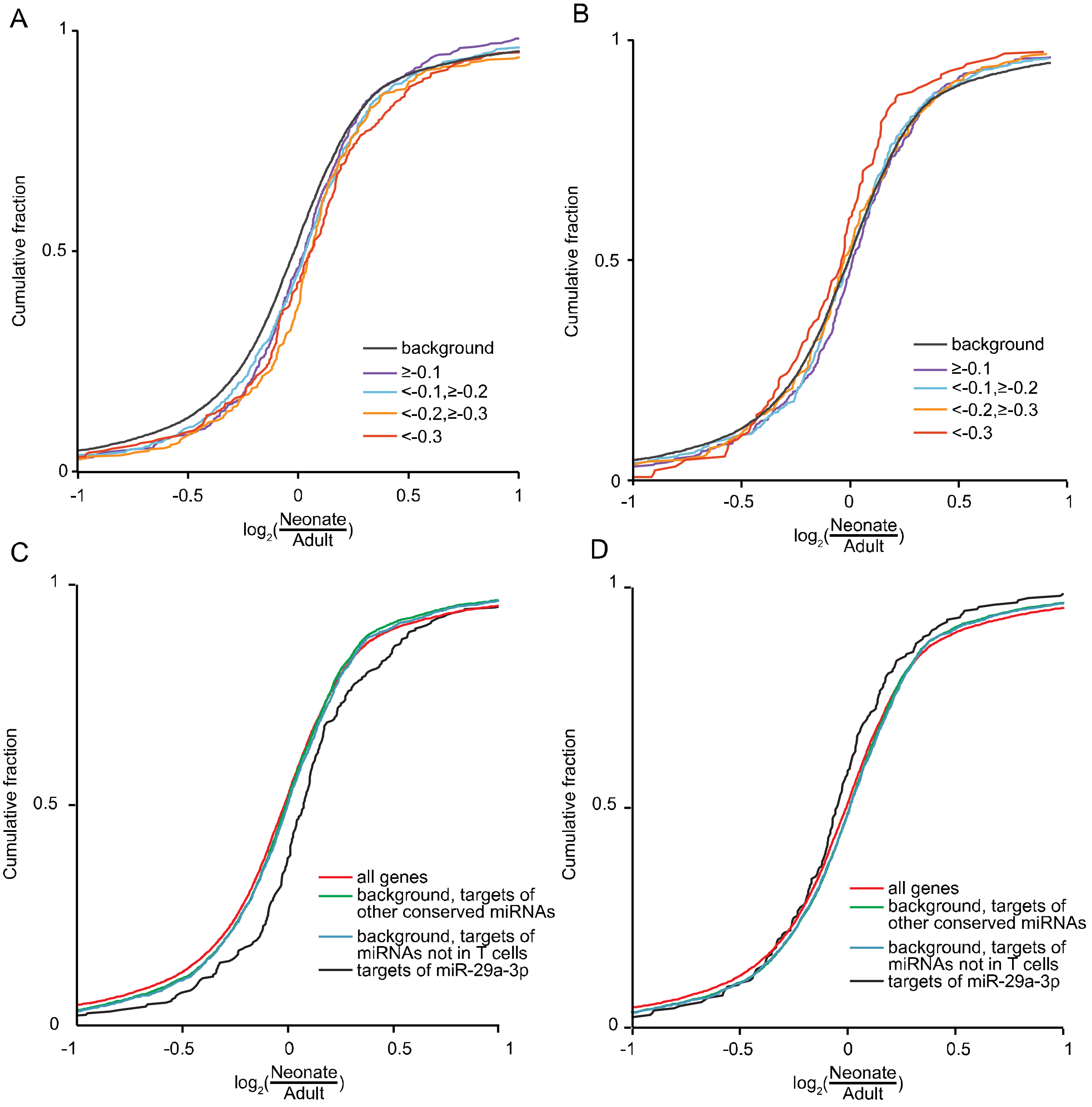

Figure S5 miRNA targeting analysis. (A and B) Targets of miR-29a-3p (A) and miR-130b-3p (B) were binned by context score, regardless of conservation status, to confirm that stronger targets were more repressed by their cognate miRNA than were weaker targets. The background set used was all well-expressed genes, excluding targets for the miRNA being tested. For miR-29a-3p, all context score bins are significantly different from background (context ≥-0.1, $p<0.05$; context <-0.1, ≥-0.2, $p<0.005$; context <-0.2, ≥-0.3, $p<10^{-6}$; context <-0.3, $p<0.05$). For miR-130b-3p, targets with context scores <-0.3 were significantly different from background ($p<0.05$). (C and D) MicroRNA targeting signatures are robust to alternative background gene sets. We tested background sets consisting of all well-expressed genes (red), well-expressed genes that are strong targets of broadly conserved miRNAs (defined in Friedman *et al.* 2009, green), and well-expressed genes that are targets of broadly conserved miRNAs excluding those well-expressed in CD8+ T cells. Compared to all background sets, strong miR-29a-3p targets (C, gray) have significantly different expression ($p<0.0005$). Similarly, strong miR-130b-3p targets (D, gray) have significantly different expression ($p<0.05$) when compared to all different background sets tested.