Supplementary Table 1:

	Sampling strategy								
	a	**b**	**c**	**d**	**e**	**f**	**g**	**h**	**i**
Mean	339	466	290	1558	523	252	357	285	367
Median	204	398	182	1644	359	224	262	130	272
Mean % diff from A	na	37	-14	350	54	-25	5	-15	9
STDEV	382	363	334	918	577	191	422	426	343
MIN	32	54	36	338	31	7	20	37	44
MAX	1792	1672	1576	3366	2730	693	2116	2104	1553

The distribution of CD8 densities (per mm^2) in the 23 samples as obtained by the different sampling methods (a-i), and the percent difference of the mean compared to the whole tumor assessment (a). STDEV: standard deviation. MIN: smallest density. MAX: largest density.

Supplementary Table 2:

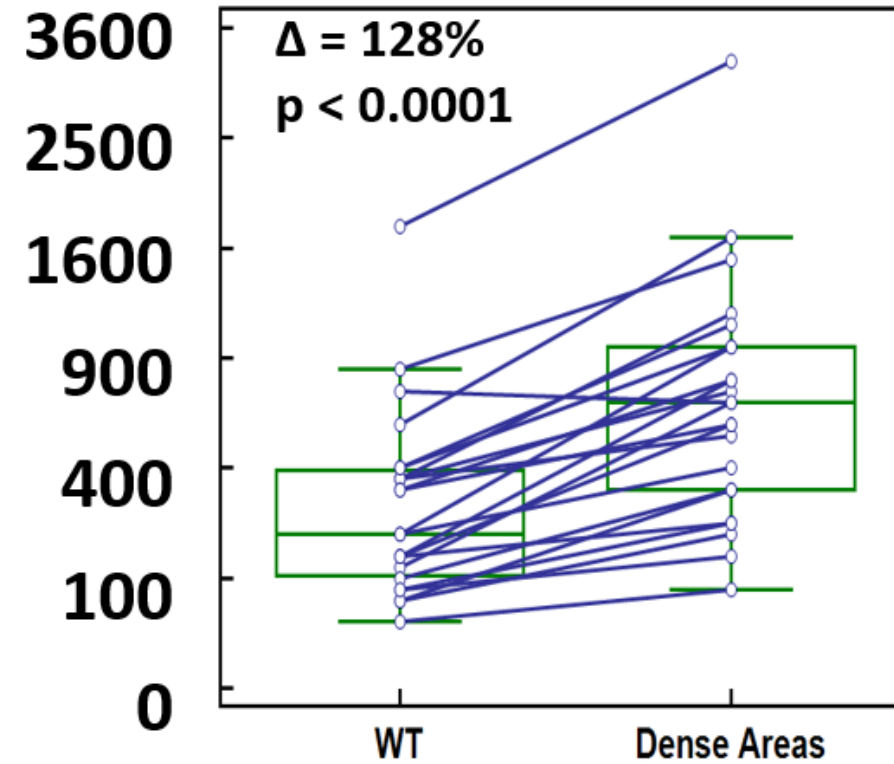|		N	Whole tumor	Central tumor	Whole tumor		Central tumor	
					CD8 Low	CD8 Hi	CD8 Low	CD8 Hi
Histology	Adenocarcinoma	**12**	329 (25 - 632)	295 (28 - 562)	6	6	6	6
	Squamous cell	**11**	350 (173 - 527)	285 (134 - 435)	5	6	5	6
Stage	**1**	**3**	443 (0 - 1279)	419 (0 - 1180)	1	2	0	1
	2	**2**	146 (0 - 883)	108(0 - 991)	1	1	2	0
	3	**18**	343 (139 - 547)	289 (112-465)	9	9	9	9
Age	**>70**	**13**	347 (67 - 628)	302 (53 - 551)	6	7	8	5
	≤70	**10**	328 (140 - 515)	275 (122 - 428)	5	5	3	7

The distribution of CD8 densities (per mm^2), and categories (Low and Hi across the median) in the 23 whole tumor and central tumor samples according to different clinical characteristics (tumor histology, clinical stage and patient age). Results are reported as mean densities per mm^2 and 95% confidence intervals are shown in parentheses.
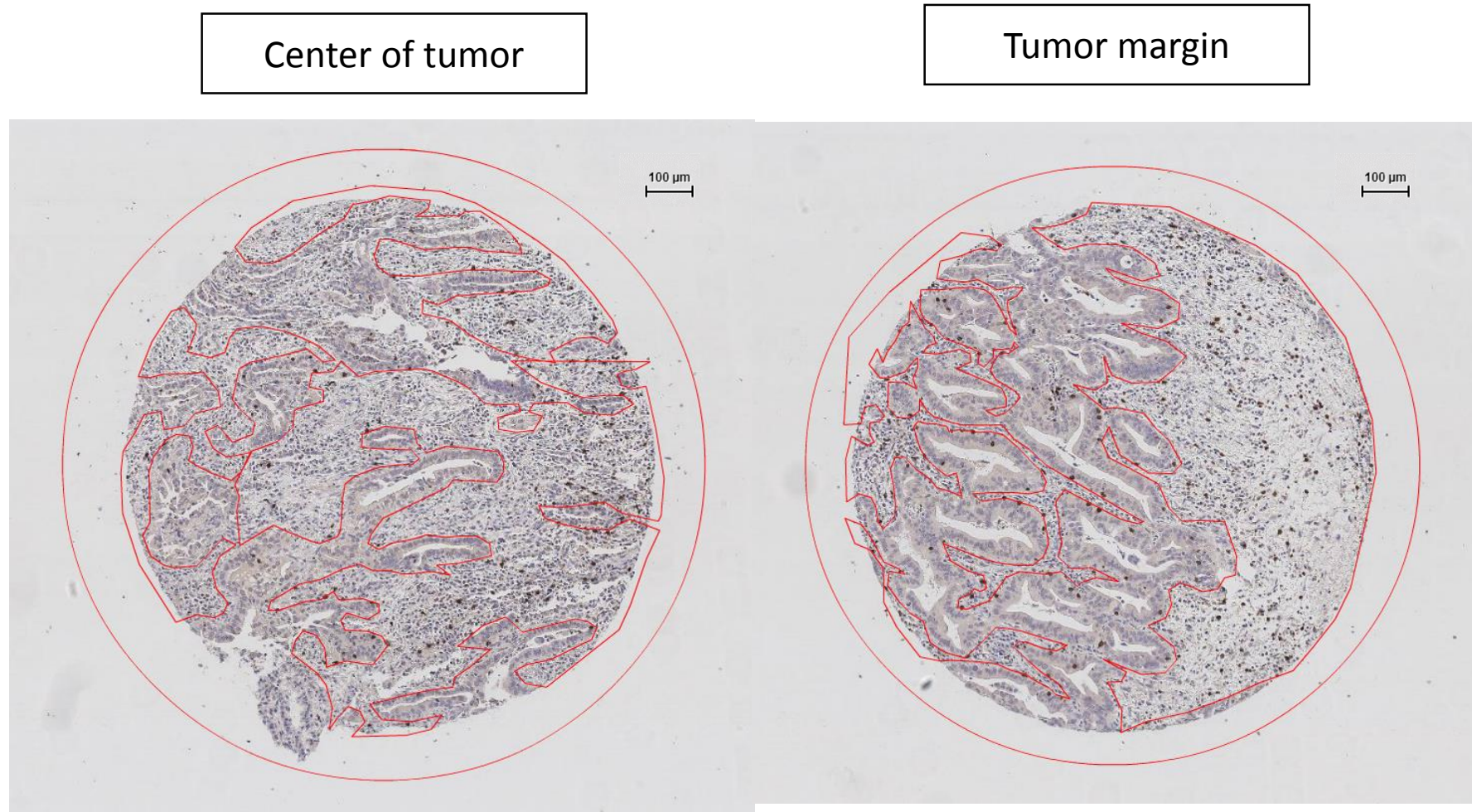
Supplementary Figure 1:

Array of Scatter Plots: Displaying inter-method associations of CD8 densities between each pair of the 9 sampling strategies used.

Supplementary Figure 2:

Three Densest Areas Vs Whole Tumor: Comparison of CD8 densities obtained from the whole to tumor to those obtained from the three densest areas that are included in the most representative areas assessment (noted B). The difference of the means is reported and the significance is tested using a paired T-test. WT: whole tumor.

Supplementary Figure 3:

Stromal and Intra-Epithelial Areas: Example of demarcation of stromal areas vs cancer cell nests within two NSCLC tissue microarray cores.