Additional file 1: Fig. S1 to Fig. S7 and Table S1

An optimized library for reference-based deconvolution of whole-blood biospecimens assayed using the Illumina HumanMethylationEPIC BeadArray

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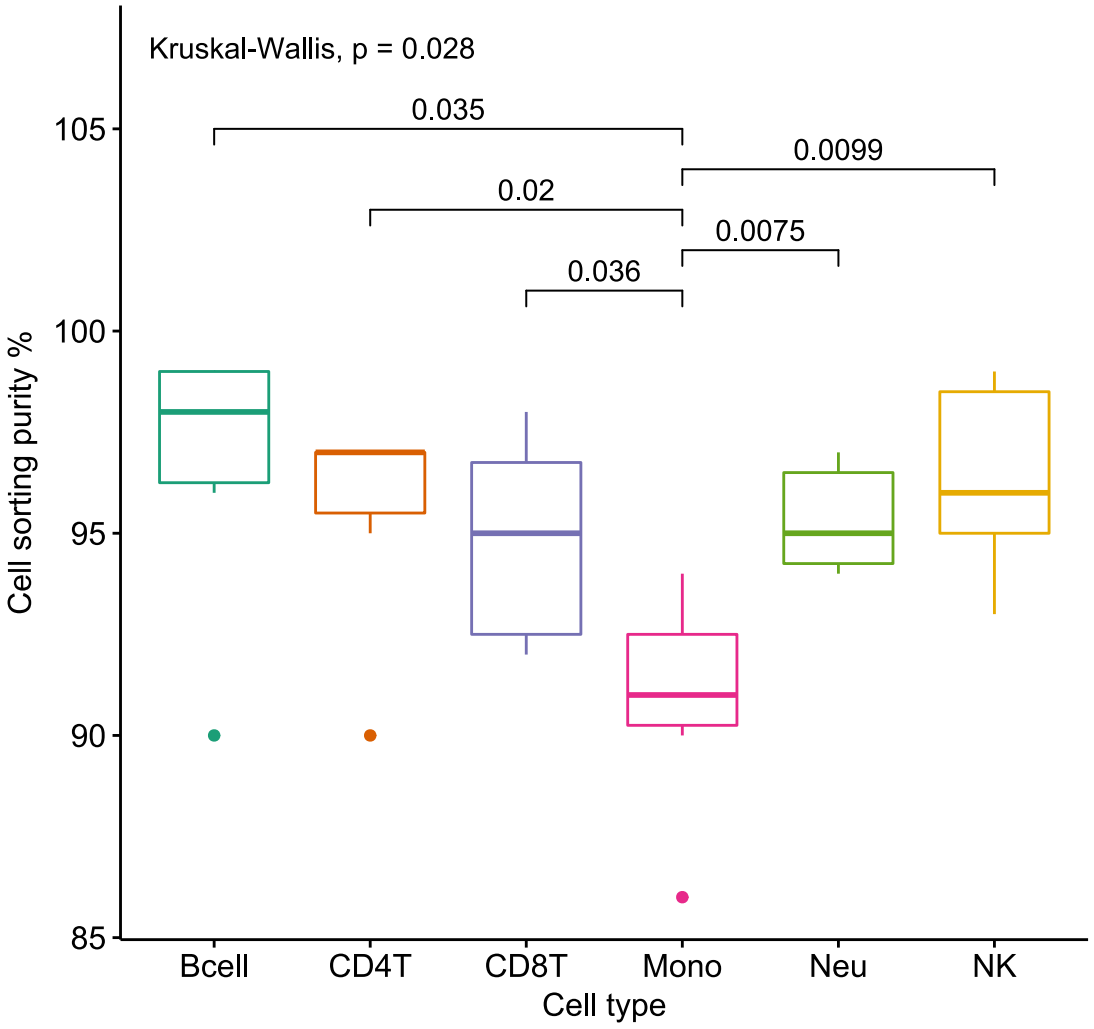
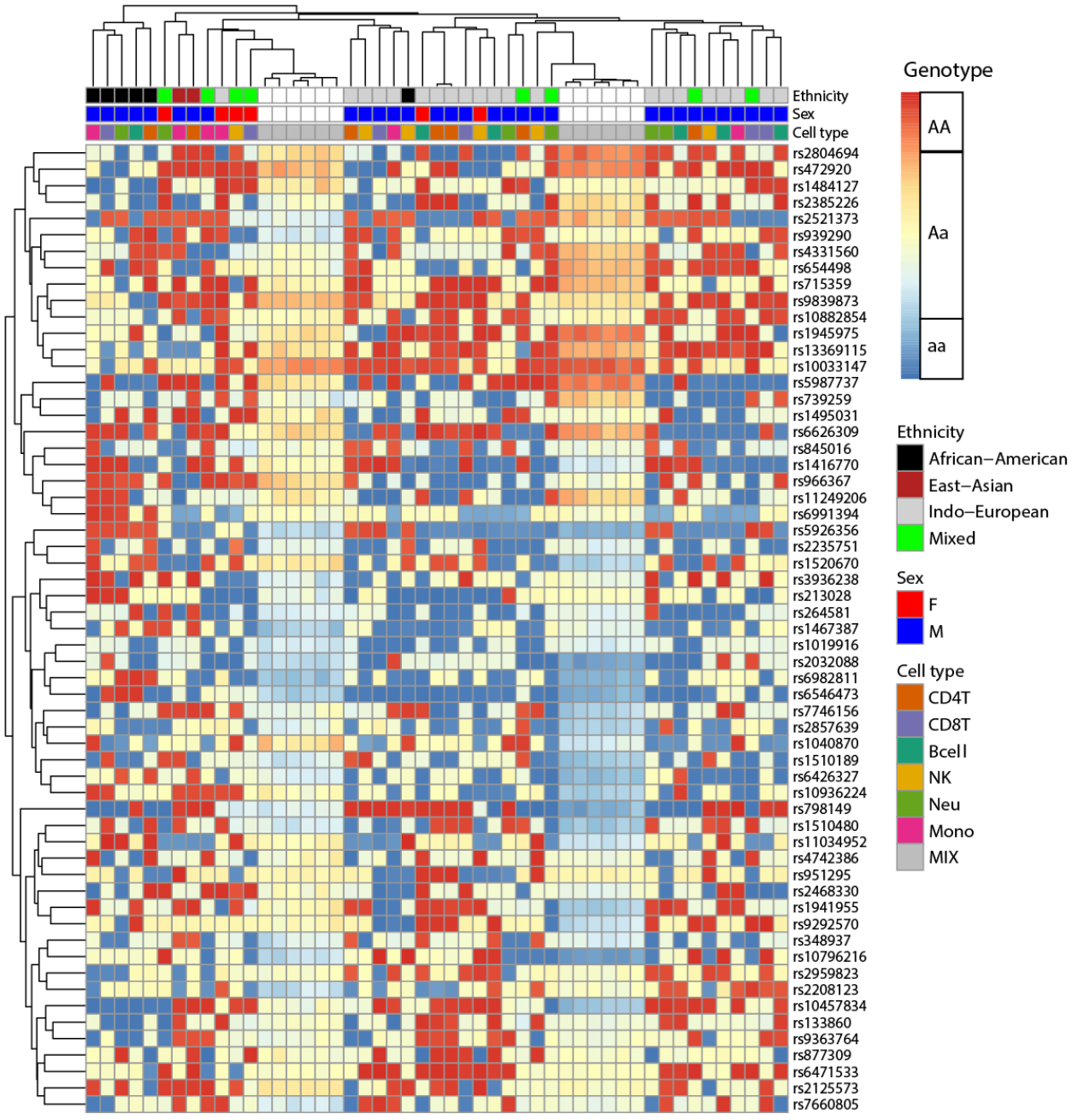
Fig. S1. Estimated cell purity by flow cytometry per cell type



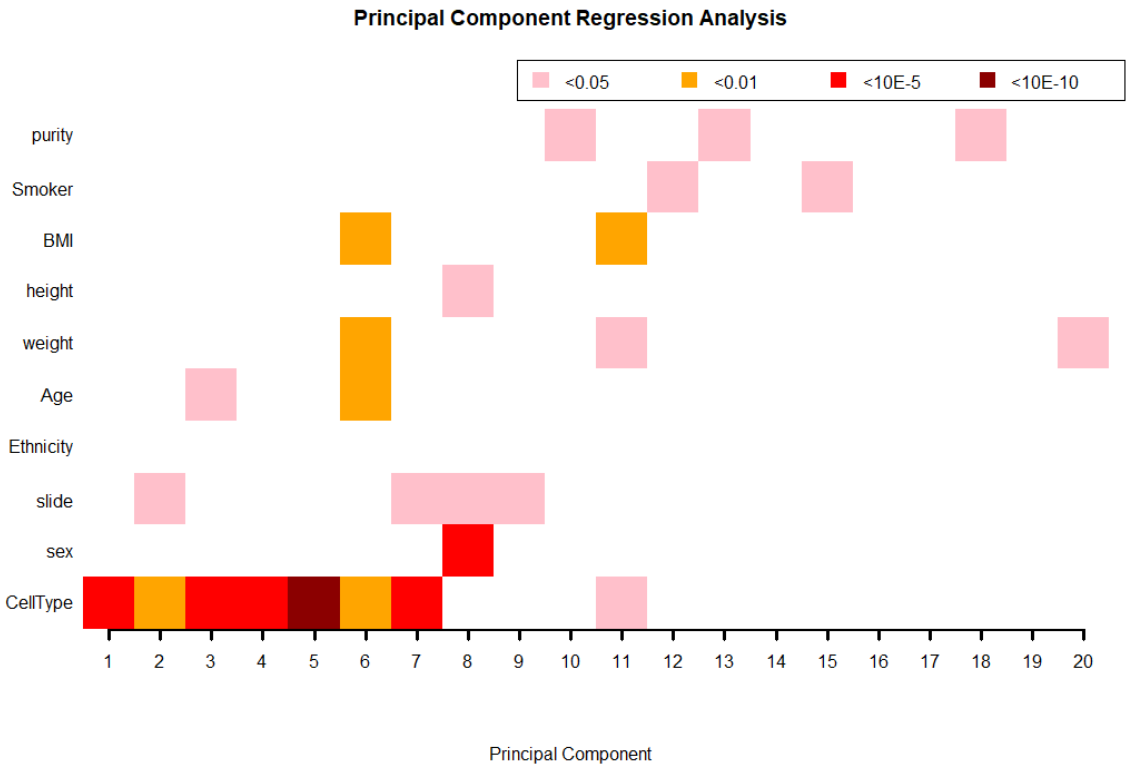
Monocyte estimates purity were statistically significant different to the other cell types.

Fig. S2. Heatmap based on a hierarchical cluster of purified cell types and cell mixtures based on the array SNPs.



Notes: 1) Most of the African American and East-Asian clustered according to the 59 control SNPs in the array. Ethnic groups correspond to a very broad categorization, for specific self-attributed ethnicity background see the database information. 2) Although the genotype scale is based on β-values, the heatmap should be interpreted as three genotype categories: red (>0.8) AA two major alleles, yellow (>0.2-≤0.8) Aa or one minor allele, and blue (≤0.2) aa or two minor alleles present on the SNP.

Fig. S3. Association between the top 20 principal components and potential confounders for DNA methylation.



Abbreviations: purity: flow sorted cell purity estimations, smoker: current vs never smoker, BMI: body mass index, age: age in years, ethnicity: African-American, East-Asian, Indo-European, Mixed (Hispanic, others).

Fig. S4. Iterative testing of different L-DMR library sizes using the IDOL optimization algorithm.

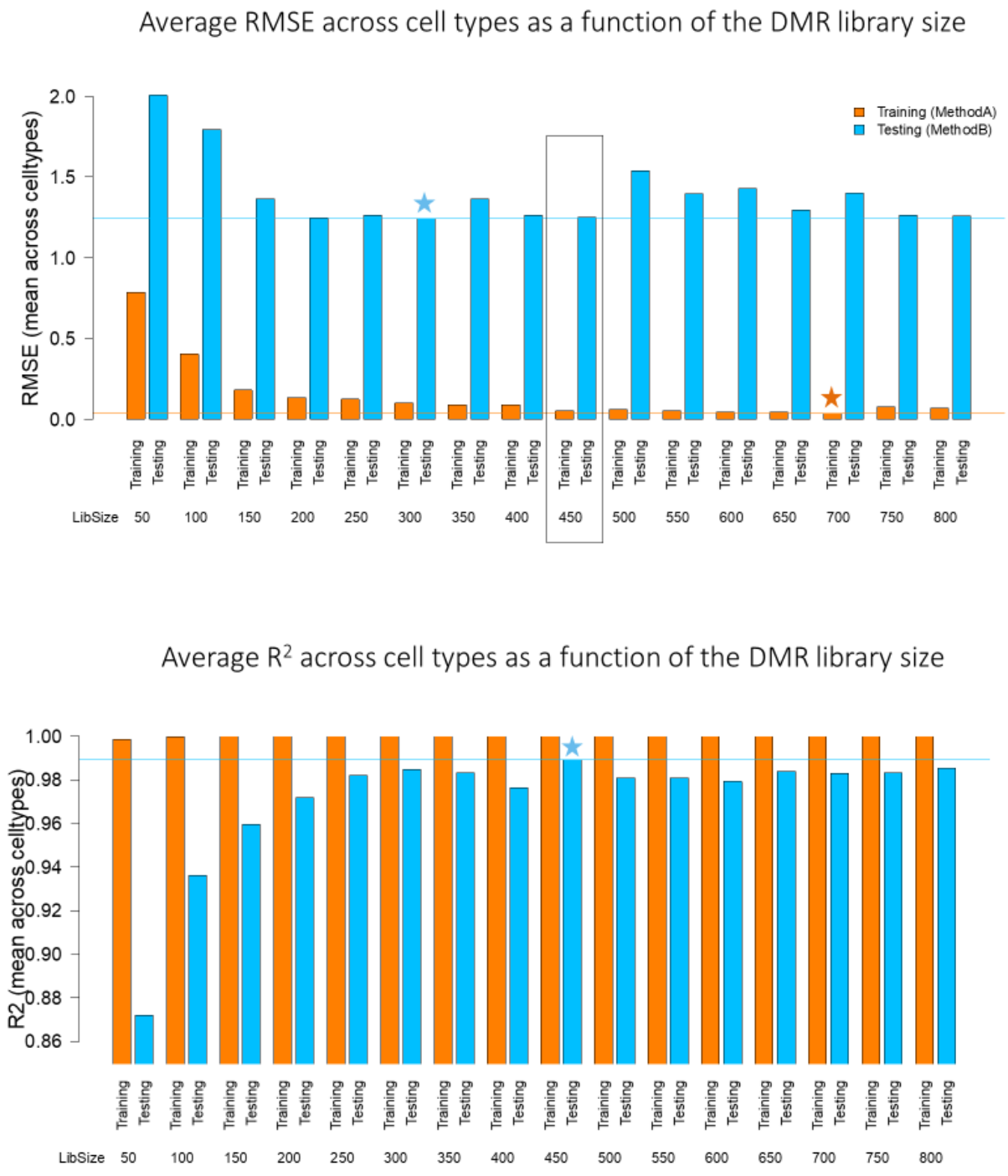


Table S1. Cell composition percentages for the artificial reconstruction samples.

Mixture Reconstruction	Sample	Cell Percentage (%)					
		Lymphoid Lineage				Myeloid Lineage	
		CD4T	CD8T	Bcell	NK	Mono	Neu
Method a	1a	13	11	16	12	23	25
	2a	7	19	19	15	19	21
	3a	6	33	8	11	19	23
	4a	16	29	7	15	22	11
	5a	11	20	20	22	10	17
	6a	18	13	26	15	22	6
Method b	1b	13	2	1	4	5	75
	2b	16	11	1	2	7	63
	3b	9	6	2	0	10	73
	4b	14	8	2	3	6	67
	5b	12	5	6	7	4	66
	6b	15	4	4	2	5	70

Fig. S5. Comparison of several probe selection methods and estimate cell proportions using constrained projection/ quadratic programming CP/QP versus the reconstructed (true) DNA fraction in the artificial DNA mixtures

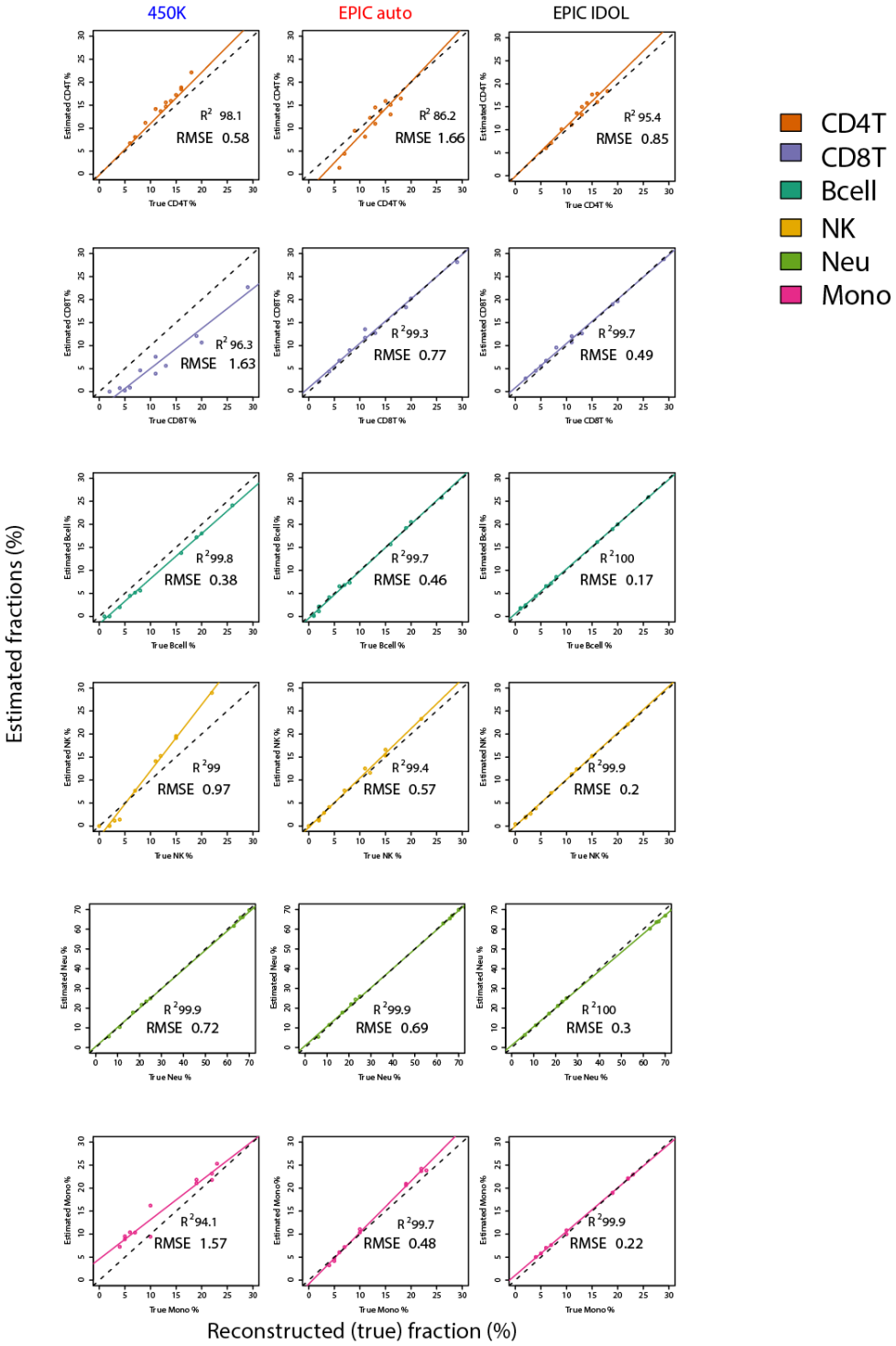
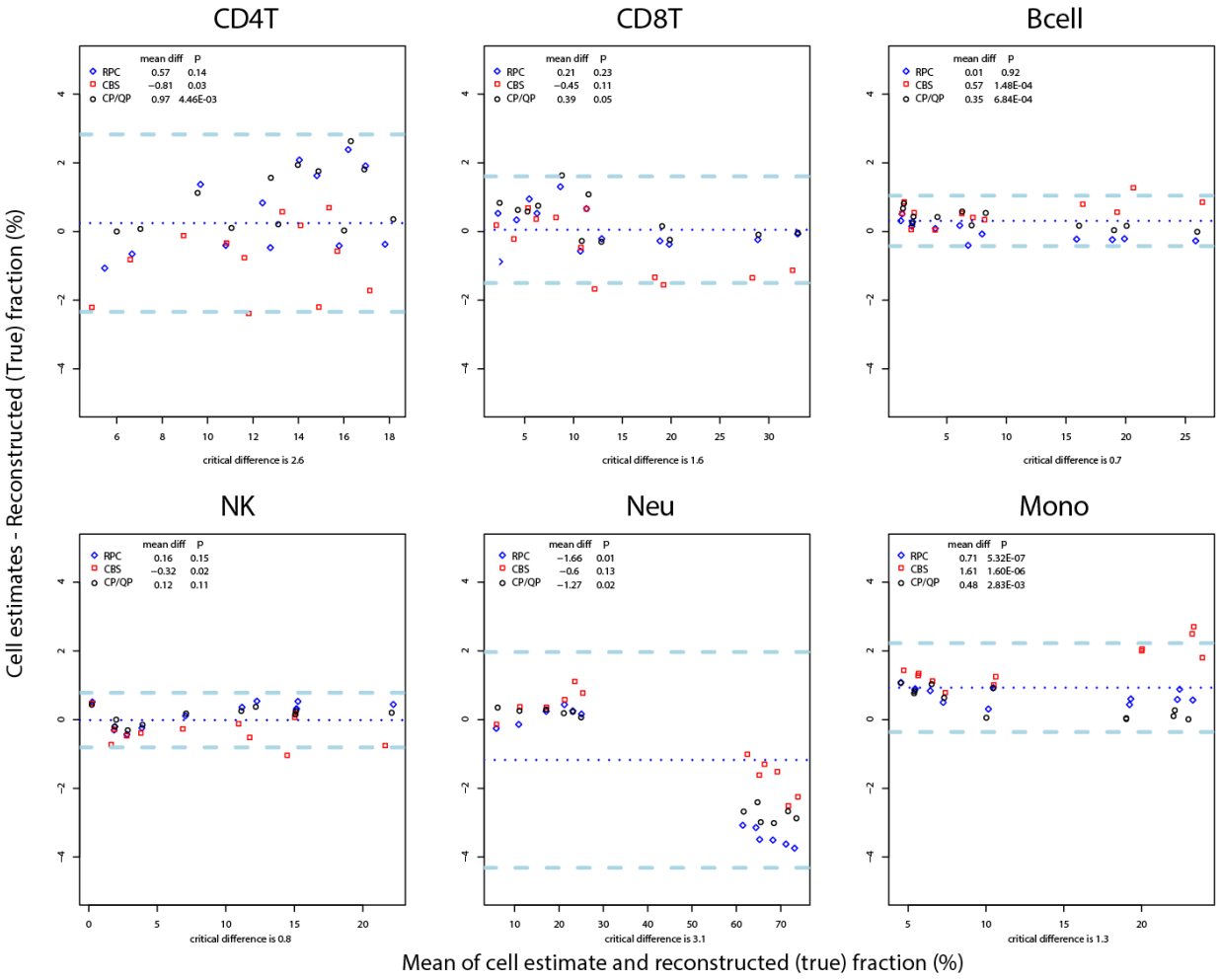


Fig. S6. Bland-Altman plots comparing the mean differences between the estimated cell fraction using three deconvolution methods and the true fraction in the artificial mixture per cell type



Notes: in the Bland Altman plots, the x axes show the mean of each estimate versus the corresponding true value, the y axes show the mean difference for Robust Partial Correlation-RPC (blue diamonds), CIBERSORT-CBS (red squares), and constrained projection/quadratic programming-CP/QP (black circles). The confidence bands (dashed horizontal lines) are 2 SD (critical 95% confidence interval difference) from the mean of the differences (dark dotted line). The mean difference per method and the paired t-test p-value are summarized on the top left of each plot.

Fig. S7. Comparison of the estimate cell proportions using constrained projection/ quadratic programming CP/QP using an IDOL optimized library restricted to the Illumina HumanMethylation 450k-450k array versus the reconstructed (true) DNA fraction in the artificial DNA mixtures arrayed in the 450k platform