



Animal Model Workshop

Lipidomic classification of clear cell Renal Cell Carcinoma reveals aggressiveness and therapeutic sensitivity

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Session 10: From Discovery to Delivery – RCC Models
Powering Therapies, Resistance Solutions, and Diagnostics



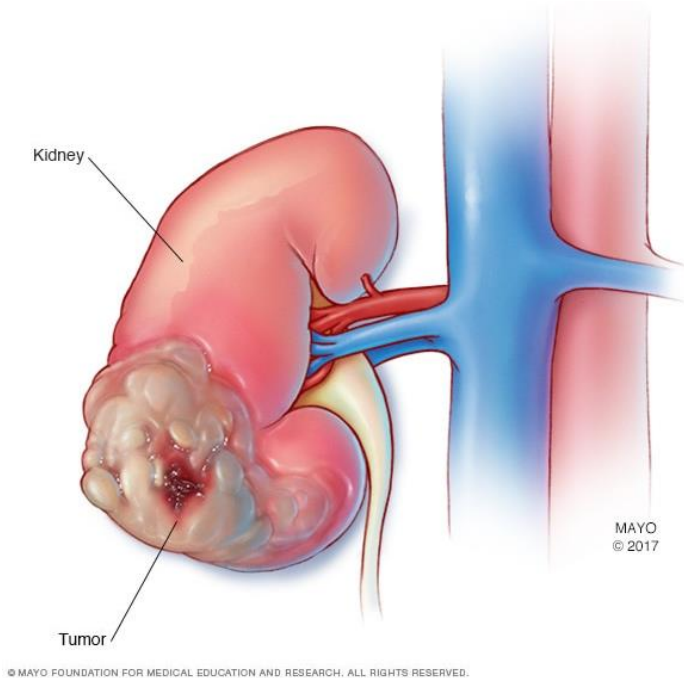
Kidney Cancer Association® IN PARTNERSHIP WITH

UT Southwestern
Medical Center
Kidney Cancer Program

Disclosures...

- There are no actual conflicts of interest to disclose.
- The speaker does hold a patent application for chemerin inhibition in renal cancer.

Renal Cell Carcinoma



- 73,750 new cases/year
45,520 ♂/28,230 ♀
- 14,830 deaths
9,860 ♂/4,970 ♀

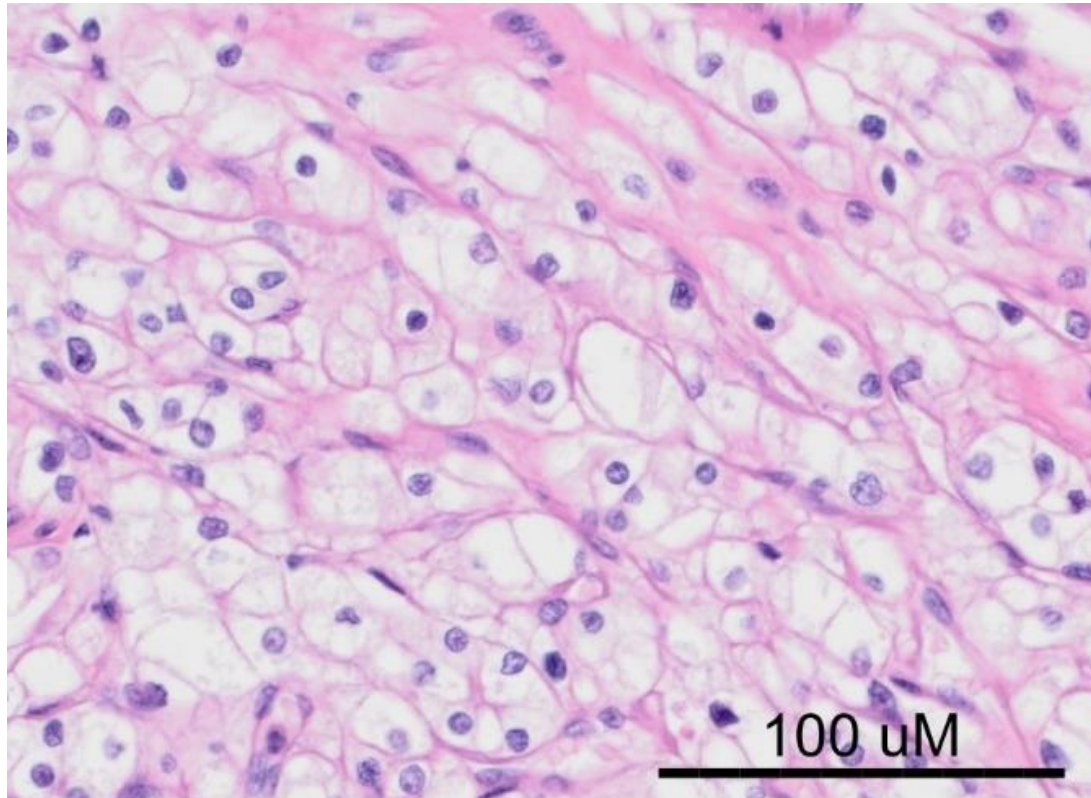
Types:

clear cell RCC (75%)
Papillary RCC (15%)
Chromophobe RCC (5%)
Oncocytoma (5%)

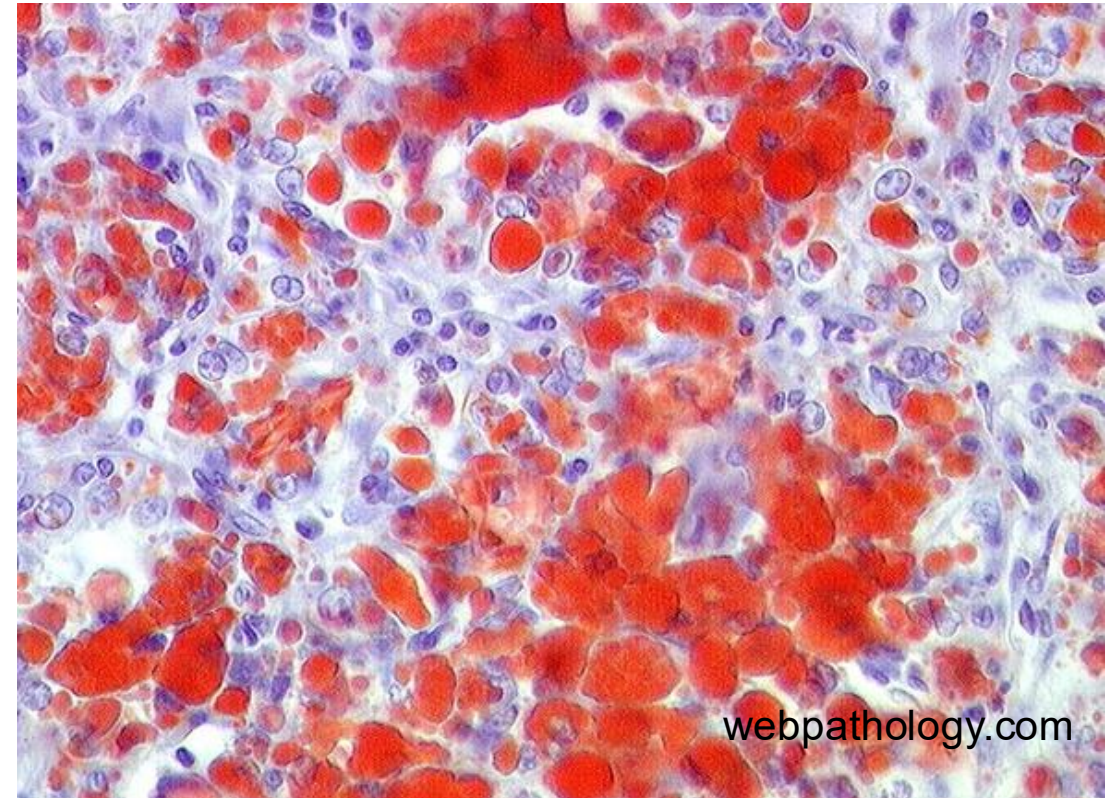
- Risk factors:
 - Smoking
 - Obesity
- Standard of care:
 - Surgical resection
 - TKI therapy
 - Immunotherapy
- 30% 5yr survival for metastatic patients

ccRCC is defined by abundant lipid accumulation

H&E

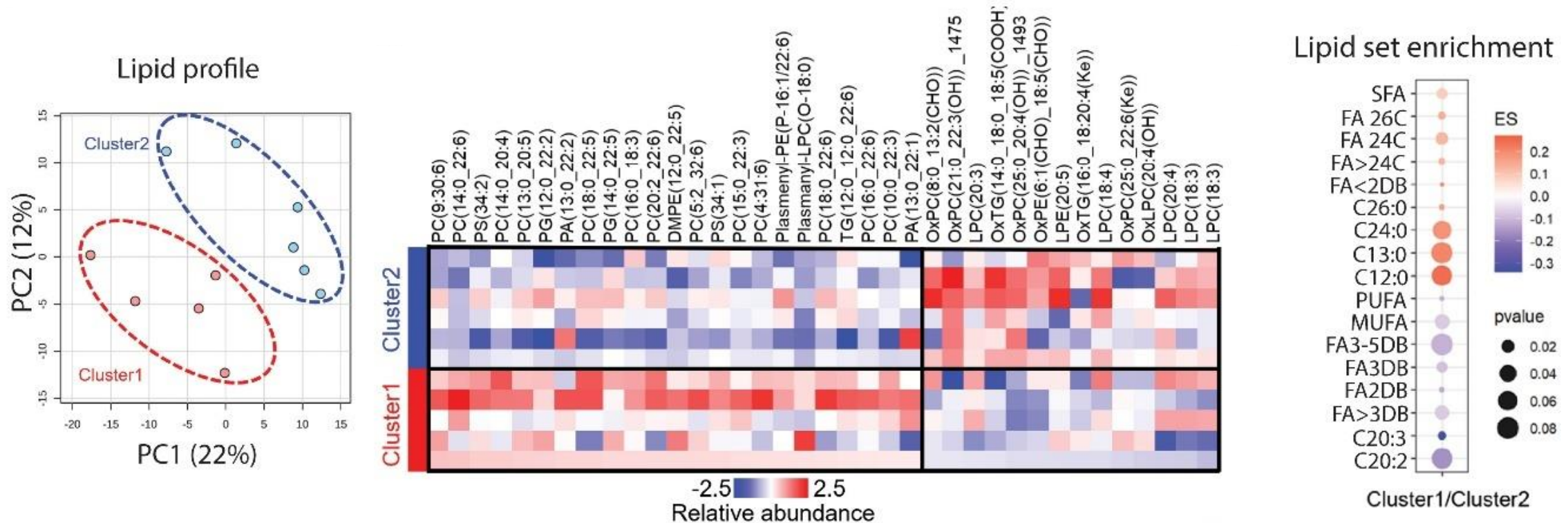


Oil Red O

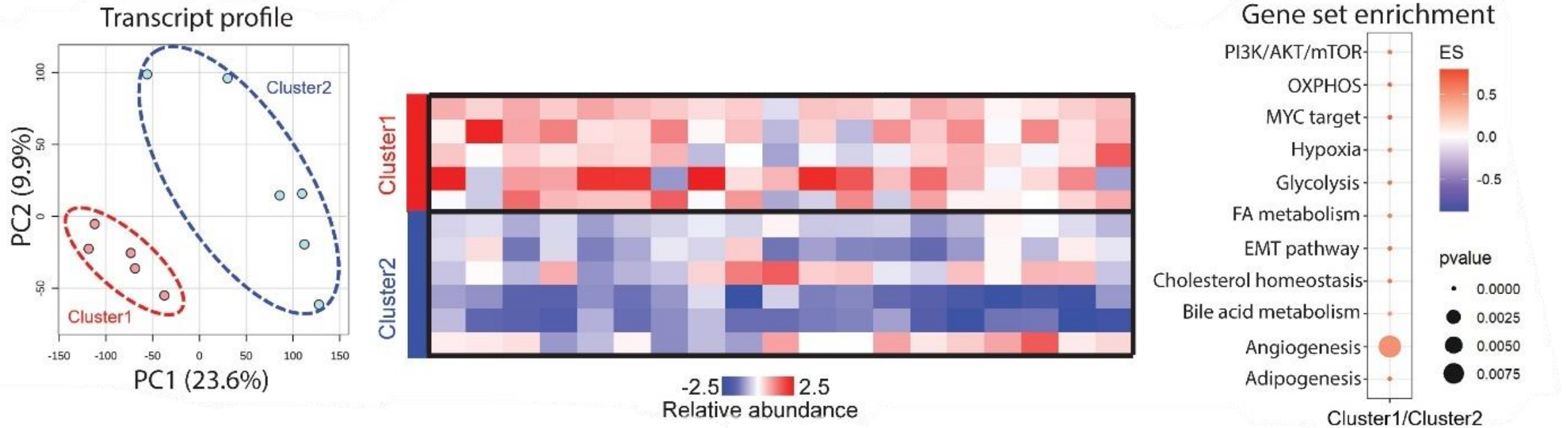


But are all lipidomes the same?

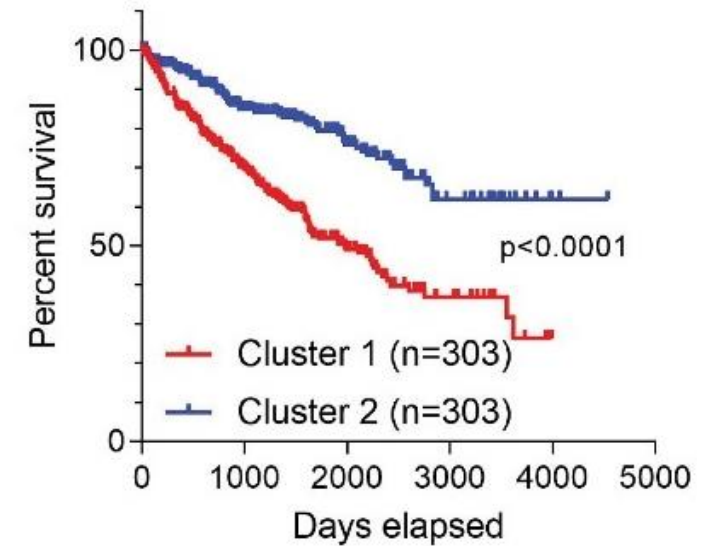
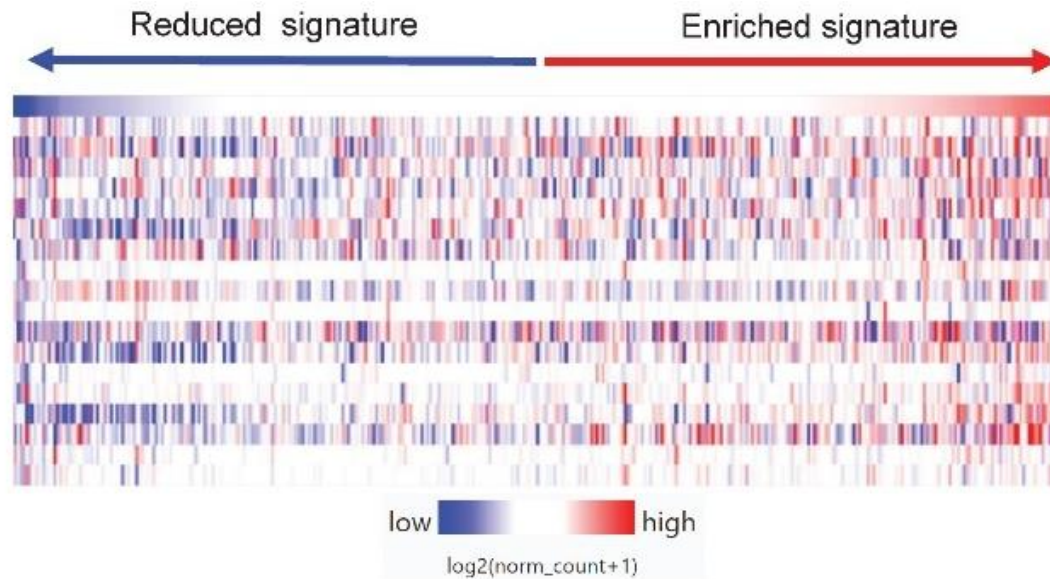
ccRCC lipidomes are not uniform



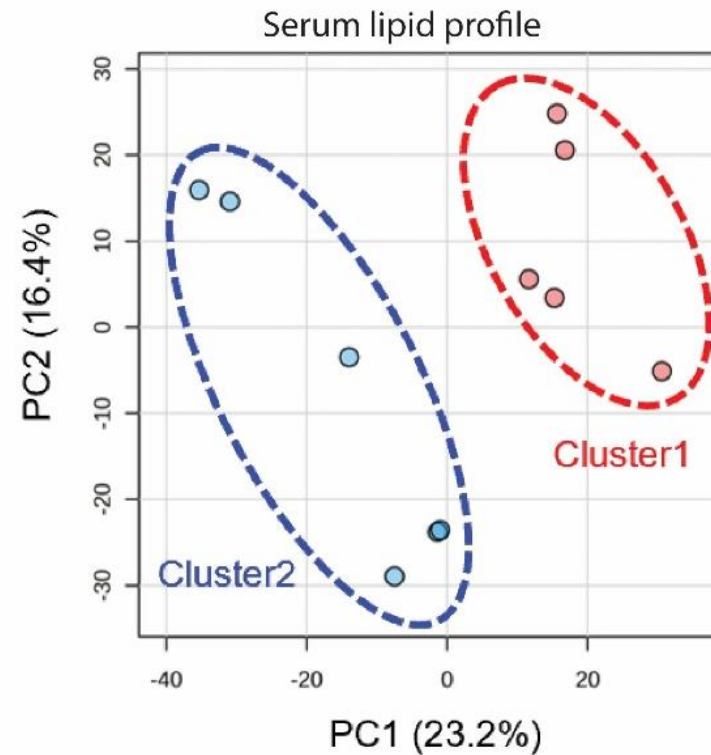
ccRCC transcriptomes are not uniform



ccRCC lipidome classes are prognostic

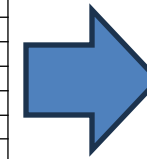


ccRCC tumor clusters can be seen in the serum

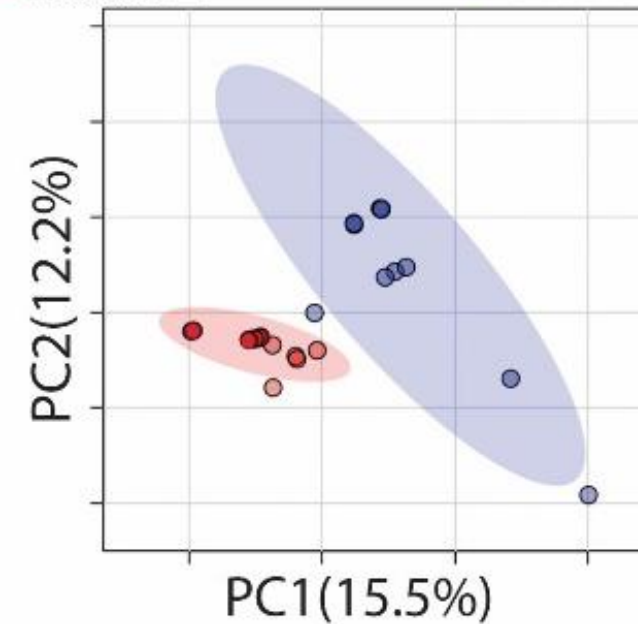


PDX tumors retain cluster classification

XP ID	RARRES2 Expression Level	Histology	VHL Status	Cohort engrafted to	Growth Rate	DMSO Implantation Success
XP673	0	ccRCC	mut	c1	11mm in 56 days	Not attempted
XP416	1.443013255	ccRCC w/sarcomatoid	mut	c29	14mm in 22 days	2 successful attempt; 1 unsuccessful attempt
XP241	2.837344468	ccRCC	mut	c3	8mm in 56 days	Not attempted
XP490	3.521287353	ccRCC w/sarcomatoid	mut	c38	16mm in 32 days	2 successful attempts
XP977	6.166977478	ccRCC	mut	c11	13mm in 42 days	Not attempted
XP685	12.36551863	ccRCC w/rhabdoid	mut	c1	16mm in 66 days	Not attempted
XP843	29.67206715	ccRCC w/rhabdoid and focal sarcoma	mut	c10	18mm in 57 days	1 unsuccessful attempt
XP579	67.30143213	ccRCC	mut	c2	14mm in 24 days	not attempted
XP610	83.83682817	ccRCC	mut	c8	11mm in 24 days	not attempted
XP669	99.6878093	ccRCC	mut	c13	18mm in 47 days	1 successful attempt
XP580	101.2834487	ccRCC	mut	c6	12mm in 48 days	Not attempted
XP144	148.6872319	ccRCC	mut	c52	15mm in 21 days	5 successful attempts; 1 unsuccessful attempt
XP166	150.9026626	ccRCC w/sarcomatoid	mut	c12	12mm in 36 days	2 unsuccessful attempts
XP785	175.7478776	ccRCC	mut	c7	11mm in 35 days	not attempted
XP681	197.6449218	ccRCC w/sarcomatoid	mut	c5	11mm in 46 days	not attempted
XP259	203.9235783	ccRCC w/sarcomatoid	mut	c1	14mm in 89 days	not attempted
XP955p	253.5192669	ccRCC	mut	c29	18mm in 38 days	not attempted
XP115	266.9668311	ccRCC	mut	c5	10mm in 163 days	not attempted
XP391	369.0081661	ccRCC	mut	c5	18mm in 68 days	1 unsuccessful attempt
XP289	381.7827564	ccRCC	mut	c18	15mm in 69 days	2 successful; 1 unsuccessful attempt
XP332	464.6456044	ccRCC	mut	c3	10mm in 91 days	1 successful attempt
XP316	481.85308	ccRCC	mut	c3	7mm in 129 days	2 successful attempts
XP264	663.9298384	ccRCC	mut	c0	7mm in 96 days	not attempted
XP191	779.1837903	ccRCC	mut	c2	13mm in 71 days	not attempted
XP470	792.0712928	ccRCC	mut	c2	12mm in 67 days	2 unsuccessful attempts
XP600	829.8460497	ccRCC	mut	c1	14mm in 101 days	not attempted
XP206	865.2757326	ccRCC	mut	c24	14mm in 56 days	currently attempting
XP1084	916.1799093	ccRCC	mut	c12	13mm in 48 days	not attempted
XP536	928.1096515	ccRCC w/sarcomatoid	mut	c4	13mm in 120 days	not attempted
XP243	931.2492766	ccRCC	mut	c2	9mm in 128 days	not attempted
XP474	1002.354842	ccRCC	mut	c14	13mm in 89 days	1 successful attempt; 1 unsuccessful attempt
XP250	1012.007767	ccRCC	mut	c2	20mm in 74 days	not attempted
XP283	1067.397856	ccRCC	mut	c15	7mm in 158 days	2 successful attempts; 1 unsuccessful attempt
XP284	1077.83728	ccRCC	mut	c1	15mm in 96 days	not attempted
XP418	1080.948685	ccRCC	mut	c1	11mm in 174 days	not attempted
XP127	1089.280388	ccRCC	mut	c8	17mm in 189 days	2 successful attempts
XP967	1131.267441	ccRCC	mut	c1	9mm in 140 days	not attempted
XP296	1146.654542	ccRCC	mut			



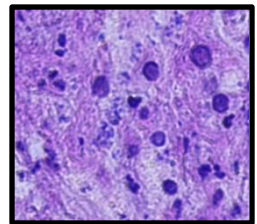
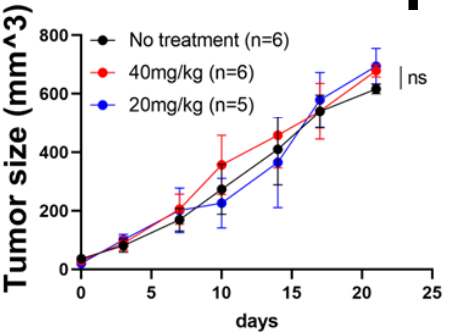
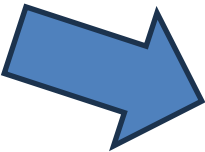
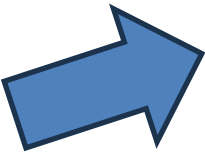
● Chemerin high PDX
 ● Chemerin low PDX
● Cluster 1
 ● Cluster 2



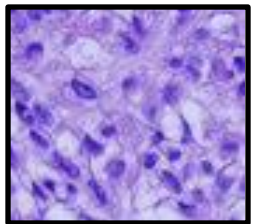
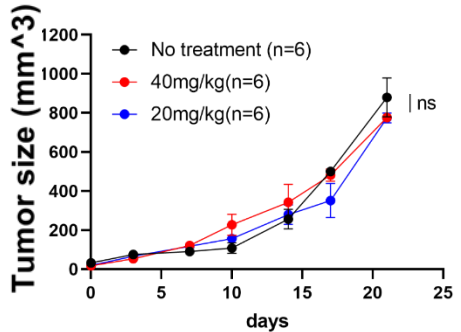
**PDX models from the
Brugarolas collection**

Clusters reveal Chemerin dependence

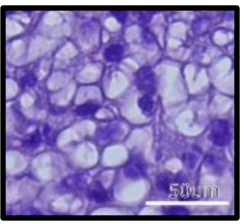
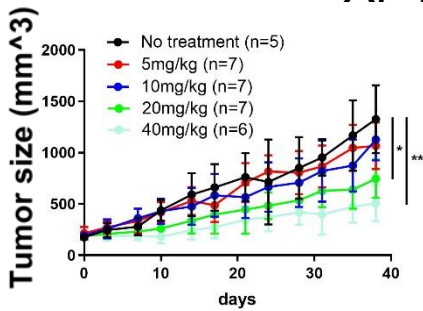
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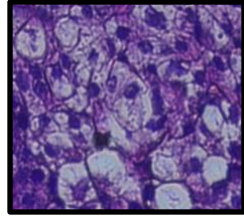
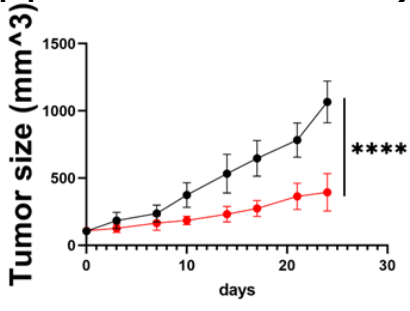
XP144



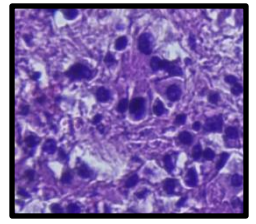
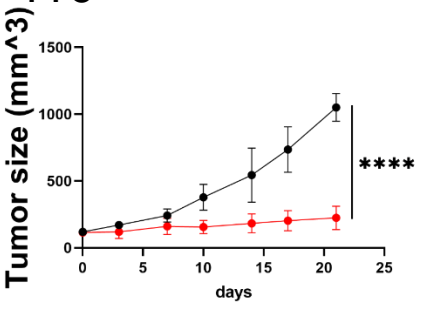
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XP296

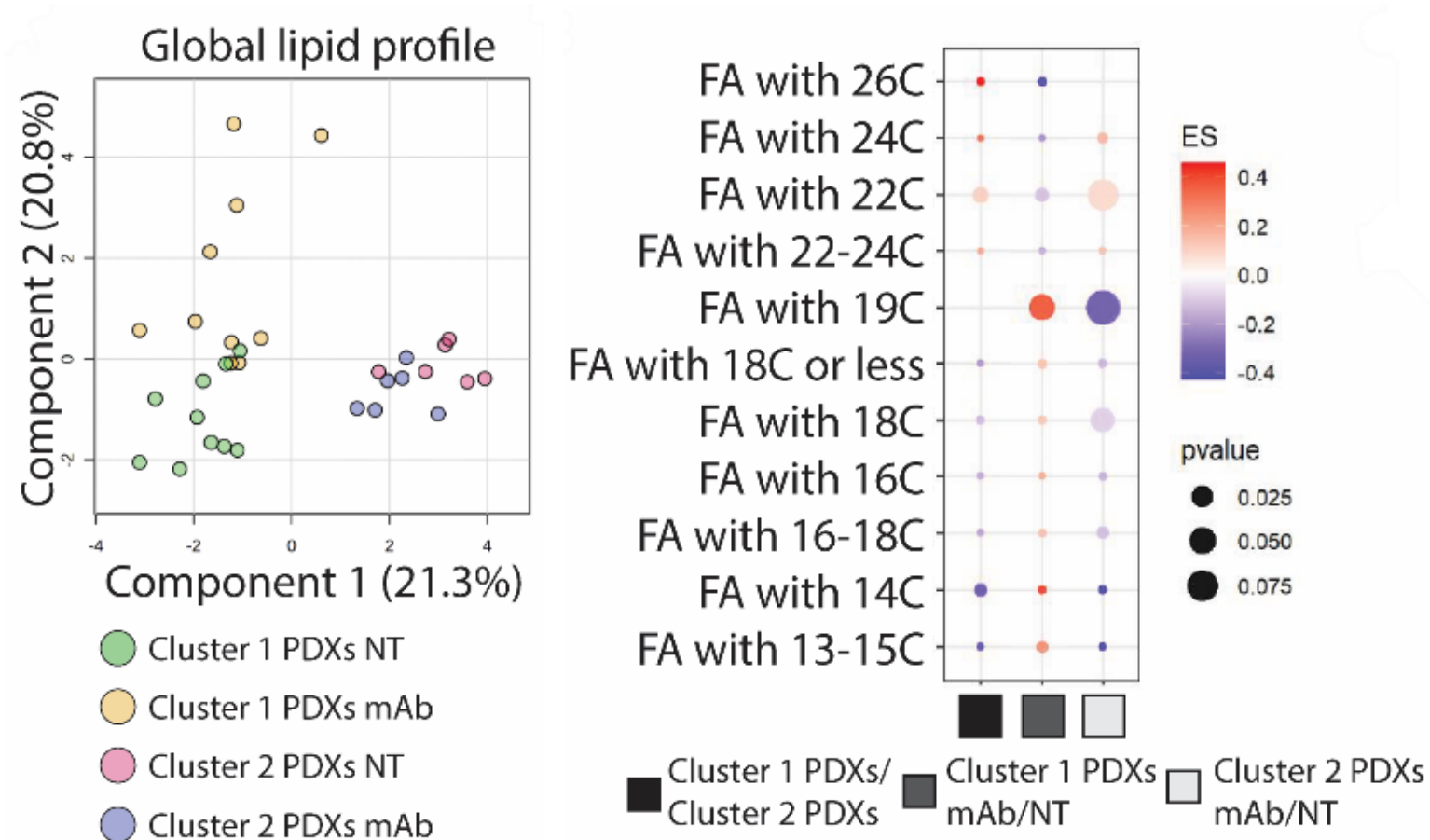


XP334

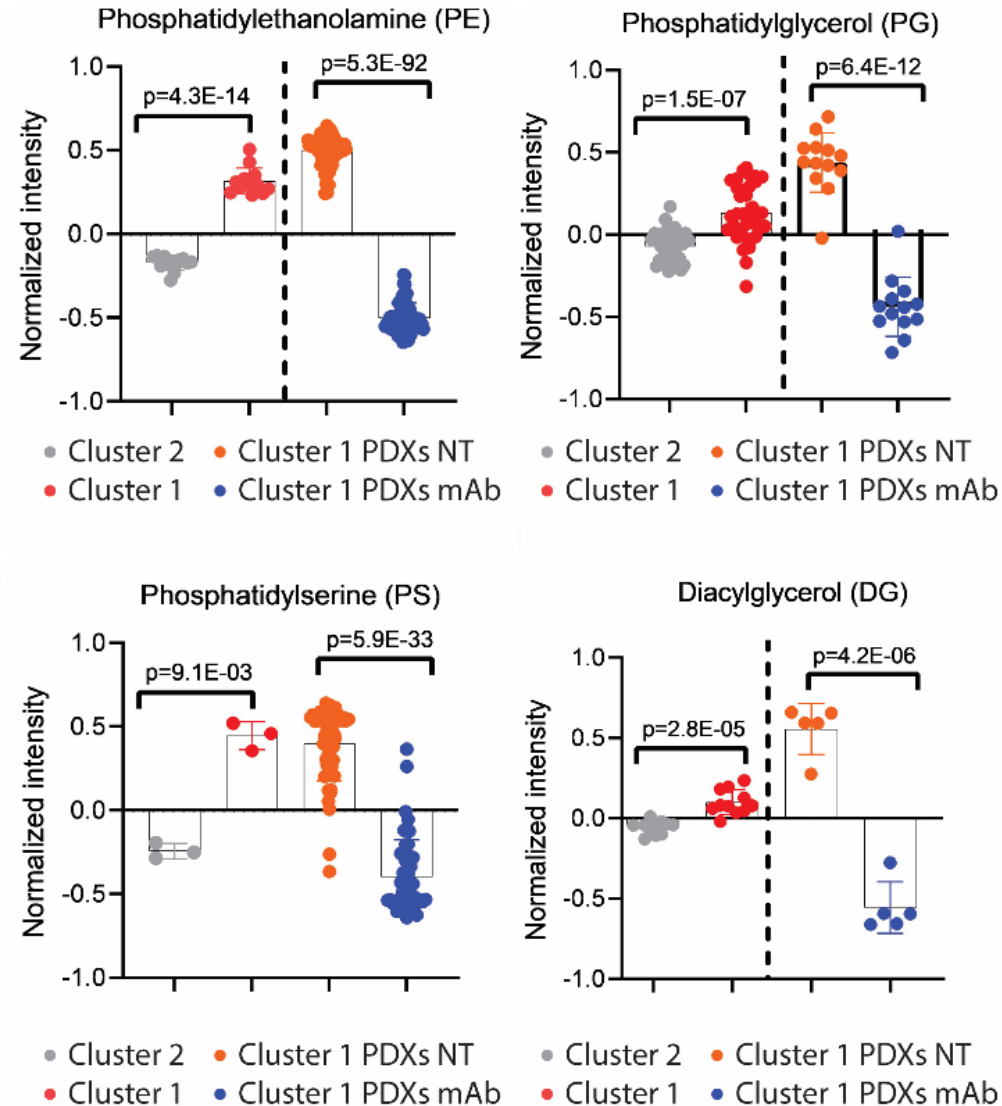


XP754

Chemerin targeting reprograms the lipidomes of Cluster 1 tumors

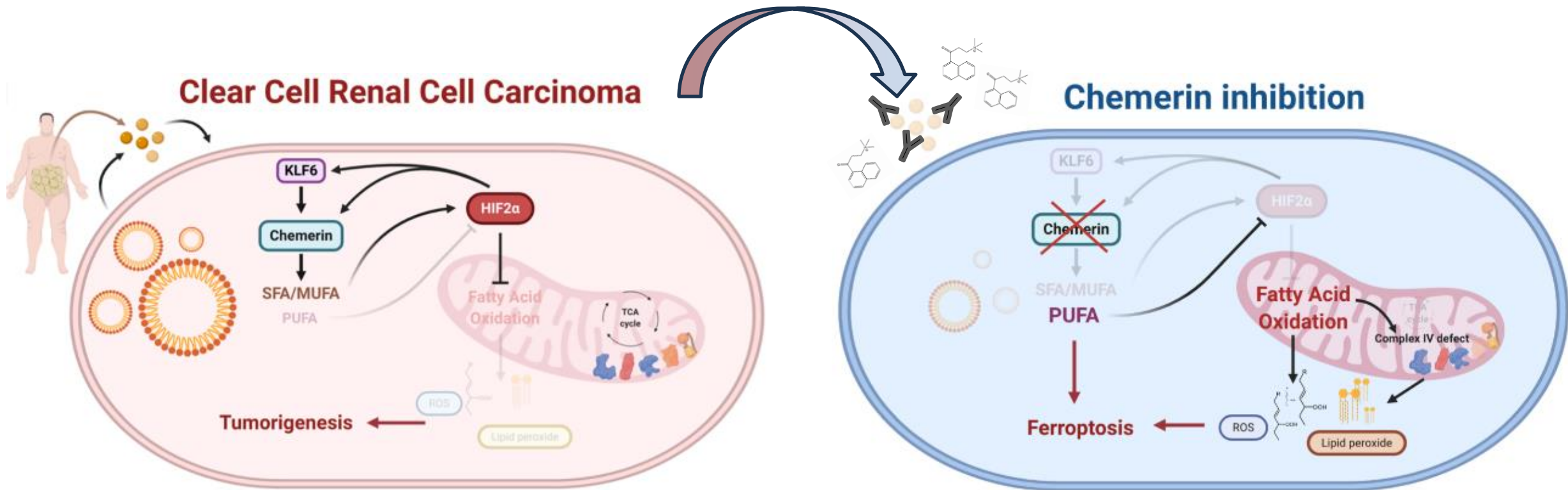


Chemerin targeting reprograms the lipidomes of Cluster 1 tumors



Summary:

Lipidome-based precision medicine for ccRCC



- Opportunities for patient selection?
- Opportunities for dietary intervention?
- What drives the lipidome in chemerin-low tumors?

Acknowledgements:

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UTSW

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- Timothy J. Garrett

