

**Table S11. Performance of markers in simulated dilutions of tumor DNA into WBC DNA**

Biomarker	ctDNA fraction <sup>a</sup>	AUC	Threshold <sup>b</sup>	Specificity	Sensitivity														
					ALL <sup>c</sup>	BLCA	BRCA	COAD	HNSC	KIRC	KRIP	LIHC	LUAD	LUSC	PAAD	PRAD	READ	STAD	UCEC
G	0.01	0.523	0.49	34%	70%	73%	70%	72%	73%	67%	64%	70%	66%	68%	68%	70%	73%	77%	72%
T		0.559	0.50	57%	54%	56%	55%	57%	55%	45%	49%	59%	51%	53%	37%	58%	53%	57%	53%
Z		0.554	0.48	41%	69%	69%	65%	72%	71%	61%	62%	71%	67%	68%	69%	69%	86%	77%	71%
GT		0.559	0.49	51%	58%	60%	59%	62%	61%	47%	55%	66%	56%	58%	43%	63%	56%	61%	58%
GZ		0.554	0.47	29%	80%	81%	78%	86%	81%	72%	70%	80%	78%	79%	74%	81%	92%	83%	84%
TZ		0.566	0.48	48%	64%	64%	63%	70%	66%	51%	56%	66%	61%	60%	54%	68%	71%	70%	67%
GTZ		0.568	0.48	44%	67%	70%	66%	73%	67%	57%	61%	73%	67%	64%	54%	70%	73%	72%	70%
G	0.1	0.700	0.45	57%	75%	87%	79%	89%	85%	53%	42%	57%	77%	72%	69%	63%	85%	91%	73%
T		0.848	0.53	85%	74%	69%	75%	93%	85%	26%	28%	70%	69%	80%	49%	89%	95%	90%	80%
Z		0.835	0.48	80%	76%	88%	67%	97%	92%	34%	32%	77%	61%	77%	57%	84%	99%	91%	98%
GT		0.848	0.53	86%	73%	68%	75%	93%	85%	25%	28%	70%	69%	80%	49%	88%	95%	90%	80%
GZ		0.836	0.51	81%	75%	88%	65%	97%	91%	32%	29%	77%	61%	76%	55%	83%	99%	88%	98%
TZ		0.881	0.48	83%	79%	85%	77%	95%	93%	32%	38%	80%	71%	84%	54%	90%	98%	94%	94%
GTZ		0.881	0.49	84%	79%	82%	77%	96%	92%	30%	37%	80%	70%	86%	55%	92%	98%	92%	95%
G	0.25	0.815	0.56	87%	70%	88%	77%	94%	88%	39%	14%	36%	76%	65%	68%	45%	81%	95%	65%
T		0.897	0.58	96%	76%	71%	79%	96%	90%	24%	23%	68%	74%	83%	57%	93%	97%	95%	80%
Z		0.900	0.65	97%	76%	93%	66%	100%	96%	23%	21%	77%	61%	81%	52%	90%	100%	94%	100%
GT		0.911	0.52	94%	79%	76%	83%	96%	92%	27%	23%	69%	79%	85%	68%	93%	97%	97%	81%
GZ		0.915	0.65	96%	77%	93%	70%	100%	96%	24%	21%	74%	65%	82%	54%	86%	100%	95%	99%
TZ		0.939	0.51	95%	85%	90%	87%	100%	99%	29%	28%	86%	83%	92%	69%	95%	100%	99%	99%
GTZ		0.939	0.61	97%	83%	87%	84%	99%	98%	25%	25%	81%	78%	91%	60%	94%	100%	97%	99%

G	0.5	0.832	0.58	95%	71%	89%	80%	95%	90%	38%	11%	34%	81%	69%	75%	46%	81%	97%	63%
T		0.903	0.58	99%	78%	74%	83%	96%	90%	26%	24%	70%	80%	84%	60%	95%	97%	96%	83%
Z		0.904	0.52	98%	82%	94%	76%	100%	99%	33%	29%	82%	68%	89%	71%	94%	100%	98%	100%
GT		0.924	0.53	97%	82%	87%	86%	98%	98%	31%	22%	70%	87%	89%	72%	94%	99%	97%	83%
GZ		0.933	0.48	96%	86%	95%	87%	100%	100%	38%	26%	79%	82%	92%	80%	94%	100%	99%	100%
TZ		0.947	0.54	99%	87%	94%	91%	100%	100%	34%	29%	88%	87%	94%	75%	96%	100%	99%	100%
GTZ		0.949	0.53	99%	88%	94%	91%	100%	100%	35%	28%	87%	89%	94%	75%	96%	100%	100%	99%
G	0.75	0.818	0.54	96%	73%	92%	84%	95%	92%	39%	12%	36%	83%	71%	77%	50%	83%	97%	63%
T		0.899	0.53	99%	80%	76%	84%	97%	91%	29%	28%	70%	82%	86%	65%	95%	97%	96%	83%
Z		0.895	0.53	99%	82%	95%	76%	100%	99%	35%	31%	82%	69%	89%	74%	94%	100%	98%	100%
GT		0.921	0.44	97%	86%	93%	90%	99%	99%	40%	26%	71%	93%	92%	80%	95%	99%	98%	86%
GZ		0.930	0.50	98%	88%	96%	91%	100%	100%	41%	26%	80%	87%	94%	83%	94%	100%	99%	100%
TZ		0.946	0.46	99%	89%	96%	93%	100%	100%	39%	33%	89%	90%	95%	82%	96%	100%	99%	100%
GTZ		0.948	0.51	99%	89%	96%	94%	100%	100%	39%	29%	89%	92%	95%	82%	96%	100%	100%	100%
G	0.9	0.812	0.58	98%	73%	90%	83%	95%	91%	39%	12%	36%	83%	69%	75%	49%	83%	97%	63%
T		0.895	0.49	99%	81%	77%	84%	97%	91%	31%	29%	71%	85%	86%	68%	95%	97%	96%	83%
Z		0.888	0.47	99%	83%	95%	77%	100%	99%	39%	31%	83%	70%	90%	74%	94%	100%	98%	100%
GT		0.919	0.44	98%	86%	93%	91%	99%	99%	41%	26%	72%	93%	92%	80%	96%	99%	98%	86%
GZ		0.927	0.49	99%	88%	96%	91%	100%	100%	43%	26%	81%	88%	94%	82%	94%	100%	99%	100%
TZ		0.944	0.42	99%	90%	97%	94%	100%	100%	41%	35%	90%	92%	95%	83%	96%	100%	99%	100%
GTZ		0.947	0.38	99%	90%	97%	95%	100%	100%	43%	34%	89%	93%	96%	85%	96%	100%	100%	100%
G	1	0.810	0.54	98%	74%	92%	84%	95%	92%	40%	12%	36%	84%	71%	77%	51%	83%	97%	63%
T		0.893	0.47	99%	81%	77%	85%	97%	91%	32%	30%	72%	85%	86%	68%	95%	97%	96%	83%
Z		0.884	0.44	99%	83%	95%	78%	100%	99%	40%	31%	84%	70%	90%	75%	95%	100%	99%	100%
GT		0.918	0.41	98%	87%	93%	92%	99%	99%	42%	28%	72%	93%	93%	85%	96%	99%	98%	86%
GZ		0.927	0.46	99%	88%	97%	91%	100%	100%	45%	26%	81%	89%	95%	85%	94%	100%	99%	100%
TZ		0.943	0.41	99%	90%	97%	94%	100%	100%	43%	35%	90%	92%	95%	83%	96%	100%	99%	100%
GTZ		0.946	0.44	99%	90%	97%	95%	100%	100%	42%	33%	89%	93%	96%	83%	96%	100%	100%	100%

<sup>a</sup> Methylation value from TCGA tumor samples were computationally diluted at different concentrations into the methylation value of white blood cell DNA, to simulate the circulating tumor DNA (ctDNA) found in plasma.

<sup>b</sup> Probability threshold obtained by applying Youden's Index after logistic regression and ROC curve analysis

<sup>c</sup> Tumor samples from all 14 TCGA tumor types combined into one cohort.

Abbreviations: G = GALR1, T = TLX1, Z = ZNF154, AUC = Area Under the ROC curve, ROC = Receiver Operating Characteristics, BLCA = bladder urothelial carcinoma, BRCA = breast invasive carcinoma, COAD = colon adenocarcinoma, HNSC = head and neck squamous cell carcinoma, KIRC = kidney renal clear cell carcinoma, KIRP = kidney renal papillary cell carcinoma, LIHC = liver hepatocellular carcinoma, LUAD = lung adenocarcinoma, LUSC = lung squamous cell carcinoma, PAAD = pancreatic adenocarcinoma, PRAD = prostate adenocarcinoma, READ = rectum adenocarcinoma, STAD = stomach adenocarcinoma, UCEC = uterine corpus endometrioid carcinoma.