

Supporting information

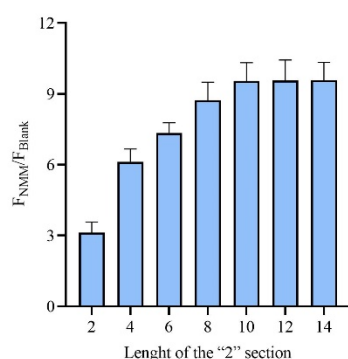


Figure S1. Fluorescence signal-to-background (F_{NMM}/F_{Blank}) of the approach when detecting exosomes with length of "2" section in L probes.

Table S1. All of the oligonucleotides used in this work.

Title	Sequences (5' to 3')
L1	AAG CGT CTT TTT TGC GTT GTT AAT TTA AGA CGC TTG ACG CTA ATA GTT TTT TTT TTT TTA TAT ACA CCC CAC CTC GCT CCC GTG ACA CTA ATG CTA TT
L2	Cholesterol- GA CCC TAA GCA TAC ATG CTC ACT GAC GCT AGG TTT TTT TT TTT TTT TCT ATT AGC TCA AGC GTC TTA AAT TCT AAC CGT ATC GTG C
H1	CTA ACC GTA TCG TGC TTT TTT TTT TTT GCA CGA TAC GGT TAG AAT ATT AAC AAC GCA
G-rich	GCA CGA TAC GGT TAG AGG GTA GGG CGG GTT GGG A
"9"	TCC CAA CTT TCT AAC CGT AT
H2 probe	CGG TTA GAA AGT TGC TAA CCG TAT CGT GCC AAC TTT CTA A

Table S2. A brief comparisons of the method with former exosomes detection methods.

Name	Principle	Recognizing target	Signal mode	LOD	Detection range	Anti-interference capability	Label-free	Ref
The method	Dual recognition+ chain displacement+ proximity ligation	CD63; Lipid bilayer	Fluorescence	36 particles/ μL	10^2 to 10^6 particles/ μL	Yes	Yes	
CRISPR-Cas based	CD63 aptamer based recognition+ CRISPR-Cas12a system	CD63 protein	Fluorescence	10^3 particles/ μL	3×10^3 to 6×10^7 particles/ μL	No	No	[1]
Allosteric probe	CD63 aptamer based recognition+ CRISPR-Cas12a system+ reverse transcription	CD63 protein	Fluorescence	10^2 particles/ μL	10^2 to 10^6 particles/ μL	No	No	[2]
AcmPLA	Dual recognition+ chain displacement+ proximity ligation RCA	CD63; Lipid bilayer	Fluorescence	10^2 particles/ μL	10^2 to 10^6 particles/ μL	Yes	No	[3]
Colorimetric biosensor	CD63 aptamer based recognition+ hybridization chain reaction	CD63;	Color change	1.6×10^2 particles/ μL	1.4×10^3 to 2.8×10^5 particles/ μL	No	Yes	[4]

RCA, rolling circle amplification.

References:

1. Zhao X, Zhang W, Qiu X, Mei Q, Luo Y, Fu W. 2020. Rapid and sensitive exosome detection with CRISPR/Cas12a. *Anal. Bioanal. Chem.* **412**: 601-609.
2. Zhao X, Zeng L, Mei Q, Luo Y. 2020. Allosteric Probe-Initiated Wash-Free Method for Sensitive Extracellular Vesicle Detection through Dual Cycle-Assisted CRISPR-Cas12a. *ACS Sens.* **5**: 2239-2246.
3. Zhao X, Luo C, Mei Q, Zhang H, Zhang W, Su D, *et al.* 2020. Aptamer-Cholesterol-Mediated Proximity Ligation Assay for Accurate Identification of Exosomes. *Anal. Chem.* **92**: 5411-5418.
4. Zhang Y, Wang D, Yue S, Lu Y, Yang C, Fang J, *et al.* 2019. Sensitive Multicolor Visual Detection of Exosomes via Dual Signal Amplification Strategy of Enzyme-Catalyzed Metallization of Au Nanorods and Hybridization Chain Reaction. *ACS Sens.* **4**: 3210-3218.