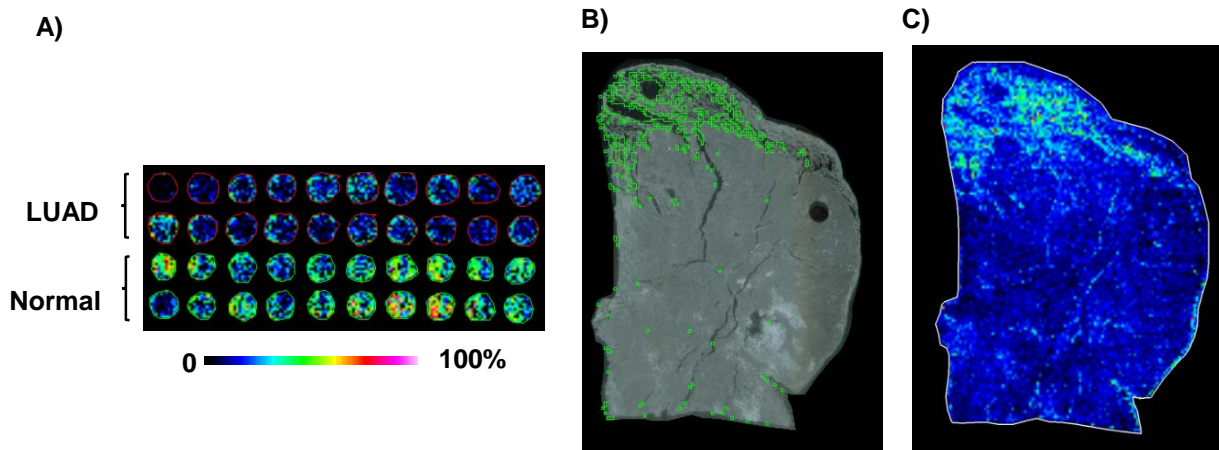
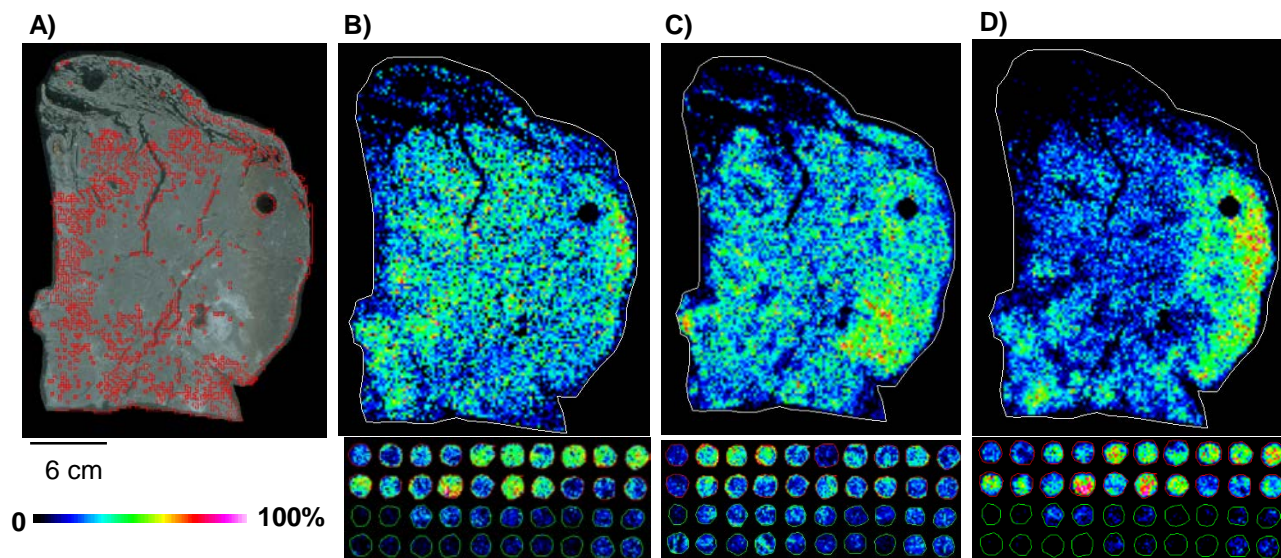


## Supplemental Figure 1



**Supplemental Figure 1.** Correlation to spatial distribution of TMA peaks detected as significantly increased in healthy lung tissue. A total of 10 peaks (Figure 2, manuscript Figures) that were elevated in normal tissue were compared by correlation coefficient to regions of normal adjacent tissue (green, Supplemental Figure 1B). Most peaks elevated in healthy lung tissue were not found in normal adjacent tissue. A single peak,  $m/z$  1022.0978 ( $m/z$  1022), showed a correlation of 0.54 signifying some spatial distribution correlation to normal adjacent regions. A) TMA data for  $m/z$  1022. Area under the receiver operating curve was 0.96 p-value  $<0.001$ , between LUAD and healthy lung tissue cores. B) Region of normal adjacent lung tissue, pathologist confirmed. C) Image map of  $m/z$  1022 showing high expression in the normal adjacent region. Calculated correlation coefficient was 0.54 for matching of spatial distribution between  $m/z$  1022 and NAT.

## Supplemental Figure 2



**Supplemental Figure 2.** Correlation to spatial distribution of TMA peaks detected as significantly increased in lung adenocarcinoma (LUAD) tissue. A total of 15 peaks (Figure 2, manuscript Figures) that were elevated in LUAD tissue microarray cores were compared by correlation coefficient to regions of LUAD in a lung wedge resection (red, Supplemental Figure 2A). A total of three peaks  $m/z$  919.4218 ( $m/z$  919),  $m/z$  943.5080 ( $m/z$  943), and  $m/z$  1019.5878 ( $m/z$  1019.58) showed some correlation with the tissue region marked with LUAD on the wedge resection (Spatial correlation coefficient 1.00, 0.568, and 0.686, respectively). A) Region of defined as tumor, pathologist confirmed. B)  $m/z$  919 expression patterns throughout tumor region and negligible within normal adjacent region. C)  $m/z$  943 greater relative intensity in the lower tumor region, higher overall expression in the TMA tumor cores. D)  $m/z$  1019.58 in the primary tumor site but with relatively lower expression throughout the tumor.

**Supplemental Table 1: TMA Map**

s.	No.	Age	Sex	Anatom	Pathology diagnosis	TNM	Grade	Stage	Type	Image
<a href="#">A1</a>	1	66	M	Lung	Papillary adenocarcinoma	T2N0M0	1	I	Malignant	
<a href="#">A2</a>	2	61	M	Lung	Papillary adenocarcinoma	T2N1M0	1	II	Malignant	
<a href="#">A3</a>	3	50	M	Lung	Acinar adenocarcinoma	T1N0M0	1	I	Malignant	
<a href="#">A4</a>	4	55	M	Lung	Acinar adenocarcinoma	T2N0M0	1	I	Malignant	
<a href="#">A5</a>	5	65	M	Lung	Acinar adenocarcinoma	T2N0M0	1	I	Malignant	
<a href="#">A6</a>	6	42	F	Lung	Acinar adenocarcinoma	T3N1M0	1	IIIA	Malignant	
<a href="#">A7</a>	7	62	M	Lung	Papillary adenocarcinoma	T2N0M0	1	I	Malignant	
<a href="#">A8</a>	8	60	M	Lung	Papillary adenocarcinoma	T2N0M0	1	I	Malignant	
<a href="#">A9</a>	9	70	M	Lung	Acinar adenocarcinoma	T2N0M0	1	I	Malignant	
<a href="#">A10</a>	10	70	M	Lung	Acinar adenocarcinoma	T1N0M0	1	I	Malignant	
<a href="#">B1</a>	11	70	M	Lung	Papillary adenocarcinoma	T1N0M0	1	I	Malignant	
<a href="#">B2</a>	12	60	F	Lung	Papillary adenocarcinoma	T2N0M0	1	I	Malignant	
<a href="#">B3</a>	13	67	M	Lung	Acinar adenocarcinoma	T2N0M0	2--3	I	Malignant	
<a href="#">B4</a>	14	58	M	Lung	Acinar adenocarcinoma	T2N1M0	2--3	II	Malignant	
<a href="#">B5</a>	15	47	M	Lung	Acinar adenocarcinoma	T1N0M0	2--3	I	Malignant	
<a href="#">B6</a>	16	51	M	Lung	Acinar adenocarcinoma	T2N0M0	2--3	I	Malignant	
<a href="#">B7</a>	17	37	F	Lung	Acinar adenocarcinoma	T2N0M0	2--3	I	Malignant	
<a href="#">B8</a>	18	61	M	Lung	Acinar adenocarcinoma	T1N0M0	2--3	I	Malignant	
<a href="#">B9</a>	19	59	M	Lung	Solid adenocarcinoma	T2N1M0	3	II	Malignant	
<a href="#">B10</a>	20	50	F	Lung	Solid adenocarcinoma	T3N0M0	3	IIB	Malignant	
<a href="#">C1</a>	21	18	F	Lung	Lung tissue	-	-	-	Normal	
<a href="#">C2</a>	22	18	F	Lung	Lung tissue	-	-	-	Normal	
<a href="#">C3</a>	23	49	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">C4</a>	24	49	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">C5</a>	25	48	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">C6</a>	26	48	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">C7</a>	27	24	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">C8</a>	28	24	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">C9</a>	29	22	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">C10</a>	30	22	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">D1</a>	31	35	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">D2</a>	32	35	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">D3</a>	33	47	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">D4</a>	34	47	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">D5</a>	35	15	F	Lung	Lung tissue	-	-	-	Normal	
<a href="#">D6</a>	36	15	F	Lung	Lung tissue	-	-	-	Normal	
<a href="#">D7</a>	37	42	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">D8</a>	38	42	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">D9</a>	39	47	M	Lung	Lung tissue	-	-	-	Normal	
<a href="#">D10</a>	40	47	M	Lung	Lung tissue	-	-	-	Normal	

**Supplemental Table 2: Proteins identified from duplicate lung tissue sections (sections 1, 3; section2 was used for imaging) diagnosed with lung adenocarcinoma.**

Proteins are identified with a probability of 99% and a minimum of two peptides in combined runs.  
 Proteins are shown with exclusive unique peptides per protein and total spectrum count.

Accession	Protein Name	Gene Symbol	Exclusive unique peptides Section 1	Exclusive unique peptides Section 3	Total Spectrum Count Section 1	Total Spectrum Count Section 3	Merl-Pham et al., 2019 Matrix Biology Plus, 1:100005			Function, Description 1	Source	Function, Description 2	Source
							human primary lung fibroblasts	Idiopathic pulmonary fibrosis	Gocheva et al., 2017 Proc Natl Acad Sci U S A. 114:E5625				
							Trypsin digest, mouse lung	Trypsin digest, fresh mouse lung fibrosis and LUAD	Angel et al., 2019 Proteomics Clin Appl. 13:e1700152				
sp P08123 CO1A2	Collagen alpha-2(I)	COL1A2	23	18	63	77	x	x	x	collagen type protein			
sp P02452 CO1A1	Collagen alpha-1(I)	COL1A1	9	10	19	27	x	x	x	collagen type protein			
sp P02461 CO3A1	Collagen alpha-1(III)	COL3A1	7	8	10	12	x	x	x	collagen type protein			
sp Q03001 DYST	Dystonin	DST	5	4	5	4				Assembly of collagen fibrils	Reactome		
sp P03938 CO5A1	Collagen alpha-1(V)	COL5A1	5	7	8	10	x	x	x	collagen type protein			
sp P08670 VIME	Vimentin	VIM	41	47	51	74				Stabilization of type I collagen mRNA	Publication PMC3165730	Positive regulation of collagen biosynthesis	GO
sp P05997 CO5A2	Collagen alpha-2(V)	COL5A2	3	6	4	10	x	x	x	collagen type protein			
sp P02482 CO4A1	Collagen alpha-1(IV)	COL4A1	1	3	3	5	x	x		collagen type protein			
sp P12111 CO6A3	Collagen alpha-3(VI)	COL6A3	23	17	25	20	x		x	collagen type protein			
sp P29400 CO4A5	Collagen alpha-5(VI)	COL4A5	0	5	0	8				collagen type protein			
sp P98160 PGBM	Basement membrane-spe	HSPG2	4	7	5	8	x	x	x	Cell adhesion to collagen	Publication PMID: 11956183		
sp Q15149 PLEC	Plectin	PLEC	10	10	10	11			x	Assembly of collagen fibrils	Reactome		
sp P08572 CO4A2	Collagen alpha-2(IV)	COL4A2	1	3	2	4	x	x		collagen type protein			
sp P39060 CO1A1	Collagen alpha-1(XVIII)	COL18A1	3	3	3	5	x	x		collagen type protein			
sp P27658 CO8A1	Collagen alpha-1(VIII)	COL8A1	0	6	0	7	x	x		collagen type protein			
sp Q05707 COE1	Collagen alpha-1(XIV)	COL14A1	4	7	5	9		x		collagen type protein			
sp P29400-2 CO4A5	Isoform 2 of Collagen alpha	COL4A5	3	0	8	0				collagen type protein			
sp Q9Y6C2 EMIL1	EMILIN-1	EMILIN1	9	16	9	18	x	x	x	Negative regulation of collagen fibril organization	GO	Collagen domain present	Pfam
sp Q75445-3 USH2A	Isoform 3 of Usherin	USH2A	3	0	3	0				Collagen binding	GO	Collagen interaction	Publication PMID: 14676276 PMID: 16114888
sp Q8UVK1 CSPG4	Chondroitin sulfate proteoglycan	CSPG4	0	3	0	3	x			Cell surface receptor, type 1 collagen	Publication PMID: 11278606		
sp P12110 CO6A2	Collagen alpha-2(VI)	COL6A2	8	7	13	11	x	x	x	collagen type protein			
sp P35555 FBN1	Fibrillin-1	FBN1	3	0	3	0	x	x		Elastin fiber formation	GO	Secondary collagen-elastin interaction	Publication PMID: 28395027
sp P24821-4 TENA	Isoform 4 of Tenascin	TNC	3	12	3	12	x	x		Collagen binding	Publication PMID: 16924594		
sp P02751-8 FN1	Isoform 8 of Fibronectin	FN1	4	0	4	0	x	x	x	Collagen binding	Publication PMID: PMC1167230		
sp P02751-7 FN1	Isoform 7 of Fibronectin	FN1	0	5	0	8	x	x	x	Collagen binding	Publication PMID: PMC1167230		
sp Q9UBS9-2 SUCO	Isoform 2 of SUN domain	SUCO	3	0	3	0				Positive regulation of type I collagen	GO		
sp P07237 PDI1	Protein disulfide-isomerase	P4HB	8	10	10	14			x	Collagen modifying	Reactome		
sp Q14289 FAK2	Protein-tyrosine kinase 2-beta	PTK2B	4	0	4	0				Downstream collagen receptor signaling	Publication PMID: 25960397		
sp P02545 LMNA	Prelamin-A/C	LMNA	5	6	6	8			x	Cellular response to hypoxia	GO		
sp Q15084-2 PDI1	Isoform 2 of Protein disulfide	PDI1	5	9	5	11				Cell redox homeostasis	GO	Unfolded Protein response	GO
sp P07339 CATD	Cathepsin D	CTSD	5	5	5	8	x			Collagen catabolism	GO		
sp P30044 PRDX5	Peroxisredoxin-5, mitochond	PRDX5	5	7	6	11			x	Positive regulation of collagen	GO	Cell redox homeostasis	GO
sp P21810 PGS1	Bglycan	BGN	6	6	6	6	x	x	x	Collagen fiber assembly	Publication PMID: 12354766		
sp Q15582 BIGH3	Transforming growth factor	TGFBI	1	4	1	4	x	x		Cell-collagen adhesion	GO		
sp P07585 PGS2	Decorin	DCN	2	3	2	5	x		x	Collagen binding	GO	Amyloid fibrillar fiber formation	Reactome
sp P55083-2 MFAP4	Isoform 2 of Microfibril-asso	MFAP4	1	4	3	7		x	x	Collagen regulation by metabolism	GO		
sp P01903 DRA	HLA class II histocompatib	HLA-DRA	1	3	2	4				Interactions with denatured collagen	Publication PMID: PMC1004167		
sp P13688 CEAM1	Carcinoembryonic antigen	CEACAM1	0	5	0	6				Platelet-collagen binding	Publication PMID: 16291724		
sp P04004 VTNC	Vitronectin	VTN	2	3	2	3				Collagen binding	GO		
sp P23142-4 FBLN1	Isoform C of Fibulin-1	FBLN1	0	3	0	3				Collagen interaction	Publication PMID: 12778127	Collagen Interaction	Functional annotation
sp P13688-9 CEAM1	Isoform 9 of Carcinoembry	CEACAM1	4	0	6	0	x	x		Platelet & cell-collagen adhesion	Publication PMID: 19006452 PMID: PMC2171332		