

Figure W1. Concordance of aCGH and exome capture copy number assessments in sample WA53. (A) Overall copy number across the genome for sample WA53 by aCGH and exome sequencing. Log₂(copy number ratio) between tumor and matched normal is shown on the vertical axis; each point represents the log-transformed ratio for each aCGH probe or targeted exon, ordered by genomic coordinates. Large-scale amplifications and deletions are visible and agree in magnitude across the two technologies. (B) Copy number for sample WA53 by aCGH and exome sequencing in a 35-Mb region containing the AR gene. Both technologies reveal the same focal pattern of amplification and give similar estimates of the number of copies of the AR gene. Red line segments represent segmented copy number data. (C) Copy number for sample WA53 by aCGH and exome sequencing in a 30-Mb region containing the PTEN gene. Both technologies reveal focal 2-copy loss of PTEN in this sample. Red line segments represent segmented copy number data. (D) Classification performance of exome capture sequencing relative to aCGH for sample WA53. ROC curves are shown, using aCGH copy number assessments as a criterion standard. ROC curves are presented for classifying all aCGH segments (red), segments containing at least ten targeted exons (green), and all targeted genes (blue).

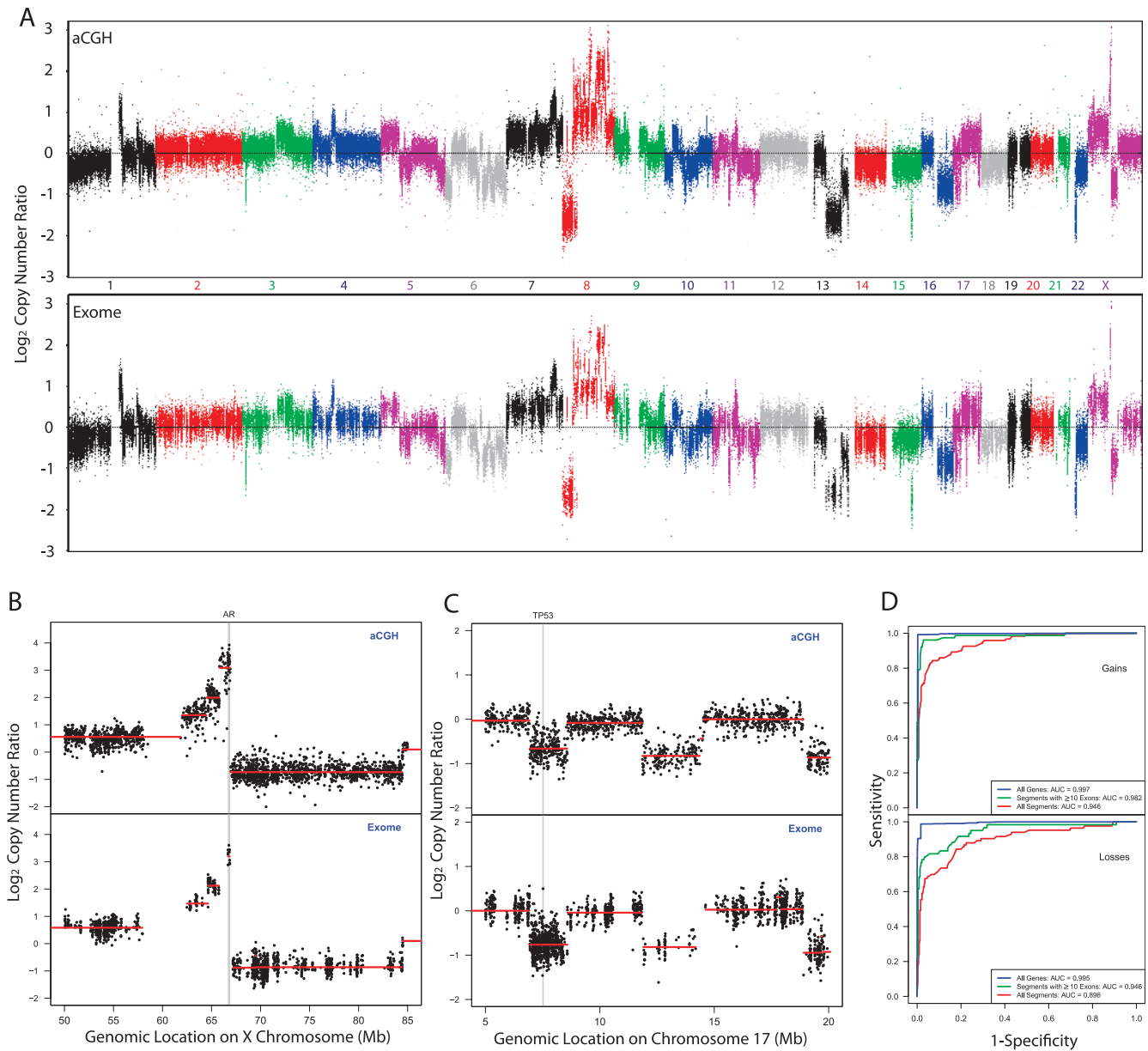


Figure W2. Concordance of aCGH and exome capture copy number assessments in sample WA55. (A) Overall copy number across the genome for sample WA55. Log₂(copy number ratio) between tumor and matched normal is shown on the vertical axis; each point represents the log-transformed ratio for each targeted exon or aCGH probe, ordered by genomic coordinates. Large-scale amplifications and deletions are visible and agree in magnitude across the two technologies. (B) Copy number for sample WA55 by aCGH and exome sequencing in a 35-Mb region containing the AR gene. Both technologies reveal the same focal pattern of amplification and give similar estimates of the number of copies of the AR gene. Red line segments represent segmented copy number data. (C) Copy number for sample WA55 by aCGH and exome sequencing in a 15-Mb region containing the TP53 gene. Both technologies reveal focal one-copy loss of TP53 in this sample. Red line segments represent segmented copy number data. (D) Classification performance of exome capture sequencing relative to aCGH for sample WA55. ROC curves are shown, using aCGH copy number assessments as a criterion standard. ROC curves are presented for classifying all aCGH segments (red), segments containing at least ten targeted exons (green), and all targeted genes (blue).

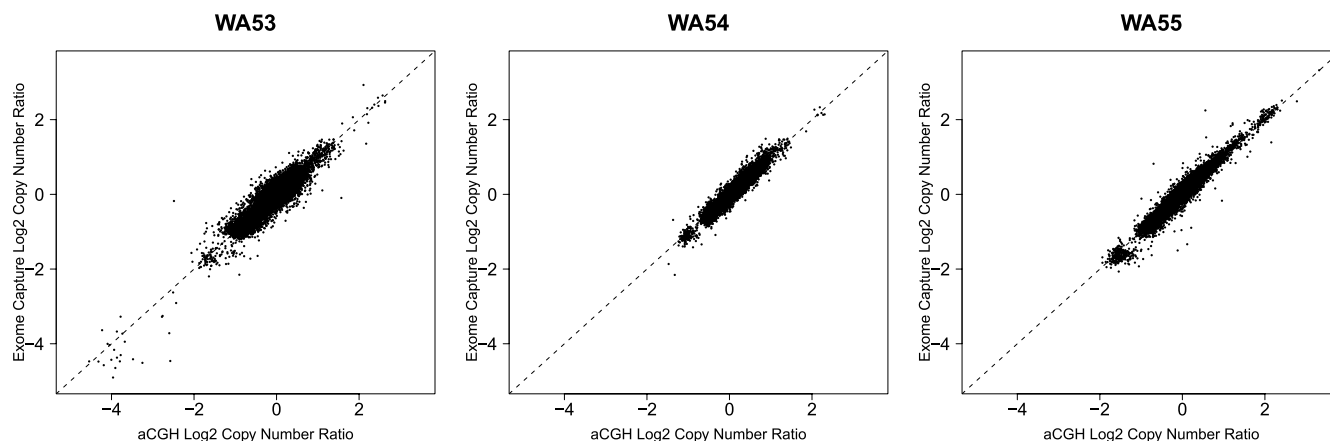


Figure W3. Concordance of copy number by aCGH and targeted exome sequencing through genomic windows analysis. Scatterplots show log₂ copy number ratios by each of aCGH and exome sequencing, computed as mean log₂ ratios over windows covering the genome. Windows were chosen to include at least five aCGH probes and at least five targeted exons to enable reliable comparison. For each sample, the mean log₂ copy number ratios were very highly correlated (WA53; 0.92, WA54; 0.96, WA55; 0.97, $P < .001$ for each sample).

Table W1. AUC Results for Exome Sequencing Compared with aCGH.

	Gain			Loss		
	WA53	WA54	WA55	WA53	WA54	WA55
All segments*	0.971	0.913	0.946	0.956	0.902	0.896
Segments containing ≥ 2 exons [†]	0.979	0.945	0.970	0.957	0.956	0.942
Segments containing ≥ 10 exons [‡]	0.979	0.977	0.982	0.951	0.958	0.946
All genes [‡]	0.993	0.989	0.997	0.994	0.993	0.995
Informative genes [§]	0.984	0.991	0.998	0.997	0.991	0.994

*ROC curves for predicting aberration status (gain *vs* no gain or loss *vs* no loss) of each segment identified from segmentation analysis of aCGH data.

[†]ROC curves for predicting aberration of each segment identified from segmentation analysis of aCGH data, excluding segments overlapping fewer than 2 (or 10) targeted exons.

[‡]ROC curves for predicting aberration status of each gene targeted by exome sequencing.

[§]ROC curves for predicting aberration status of each informative gene targeted by exome sequencing.

Table W2. Prostate Cancer Tissue Specimens Used for Exome Sequencing.

Sample Name	Disease State*	Age [†]	Gleason Score [‡]	Prior Treatment [§]	ETS/RAF Status [¶]
WA53	CRPC	68	NA	H, C, X	ERG ⁺
WA54	CRPC	73	NA	P, R, H, C, X	ERG ⁺
WA55	CRPC	72	NA	H, C, X	ERG ⁺
WA35	CRPC	71	NA	R, H, C, X	Negative
WA42	CRPC	61	NA	H, C	Negative
WA43-27 (celiac LN)	CRPC	52	NA	P, R, H, C	Negative
WA43-44 (bladder)	CRPC				
WA43-71 (right lung)	CRPC				
WA46	CRPC	71	NA	P, R, H, C, X	Negative
WA49	CRPC	68	NA	P, R, H, C	ERG ⁺
WA50	CRPC	78	NA	P, R, H, C	ERG ⁺
WA51	CRPC	65	NA	P, H, C, X	Negative
WA52	CRPC	80	NA	P, H, C	ERG ⁺
WA56	CRPC	79	NA	P, R, H, C, X	ERG ⁺
WA57	CRPC	73	NA (NE diff)	R, H, C,	ERG ⁺
WA59	CRPC	59	NA	H, C, X	Negative
WA60	CRPC	62	NA	H, C	ERG ⁺

*Localized prostate cancer (PC) or castrate-resistant metastatic PC (CRPC).

[†]Age at diagnosis (PC) or death (CRPC).

[‡]Gleason score of profiled prostatectomy specimen for PC. CRPCs with neuroendocrine (NE) differentiation are noted.

[§]C indicates chemotherapy; H, hormone therapy; P, prostatectomy; R, radiation; X, palliative radiation.

[¶]Rearrangements in ETS or RAF family genes.

Table W3. Prostate Cancer Exome Sequencing Statistics.

Sample	Status	Agilent SureSelect Human All Exon Kit (Mb)	Bases in Target Region	Reads Sequenced (after Quality Filtering)	Bases Sequenced (after Quality Filtering)	Bases Mapped to Genome	Bases Mapped to Target Region	Mean No. Reads per Targeted Base
WA35	Tumor	50	51,712,500	170,916,320	13,331,472,960	10,558,678,026	5,238,994,222	101.31
	Normal	50	51,712,500	157,827,174	12,310,519,572	9,722,413,350	4,443,761,328	85.93
WA42	Tumor	50	51,712,500	169,227,800	13,199,768,400	11,152,269,258	5,328,029,502	103.03
	Normal	50	51,712,500	160,543,858	12,522,420,924	10,584,966,288	5,238,213,050	101.29
WA43	Tumor 43-27	50	51,712,500	106,207,750	8,284,204,500	7,078,252,896	3,474,444,817	67.19
	Tumor 43-44	50	51,712,500	119,846,711	9,348,043,458	8,062,722,408	4,302,838,713	83.21
	Tumor 43-71	50	51,712,500	115,921,897	9,041,907,966	7,819,368,804	3,702,454,417	71.60
	Normal	50	51,712,500	109,694,911	8,556,203,058	7,301,239,530	3,538,639,763	68.43
WA46	Tumor	50	51,712,500	174,132,908	13,582,366,824	11,159,069,376	5,653,532,988	109.33
	Normal	50	51,712,500	174,753,667	13,630,786,026	11,418,269,070	5,428,312,362	104.97
WA49	Tumor	50	51,712,500	155,083,960	12,096,548,880	10,251,439,692	5,091,480,149	98.46
	Normal	50	51,712,500	150,941,382	11,773,427,796	9,990,123,234	5,142,727,707	199.45
WA50	Tumor	50	51,712,500	151,428,570	11,811,428,460	10,163,517,936	4,825,565,562	93.32
	Normal	50	51,712,500	146,431,894	11,421,687,732	9,712,458,132	4,918,010,589	95.10
WA51	Tumor	50	51,712,500	165,709,454	12,925,337,412	10,739,425,398	4,824,644,281	93.30
	Normal	50	51,712,500	170,866,524	13,327,588,872	11,006,378,916	5,103,100,934	98.68
WA52	Tumor	50	51,712,500	196,334,388	15,314,082,264	12,710,410,284	6,105,297,939	118.06
	Normal	50	51,712,500	182,664,677	14,247,844,806	11,851,474,518	5,394,831,142	104.32
WA53	Tumor	38	37,806,033	170,043,479	13,263,391,362	11,275,509,726	6,813,696,982	180.23
	Normal	38	37,806,033	160,836,761	12,545,267,358	10,592,709,894	6,593,161,035	174.39
WA54	Tumor	38	37,806,033	109,465,569	8,538,314,382	7,274,785,830	4,409,679,103	116.64
	Normal	38	37,806,033	168,886,512	13,173,147,936	11,227,983,078	7,016,349,732	185.59
WA55	Tumor	38	37,806,033	169,683,500	13,235,313,000	11,190,529,662	6,730,794,029	178.03
	Normal	38	37,806,033	168,001,511	13,104,117,858	11,095,714,656	6,872,481,717	181.78
WA56	Tumor	50	51,712,500	171,138,470	13,348,800,660	10,979,986,056	5,177,318,788	100.12
	Normal	50	51,712,500	173,359,773	13,522,062,294	11,245,543,686	5,497,614,730	106.31
WA57	Tumor	50	51,712,500	172,761,810	13,475,421,180	10,834,401,240	4,778,197,473	92.40
	Normal	50	51,712,500	169,816,928	13,245,720,384	10,482,745,260	5,096,773,379	98.56
WA59	Tumor	50	51,712,500	159,528,926	12,443,256,228	10,058,917,362	4,475,487,277	86.55
	Normal	50	51,712,500	167,669,729	13,078,238,862	10,418,808,036	4,900,312,121	94.76
WA60	Tumor	50	51,712,500	166,908,169	13,018,837,182	10,453,483,014	4,569,838,785	88.37
	Normal	50	51,712,500	163,743,302	12,771,977,556	10,272,887,664	4,726,398,012	91.40
Mean across samples			49,105,037	158,449,321	12,359,047,067	10,271,452,571	5,169,155,707	105.27

Table W4. Summary of Aberrations across 17 Lethal Metastatic Prostate Samples.

Sample	All Gains (Copy Number Ratio ≥ 1.25)		All Losses (Copy Number Ratio ≤ 0.75)		High-level Gains (Copy Number Ratio ≥ 2.0)		Homozygous Losses (Copy Number Ratio ≤ 0.50)	
	No. Aberrations*	Length of Altered Genome (Mb) [†]	No. Aberrations*	Length of Altered Genome (Mb) [†]	No. Aberrations*	Length of Altered Genome (Mb) [†]	No. Aberrations*	Length of Altered Genome (Mb) [†]
WA35	233	407.5	70	280.2	35	26.5	9	1.2
WA42	12	286.0	81	428.1	0	0.0	19	19.7
WA43-27	53	334.6	56	538.0	18	23.1	9	0.7
WA43-44	51	368.5	61	492.3	23	30.1	9	0.7
WA43-71	490	849.5	609	379.0	25	23.3	89	25.9
WA46	596	720.5	79	71.1	112	108.2	7	0.5
WA49	173	404.7	43	264.8	29	26.1	9	37.5
WA50	88	429.2	96	183.1	3	1.2	17	3.4
WA51	30	273.4	81	538.3	3	101.5	22	56.4
WA52	33	240.8	55	79.8	0	0.0	3	3.5
WA53	93	332.9	117	513.3	18	22.5	17	18.8
WA54	100	353.1	65	475.7	19	7.7	9	30.7
WA55	104	506.3	83	282.6	29	58.7	18	75.5
WA56	51	421.9	71	406.2	2	3.5	18	70.2
WA57	57	421.3	78	639.6	11	26.2	34	144.6
WA59	306	562.5	282	277.2	37	31.7	28	28.0
WA60	743	433.6	746	912.0	19	21.4	59	67.9
Median	93	407.5	79	406.2	19	23.3	17	25.9

*Number of aberrations refers to the number of segments identified from segmentation analysis exceeding the given threshold.

[†]Length of altered genome refers to the combined length of these aberrant segments per sample, expressed in megabases.