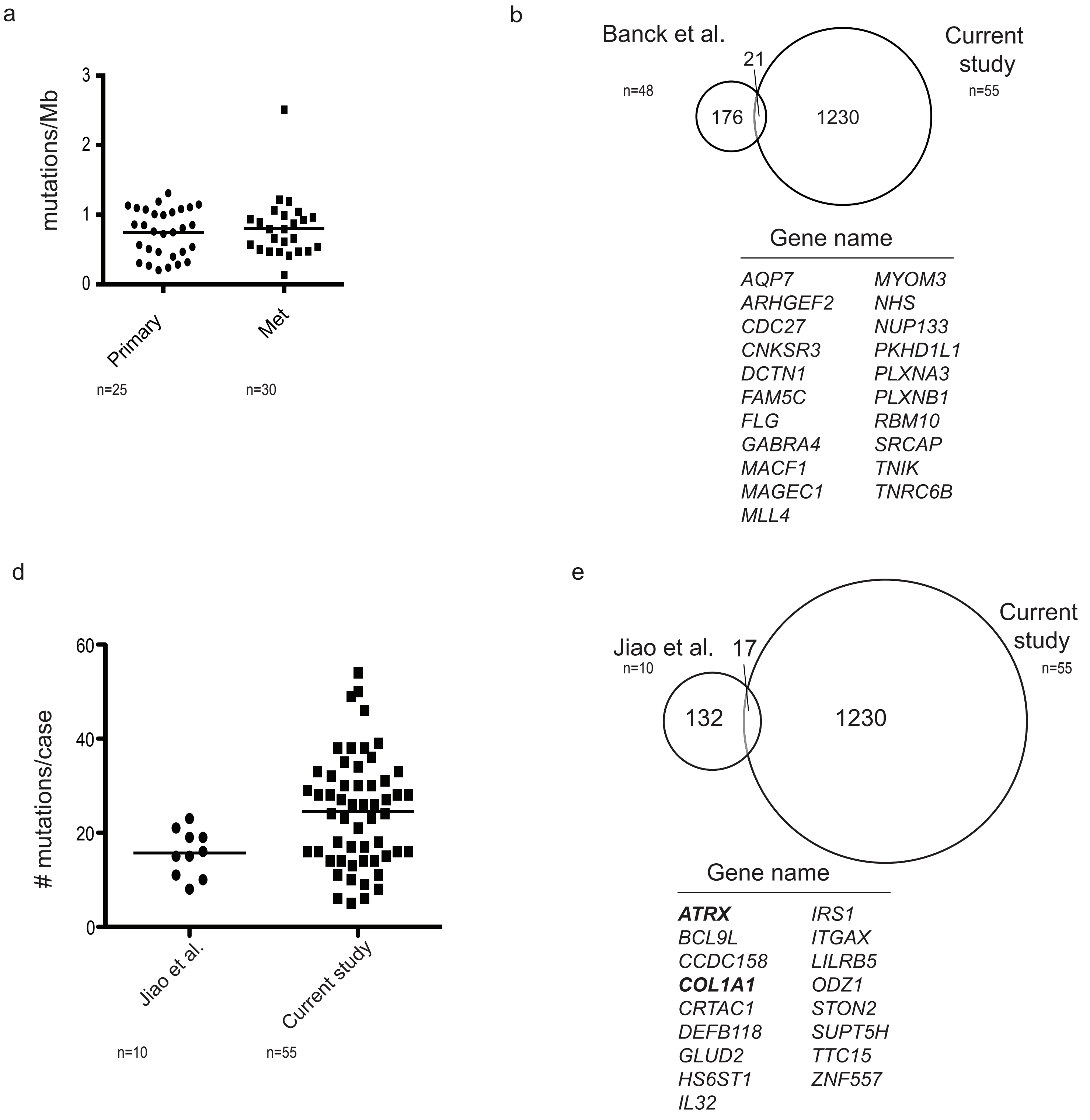


Gene name

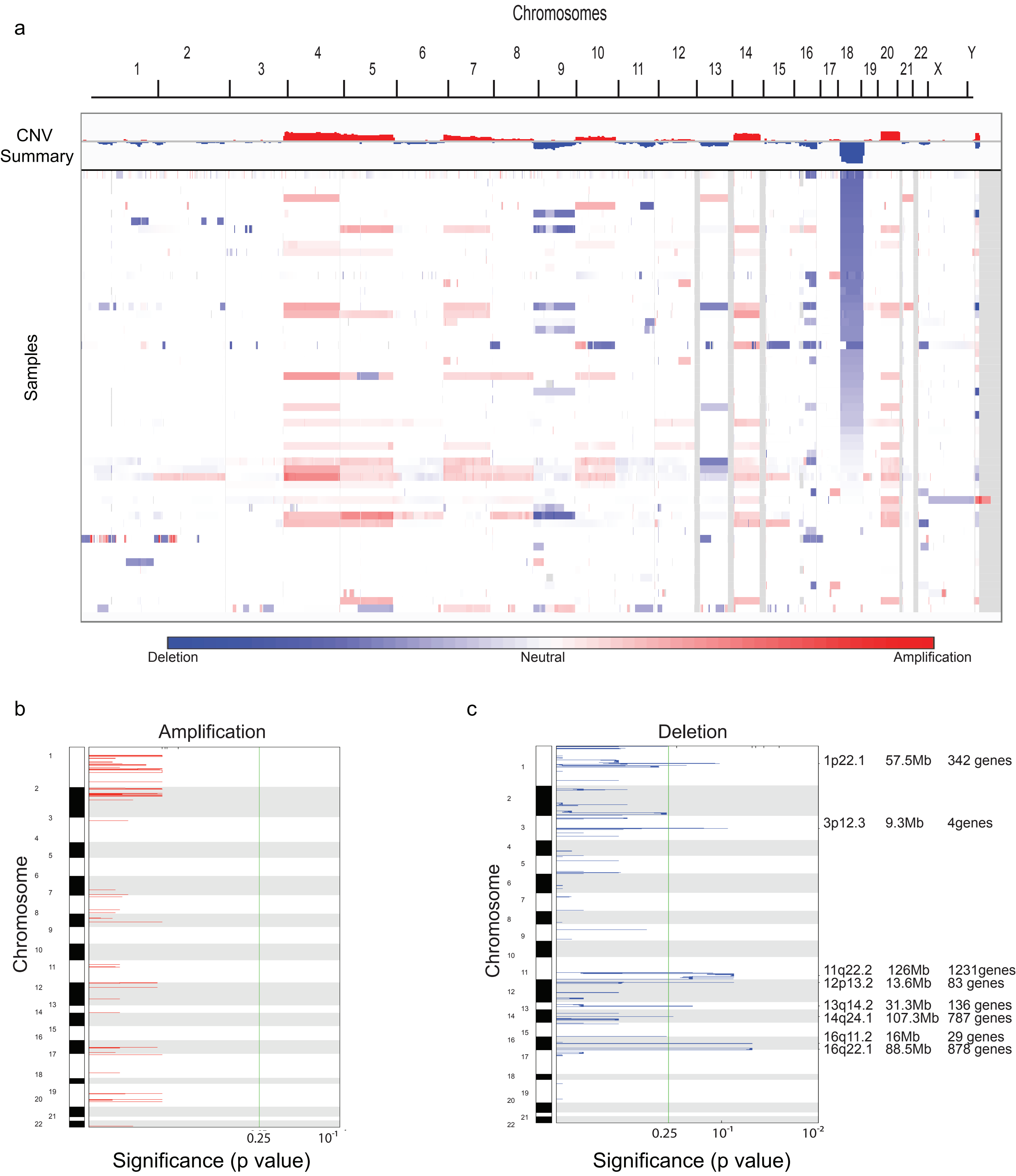
AQP7
ARHGEF2
CDC27
CNKSR3
DCTN1
FAM5C
FLG
GABRA4
MACF1
MAGEC1
MLL4
MYOM3
NHS
NUP133
PKHD1L1
PLXNA3
PLXNB1
RBM10
SRCAP
TNIK
TNRC6B

Gene name

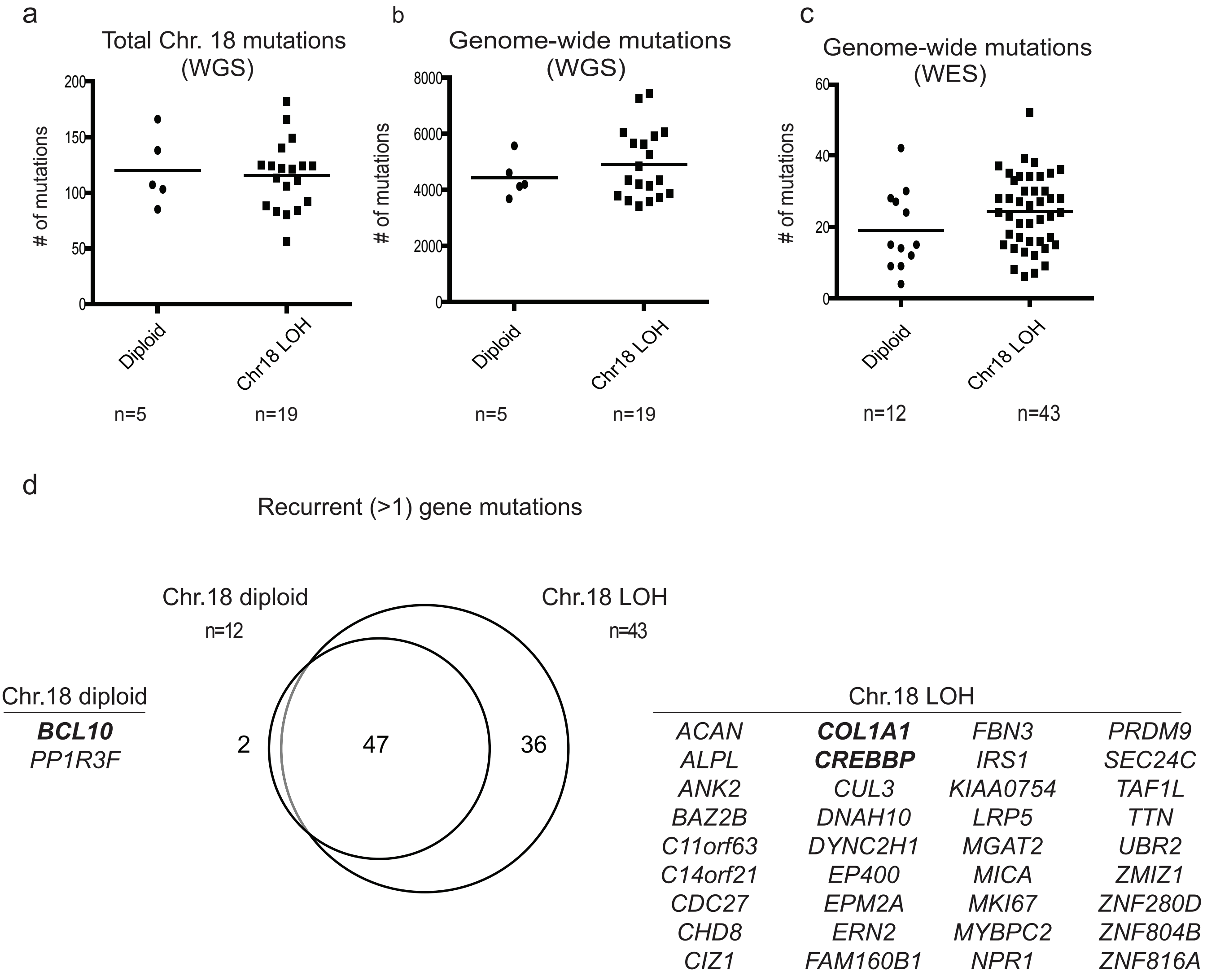
ATRX
BCL9L
CCDC158
COL1A1
CRTAC1
DEFB118
GLUD2
HS6ST1
IL32
IRS1
ITGAX
LILRB5
ODZ1
STON2
SUPT5H
TTC15
ZNF557

Supplementary Figure 1: Comparison of somatic mutation rates in our study and the published neuroendocrine tumor literature

a) Plot comparing the number of mutations per megabase (Mb) in primary and metastatic SI-NETs, the bar represents the mean. b) Venn diagram of the concordant gene mutations identified previously in SI-NETs [5] and the current study of SI-NETs. c) Plot comparing the total number of mutations per case in pancreatic NETs [2] and the current study, the bar represents the mean. d) Venn diagram of the concordant gene mutations identified in both studies (bold indicates membership in the Cancer Gene Census) [8].


a
Chromosomes
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
X
Y
CNV Summary
Samples
Deletion
Neutral
Amplification
b
Amplification
Chromosome
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
0.25
10^{-1}
Significance (p value)
c
Deletion
Chromosome
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
0.25
10^{-1}
10^{-2}
Significance (p value)
1p22.1 57.5Mb 342 genes
3p12.3 9.3Mb 4genes
11q22.2 126Mb 1231genes
12p13.2 13.6Mb 83 genes
13q14.2 31.3Mb 136 genes
14q24.1 107.3Mb 787 genes
16q11.2 16Mb 29 genes
16q22.1 88.5Mb 878 genes

Supplementary Figure 2: SCNA and GISTIC analysis of 55 small intestine and metastatic NETs.
a) Somatic copy number alterations in 55 primary and metastatic small intestine NETS. Upper panel, summary plot of SCNAs across all chromosomes. Lower panel, heat map of copy number increases (red) and decreases (blue). GISTIC 2.0 q-values for amplifications (b) and deletions (c) are plotted across the genome (y-axis). The significantly deleted peaks are labeled with the size of the region and putative gene targets (Supplementary Tables 15 and 16).



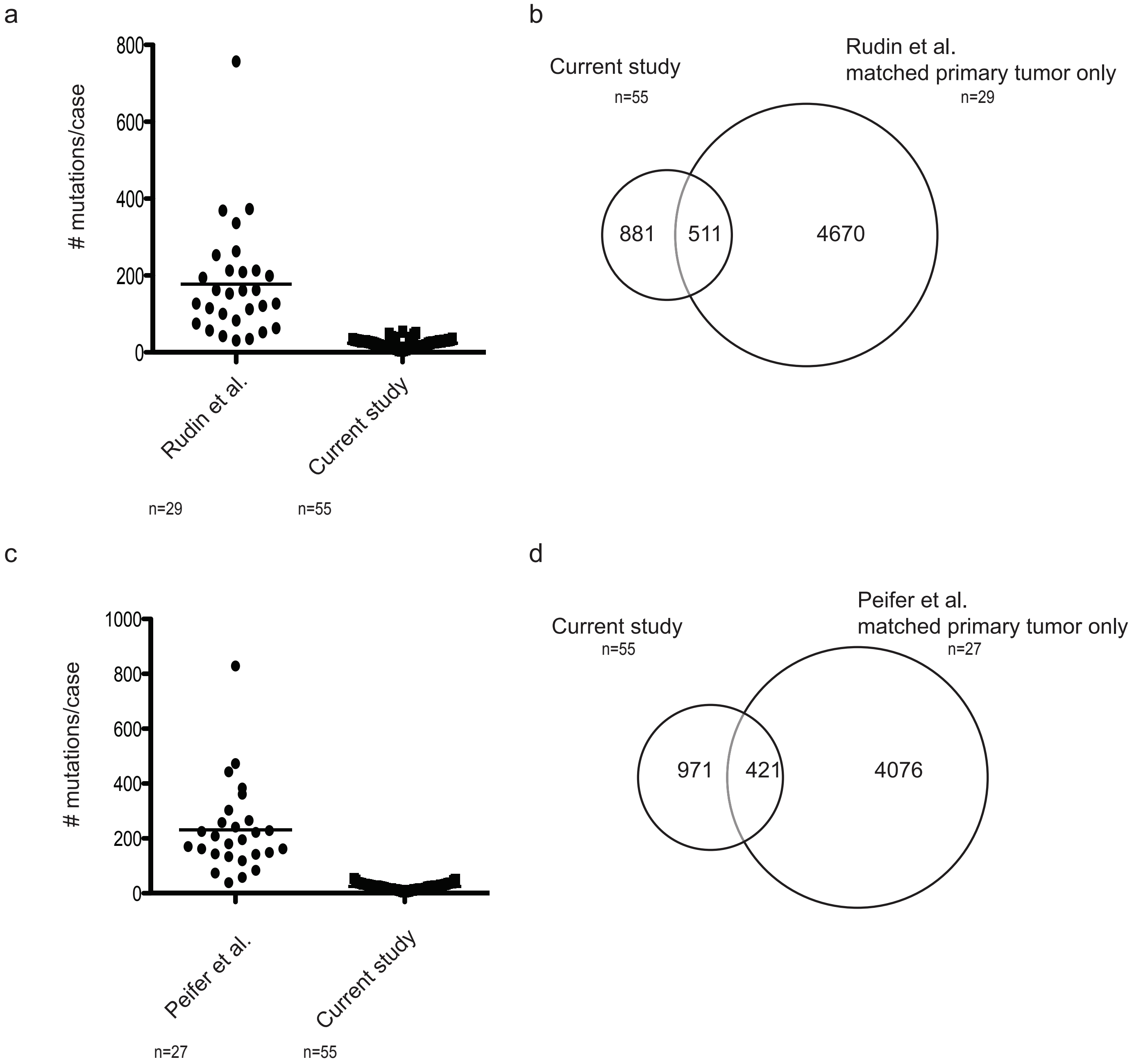
Chr.18 diploid

BCL10
PP1R3F

Chr.18 LOH

ACAN
ALPL
ANK2
BAZ2B
C11orf63
C14orf21
CDC27
CHD8
CIZ1
COL1A1
CREBBP
CUL3
DNAH10
DYNC2H1
EP400
EPM2A
ERN2
FAM160B1
FBN3
IRS1
KIAA0754
LRP5
MGAT2
MICA
MKI67
MYBPC2
NPR1
PRDM9
SEC24C
TAF1L
TTN
UBR2
ZMIZ1
ZNF280D
ZNF804B
ZNF816A

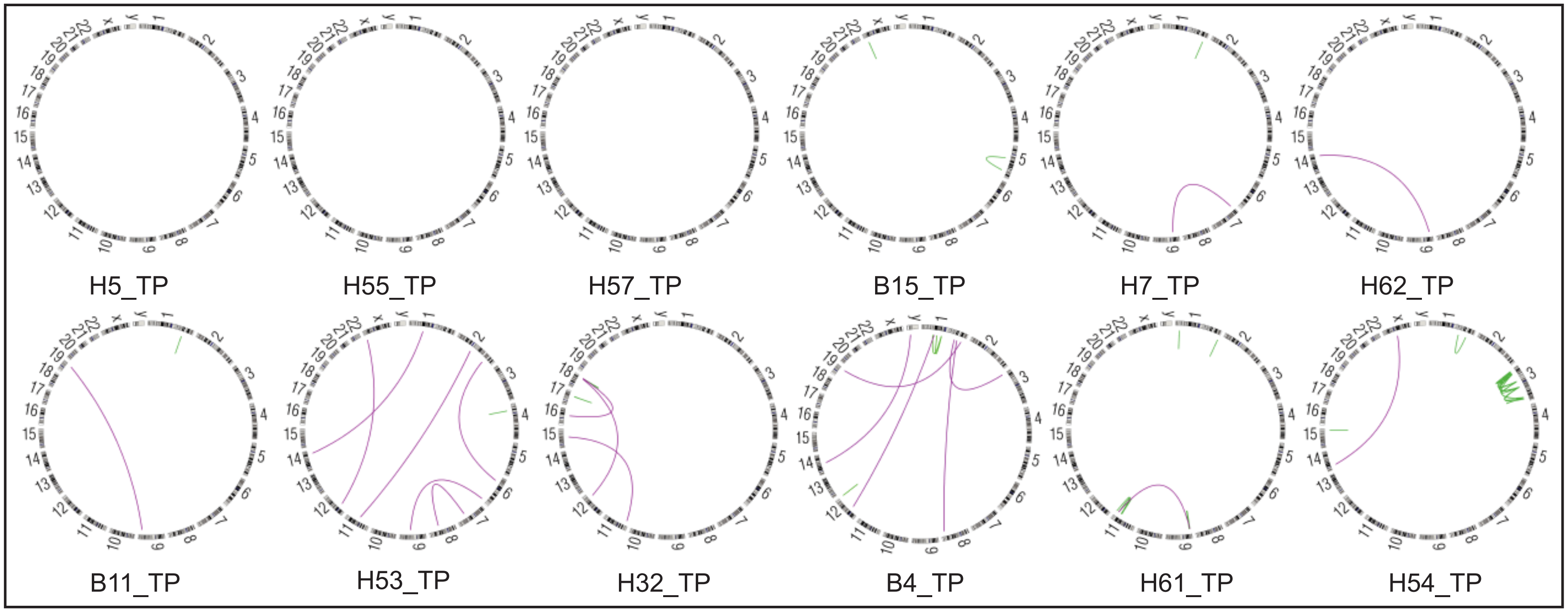
Supplementary Figure 3: Chromosome 18 centric specific analysis
a) Plot comparing the total number of somatic variants in chromosome 18 as detected by whole-genome sequencing (WGS) for cases with or without chr.18 LOH, the bar represents the mean. b) Plot comparing the total genome wide somatic variants detected by WGS for cases with or without chr.18 LOH, the bar represents the mean. c) Plot comparing the number of mutations genome-wide detected by whole-exome sequencing (WES) for cases with or without chr.18 LOH, the bar represents the mean. d) Venn diagram of gene mutations found in more than 1 case and relation to chr.18 status. Mutations in two genes were exclusive to the chr.18 diploid cases, while mutations in 47genes were present in both chr. 18 diploid and LOH cases. The greater number of gene mutations found in the chr.18 LOH cases is a reflection of the greater sample size. Genes in bold are present in the Cancer Gene Census [8].



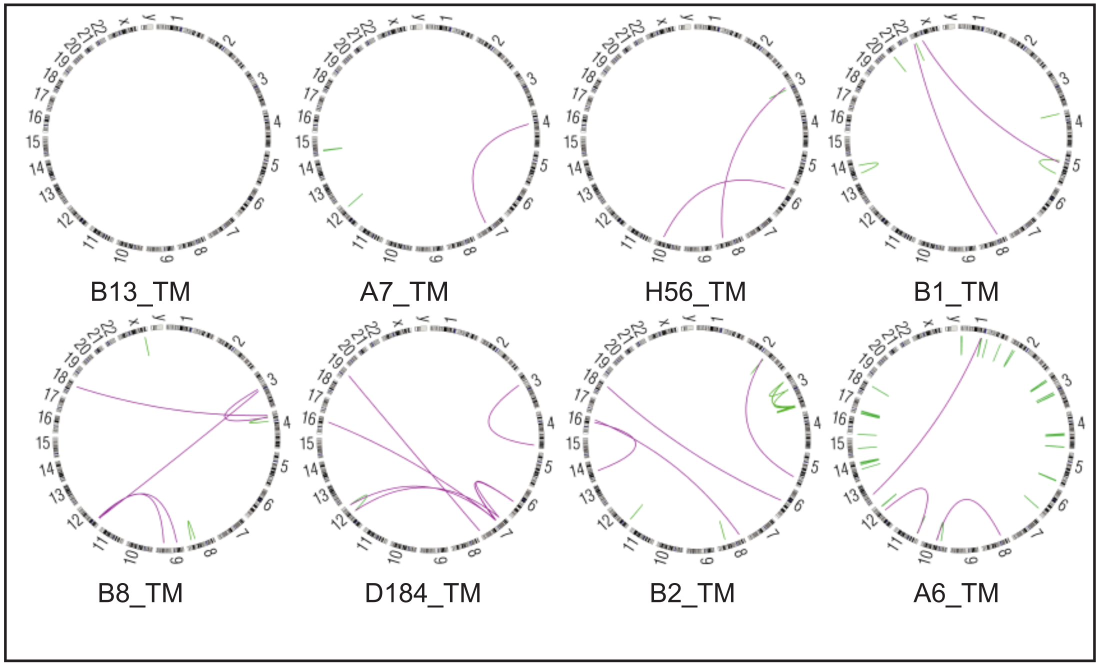
Supplementary Figure 4: Comparison of somatic variants with the published small cell lung cancer literature

a) Plot comparing the total number of mutations per case in SCLC [29] and the current study of SI-NETs. b) Venn diagram of the concordant gene mutations identified in both studies (see Supplemental Table 10 for genes). c) Plot comparing the total number of mutations per case in SCLC [30] and the current study. b) Venn diagram of the concordant gene mutations identified in both studies (see Supplemental Table 11 for genes).

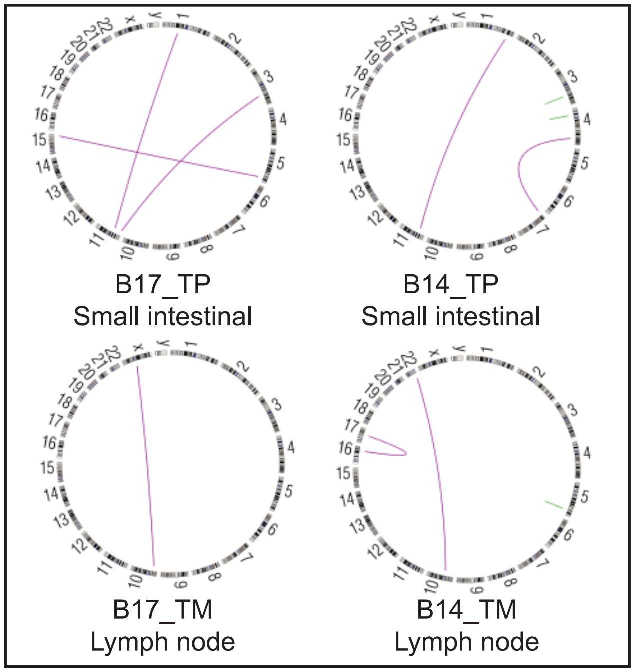
Primary small intestinal



Metastatic to liver



Small intestinal/Lymph node trio



Supplemental Figure 5: CIRCOS Plots of chromosomal rearrangements in small intestinal and metastatic NET cases. Circos plots of whole-genome sequence data depicting intrachromosomal rearrangments (green lines) and interchromosomal rearrangements (purple lines). See Supplemental Tables 12 and 13.