

Supplemental Figures 1-8

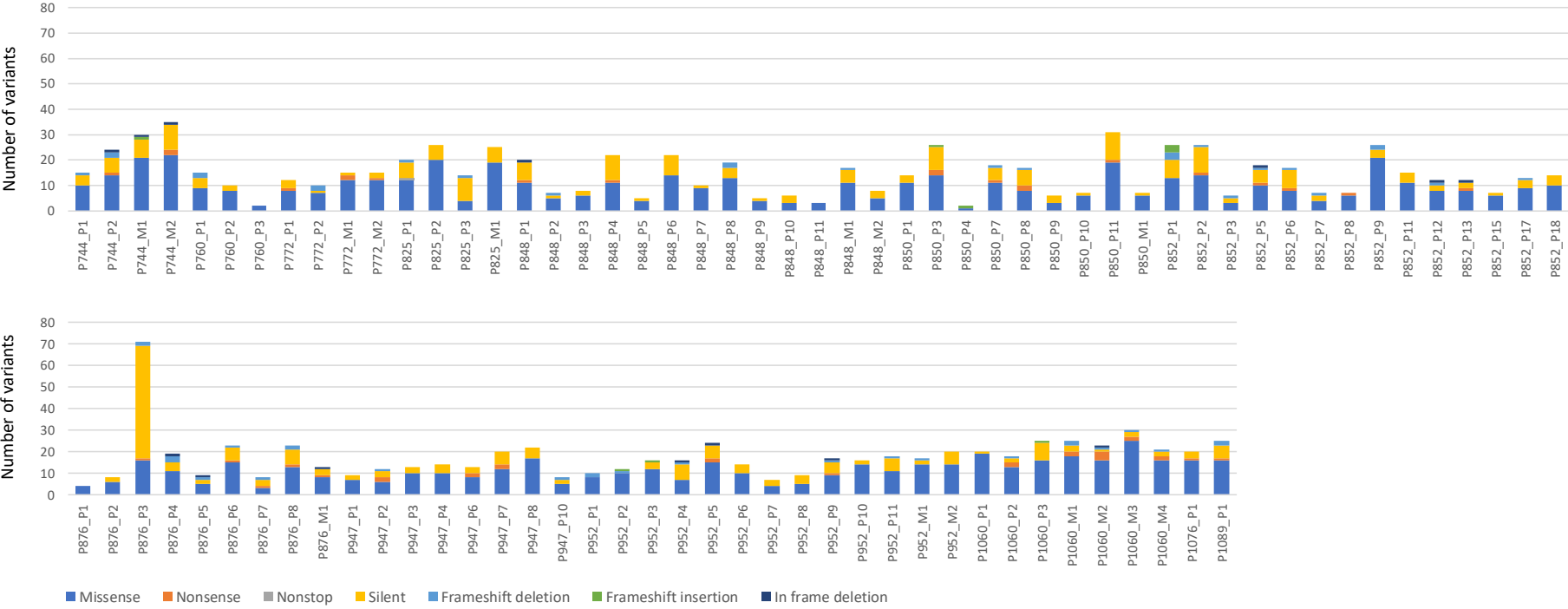


Figure S1. Classification of coding variants in 75 primary ileal NETs and 15 metastases. Majority of the coding variants were either missense (65%) or silent mutations (27%) followed by frameshift deletions (4%) and nonsense mutations (3%).

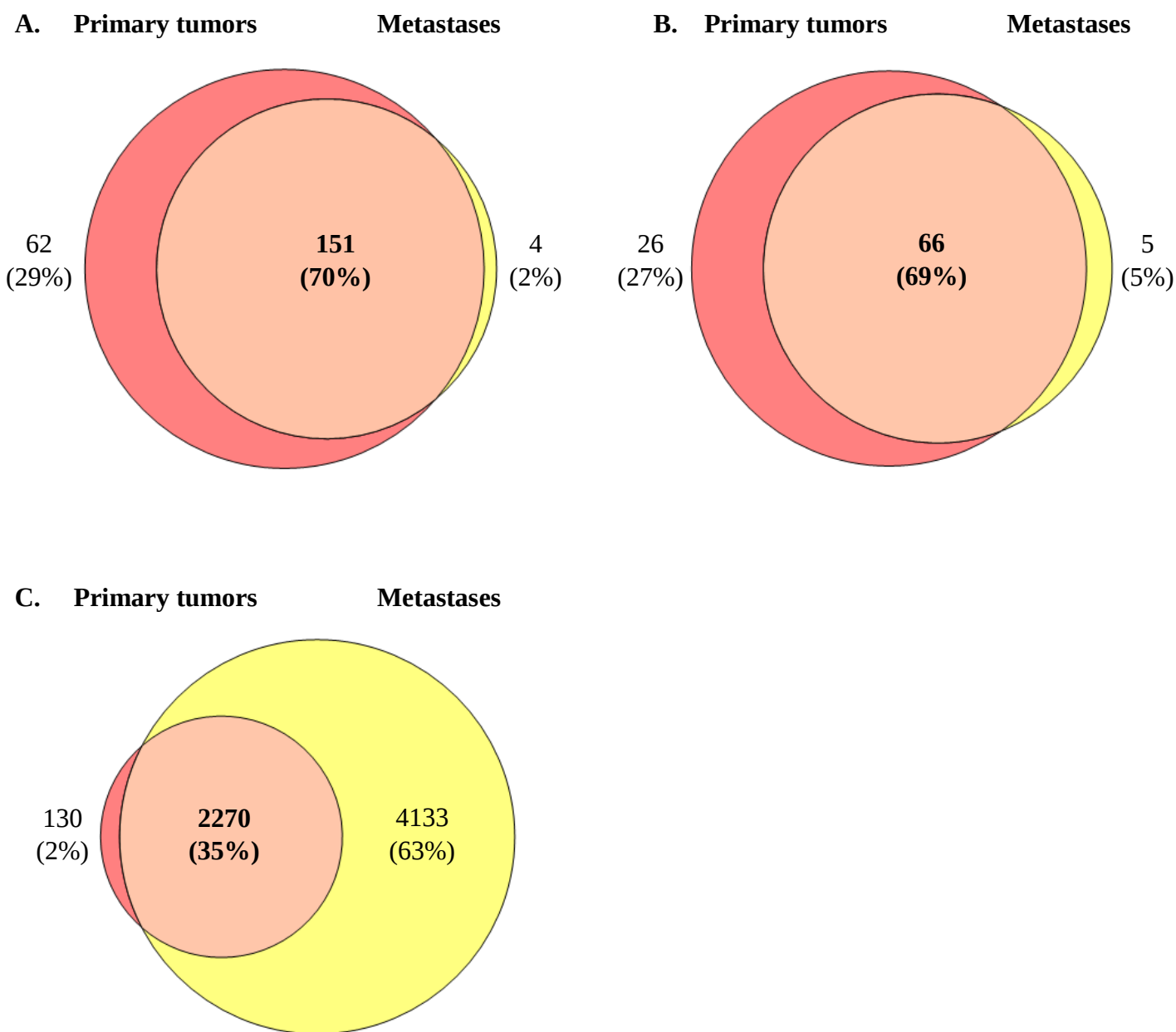
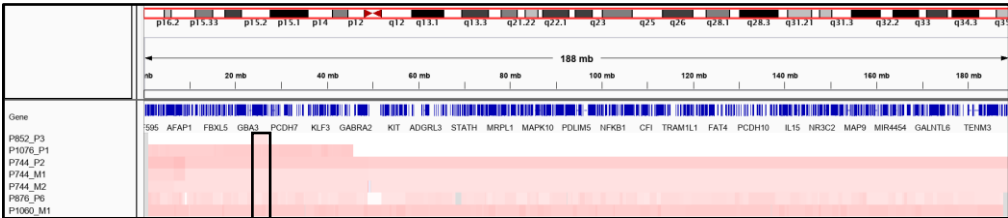


Figure S2. Overlap of somatic variation between primary ileal NETs and metastases. A) Majority of the identified CNAs (n=217) were present in both primary ileal NETs and metastases. A shared CNA indicates either exactly the same CNA or overlapping CNA. B) Majority of the recurrently mutated genes (n=96) were mutated in both primary ileal NETs and metastases. C) Metastases harbored more unique recurrent noncoding variants (n=6,533) than shared with the primary ileal NETs.

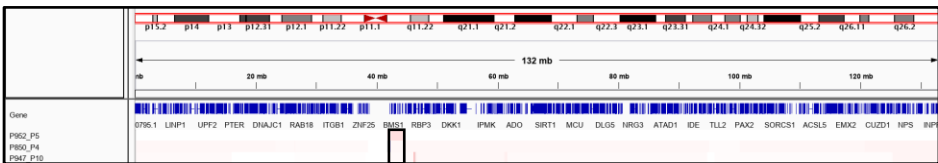
Chr4p15.2 [chr4:23699756-27292161]

3.6 Mb region; 20 genes



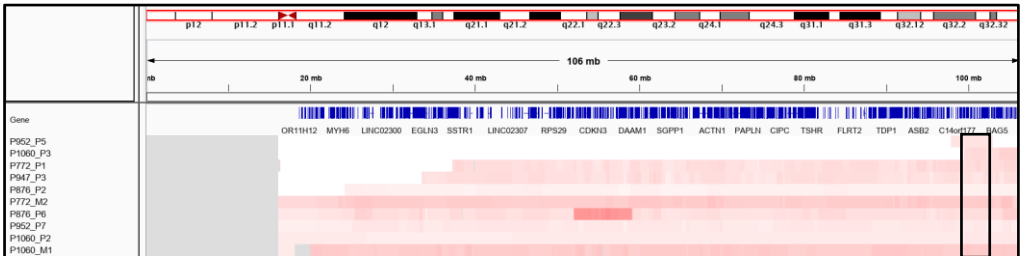
Chr10q11.21 [chr10:41911522-44544587]

2.6 Mb region; 29 genes



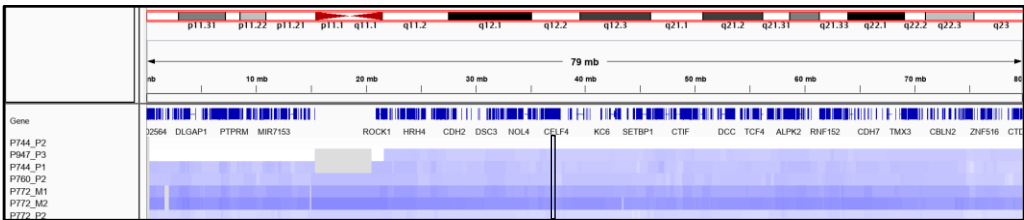
Chr14q32.2-32 [chr14:99528087-103095532]

3.6 Mb region; 80 genes



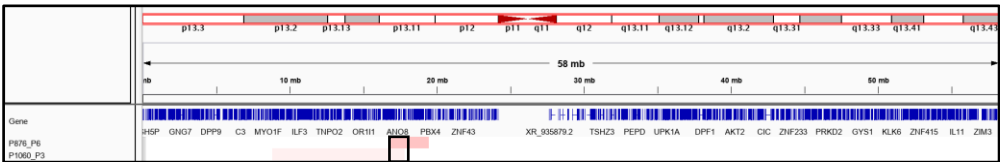
Chr18q12.2 [chr18:37090096-37238095]

0.15 Mb region; 1 gene



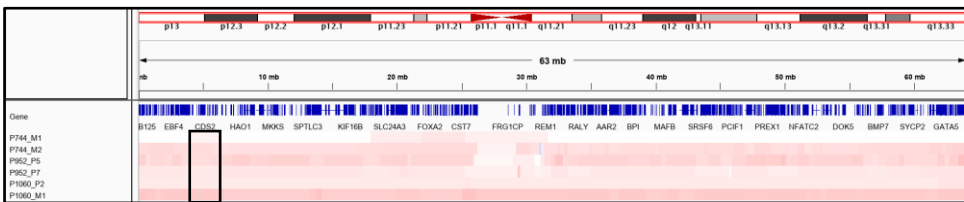
Chr19p13.11 [chr19:16820575-17850473]

1 Mb region; 34 genes



Chr20p13-12.3 [chr20:4128430-6303853]

2.2 Mb region; 25 genes



Deletion

Neutral

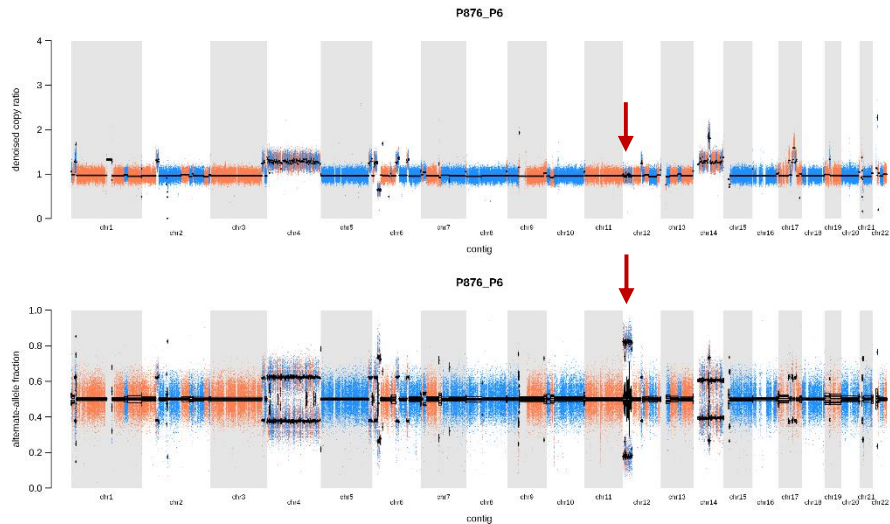
Amplification

Figure S3. Minimally targeted regions of size < 5Mb. Each minimally targeted region was observed in at least two multifocal ileal NET patients. Images of the minimally targeted regions on chr4, 14, 18 and 20 include five examples of tumors with whole chromosome alterations.

CDKN1B (chr12:12,715,058-12,721,204)



Copy-neutral LOH (P876_P6)



TNRC6B (chr22:40,177,925-40,335,808)

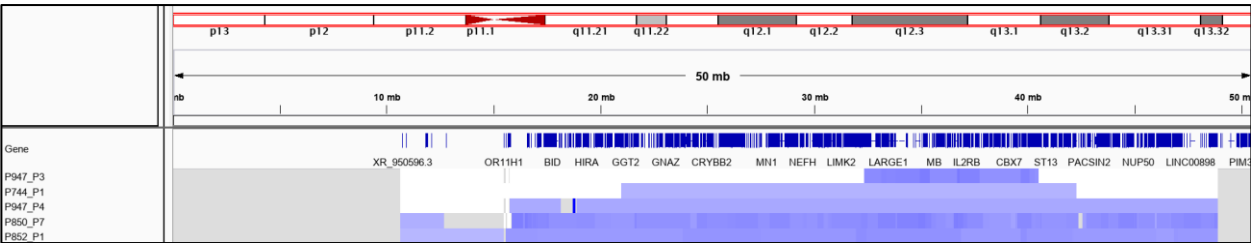
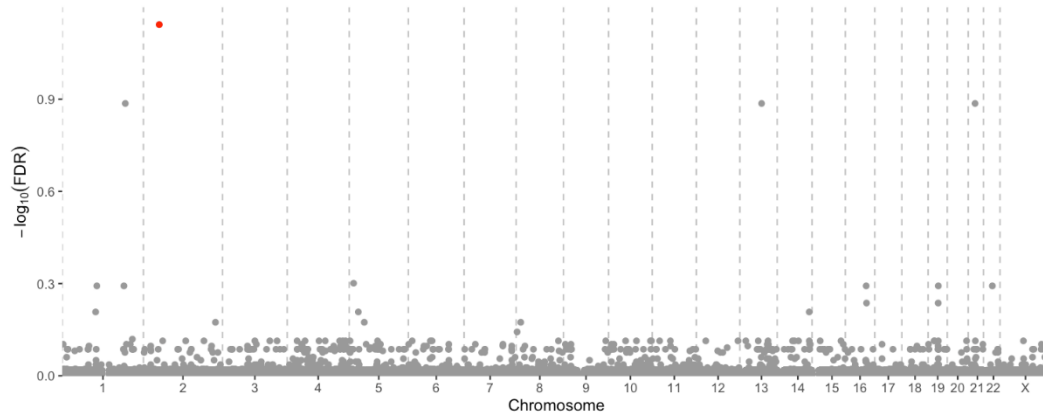


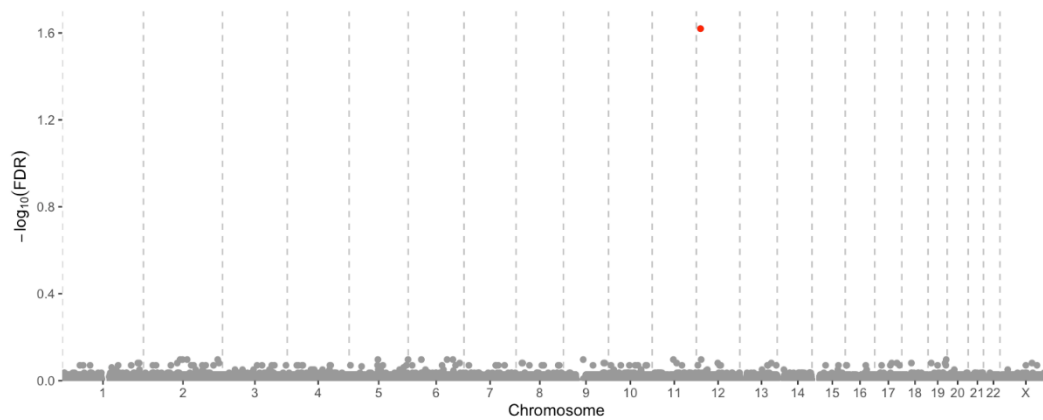
Figure S5. Deletions affecting *CDKN1B* and *TNRC6B*. *CDKN1B* was deleted in five primary ileal NETs from three multifocal ileal NET patients. Additionally, one primary ileal NET (P876_P6) displayed copy-neutral LOH on chr12p. *TNRC6B* was affected by a deletion in five primary ileal NETs from four multifocal ileal NET patients.

A.



Chr	Start position	End position	Width	P-value	FDR	Count
2	48340001	48350000	10000	2.80E-07	0.072	8
21	20980001	20990000	10000	1.60E-06	0.13	7
13	66640001	66650000	10000	1.80E-06	0.13	7
1	193350001	193360000	10000	2.10E-06	0.13	7
5	13510001	13520000	10000	9.80E-06	0.5	6

B.



Chr	Start position	End position	Width	P-value	FDR	Count
12	12700001	12800000	100000	9.00E-07	0.024	5
6	118800001	118900000	100000	8.20E-05	0.8	3
2	227000001	227100000	100000	0.00016	0.8	3
9	60500001	60600000	100000	2.00E-04	0.8	4
6	39900001	40000000	100000	0.00022	0.8	3

Figure S7. Statistically enriched regions of SNVs and indels in 75 primary ileal NETs and 15 metastases. A) Results of a fishHook analysis for SNVs. Five top hits are reported under the scatter plot, one of them being statistically significant after multiple testing correction. B) Results of a fishhook analysis for indels. Five top hits are reported under the scatter plot, one of them being statistically significant after multiple testing correction. FDR < 0.1 was considered statistically significant.

