FIGURE LEGENDS

FIGURE 1. Low-density array analysis of serum miRNA in pediatric CD patients. (A) Dendrogram showing hierarchical cluster analysis using 68 miRNAs detected in all samples by LDA. (B) Scatterplot of relative serum miRNA levels of 11 CD-associated miRNAs and 2 unaltered control miRNAs as determined by LDA and individual qRT-PCR. Open circles, control samples; filled circles, CD samples. ρ, Spearman's rank correlation coefficient. (C) Comparison of relative levels of CD-associated miRNAs in control and CD samples determined by individual qRT-PCR. Data is presented as fold change in comparison to controls. * $p < 0.05$

FIGURE 2. Validation of CD-associated circulating miRNAs. (A) Box-whisker plots of CD-associated serum miRNAs validated in an independent set of controls (n=32) and CD cases (n=46) as well as celiac cases (n=12) and associated controls (n=12). Box, 25-75%; whisker, upper, lower adjacent values; line, median; points, outside values. Data is presented as fold change in comparison to controls. * $p < 0.0001$; n.s., not significant. (B) Receiver operating characteristic curves of 2 CD-associated miRNAs in sera of pediatric CD patients (n=46) and healthy controls (n=32). AUC, area under the curve.

FIGURE 3. Response of CD-associated circulating miRNAs following treatment. (A) Dot plots of 2 CD-associated miRNAs in sera of pediatric CD patients at diagnosis and following 6 months of treatment (n=24). Data is presented as fold change relative to level at diagnosis. Solid lines connect data points for each patient. Dashed line, median. * $p = 0.003$; n.s., not significant, using the Wilcoxon matched-pairs signed-rank test. (B) Serum miRNA levels in pediatric CD patients at diagnosis and following 6 months of treatment (n=24). Data is presented as fold change relative to level at diagnosis. * $p = 0.003$ for miR-484 and $p = 0.037$ for miR-195 using the Wilcoxon matched-pairs signed-rank test.

SUPPLEMENTAL DIGITAL CONTENT

SUPPLEMENTAL FIGURE 1. SAM plot of 130 miRNAs detected in at least 50% of both control and CD samples by LDA. Dashed lines, upper and lower Delta; open circles, significantly elevated miRNAs; filled circles, unaltered miRNAs.

SUPPLEMENTAL FIGURE 2. Correlation between CD-associated circulating miRNAs. (A) Heat map of Spearman's rank correlation coefficient values for each serum miRNA pairing in the validation sample set. The serum levels of each miRNA were significantly correlated with the levels of any other miRNA at $p < 0.0001$. (B) Scatter plots in logarithmic scale of relative miRNA expression levels. Shown are the strongest and weakest correlations of CD-associated circulating miRNAs as determined by Spearman's rank correlation. Open circles, controls; filled circles, CD; ρ, Spearman's rank correlation coefficient.

SUPPLEMENTAL FIGURE 3. Analysis of CD-associated circulating miRNAs using internal reference miRNAs. (A) Two miRNAs identified by LDA as unchanged between control and CD samples (n=6). Fold change presented as relative to controls. (B) CD-associated circulating miRNAs in CD samples as determined using either exogenous miRNAs (spike) or miR-150 and miR-342-3p (internal) to normalize data (n=46). No significant differences between normalization methods were seen for any CD-associated miRNA. Fold change presented as relative to controls.

Supplemental Figure 1

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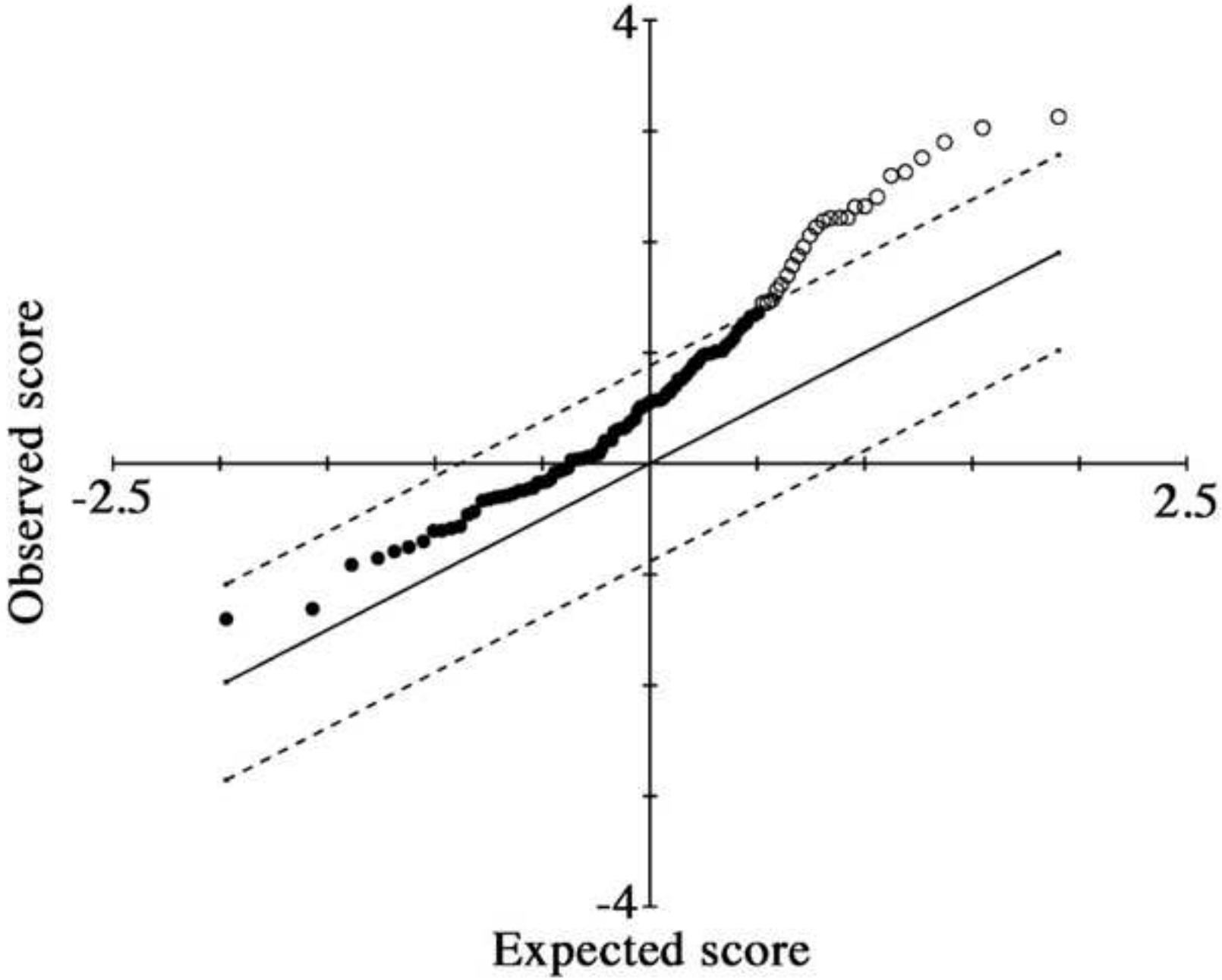

Supplemental Figure 2

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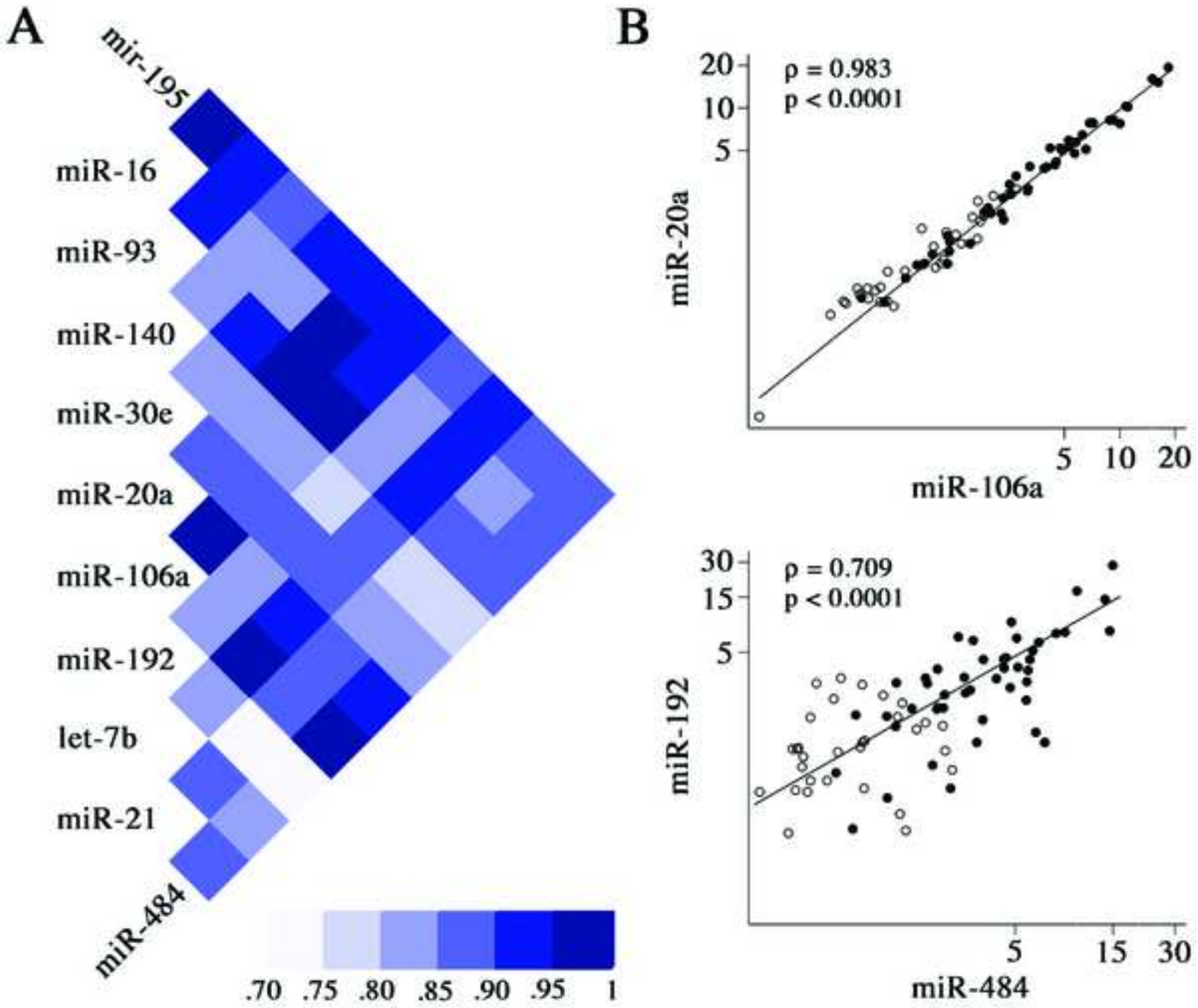

Supplemental Figure 3

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