Supporting Information

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SI Materials and Methods

For cDNA synthesis, 1 μL of 100 μM selective primer mix was combined with 1 μL (500 ng) of template and 3 μL of water. The mix was heated at 65 °C for 5 min and chilled at 4 °C before adding 5 μL of reverse transcription master mix (2 μL of 5× first-strand buffer, 0.5 μL of 100 mM DTT, 2 μL of 10 mM dNTP, and 0.5 μL of SuperScript III enzyme). The reaction mixture was incubated at 40 °C for 90 min and cooled to 4 °C. For second-strand synthesis, 10 μL of the first-strand reaction was added to 65 μL of the nick-translation mix (45.5 μL of water, 15 μL of 5× second-strand buffer, 1.5 μL of 10 mM dNTP, 0.5 μL of *Escherichia coli* DNA Ligase, 2.0 μL of *E. coli* DNA Pol I, 0.5 μL of *E. coli* RNase H) (New England Biolabs, Inc.). The reaction mixture was incubated at 16 °C for 2 h and was stopped by adding 25 μL of 0.2 M EDTA.

DNA was purified in 35 μL elution buffer by using a QIAquick PCR Purification kit (Qiagen, Inc.).Ten microliters of the eluate was added to 3 μL of quick-blunting mix (1.25 μL 10× buffer, 1.25 μL 1 mM dNTP, 0.5 μL Blunting enzyme mix) (New England Biolabs, Inc.). The reaction mixture was incubated at 23 °C for 30 min and at 70 °C for 10 min and then was chilled before 1 μL of 12.5 μM forward and reverse adaptor mix was added. Forward adaptors were engineered with three-base barcode tags to allow sample multiplexing. The sample-adaptor mix was added to 16.5 μL of the ligation mix (15 μL of 2× Quick Ligase Buffer and 1.5 μL of Quick ligase) (New England Biolabs, Inc.) and was incubated at 23 °C for 15 min. For PCR amplification, 10 μL of the ligated sample was combined with 90 μL of PCR mix [39 μL of water, 10 μL of 10× reaction buffer (+ Mg), 10 μL of 25 mM $MgCl_2$, 5 μL of DMSO, 5 μL of 10 mM dNTPs, 10 μL of 10 μM forward primer, 10 μL of 10 μM reverse primer, 1 μL of Taq DNA Polymerase] (New England Biolabs, Inc.). The nick resulting from the previous adaptor ligation step was repaired by incubating the samples at 72 °C for 2 min and at 95 °C for 2 min followed by 20 cycles of 95 °C for 30 s, 60 °C for 30 s, 72 °C for 1 min and then at 72 °C for 5 min to polish ends before cooling to 4 °C. Double-stranded DNA was purified using AMPure XP magnetic beads (Agencourt).

Other Supporting Information Files

Table S1 (DOC)
Table S2 (DOCX)
Dataset S1 (XLSX)