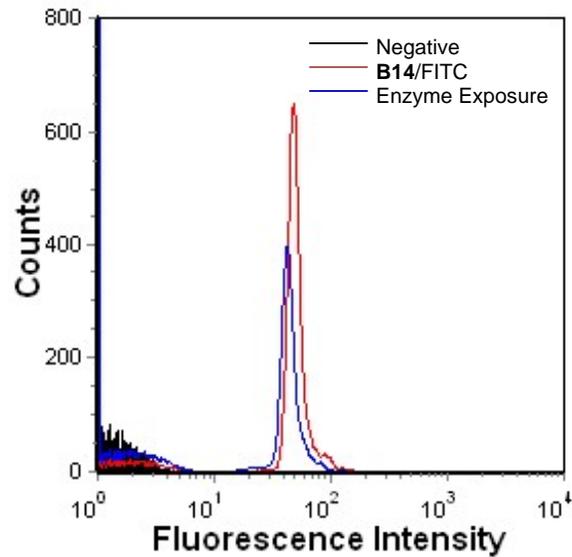
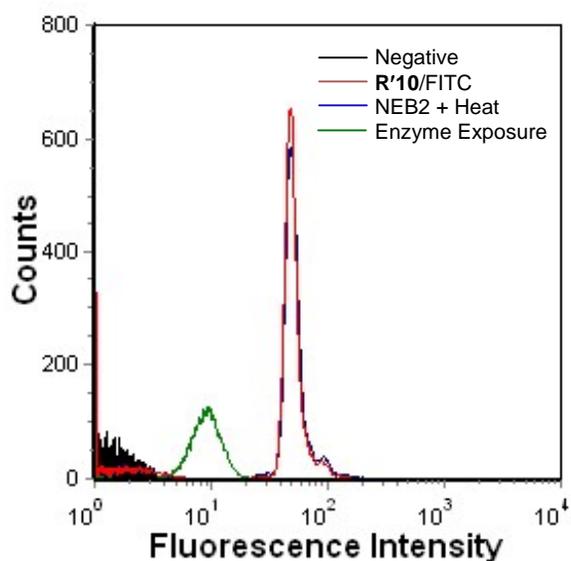


Supporting Information



Supplementary Figure 1: Representative histogram of fluorescence intensities associated with **A20**-functionalized microspheres hybridized to FITC-labeled **B14** target strands (**B14/FITC**) and then incubated with restriction enzyme *AluI* (enzyme exposure). Note: The **A20:B14** duplexes do not possess the recognition motif for cleavage by *AluI*. The negligible shift in fluorescence intensity following incubation indicates that nonspecific cleavage by *AluI* is negligible. The negative control is a suspension of 100% **A20**-functionalized microspheres alone (negative).



Supplementary Figure 2: Representative histogram of fluorescence intensities associated with **R10**-functionalized microspheres hybridized to FITC-labeled **R'10** targets before (**R'10/FITC**) and after incubation with *AluI* (enzyme exposure). Note: The **R10:R'10** duplexes do possess the recognition motif for cleavage by *AluI*. The decrease in fluorescence intensity following enzyme incubation is attributed to specific clipping by *AluI*. One control experiment (NEB2 + Heat) involves the incubation in identical buffer conditions as the enzyme-digested samples, but with no *AluI* present. The identical peak values between this control and the hybridized sample prior to digestion (**R'10/FITC**) indicates negligible changes occur in duplex density due to **R10:R'10** duplex dissociation. The negative control is a suspension of 100% **R10**-functionalized microsphere alone (negative).