

**Supplementary Table 1.** Oligonucleotides used in this study

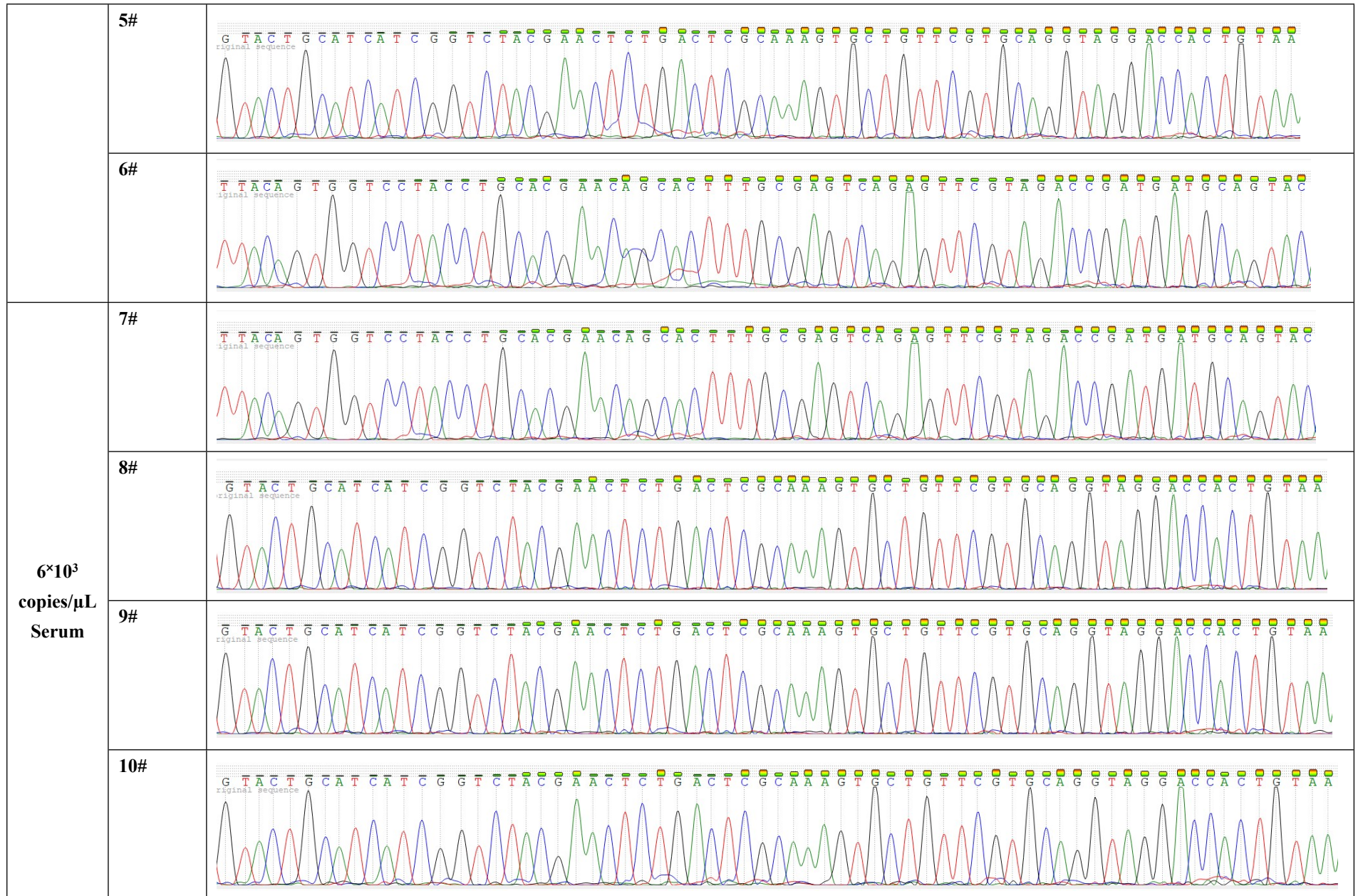
miRNA	oligonucleotides	Sequence (5'-3')
miR-16	Sequences	UAGCAGCACGUAAAUAUUGGCG
	Primer-F	GTACTGCATCATCGGTCTAC
	Primer-R	CCTACAGACTACGCCAATAT
	Linker	GTACTGCATCATCGGTCTACGTACCAGAGCCAAGTAGCAGCACGT-POOH
	Probe	FAM-CAGAGCCAAGTAGC-MGB
cel-miR-39	Sequences	UCACCGGGUGUAAAUCAGCUUG
	Primer-F	GTACTGCATCATCGGTCTAC
	Primer-R	GAGTAACAACGCAAGCTGATTT
	Linker	GTACTGCATCATCGGTCTACGAACCAACTCAACATCACCGGGTGT-POOH
	Probe	FAM-CCAAGTCAACATCA-MGB
miR-93	Sequences	CAAAGUGCUGUUCGUGCAGGUAG
	Primer-F	GTACTGCATCATCGGTCTAC
	Primer-R	TTACAGTGGTCCTACCTGCACG
	Linker	GTACTGCATCATCGGTCTACGAACTCTGACTCGCAAAGTGCTGTTC-POOH
	Probe	FAM-TCTGACTCGCAAAG-MGB
miR-21	Sequences	UAGCUUAUCAGACUGAUGUUGA
	Primer-F	GTACTGCATCATCGGTCTAC
	Primer-R	CTCAGCGTCTCAACATCAGT
	Linker	GTACTGCATCATCGGTCTACGAACATGTCCGCCTAGCTTATCAG-POOH
	Probe	FAM-ATGTCCGCCTAGCT-MGB

**Supplementary Table 2.** The results of LoD analysis for serum direct SMOS-qPCR

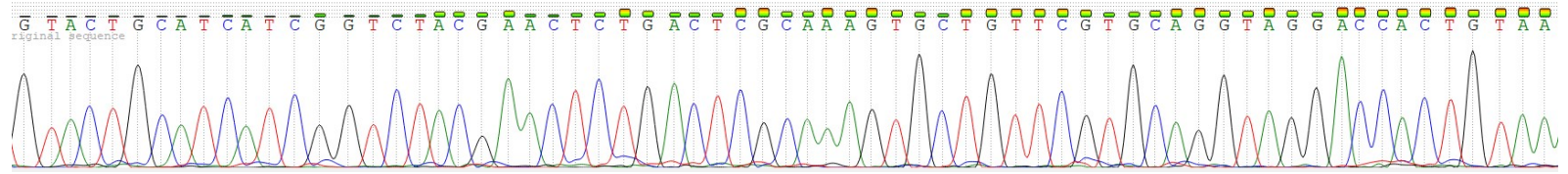
Concentration	Replicates	Positive number (n)	Positive rate (%)
6×10 <sup>3</sup> copies/μL	20	18	90.0
3×10 <sup>3</sup> copies/μL	20	7	35.0
1.5×10 <sup>3</sup> copies/μL	20	1	5.0

**Supplementary Table 3.** The Sanger sequencing results of  $6 \times 10^4$  copies/ $\mu\text{L}$  and  $6 \times 10^3$  copies/ $\mu\text{L}$  4-plex miRNAs with the treated serum as background.

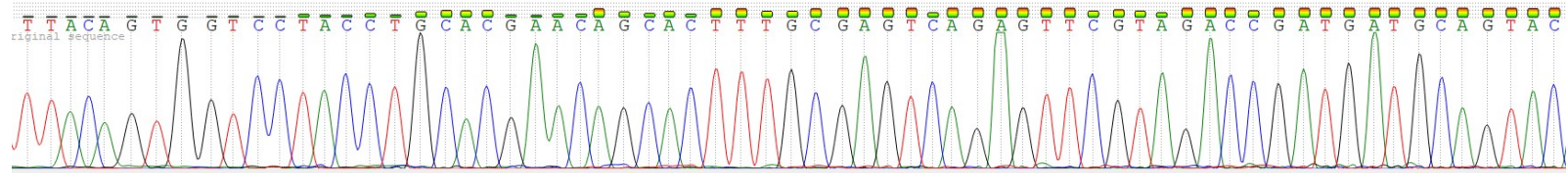
Sample	ID	Sequence (5'-3')
Reference	Sense strand	GTACTGCATCATCGGTCTACGAACTCTGACTCGCAAAGTGCTGTTTCGTGCAGGTAGGACCACTGTAA (miR-93)
	Antisense strand	TTACAGTGGTCCTACCTGCACGAACAGCACTTTGCGAGTCAGAGTTCGTAGACCGATGATGCAGTAC (miR-93)
$6 \times 10^4$ copies/ $\mu\text{L}$ Serum	1#	
	2#	
	3#	
	4#	

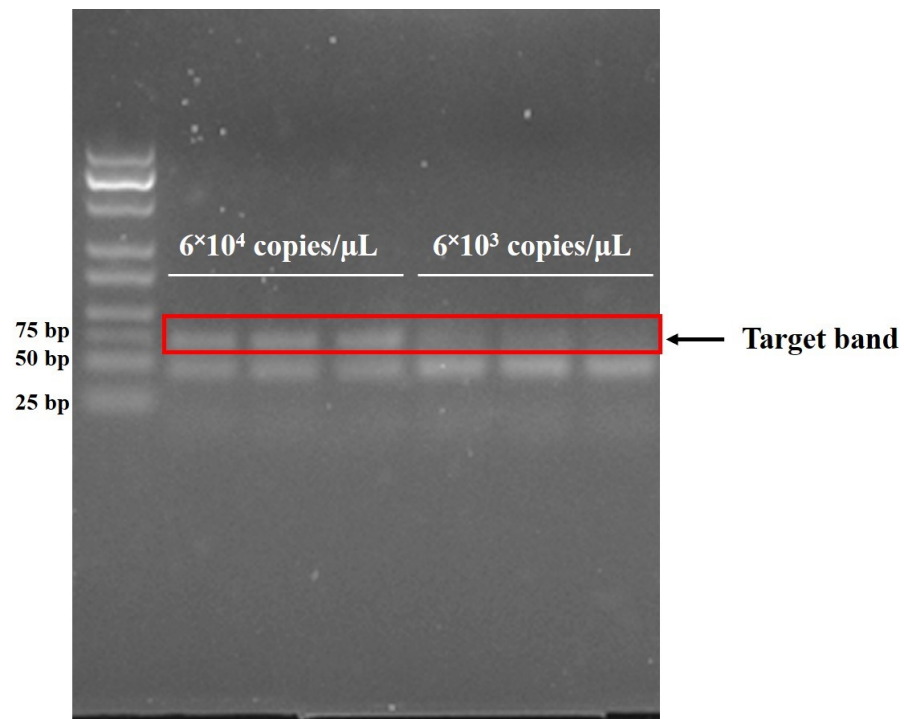


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**Figure S1.** The agarose gel electrophoresis analysis for  $6 \times 10^4$  copies/ $\mu\text{L}$  and  $6 \times 10^3$  copies/ $\mu\text{L}$  4-plex miRNAs with the treated serum as background.