	TAG48:2-FA18:2	TAG
41	DAG(18:1/22:6)	DAG	116	PE(18:2/16:1)	PE	191	TAG48:3-FA12:0	TAG
42	DAG(20:0/20:0)	DAG	117	PE(O-16:0/20:4)	PE	192	TAG48:3-FA14:0	TAG
43	FFA(17:0)	FFA	118	PE(P-16:0/18:2)	PE	193	TAG48:3-FA14:1	TAG
44	FFA(20:5)	FFA	119	PE(P-16:0/20:3)	PE	194	TAG48:3-FA16:0	TAG
45	FFA(22:6)	FFA	120	PE(P-16:0/22:6)	PE	195	TAG48:3-FA16:1	TAG
46	FFA(24:0)	FFA	121	PE(P-18:0/18:1)	PE	196	TAG48:3-FA18:1	TAG
47	LPC(15:0)	LPC	122	PE(P-18:0/18:2)	PE	197	TAG48:3-FA18:2	TAG
48	LPC(16:0)	LPC	123	PE(P-18:0/20:3)	PE	198	TAG48:3-FA18:3	TAG
49	LPC(17:0)	LPC	124	PE(P-18:0/22:6)	PE	199	TAG48:4-FA12:0	TAG
50	LPC(18:0)	LPC	125	PE(P-18:1/18:1)	PE	200	TAG48:4-FA14:0	TAG
51	LPC(18:1)	LPC	126	PE(P-18:1/18:2)	PE	201	TAG48:4-FA14:1	TAG
52	LPC(18:2)	LPC	127	PE(P-18:1/20:3)	PE	202	TAG48:4-FA16:0	TAG
53	LPC(20:2)	LPC	128	PE(P-18:1/20:4)	PE	203	TAG48:4-FA16:1	TAG
54	LPC(20:3)	LPC	129	PE(P-18:1/22:6)	PE	204	TAG48:4-FA18:1	TAG
55	LPC(20:4)	LPC	130	SM(14:0)	SM	205	TAG48:4-FA18:2	TAG
56	LPC(22:5)	LPC	131	SM(18:1)	SM	206	TAG48:4-FA18:3	TAG
57	LPC(22:6)	LPC	132	SM(20:1)	SM	207	TAG48:5-FA18:2	TAG
58	LPE(16:0)	LPE	133	SM(22:0)	SM	208	TAG49:0-FA15:0	TAG
59	LPE(18:0)	LPE	134	SM(22:1)	SM	209	TAG49:0-FA16:0	TAG
60	LPE(18:1)	LPE	135	SM(24:0)	SM	210	TAG49:0-FA17:0	TAG
61	PC(14:0/18:1)	PC	136	SM(24:1)	SM	211	TAG49:0-FA18:0	TAG
62	PC(14:0/18:2)	PC	137	SM(26:0)	SM	212	TAG49:1-FA14:0	TAG
63	PC(14:0/20:3)	PC	138	SM(26:1)	SM	213	TAG49:1-FA15:0	TAG
64	PC(14:0/20:4)	PC	139	TAG44:0-FA16:0	TAG	214	TAG49:1-FA16:0	TAG
65	PC(15:0/18:1)	PC	140	TAG44:1-FA16:0	TAG	215	TAG49:1-FA16:1	TAG
66	PC(15:0/18:2)	PC	141	TAG44:1-FA18:1	TAG	216	TAG49:1-FA17:0	TAG
67	PC(16:0/14:0)	PC	142	TAG44:2-FA16:0	TAG	217	TAG49:1-FA18:1	TAG
68	PC(16:0/16:1)	PC	143	TAG44:2-FA18:2	TAG	218	TAG49:2-FA14:0	TAG
69	PC(16:0/18:0)	PC	144	TAG45:1-FA16:0	TAG	219	TAG49:2-FA15:0	TAG
70	PC(16:0/18:1)	PC	145	TAG46:0-FA14:0	TAG	220	TAG49:2-FA16:0	TAG
71	PC(16:0/18:2)	PC	146	TAG46:0-FA16:0	TAG	221	TAG49:2-FA16:1	TAG
72	PC(16:0/18:3)	PC	147	TAG46:1-FA12:0	TAG	222	TAG49:2-FA17:0	TAG
73	PC(16:0/20:2)	PC	148	TAG46:1-FA14:0	TAG	223	TAG49:2-FA18:1	TAG
74	PC(16:0/20:3)	PC	149	TAG46:1-FA14:1	TAG	224	TAG49:2-FA18:2	TAG
75	PC(16:0/20:4)	PC	150	TAG46:1-FA16:0	TAG	225	TAG49:3-FA15:0	TAG

<b>Metabolite</b>	<b>Class</b>	<b>Metabolite</b>	<b>Class</b>	<b>Metabolite</b>	<b>Class</b>			
226	TAG49:3-FA16:0	TAG	301	TAG52:2-FA18:0	TAG	376	TAG54:2-FA16:0	TAG
227	TAG49:3-FA16:1	TAG	302	TAG52:2-FA18:1	TAG	377	TAG54:2-FA18:0	TAG
228	TAG49:3-FA18:2	TAG	303	TAG52:2-FA18:2	TAG	378	TAG54:2-FA18:1	TAG
229	TAG49:3-FA18:3	TAG	304	TAG52:2-FA20:0	TAG	379	TAG54:2-FA18:2	TAG
230	TAG50:0-FA14:0	TAG	305	TAG52:2-FA20:1	TAG	380	TAG54:2-FA20:0	TAG
231	TAG50:0-FA16:0	TAG	306	TAG52:2-FA20:2	TAG	381	TAG54:2-FA20:1	TAG
232	TAG50:0-FA18:0	TAG	307	TAG52:3-FA14:0	TAG	382	TAG54:2-FA20:2	TAG
233	TAG50:1-FA14:0	TAG	308	TAG52:3-FA16:0	TAG	383	TAG54:3-FA16:0	TAG
234	TAG50:1-FA16:0	TAG	309	TAG52:3-FA16:1	TAG	384	TAG54:3-FA16:1	TAG
235	TAG50:1-FA16:1	TAG	310	TAG52:3-FA18:0	TAG	385	TAG54:3-FA18:0	TAG
236	TAG50:1-FA18:0	TAG	311	TAG52:3-FA18:1	TAG	386	TAG54:3-FA18:1	TAG
237	TAG50:1-FA18:1	TAG	312	TAG52:3-FA18:2	TAG	387	TAG54:3-FA18:2	TAG
238	TAG50:2-FA14:0	TAG	313	TAG52:3-FA18:3	TAG	388	TAG54:3-FA18:3	TAG
239	TAG50:2-FA14:1	TAG	314	TAG52:3-FA20:0	TAG	389	TAG54:3-FA20:1	TAG
240	TAG50:2-FA16:0	TAG	315	TAG52:3-FA20:1	TAG	390	TAG54:3-FA20:2	TAG
241	TAG50:2-FA16:1	TAG	316	TAG52:3-FA20:2	TAG	391	TAG54:3-FA20:3	TAG
242	TAG50:2-FA18:0	TAG	317	TAG52:3-FA20:3	TAG	392	TAG54:4-FA16:0	TAG
243	TAG50:2-FA18:1	TAG	318	TAG52:3-FA22:1	TAG	393	TAG54:4-FA16:1	TAG
244	TAG50:2-FA18:2	TAG	319	TAG52:4-FA14:0	TAG	394	TAG54:4-FA18:0	TAG
245	TAG50:3-FA14:0	TAG	320	TAG52:4-FA16:0	TAG	395	TAG54:4-FA18:1	TAG
246	TAG50:3-FA14:1	TAG	321	TAG52:4-FA18:0	TAG	396	TAG54:4-FA18:2	TAG
247	TAG50:3-FA16:0	TAG	322	TAG52:4-FA18:1	TAG	397	TAG54:4-FA18:3	TAG
248	TAG50:3-FA16:1	TAG	323	TAG52:4-FA18:2	TAG	398	TAG54:4-FA20:1	TAG
249	TAG50:3-FA18:0	TAG	324	TAG52:4-FA18:3	TAG	399	TAG54:4-FA20:2	TAG
250	TAG50:3-FA18:1	TAG	325	TAG52:4-FA20:0	TAG	400	TAG54:4-FA20:3	TAG
251	TAG50:3-FA18:2	TAG	326	TAG52:4-FA20:2	TAG	401	TAG54:4-FA20:4	TAG
252	TAG50:3-FA18:3	TAG	327	TAG52:4-FA20:3	TAG	402	TAG54:4-FA22:1	TAG
253	TAG50:4-FA14:0	TAG	328	TAG52:4-FA20:4	TAG	403	TAG54:4-FA22:4	TAG
254	TAG50:4-FA14:1	TAG	329	TAG52:4-FA22:1	TAG	404	TAG54:5-FA16:0	TAG
255	TAG50:4-FA16:0	TAG	330	TAG52:4-FA22:4	TAG	405	TAG54:5-FA16:1	TAG
256	TAG50:4-FA16:1	TAG	331	TAG52:5-FA14:0	TAG	406	TAG54:5-FA18:0	TAG
257	TAG50:4-FA18:1	TAG	332	TAG52:5-FA16:0	TAG	407	TAG54:5-FA18:1	TAG
258	TAG50:4-FA18:2	TAG	333	TAG52:5-FA18:2	TAG	408	TAG54:5-FA18:2	TAG
259	TAG50:4-FA18:3	TAG	334	TAG52:5-FA18:3	TAG	409	TAG54:5-FA18:3	TAG
260	TAG50:4-FA20:4	TAG	335	TAG52:5-FA20:3	TAG	410	TAG54:5-FA20:2	TAG
261	TAG50:5-FA14:0	TAG	336	TAG52:5-FA20:4	TAG	411	TAG54:5-FA20:3	TAG
262	TAG50:5-FA16:0	TAG	337	TAG52:5-FA20:5	TAG	412	TAG54:5-FA20:4	TAG
263	TAG50:5-FA16:1	TAG	338	TAG52:5-FA22:5	TAG	413	TAG54:5-FA20:5	TAG
264	TAG50:5-FA18:1	TAG	339	TAG52:6-FA14:0	TAG	414	TAG54:5-FA22:4	TAG
265	TAG50:5-FA18:2	TAG	340	TAG52:6-FA16:0	TAG	415	TAG54:5-FA22:5	TAG
266	TAG50:5-FA18:3	TAG	341	TAG52:6-FA18:1	TAG	416	TAG54:6-FA16:0	TAG
267	TAG50:5-FA20:4	TAG	342	TAG52:6-FA18:2	TAG	417	TAG54:6-FA16:1	TAG
268	TAG51:0-FA17:0	TAG	343	TAG52:6-FA18:3	TAG	418	TAG54:6-FA18:1	TAG
269	TAG51:0-FA18:0	TAG	344	TAG52:6-FA20:4	TAG	419	TAG54:6-FA18:2	TAG
270	TAG51:1-FA15:0	TAG	345	TAG52:6-FA20:5	TAG	420	TAG54:6-FA18:3	TAG
271	TAG51:1-FA16:0	TAG	346	TAG52:6-FA22:6	TAG	421	TAG54:6-FA20:3	TAG
272	TAG51:1-FA17:0	TAG	347	TAG52:7-FA18:1	TAG	422	TAG54:6-FA20:4	TAG
273	TAG51:1-FA18:0	TAG	348	TAG52:7-FA20:5	TAG	423	TAG54:6-FA20:5	TAG
274	TAG51:1-FA18:1	TAG	349	TAG52:7-FA22:6	TAG	424	TAG54:6-FA22:5	TAG
275	TAG51:2-FA15:0	TAG	350	TAG52:8-FA16:1	TAG	425	TAG54:6-FA22:6	TAG
276	TAG51:2-FA16:0	TAG	351	TAG52:8-FA18:2	TAG	426	TAG54:7-FA16:1	TAG
277	TAG51:2-FA16:1	TAG	352	TAG53:0-FA16:0	TAG	427	TAG54:7-FA18:1	TAG
278	TAG51:2-FA17:0	TAG	353	TAG53:1-FA16:0	TAG	428	TAG54:7-FA18:2	TAG
279	TAG51:2-FA18:1	TAG	354	TAG53:1-FA17:0	TAG	429	TAG54:7-FA18:3	TAG
280	TAG51:2-FA18:2	TAG	355	TAG53:1-FA18:0	TAG	430	TAG54:7-FA20:4	TAG
281	TAG51:3-FA15:0	TAG	356	TAG53:1-FA18:1	TAG	431	TAG54:7-FA20:5	TAG
282	TAG51:3-FA16:1	TAG	357	TAG53:2-FA16:0	TAG	432	TAG54:7-FA22:5	TAG
283	TAG51:3-FA17:0	TAG	358	TAG53:2-FA17:0	TAG	433	TAG54:7-FA22:6	TAG
284	TAG51:3-FA18:2	TAG	359	TAG53:2-FA18:1	TAG	434	TAG54:8-FA18:2	TAG
285	TAG51:3-FA18:3	TAG	360	TAG53:2-FA18:2	TAG	435	TAG54:8-FA18:3	TAG
286	TAG51:4-FA15:0	TAG	361	TAG53:3-FA16:0	TAG	436	TAG54:8-FA20:4	TAG
287	TAG51:4-FA18:2	TAG	362	TAG53:3-FA17:0	TAG	437	TAG54:8-FA20:5	TAG
288	TAG51:4-FA18:3	TAG	363	TAG53:3-FA18:2	TAG	438	TAG54:8-FA22:6	TAG
289	TAG51:5-FA18:2	TAG	364	TAG53:4-FA16:0	TAG	439	TAG55:1-FA16:0	TAG
290	TAG52:0-FA16:0	TAG	365	TAG53:4-FA17:0	TAG	440	TAG55:1-FA18:1	TAG
291	TAG52:0-FA18:0	TAG	366	TAG53:4-FA18:2	TAG	441	TAG55:2-FA18:2	TAG
292	TAG52:1-FA16:0	TAG	367	TAG53:4-FA18:3	TAG	442	TAG55:3-FA18:1	TAG
293	TAG52:1-FA16:1	TAG	368	TAG53:4-FA20:4	TAG	443	TAG55:3-FA18:2	TAG
294	TAG52:1-FA18:0	TAG	369	TAG53:5-FA20:4	TAG	444	TAG55:4-FA18:1	TAG
295	TAG52:1-FA18:1	TAG	370	TAG54:0-FA18:0	TAG	445	TAG55:4-FA18:2	TAG
296	TAG52:1-FA20:0	TAG	371	TAG54:1-FA16:0	TAG	446	TAG55:5-FA18:1	TAG
297	TAG52:1-FA20:1	TAG	372	TAG54:1-FA18:0	TAG	447	TAG55:5-FA18:2	TAG
298	TAG52:2-FA14:0	TAG	373	TAG54:1-FA18:1	TAG	448	TAG55:5-FA20:4	TAG
299	TAG52:2-FA16:0	TAG	374	TAG54:1-FA20:0	TAG	449	TAG55:7-FA22:6	TAG
300	TAG52:2-FA16:1	TAG	375	TAG54:1-FA20:1	TAG	450	TAG56:1-FA16:0	TAG

	<u>Metabolite</u>	<u>Class</u>		<u>Metabolite</u>	<u>Class</u>
451	TAG56:1-FA18:1	TAG	526	TAG58:6-FA18:0	TAG
452	TAG56:2-FA16:0	TAG	527	TAG58:6-FA18:1	TAG
453	TAG56:2-FA18:0	TAG	528	TAG58:6-FA20:4	TAG
454	TAG56:2-FA20:0	TAG	529	TAG58:6-FA22:4	TAG
455	TAG56:2-FA20:1	TAG	530	TAG58:6-FA22:5	TAG
456	TAG56:3-FA16:0	TAG	531	TAG58:7-FA18:1	TAG
457	TAG56:3-FA18:0	TAG	532	TAG58:7-FA18:2	TAG
458	TAG56:3-FA18:1	TAG	533	TAG58:7-FA20:4	TAG
459	TAG56:3-FA18:2	TAG	534	TAG58:7-FA22:6	TAG
460	TAG56:3-FA20:0	TAG	535	TAG58:8-FA18:1	TAG
461	TAG56:3-FA20:1	TAG	536	TAG58:8-FA18:2	TAG
462	TAG56:3-FA20:2	TAG	537	TAG58:8-FA20:3	TAG
463	TAG56:4-FA16:0	TAG	538	TAG58:8-FA20:4	TAG
464	TAG56:4-FA18:0	TAG	539	TAG58:8-FA22:5	TAG
465	TAG56:4-FA18:1	TAG	540	TAG58:8-FA22:6	TAG
466	TAG56:4-FA18:2	TAG	541	TAG58:9-FA18:1	TAG
467	TAG56:4-FA20:1	TAG	542	TAG58:9-FA18:2	TAG
468	TAG56:4-FA20:2	TAG	543	TAG58:9-FA20:4	TAG
469	TAG56:4-FA20:3	TAG	544	TAG58:9-FA22:5	TAG
470	TAG56:4-FA20:4	TAG	545	TAG58:9-FA22:6	TAG
471	TAG56:4-FA22:4	TAG	546	TAG60:11-FA22:6	TAG
472	TAG56:5-FA16:0	TAG			
473	TAG56:5-FA18:0	TAG			
474	TAG56:5-FA18:1	TAG			
475	TAG56:5-FA18:2	TAG			
476	TAG56:5-FA20:1	TAG			
477	TAG56:5-FA20:2	TAG			
478	TAG56:5-FA20:3	TAG			
479	TAG56:5-FA20:4	TAG			
480	TAG56:5-FA22:4	TAG			
481	TAG56:5-FA22:5	TAG			
482	TAG56:6-FA16:0	TAG			
483	TAG56:6-FA18:0	TAG			
484	TAG56:6-FA18:1	TAG			
485	TAG56:6-FA18:2	TAG			
486	TAG56:6-FA18:3	TAG			
487	TAG56:6-FA20:2	TAG			
488	TAG56:6-FA20:3	TAG			
489	TAG56:6-FA20:4	TAG			
490	TAG56:6-FA20:5	TAG			
491	TAG56:6-FA22:4	TAG			
492	TAG56:6-FA22:5	TAG			
493	TAG56:6-FA22:6	TAG			
494	TAG56:7-FA16:0	TAG			
495	TAG56:7-FA16:1	TAG			
496	TAG56:7-FA18:1	TAG			
497	TAG56:7-FA18:2	TAG			
498	TAG56:7-FA18:3	TAG			
499	TAG56:7-FA20:3	TAG			
500	TAG56:7-FA20:4	TAG			
501	TAG56:7-FA20:5	TAG			
502	TAG56:7-FA22:6	TAG			
503	TAG56:8-FA16:0	TAG			
504	TAG56:8-FA16:1	TAG			
505	TAG56:8-FA18:1	TAG			
506	TAG56:8-FA18:2	TAG			
507	TAG56:8-FA18:3	TAG			
508	TAG56:8-FA20:4	TAG			
509	TAG56:8-FA20:5	TAG			
510	TAG56:8-FA22:5	TAG			
511	TAG56:8-FA22:6	TAG			
512	TAG56:9-FA18:3	TAG			
513	TAG56:9-FA20:4	TAG			
514	TAG56:9-FA20:5	TAG			
515	TAG56:9-FA22:6	TAG			
516	TAG57:2-FA18:1	TAG			
517	TAG57:3-FA18:2	TAG			
518	TAG58:10-FA18:2	TAG			
519	TAG58:10-FA20:4	TAG			
520	TAG58:10-FA22:5	TAG			
521	TAG58:10-FA22:6	TAG			
522	TAG58:2-FA18:1	TAG			
523	TAG58:3-FA18:1	TAG			
524	TAG58:5-FA18:1	TAG			
525	TAG58:6-FA16:0	TAG			

**Table S3. Plasma concentrations ( $\mu\text{M}$ ) for representative lipid species by class.** Within each lipid class, the mean, minimum, and maximum concentrations in control participants (A: Fred Hutch, B: Roswell Park) for two individual lipid metabolites are presented—the species with the lowest, or the highest, mean concentration.

**A. Fred Hutch (FH)**

<u>Class</u>	<u>Metabolite</u>	<u>Mean</u>	<u>Min</u>	<u>Max</u>
CE	CE(22:2)	0.31	0.16	0.65
CE	CE(18:2)	1761.50	991.47	2560.56
CER	CER(18:0)	0.18	0.07	0.39
CER	CER(24:0)	3.23	1.76	6.88
DAG	DAG(18:1/22:6)	0.27	0.06	1.11
DAG	DAG(18:1/18:2)	7.77	3.20	17.88
FFA	FFA(20:5)	1.13	0.48	3.33
FFA	FFA(17:0)	8.50	4.52	68.15
LPC	LPC(22:5)	0.50	0.23	1.04
LPC	LPC(16:0)	122.89	70.46	194.16
LPE	LPE(16:0)	0.91	0.57	1.73
LPE	LPE(18:0)	1.70	0.97	3.08
PC	PC(15:0/18:1)	1.08	0.54	1.99
PC	PC(16:0/18:2)	573.08	393.32	827.95
PE	PE(18:2/16:1)	0.49	0.17	1.56
PE	PE(16:0/22:6)	10.95	3.38	24.81
SM	SM(26:0)	0.65	0.46	0.98
SM	SM(22:0)	162.68	93.12	272.33
TAG	TAG52:2-FA20:0	0.17	0.07	0.32
TAG	TAG52:2-FA18:1	439.97	118.76	949.63

**B. Roswell Park (RP)**

<u>Class</u>	<u>Metabolite</u>	<u>Mean</u>	<u>Min</u>	<u>Max</u>
CE	CE(22:2)	0.25	0.16	0.58
CE	CE(18:2)	1936.11	1052.26	2922.62
CER	CER(18:0)	0.17	0.07	0.34
CER	CER(24:0)	3.70	1.27	7.07
DAG	DAG(18:1/22:6)	0.23	0.08	0.81
DAG	DAG(18:1/18:2)	8.75	2.09	31.22
FFA	FFA(24:0)	0.73	0.48	1.17
FFA	FFA(17:0)	5.74	3.29	9.64
LPC	LPC(22:5)	0.56	0.20	1.04
LPC	LPC(16:0)	138.00	80.54	206.27
LPE	LPE(16:0)	0.96	0.42	1.58
LPE	LPE(18:0)	1.72	0.71	2.80
PC	PC(15:0/18:1)	1.03	0.55	2.54
PC	PC(16:0/18:2)	628.72	338.78	939.06
PE	PE(18:2/16:1)	0.57	0.27	1.08
PE	PE(P-18:1/20:4)	9.63	2.51	24.21
SM	SM(26:0)	0.59	0.38	0.83
SM	SM(22:0)	216.67	97.73	313.71
TAG	TAG52:2-FA20:0	0.24	0.08	0.66
TAG	TAG52:2-FA18:1	538.12	182.55	2356.39

**Table S4. Selected top differential metabolites by case status.** 249 lipid species satisfying FDR  $q < 0.05$  in both cohorts (Figure 1B, bottom) were sorted and rank ordered by P value (FH). Beta coefficients, P values, and FDR q values derived from linear regression analyses are shown, by cohort, for the top ten metabolites.

	Class	Metabolite	FH				RP			
			N	Beta	P	q	N	Beta	P	q
1	TAG	TAG44:1-FA18:1	90	-1.16	5.54E-06	9.16E-04	116	-1.06	1.89E-03	3.29E-03
2	PC	PC(14:0/18:2)	94	-0.71	6.43E-06	9.16E-04	118	-0.64	1.28E-05	1.02E-04
3	TAG	TAG50:5-FA18:3	94	-0.88	7.33E-06	9.16E-04	118	-1.00	2.31E-06	4.06E-05
4	PC	PC(16:0/18:3)	94	-0.50	9.79E-06	9.16E-04	118	-0.60	3.13E-07	2.22E-05
5	CE	CE(18:4)	94	-0.79	1.23E-05	9.16E-04	118	-0.81	1.79E-05	1.27E-04
6	PC	PC(14:0/20:4)	92	-0.65	1.29E-05	9.16E-04	112	-0.43	2.53E-04	6.69E-04
7	TAG	TAG48:4-FA18:3	88	-1.04	1.38E-05	9.16E-04	117	-1.34	5.03E-07	2.22E-05
8	TAG	TAG50:4-FA18:3	94	-0.88	1.40E-05	9.16E-04	118	-0.95	1.36E-06	3.22E-05
9	PC	PC(18:2/20:3)	91	-0.66	1.64E-05	9.16E-04	117	-0.66	8.88E-06	8.08E-05
10	TAG	TAG46:2-FA14:0	92	-1.26	1.73E-05	9.16E-04	118	-1.36	9.82E-06	8.42E-05

**Table S5. Selected top differential metabolites by case status in stage-stratified analyses.** Lipid species with concentration differences in (A) early-stage (I-II) cases or (B) late-stage (III-IV) cases, relative to controls, were sorted and rank ordered by P value. Beta coefficients, P values, and FDR q values derived from linear regression analyses are shown for the top ten metabolites in each analysis.

**A.**

	<b>Class</b>	<b>Metabolite</b>	<b>N</b>	<b>Beta</b>	<b>P</b>	<b>q</b>
<b>1</b>	TAG	TAG56:2-FA16:0	83	-0.97	1.3E-05	6.2E-03
<b>2</b>	PC	PC(16:0/18:3)	84	-0.62	6.1E-05	6.2E-03
<b>3</b>	TAG	TAG52:4-FA18:0	84	-0.89	6.6E-05	6.2E-03
<b>4</b>	TAG	TAG54:2-FA20:0	84	-0.74	7.1E-05	6.2E-03
<b>5</b>	TAG	TAG50:3-FA18:0	83	-1.07	7.4E-05	6.2E-03
<b>6</b>	TAG	TAG52:2-FA14:0	78	-0.92	8.9E-05	6.2E-03
<b>7</b>	TAG	TAG52:8-FA16:1	76	-0.97	9.9E-05	6.2E-03
<b>8</b>	TAG	TAG54:1-FA16:0	84	-0.93	1.1E-04	6.2E-03
<b>9</b>	DAG	DAG(14:0/18:1)	76	-0.83	1.2E-04	6.2E-03
<b>10</b>	TAG	TAG50:3-FA18:3	84	-0.95	1.3E-04	6.2E-03

**B.**

	<b>Class</b>	<b>Metabolite</b>	<b>N</b>	<b>Beta</b>	<b>P</b>	<b>FDR</b>
<b>1</b>	CE	CE(14:0)	92	-0.81	9.7E-07	3.1E-04
<b>2</b>	TAG	TAG50:5-FA16:1	92	-1.23	1.5E-06	3.1E-04
<b>3</b>	CE	CE(14:1)	92	-0.95	1.7E-06	3.1E-04
<b>4</b>	LPC	LPC(16:0)	92	-0.37	3.1E-06	3.1E-04
<b>5</b>	TAG	TAG48:4-FA18:3	91	-1.50	3.3E-06	3.1E-04
<b>6</b>	LPC	LPC(18:0)	92	-0.45	4.3E-06	3.1E-04
<b>7</b>	TAG	TAG52:2-FA14:0	86	-1.05	4.3E-06	3.1E-04
<b>8</b>	TAG	TAG48:4-FA14:1	90	-1.16	4.5E-06	3.1E-04
<b>9</b>	TAG	TAG48:3-FA18:3	92	-1.52	6.5E-06	3.1E-04
<b>10</b>	TAG	TAG52:5-FA20:3	92	-1.06	7.2E-06	3.1E-04



**Table S6. Performance characteristics for selected lipid species (Table 4) using data from FH cohort.** Single lipid species were combined with CA125, age, and BMI, to classify early-stage (I-II) cases versus controls (FH cohort). Logistic regression was used to model the log odds of case status as a linear function of  $\log_2$  CA125, age, and BMI, with or without a given lipid metabolite (M), after imputing missing values for each species to  $\frac{1}{2}$  the minimum concentration detected for that species across all participants. ROC curve analysis was conducted to estimate AUC and *spec90* conferred by the joint model (with M) versus the base model (without M: AUC=0.802, *spec90*=0.532). Species with  $\Delta\text{spec90}>0.05$  are listed in red.

	<b>Class</b>	<b>Metabolite</b>	<b><i>spec90</i></b>	<b><math>\Delta\text{spec90}</math></b>	<b><math>P_{\Delta s}</math></b>	<b>AUC</b>	<b><math>\Delta\text{AUC}</math></b>	<b><math>P_{\Delta A}</math></b>
<b>1</b>	DAG	DAG(16:1/18:1)	0.68	0.15	0.25	0.88	0.08	0.10
<b>2</b>	CE	CE(18:1)	0.51	-0.02	0.70	0.82	0.02	0.54
<b>3</b>	CE	CE(17:0)	0.55	0.02	0.38	0.80	0.00	0.79
<b>4</b>	DAG	DAG(20:0/20:0)	0.53	0.00		0.80	0.00	
<b>5</b>	TAG	TAG52:2-FA20:2	0.40	-0.13	0.25	0.83	0.02	0.57
<b>6</b>	TAG	TAG54:3-FA20:3	0.43	-0.11	0.31	0.84	0.03	0.46
<b>7</b>	PE	PE(P-16:0/20:3)	0.57	0.04	0.43	0.81	0.01	0.82
<b>8</b>	DAG	DAG(18:0/18:2)	0.72	0.19	0.24	0.92	0.12	0.08
<b>9</b>	TAG	TAG56:4-FA18:0	0.74	0.21	0.02	0.91	0.11	0.02
<b>10</b>	CE	CE(20:0)	0.53	0.00	1.00	0.79	-0.01	0.68

**Table S7. Patient and tumor characteristics (GEO samples).**

	<b>GSE4122 (n=50)</b>		<b>GSE57477 (n=54)</b>		<b>GSE7463 (n=19)</b>		<b>GSE6822 (n=34)</b>		<b>Pooled (n=157)</b>	
	Malignant	Benign	Malignant	Benign	Malignant	Benign	Malignant	Benign	Malignant	Benign
Age [mean (sd)]	NA		67.1 (11.3)	62.5 (6.4)	58.4 (11.5)	63.4 (9.0)	NA		106	51
<b>Histology</b>										
Serous	16	7	37	17	7	4	28	6	88	34
Non-serous	15	6	0	0	2	0	0	0	17	6
N/A	1	5	0	0	0	6	0	0	1	11
<b>Stage</b>										
I	1		2		1		2		6	
II	6		4		1		2		13	
III	14		26		6		20		66	
IV	0		5		1		0		6	
NA	11		0		0		4		15	

**[GSE4122]**

GSM94332, GSM94339, GSM94341, GSM94344, GSM94346, GSM94347, GSM94349, GSM94352, GSM94359, GSM94368, GSM94372, GSM94375, GSM94377, GSM94386, GSM94393, GSM94396, GSM94402, GSM94404, GSM94405, GSM94408, GSM94409, GSM94411, GSM94412, GSM94413, GSM94414, GSM94415, GSM94417, GSM94420, GSM94421, GSM94423, GSM94425, GSM94426, GSM94348, GSM94363, GSM94366, GSM94373, GSM94379, GSM94381, GSM94382, GSM94383, GSM94388, GSM94390, GSM94392, GSM94395, GSM94398, GSM94400, GSM94401, GSM94416, GSM94422, GSM94424

**[GSE57477]**

GSM1383532, GSM1383530, GSM1383529, GSM1383526, GSM1383525, GSM1383523, GSM1383522, GSM1383519, GSM1383514, GSM1383511, GSM1383507, GSM1383504, GSM1383503, GSM1383502, GSM1383501, GSM1383499, GSM1383498, GSM1383495, GSM1383494, GSM1383492, GSM1383491, GSM1383490, GSM1383488, GSM1383487, GSM1383485, GSM1383484, GSM1383482, GSM1383480, GSM1383479, GSM1383478, GSM1383476, GSM1383474, GSM1383473, GSM1383471, GSM1383469, GSM1383468, GSM1383467, GSM1383527, GSM1383524, GSM1383520, GSM1383518, GSM1383515, GSM1383513, GSM1383510, GSM1383509, GSM1383508, GSM1383506, GSM1383505, GSM1383496, GSM1383489, GSM1383481, GSM1383475, GSM1383472, GSM1383470

**[GSE7463]**

GSM180636, GSM180637, GSM180638, GSM180639, GSM180640, GSM180641, GSM180642, GSM180643, GSM180644, GSM180626, GSM180627, GSM180628, GSM180629, GSM180630, GSM180631, GSM180632, GSM180633, GSM180634, GSM180635

**[GSE6822]**

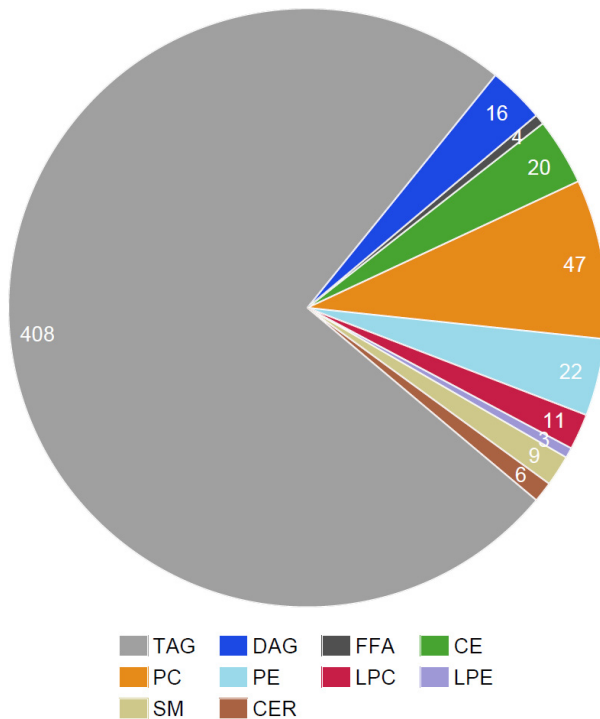
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**Table S8. Lipid transport-related GO gene sets selected and individual genes available for analysis.** 180 GO gene sets with “lipid” or “lipoprotein” included in the set name were identified. 61 of the 180 were retained based on relationships to lipid transport. 145 of 402 unique genes captured by these 61 GO gene sets had expression profiling data available for analysis in all four GEO datasets and for subsequent meta-analysis.

- 1 GO\_APOLIPOPROTEIN\_A\_I\_BINDING
- 2 GO\_APOLIPOPROTEIN\_A\_I\_MEDIATED\_SIGNALING\_PATHWAY
- 3 GO\_APOLIPOPROTEIN\_BINDING
- 4 GO\_APOLIPOPROTEIN\_RECEPTOR\_BINDING
- 5 GO\_ATPASE\_COUPLED\_INTRAMEMBRANE\_LIPID\_TRANSPORTER\_ACTIVITY
- 6 GO\_ATPASE\_COUPLED\_LIPID\_TRANSMEMBRANE\_TRANSPORTER\_ACTIVITY
- 7 GO\_BIOACTIVE\_LIPID\_RECEPTOR\_ACTIVITY
- 8 GO\_HIGH\_DENSITY\_LIPOPROTEIN\_PARTICLE
- 9 GO\_HIGH\_DENSITY\_LIPOPROTEIN\_PARTICLE\_ASSEMBLY
- 10 GO\_HIGH\_DENSITY\_LIPOPROTEIN\_PARTICLE\_BINDING
- 11 GO\_HIGH\_DENSITY\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 12 GO\_HIGH\_DENSITY\_LIPOPROTEIN\_PARTICLE\_REMODELING
- 13 GO\_INTERMEDIATE\_DENSITY\_LIPOPROTEIN\_PARTICLE
- 14 GO\_INTERMEMBRANE\_LIPID\_TRANSFER
- 15 GO\_INTRACELLULAR\_LIPID\_TRANSPORT
- 16 GO\_INTRAMEMBRANE\_LIPID\_TRANSPORTER\_ACTIVITY
- 17 GO\_LIPID\_EXPORT\_FROM\_CELL
- 18 GO\_LIPID\_IMPORT\_INTO\_CELL
- 19 GO\_LIPID\_TRANSFER\_ACTIVITY
- 20 GO\_LIPID\_TRANSLOCATION
- 21 GO\_LIPID\_TRANSPORTER\_ACTIVITY
- 22 GO\_LIPOPROTEIN\_PARTICLE\_RECEPTOR\_ACTIVITY
- 23 GO\_LIPOPROTEIN\_PARTICLE\_RECEPTOR\_BINDING
- 24 GO\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE
- 25 GO\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_BINDING
- 26 GO\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 27 GO\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_RECEPTOR\_ACTIVITY
- 28 GO\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_RECEPTOR\_BINDING
- 29 GO\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_RECEPTOR\_BIOSYNTHETIC\_PROCESS
- 30 GO\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_RECEPTOR\_CATABOLIC\_PROCESS
- 31 GO\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_REMODELING
- 32 GO\_LOW\_DENSITY\_LIPOPROTEIN\_RECEPTOR\_PARTICLE\_METABOLIC\_PROCESS
- 33 GO\_NEGATIVE\_REGULATION\_OF\_LIPID\_TRANSPORT
- 34 GO\_NEGATIVE\_REGULATION\_OF\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 35 GO\_NEGATIVE\_REGULATION\_OF\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 36 GO\_PHOSPHOLIPID\_TRANSFER\_ACTIVITY
- 37 GO\_PHOSPHOLIPID\_TRANSPORT
- 38 GO\_PHOSPHOLIPID\_TRANSPORTER\_ACTIVITY
- 39 GO\_PLASMA\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 40 GO\_POSITIVE\_REGULATION\_OF\_LIPID\_TRANSPORT
- 41 GO\_POSITIVE\_REGULATION\_OF\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 42 GO\_POSITIVE\_REGULATION\_OF\_PHOSPHOLIPID\_TRANSPORT
- 43 GO\_REGULATION\_OF\_HIGH\_DENSITY\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 44 GO\_REGULATION\_OF\_LIPID\_TRANSPORT
- 45 GO\_REGULATION\_OF\_LIPID\_TRANSPORTER\_ACTIVITY
- 46 GO\_REGULATION\_OF\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 47 GO\_REGULATION\_OF\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 48 GO\_REGULATION\_OF\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_RECEPTOR\_BINDING
- 49 GO\_REGULATION\_OF\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_RECEPTOR\_CATABOLIC\_PROCESS
- 50 GO\_REGULATION\_OF\_PLASMA\_LIPOPROTEIN\_PARTICLE\_LEVELS
- 51 GO\_REGULATION\_OF\_VERY\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 52 GO\_REGULATION\_OF\_VERY\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_REMODELING
- 53 GO\_SPHERICAL\_HIGH\_DENSITY\_LIPOPROTEIN\_PARTICLE
- 54 GO\_SPHINGOLIPID\_TRANSFER\_ACTIVITY
- 55 GO\_SPHINGOLIPID\_TRANSPORTER\_ACTIVITY
- 56 GO\_TRIGLYCERIDE\_RICH\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 57 GO\_TRIGLYCERIDE\_RICH\_LIPOPROTEIN\_PARTICLE\_REMODELING
- 58 GO\_TRIGLYCERIDE\_RICH\_PLASMA\_LIPOPROTEIN\_PARTICLE
- 59 GO\_VERY\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_ASSEMBLY
- 60 GO\_VERY\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_CLEARANCE
- 61 GO\_VERY\_LOW\_DENSITY\_LIPOPROTEIN\_PARTICLE\_REMODELING

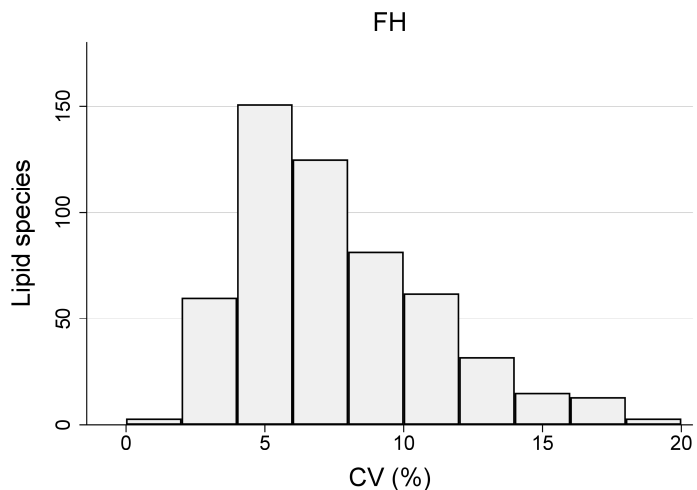


**Figure S1. Lipid class assignments for 546 analyzed lipid species.** ~75% are triacylglycerols (TAG). The remaining 138 species are classified as diacylglycerols (DAG), free fatty acids (FFA), cholesterol esters (CE), phosphatidylcholines (PC), phosphatidylethanolamines (PE), lysophosphatidylcholines (LPC), lysophosphatidylethanolamines (LPE), sphingomyelins (SM), and ceramides (CER).



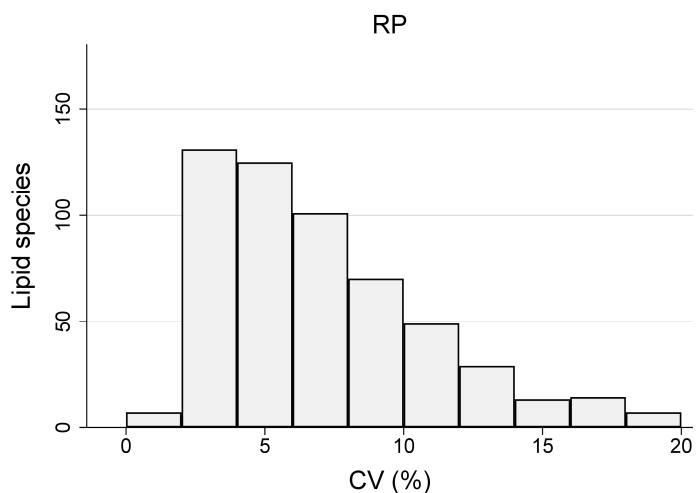
**Figure S2. Distributions of coefficients of variation (CV) for 546 analyzed lipid species.** Mean, minimum (Min), and maximum (Max) CV listed for each lipid class (A: Fred Hutch, B: Roswell Park).

**A.**



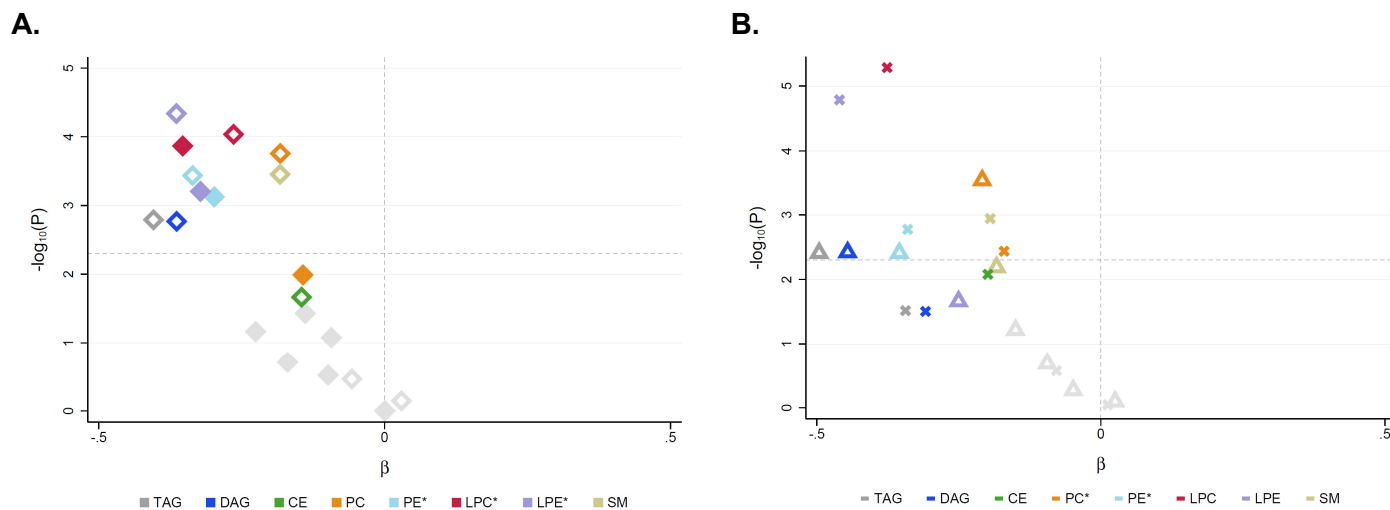
<u>Class</u>	<u>N</u>	<u>Mean</u>	<u>Min</u>	<u>Max</u>
CE	20	<b>4.0</b>	1.4	9.3
CER	6	<b>7.6</b>	4.4	15.4
DAG	16	<b>10.6</b>	7.7	15.3
FFA	4	<b>7.6</b>	3.1	12.0
LPC	11	<b>11.3</b>	3.8	17.8
LPE	3	<b>10.7</b>	6.9	17.5
PC	47	<b>10.7</b>	3.7	19.2
PE	22	<b>13.0</b>	7.6	17.4
SM	9	<b>7.9</b>	3.2	11.3
TAG	408	<b>6.8</b>	1.9	19.9

**B.**

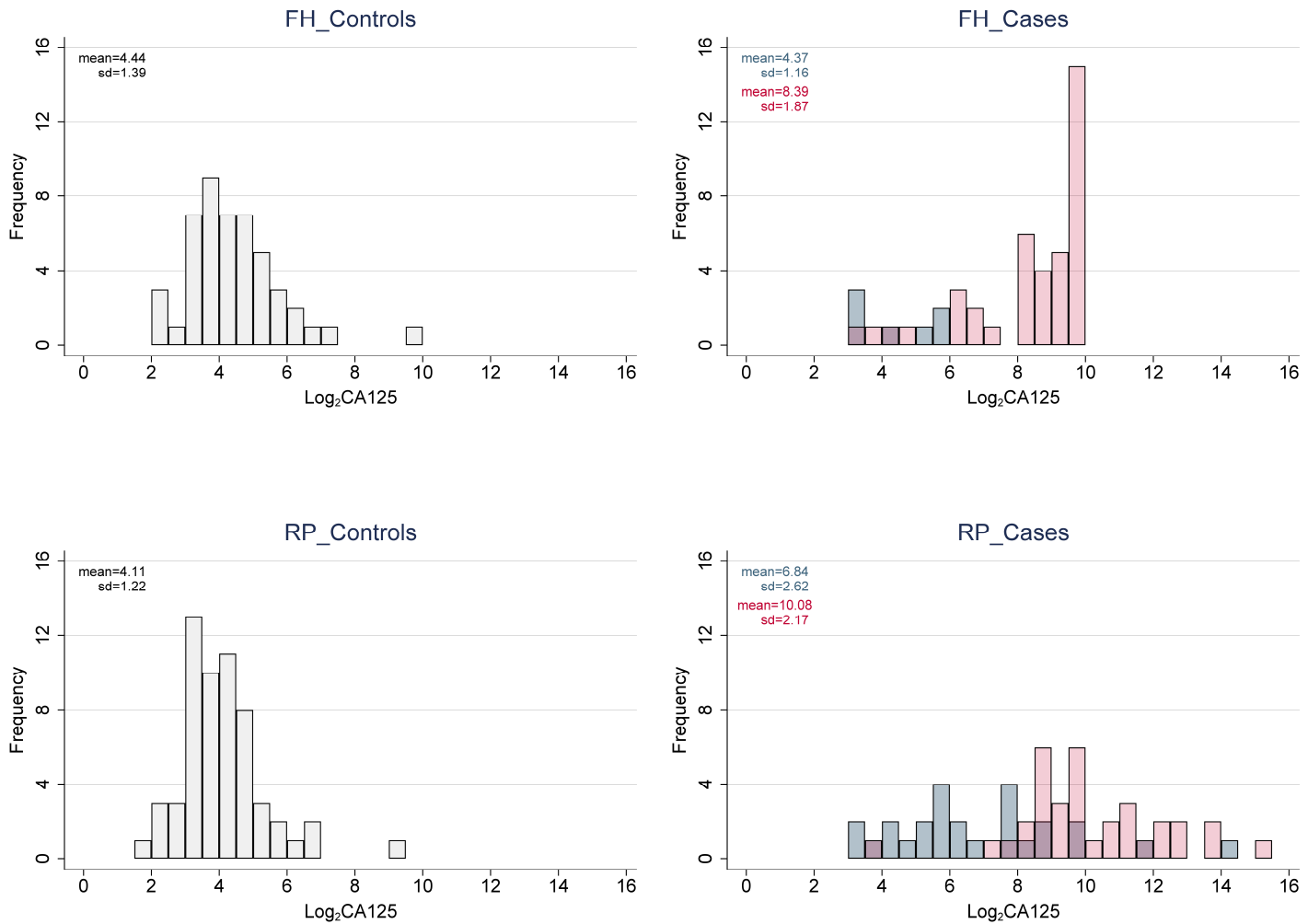


<u>Class</u>	<u>N</u>	<u>Mean</u>	<u>Min</u>	<u>Max</u>
CE	20	<b>3.8</b>	1.1	9.4
CER	6	<b>6.3</b>	3.8	11.1
DAG	16	<b>11.4</b>	7.7	16.0
FFA	4	<b>7.6</b>	4.5	9.5
LPC	11	<b>10.1</b>	3.7	16.7
LPE	3	<b>8.0</b>	3.7	13.1
PC	47	<b>8.8</b>	3.0	16.7
PE	22	<b>14.2</b>	7.9	19.7
SM	9	<b>5.4</b>	1.8	8.3
TAG	408	<b>6.4</b>	1.8	20.0

**Figure S3. Lipid class differences in cases versus controls.** Within each cohort, missing values for each species were imputed to  $\frac{1}{2}$  the minimum concentration detected for that species across all participants. Concentrations for all species in a given class were summed and  $\log_2$ -transformed to generate class-level variables, and regressed on case status with adjustment for age and BMI. (A) All cases vs. controls, by cohort (FH: solid, RP: outlined). (B) Early-stage (I-II: “ $\Delta$ ”) or late-stage (III-IV: “ $\times$ ”) cases vs. controls (RP only). \*Lipid classes with  $P < 0.005$  ( $=0.05/10$ ) in both cohorts (A), or both subgroups (B). FFA, CER:  $P > 0.05$  (gray).



**Figure S4. Plasma CA125 values (U/mL) for cases and controls.** Distributions for both early-stage (blue) and late-stage (red) cases, as indicated.

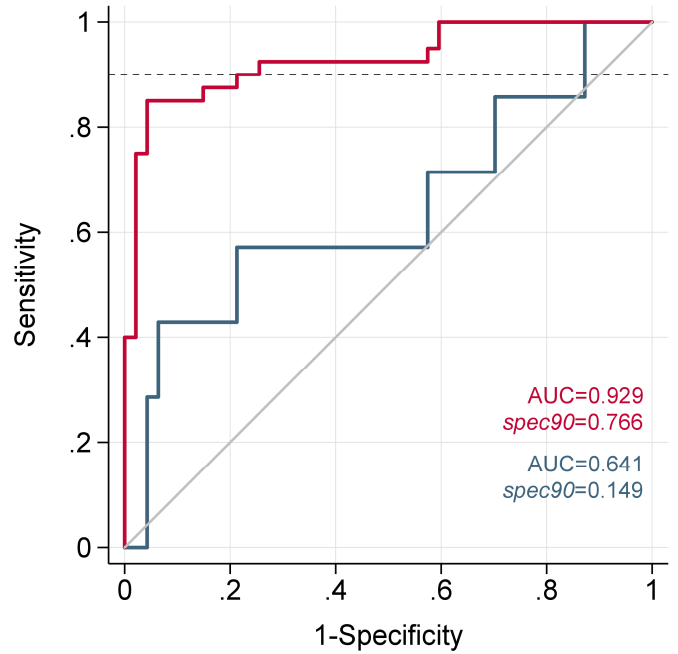
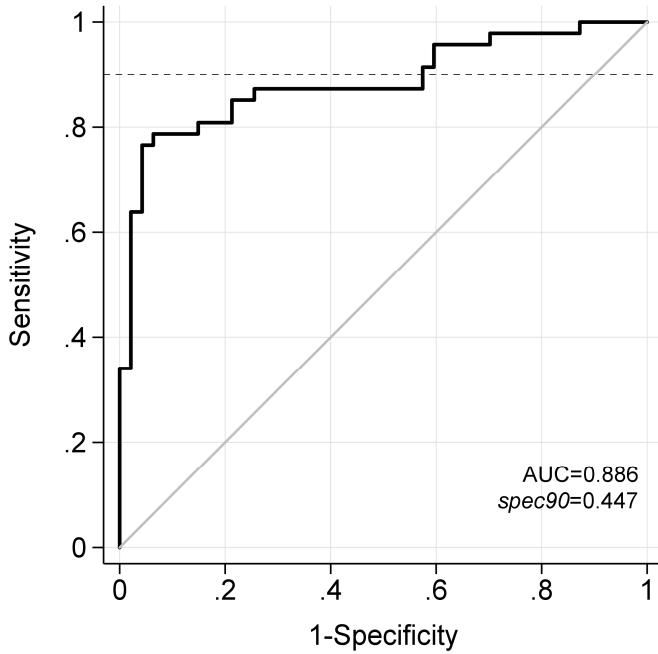


\*NOTE: N=14 CA125 values >1000 U/mL (FH) could not be further resolved due to limited remaining plasma and were recorded as  $\geq 1000$  U/mL.

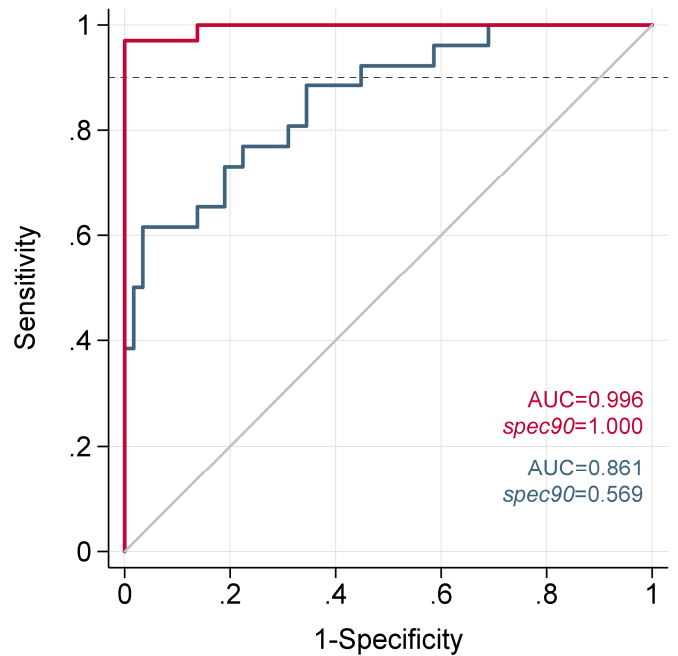
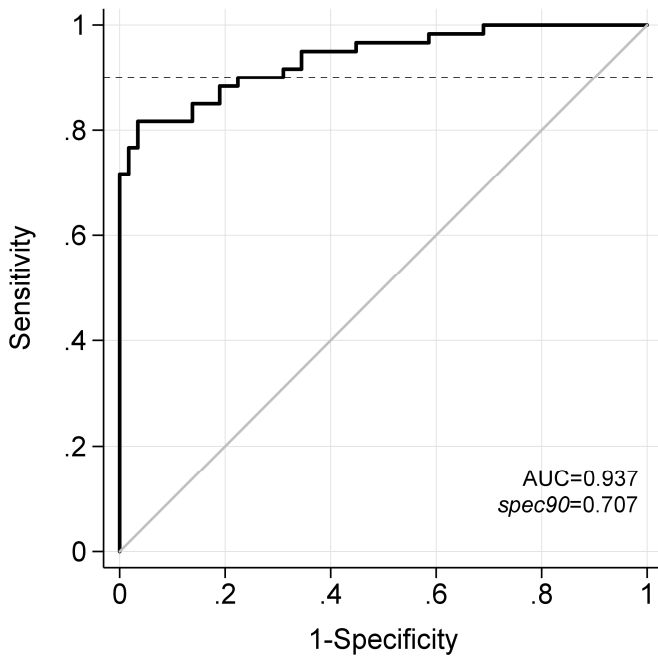


**Figure S5. ROC curves and performance metrics for base models comprised of CA125, age, and BMI.** Models were built using data from all cases and controls in the Fred Hutch (A) or Roswell Park (B) patient cohorts. Performance was assessed across all patients in a given cohort (left), or in subgroups (right) comprised of controls and early-stage cases (blue), or controls and late-stage cases (red).

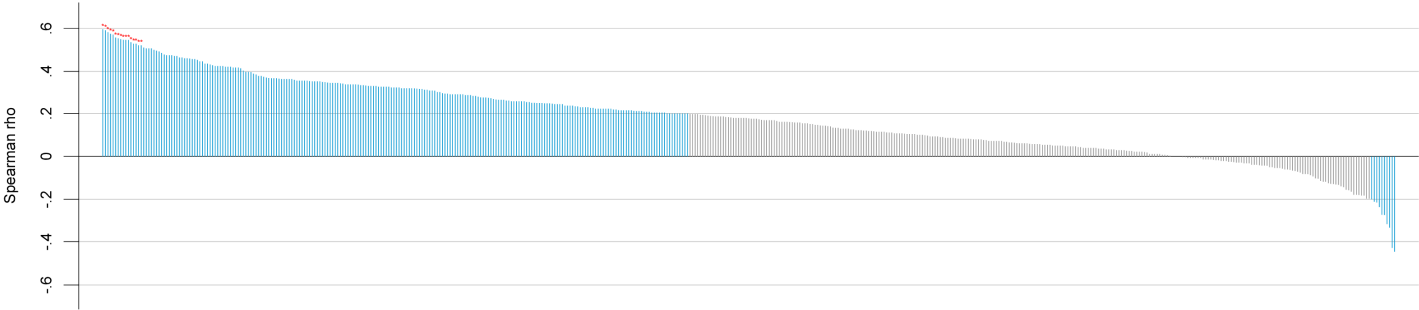
**A. Fred Hutch (FH)**



**B. Roswell Park (RP)**



**Figure S6.** Spearman correlation analysis of lipid concentrations in paired ascites and plasma specimens isolated from 15 patients with late-stage OC. Correlation coefficients ( $\rho$ ) plotted for >500 individual lipid species analyzed (gray:  $|\rho| < 0.2$ , blue:  $|\rho| \geq 0.2$ ). 16 metabolites with  $P_{\rho} < 0.05$  are marked (\*).



**Figure S7. Schematic summary.** Relative differences in plasma lipid metabolite levels and tissue gene expression levels in women with malignant, versus benign, adnexal mass.

