

Figure S1 Six base substitution type spectra of mutations in 16 high-grade fetal adenocarcinomas (H-FLACs) and The Cancer Genome Atlas (TCGA) lung adenocarcinomas (LUADs). Six base substitution type spectra of mutations of H-FLACs were compared with those of the TCGA LUADs.

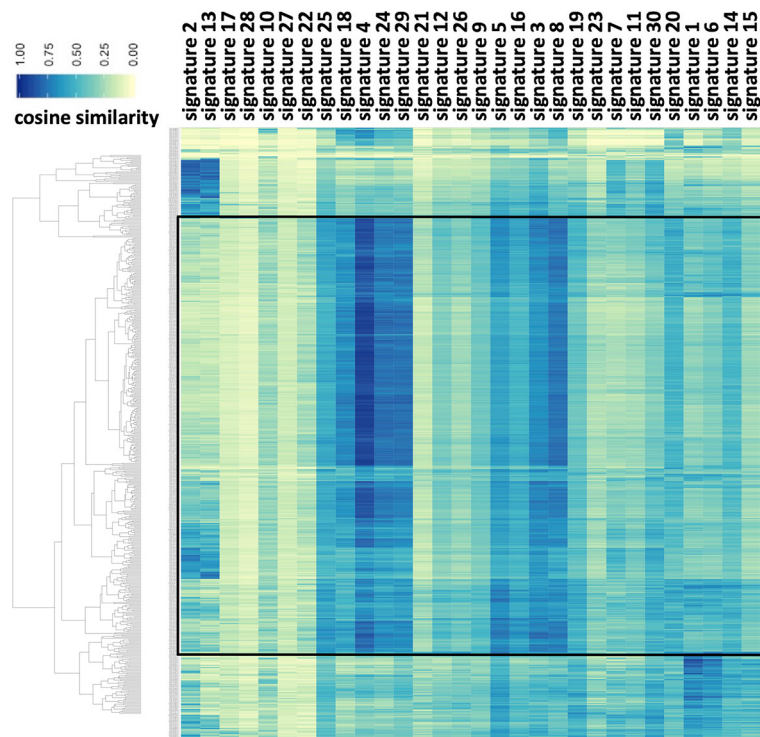


Figure S2 Heatmap of cosine similarity with the 30 mutational signatures of the 514 The Cancer Genome Atlas (TCGA) lung adenocarcinomas. The black-boxed cases resemble the common adenocarcinoma-like cluster of high-grade fetal adenocarcinomas.

Table S1 Depth of whole-exome sequencing in this study

Case	Tumor/normal	Mapped bases	Total reads	Mapped reads	Average depth
1	Normal	14,207,250,876	145,588,534	145,567,663	173.4
	Tumor	10,549,991,287	108,989,542	108,978,966	120.3
2	Normal	10,298,302,219	107,095,830	106,331,339	118.8
	Tumor	9,516,642,628	98,964,910	98,264,021	125.8
3	Normal	12,682,724,915	130,077,950	130,044,402	176.2
	Tumor	17,464,278,431	179,188,518	179,147,506	249.4
4	Normal	20,852,408,890	213,940,710	213,918,518	236.6
	Tumor	16,681,722,588	170,880,258	170,866,769	176.0
5	Normal	16,012,910,291	163,063,046	163,047,551	197.3
	Tumor	9,201,544,823	93,860,074	93,851,652	129.6
6	Normal	9,406,739,344	96,408,052	96,386,977	132.5
	Tumor	14,296,561,905	146,616,016	146,577,527	207.3
7	Normal	6,794,952,150	69,226,006	69,220,129	196.2
	Tumor	7,765,555,835	79,415,868	79,409,065	109.3
8	Normal	7,030,664,437	72,716,628	72,222,492	227.3
	Tumor	10,286,952,074	106,927,174	106,153,003	129.1
9	Normal	5,273,558,726	53,633,592	53,628,956	176.0
	Tumor	3,922,298,094	39,910,676	39,907,336	162.4
10	Normal	22,138,805,708	227,217,152	227,164,600	309.9
	Tumor	14,965,894,854	153,125,194	153,087,820	209.0
11	Normal	3,741,774,558	38,021,092	38,018,030	140.8
	Tumor	7,912,218,220	80,486,498	80,481,374	169.2
12	Normal	10,561,042,636	107,402,422	107,387,426	147.4
	Tumor	10,745,806,494	109,531,452	109,516,062	154.2
13	Normal	5,732,584,430	58,236,288	58,231,333	149.1
	Tumor	8,346,102,076	84,717,568	84,706,190	116.9
14	Normal	7,562,510,568	78,990,740	78,982,023	100.5
	Tumor	10,458,370,047	106,369,746	106,360,625	120.8
15	Normal	7,334,071,274	74,404,062	74,399,424	190.9
	Tumor	10,418,159,370	106,539,070	106,533,342	133.8
16	Normal	8,269,812,792	84,597,748	84,592,882	149.5
	Tumor	6,502,322,511	66,481,680	66,478,559	155.3

Table S2 Summary of nonsynonymous somatic mutations of high-grade fetal adenocarcinomas

Gene	Patient ID															
	1	2	3 [#]	4 ^â	5	6 [#]	7	8	9	10	11	12	13	14	15 ^â	16 ^â
<i>KMT2C</i>				C391X	Y512C			K339N		C391X		Multiple*	D2703E			
<i>TP53</i>			S241F				Splice site					L130F	L194R	Splice site	P250L	240_243del
<i>KRAS</i>			G12D			G12C				G12D					G12D	
<i>STK11</i>	Q37X				Splice site									E256X		
<i>SMAD4</i>								D351Y								528_530del
<i>RB1</i>					R320P								Y813X			
<i>NF1</i>					Splice site		Multiple*	L2089X								
<i>MET</i>						C180X							V444G			
<i>CTNNB1</i>			D32Y		D32V											
<i>CDKN2A</i>										G110C		A76fX				
<i>BRAF</i>											E715X		L711F			
<i>STX2</i>										R150C						
<i>SMARCA4</i>						R1135L										
<i>SLC4A5</i>										Q1100H						
<i>PIK3CA</i>		W498L														
<i>MBD1</i>								Q403H								
<i>MAP2K1</i>							E233K									
<i>KEAP1</i>	515_519del															
<i>FAT1</i>										P546L						
<i>ERBB2</i>	R978H															
<i>EGFR</i>													746_750del*			
<i>CDK12</i>			S288R													
<i>ARID1A</i>													P1592fX			
<i>ARHGAP35</i>		P1038H														
<i>APC</i>													P421T			
<i>PTEN</i>			K13E													
<i>COBL</i>								E480D								
<i>ACVR1B</i>								R485X								
<i>SHROOM1</i>								P300H								
<i>NKX2-1</i>		A154fX		P232L		V235G										
<i>SFTPC</i>		Splice site					Splice site									

[#], patients with severe emphysema; ^â, patients with UIP. *KMT2C* multiple*: E5X, G568C and S2350Y; *NF1* multiple*: S521C and A1453fX. UIP, usual interstitial pneumonia.