Genomic landscape of atypical adenomatous hyperplasia reveals divergent modes to lung adenocarcinoma

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SUPPLEMENTARY FIGURES

Figure S1

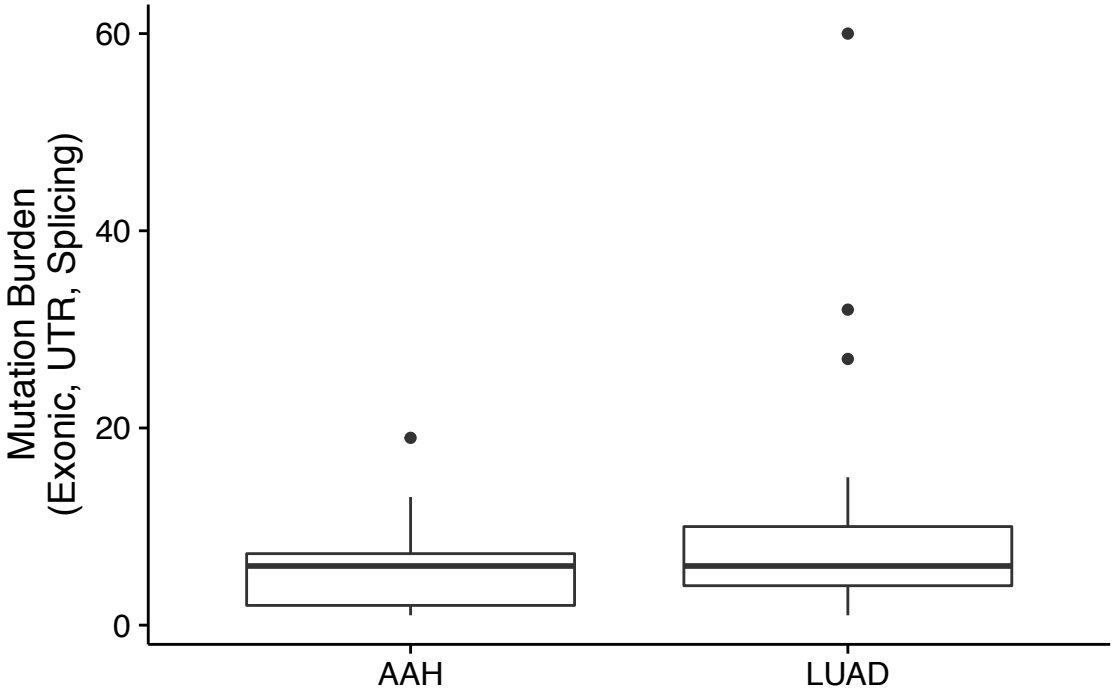


Figure S2

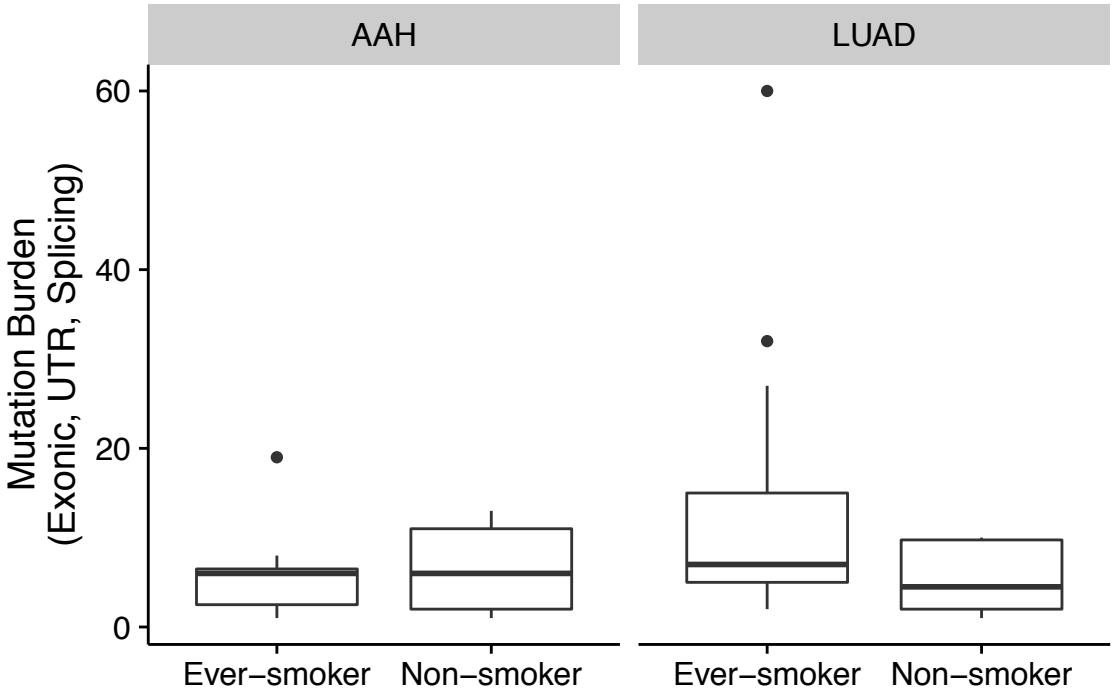

AAH
LUAD
Mutation Burden
(Exonic, UTR, Splicing)
60
40
20
0
Ever−smoker
Non−smoker
Ever−smoker
Non−smoker

Figure S3

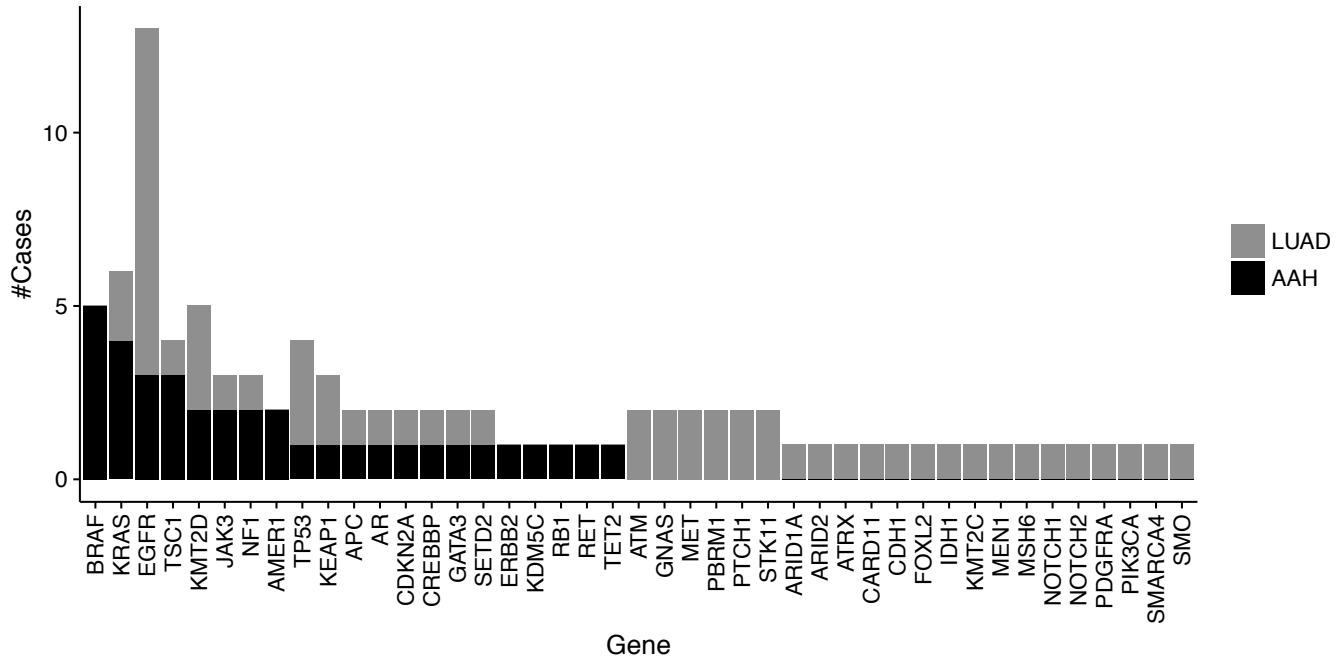
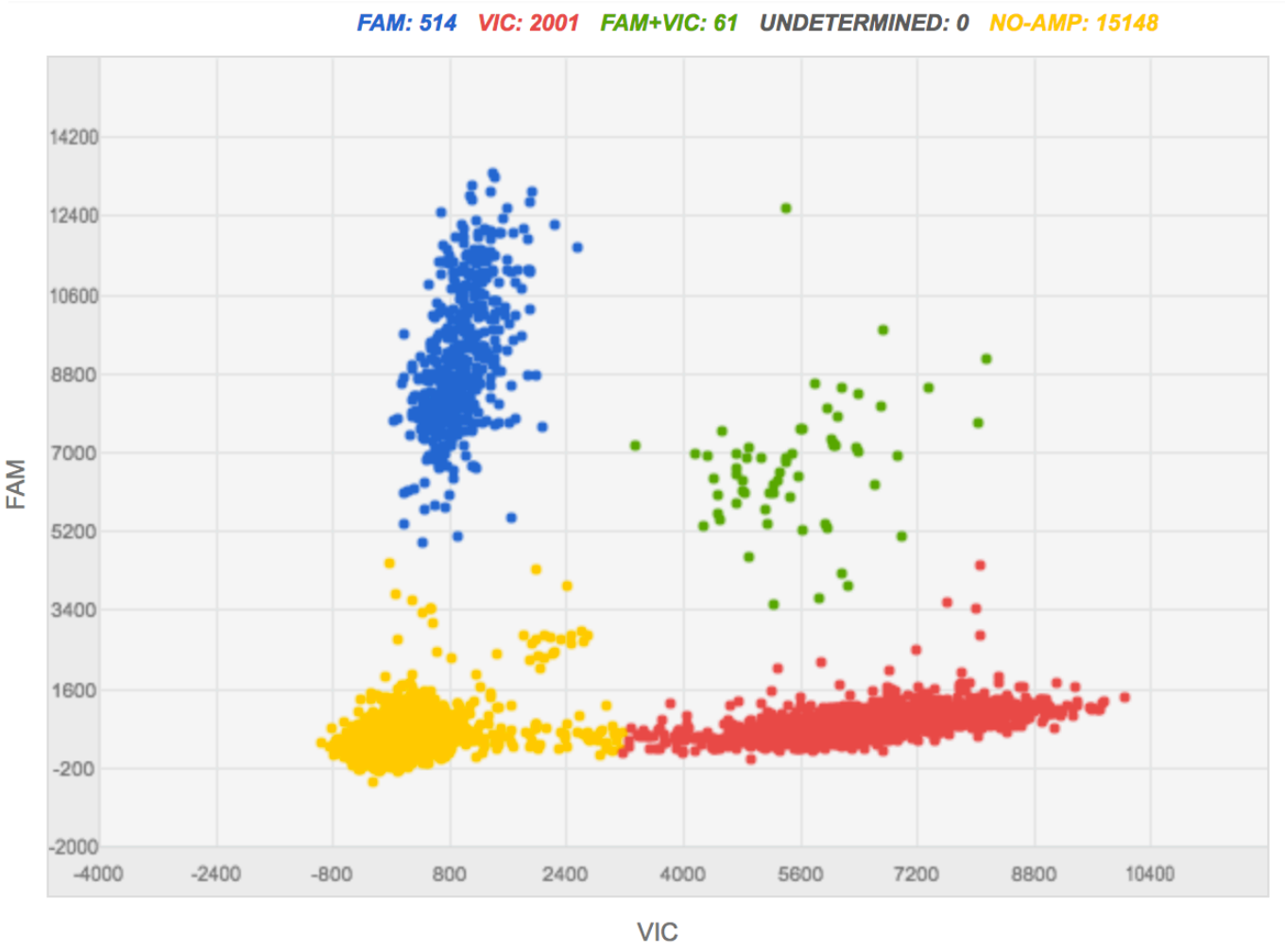

#Cases
10
5
0
LUAD
AAH
BRAF
KRAS
EGFR
TSC1
KMT2D
JAK3
NF1
AMER1
TP53
KEAP1
APC
AR
CDKN2A
CREBBP
GATA3
SETD2
ERBB2
KDM5C
RB1
RET
TET2
ATM
GNAS
MET
PBRM1
PTCH1
STK11
ARID1A
ARID2
ATRX
CARD11
CDH1
FOXL2
IDH1
KMT2C
MEN1
MSH6
NOTCH1
NOTCH2
PDGFRA
PIK3CA
SMARCA4
SMO
Gene

Figure S4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1600
-200
-2000
FAM
-4000
-2400
-800
800
2400
4000
5600
7200
8800
10400
VIC

SUPPLEMENTARY FIGURE LEGENDS

Figure S1. Mutation burden in atypical adenomatous hyperplasia and lung adenocarcinoma. Somatic point mutations in exonic, splicing and UTR regions within the 409 genes sequenced in the panel were identified for the 45 specimens (22 AAH and 23 LUAD) as described in the Materials and Methods section. Mutation burdens for AAH and LUAD were plotted.

Figure S2. Mutation burden in atypical adenomatous hyperplasia and lung adenocarcinoma based on tobacco history. Analysis of somatic mutations was performed as described in Figure S1 and in the Materials and Methods section. Specimens (AAH and LUAD) were classified based on tobacco history (non-smoker and ever-smoker) in all 22 patients. Mutation burdens for AAH and LUAD were plotted.

Figure S3. Mutation in cancer driver genes in atypical adenomatous hyperplasia and lung adenocarcinoma. For the genes previously established to be significantly mutated in lung adenocarcinomas [1] as well as other known cancer associated genes [2], we identified the distribution of number of AAH and LUAD specimens exhibiting mutations in these genes. The genes are sorted on two levels - first by the number of cases in AAH, followed by the number of cases in LUAD.

Figure S4. An example result of digital PCR used to validate somatic mutations. An example screenshot of the validation of the *BRAF* p.K601E mutation in a single sample using digital PCR is shown. In the scatter plot, the x-axis shows fluorescence of the reference allele probe in the VIC fluorophore channel, and the y-axis shows the fluorescence of the alternate allele probe in the FAM fluorophore channel. *BRAF, KRAS* and *EGFR* mutations were detected on the QuantStudio 3D Digital PCR System and their allele frequencies were inferred from the QuantStudio 3D AnalysisSuite Cloud Software.

REFERENCES

1. Cancer Genome Atlas Research Network. Comprehensive molecular profiling of lung adenocarcinoma. Nature. 2014;511: 543–550.

2. Vogelstein B, Papadopoulos N, Velculescu VE, Zhou S, Diaz LA, Kinzler KW. Cancer Genome Landscapes. Science. 2013;339: 1546–1558.