CLAIMS

1. A composition for nucleic acid hybridization comprising:

a first polynucleotide library;

a second polynucleotide library, wherein at least one polynucleotide in the first library is at least partially complimentary to at least one polynucleotide of the second library; and

an additive, wherein the additive reduces off-target hybridization of the at least one polynucleotide of the first library with the at least one polynucleotide of the second library by decreasing a local concentration of the first polynucleotide library or the second polynucleotide library at an air-liquid interface.

2. The composition of claim 1, wherein the additive is mineral oil, a nucleotide triphosphate, polyether, or urea.
3. The composition of any one of claims 1-2, wherein the additive is a hydrocarbon comprising at least six carbon atoms.
4. The composition of any one of claims 1-3, wherein the additive is silicon oil.
5. The composition of claim 1, wherein the oil is derived from plant sources.
6. The composition of any one of claims 1-4, wherein the composition further comprises dimethyl sulfoxide.
7. The composition of any one of claims 1-5, wherein the composition does not comprise a formamide.
8. The composition of any one of claims 1-6, wherein the size of the first polynucleotide library is less than 10 million bases.
9. The composition of any one of claims 1-6, wherein the size of the first polynucleotide library is less than 1 million bases.
10. The composition of any one of claims 1-6, wherein the size of the first polynucleotide library is less than 0.5 million bases.
11. The composition of any one of claims 1-10, wherein the first polynucleotide library comprises as least one exon sequence.
12. The composition of any one of claims 1-11, wherein the first polynucleotide library comprises polynucleotides encoding for at least 10 genes.
13. The composition of any one of claims 1-11, wherein the first polynucleotide library comprises polynucleotides encoding for at least 100 genes.

14. The composition of any one of claims 1-13, wherein the first polynucleotide library comprises at least one genomic fragment.
15. The composition of any one of claims 1-13, wherein the first polynucleotide library comprises RNA, DNA, cDNA, or genomic DNA.
16. The composition of any one of claims 1-15, wherein the first polynucleotide library comprises genomic DNA.
17. The composition of any one of claims 1-16, wherein the additive decreases off-target binding by at least 10%.
18. The composition of any one of claims 1-16, wherein the additive decreases off-target binding by at least 20%.
19. The composition of any one of claims 1-16, wherein the additive decreases off-target binding by at least 30%.
20. The composition of any one of claims 1-19, wherein the off-target binding is random off-target binding.