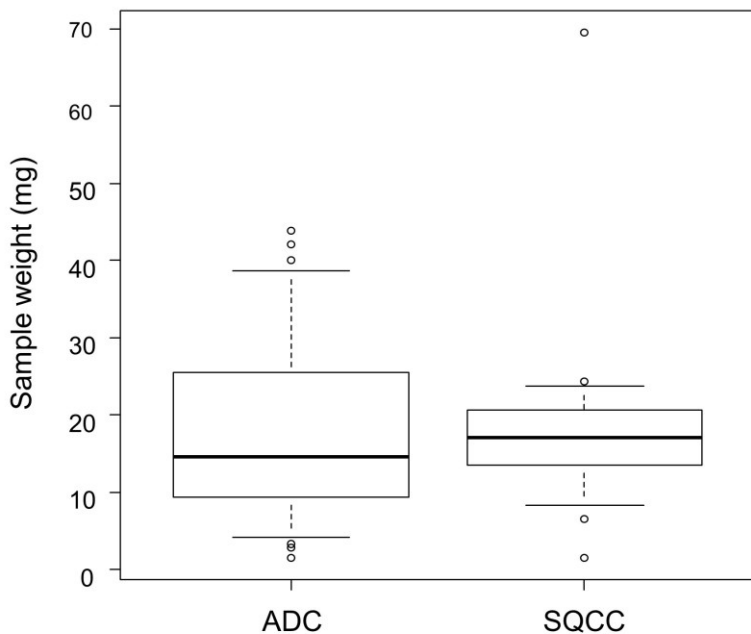
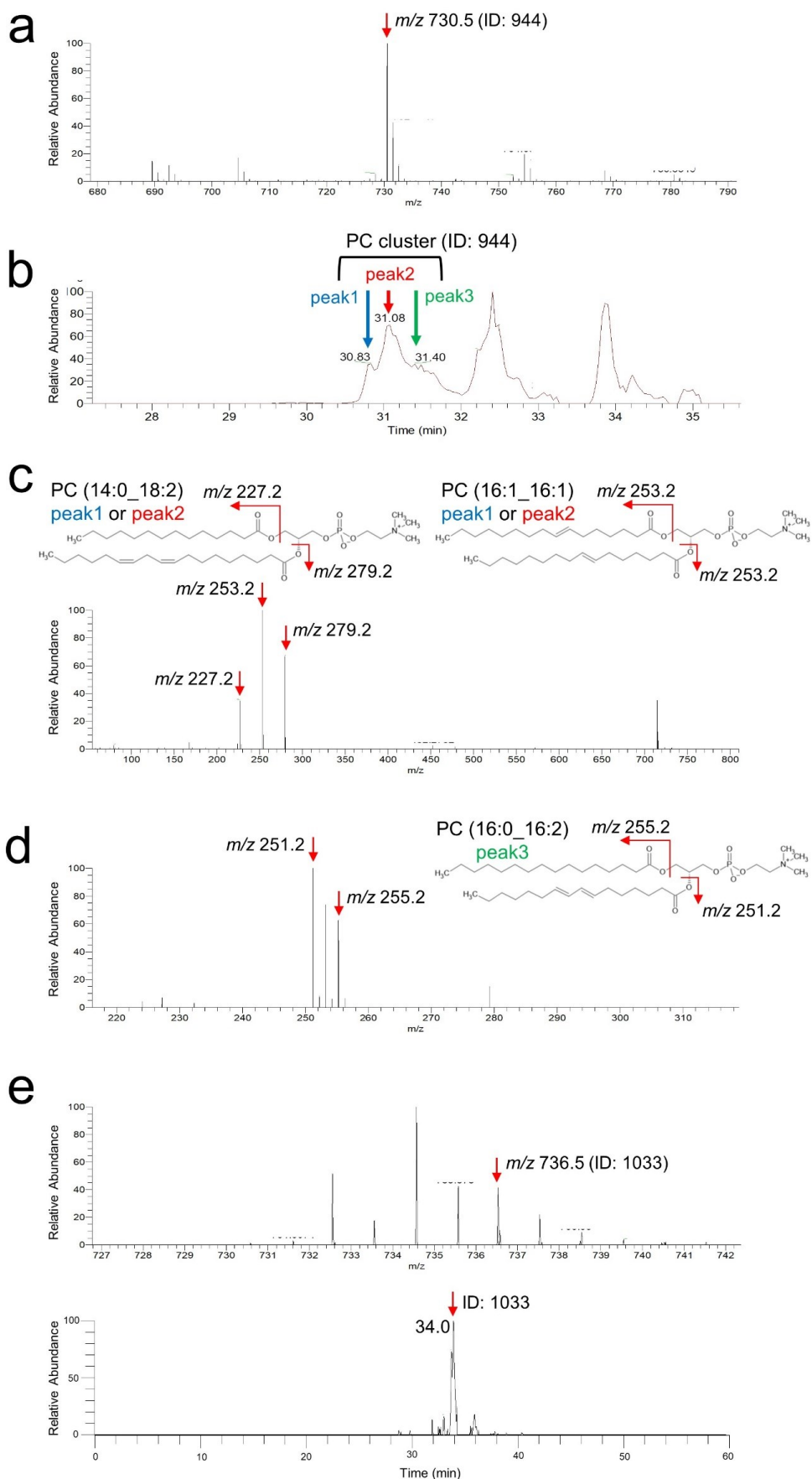




**Supplemental Figure 1.** Frozen tissue sample weights. The average sample weights recruited in this study were 18.2 mg (range: 1.5–43.9 mg) and 18.6 mg (range: 1.5–69.6 mg) in the ADC and SQCC cohorts, respectively. Abbreviations: ADC, Adenocarcinoma; SQCC, Squamous cell carcinoma.

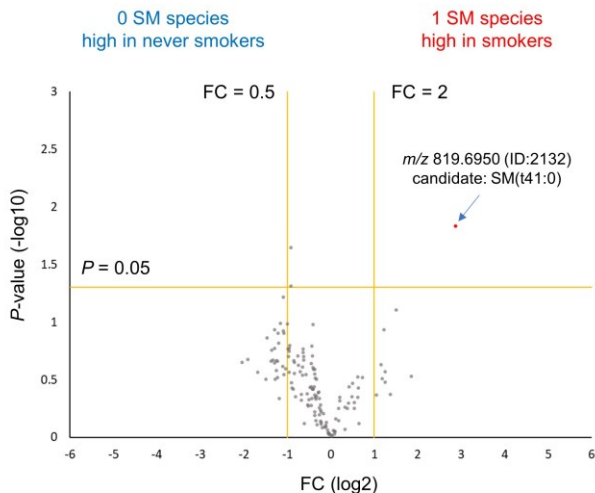


**Supplemental Figure 2.** The MS findings and MS/MS analysis of the identified lipids.

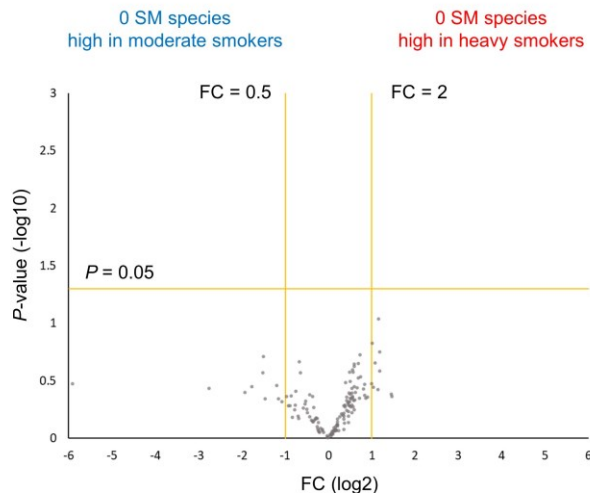
The MS peak of  $m/z$  730.5 (ID: 944) (a) identified in the adenocarcinoma cohort was regarded as a PC cluster composed of three isomers in the chromatogram (peak 1–3) (b). (c) Among MS/MS analysis of the three isomers, peaks 1 and 2 were compatible as PC (14:0\_18:2) or PC (16:1\_16:1), demonstrating fragments of FA (14:0) ( $m/z$  227.2), FA (18:2) ( $m/z$  279.2), and FA (16:1) ( $m/z$  253.2). (d) For peak 3, the detected fragments, FA (16:0) ( $m/z$  255.2) and FA (16:2) ( $m/z$  251.2), were compatible as product ions from PC (16:0\_16:2). (e) For the MS peak of  $m/z$  736.5 (ID: 1033) (upper panel) in the squamous cell carcinoma cohort, the corresponding peak in the chromatogram had a single peak (lower panel). However, the MS/MS analysis was not performed because of its weak signal intensity.

Abbreviations: FA, Fatty acid; ID, Identification number; MS, Mass spectrometry; MS/MS, Tandem mass spectrometry; PC, Phosphatidylcholine.

### (a) ADC



### (b) SQCC



**Supplemental Figure 3.** Volcano plots described on lipid peaks for which SM species were assigned as candidate molecules by LipidSearch™ software.

Only one significant lipid peak ( $m/z$  819.6950 [ID: 2132]) in the smoker group of the ADC cohort was identified; the assigned candidate molecule was SM (t41:0) (a). On the other hand, no significant lipid peak was identified in the SQCC cohort (b).

Abbreviations: ADC, Adenocarcinoma; FC, Fold change; SM, sphingomyelin; SQCC, Squamous cell carcinoma.