Table S1. Clinical sample detection by SERS-LFIA using SERS tags.

NO.	Target	SERS tags	Biorecognition molecules	Sensitivity enhancement	LOD	Detection time	Ref.
1.	H1N1/SARS-CoV-2/RSV	Fe_3O_4@Au		100-fold increase	85 copies/mL,8 pg/mL, 8pg/mL, respectively	30 min	[1]
2.	Aflatoxin B_1/ zearalenone/ fumonisin B_1/ deoxynivalenol/ ochratoxin A/ toxin	Au@Ag core-shell		The results were consistent with that of LC-MS	0.96pg/mL, 6.2 pg/mL, 0.26 ng/mL, 0.11 ng/mL, 15.7 pg/mL, 8.6 pg/mL, respectively	20 min	[2]
3.	Anti-SARS-CoV-2 IgM and IgG	SiO_2@Ag	S protein	800-fold increase		25 min	[3]
4.	Ricin, staphylococcal enterotoxin B, and botulinum neurotoxin type A	SiO_2@Au		100-fold increase	0.1, 0.05, and 0.1 ng/mL, respectively	15min	[4]
5.	*Salmonella typhimurium* , *Staphylococcus aureus*	Fe_3O_4@Au			12 and 9 cells/mL, respectively	30 min	[5]

6.	Fumonisin B1, aflatoxin B1， zearalenone	GO@Au-Au		500-fold increase	0.529, 0.745, 5.90 pg/mL, respectively	20 min	6
7.	*Salmonella typhimurium, Escherichia coli,*	GO@Au/Ag			9 cells/mL level	20 min	7
8.	*Escherichia coli O157:H7*	Prussian blue nanoparticles			10^2 cfu/mL		8
9.	HIV-1 DNA	SiO_2@Au			0.3 fM	1 h	9
10.	Two SARS-CoV-2	SARS-CoV-2		22- and 225-fold increase, respectively	23 and 2 pg/mL, respectively,	30 min	10
11.	*Staphylococcus aureus*	Au–Ag@Pt	4-MPBA	330-fold, 37-fold, and 55-fold	3 CFU/mL for SERSLFIA,27 CFU/mL for PT-LFIA, and 18 CFU/mL for CL-LFIA,	12min	11
12.	*Campylobacter jejuni*	AuNR@Pt			50 cfu/mL		12
13.	SARS-CoV-2 N protein antibody	Fe_3O_4-Ag^{MBA}@Au NPs	nucleocapsid	three orders of magnitude	0.08 pg/mL	20 min	13
14.	SARS-CoV-2 IgG	Ag^{MBA}@Au		A sensitivity four	0.22 pg/mL	20 min	14

				orders of magnitude higher			
15.	COVID-19	AuNPs		One increse in the order of magnitude	1 ng/mL	15 min	15
16.	SARS-CoV-2 neutralizing antibodies	Au-Ag HNSs		10-fold increase	20 ng/mL	15 min	16
17.	SARS - CoV - 2	AuNPs			1 ng/ml	15 min	17
18.	*Clostridium difficile*	AuNPs			0.01 pg/μL	20 min	18
19.	SARS-CoV-2 and influenza A virus	AuNPs		10 and 40 times more sensitive than the ELISA			19
20.	SARS-CoV-2 S1 protein	Gold nanocrown		3 orders of magnitude increase	57.21 fg/mL	15min	20
21.	Staphylococcus aureus, Pseudomonas aeruginosa, and Salmonella typhimurium	2D GFe–DAu–D/M	MPBA		10 cells mL^{-1}	15min	21
22.	Influenza A, parainfluenza 1,	Ag^{NBA}@Au NPs	nucleic acids		0.031 pM, 0.030	7 min	22

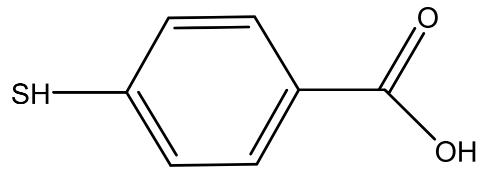
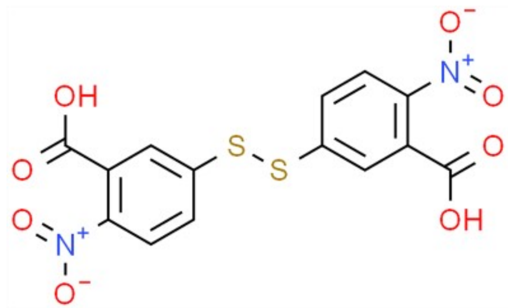
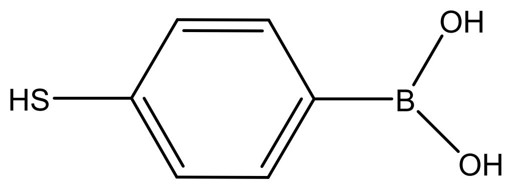
	parainfluenza 3, respiratory syncytial virus, coxiella burnetii, legionella pneumophila, influenza B, parainfluenza 2, adenovirus, chlamydophila pneumoniae, and mycoplasma pneumoniae	Ag^{MB}@Au NPs			pM, 0.038 pM, 0.038 pM, 0.040 pM, 0.039 pM, 0.035 pM, 0.032 pM, 0.040 pM, 0.039 pM, and 0.041 pM, respectively		
23.	Carcinoembryonic antigen neuron-specific enolase	Au@MBA@Ag @CEA， Au@MMTAA@ Ag@NSE NPs	Antibody	3.2-fold	0.032 and 0.046 ng/mL	15 min	[23]
24.	H1N1, SARSCoV-2 and RSV	Fe_3O_4/DTNB@Au/DTNB	Antibody	100 and 5-500 times	85 copies mL^{-1}, 8 pg mL^{-1}, and 8 pg mL^{-1}	15 min	[1]
25.	SARS-CoV-2 and influenza a virus	MGITC-labeled AuNP	Antibody	10 times and 40 times	5.2 PFU/mL and 23 HAU/mL,		[19]
26.	*E. coli*	AuNF-PMBA	Antibody			45 min	[24]

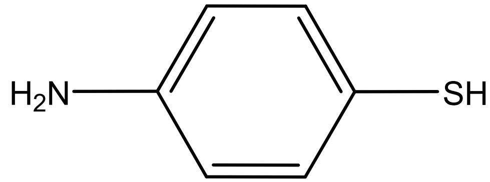
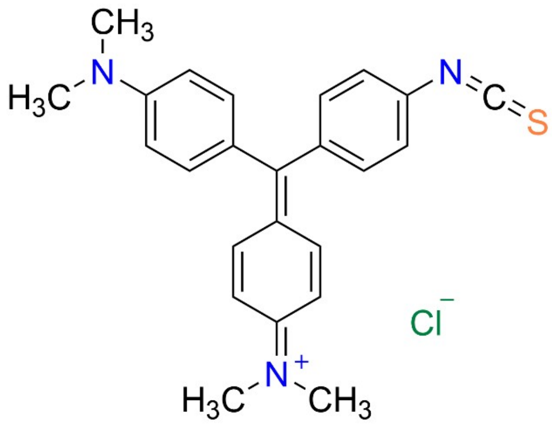
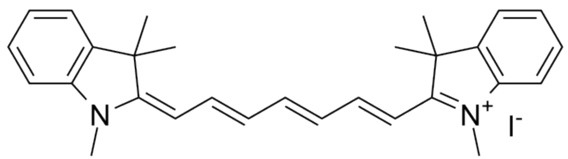
		NMs		three orders of magnitude lower	10^3 cfu/mL in colorimetric mode, 10^2 cfu/mL in Raman mode and 10^2 cfu/mL in photothermal mode		
27.	Cardiac troponin I , N-terminal natriuretic peptide precursor	Au@PS	Monoclonal antibodies	10–20 folds	1 pg/mL and 10 pg/mL	15 min	[25]
28.	Amyloid A and C-reactive protein	Fe_3O_4@Au	Antibody	100-fold and 1000-fold	0.1 ng/mL and 0.01 ng/mL	30 min	[26]
29.	Alzheimer's disease biomarkers (Aβ42 and Aβ40)	Au@SiO_2	Antibody	10 times	15.3 and 16.8 fg mL^{-1}		[27]
30.	Prostate-specific antigen	Au@MBN@Ag@PSA	Antibody	3.5-fold increase	0.08 ng/mL	20 min	[28]
31.	*Mycoplasma pneumoniae*	Au/DTNB@Ag/DTNB		100 times	0.1 ng mL^{-1}		[29]
32.	SARS-CoV-2 S and NP antigens	Fe_3O_4@Au (Mag@Au)	Antibody	22 and 225-fold	23 pg mL^{-1} and 2 pg mL^{-1}	30 min	[10]

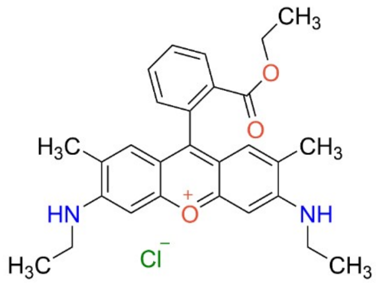
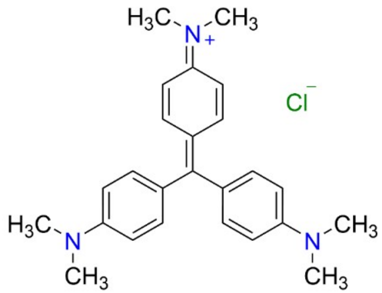
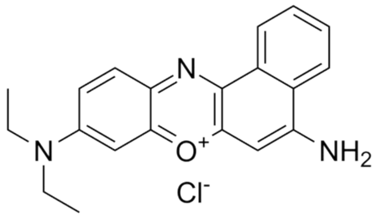
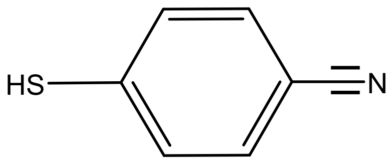
33.	*Streptococcus pneumoniae* and *influenza A virus*		Antibody	172 and 312 times	16 cells/mL and 29 pfu/mL		30
34.	Dehydroepiandrosterone	DTNB-Au@Pt@Ag NPs	Antibody	100-fold, 200-fold and 7 000-fold	1.0 ng mL^{-1} for CM-LFIA, 0.42 ng mL^{-1} 1 for PT-LFIA, and 0.013 ng mL^{-1} for SERS-LFIA	5 min	31
35.	Anti-SARS-CoV-2 IgM and IgG antibodies	GERTs	Antigen	100 times	1 ng/mL and 0.1 ng/mL	15 min	32
36.	Matrix metalloproteinase-9, S100 calcium-binding protein B protein, and neuro-specific enolase	Gold nanoparticles	Antibody		0.01 pg/mL		33
37.	Prostate specific antigen, alpha-fetoprotein, and for carcinoembryonic antigen	Fe_3O_4@Au magnetic NPs	Antibody	10^4 and 60 times	1.43 pg mL^{-1}.92 pg mL^{-1},.84 pg mL^{-1}	30 min	34

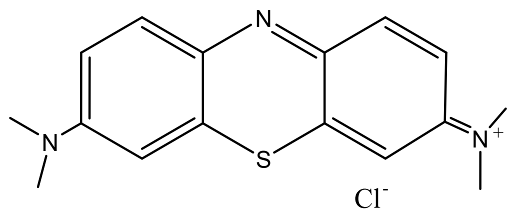
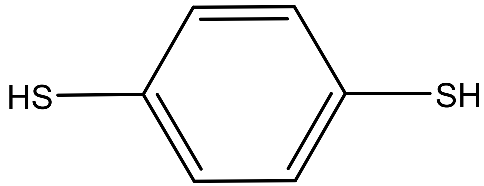
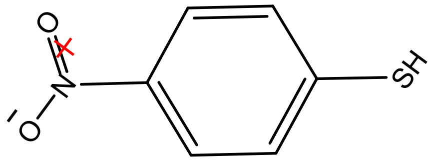
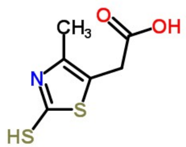
38.	Free and total prostate-specific antigens	Au NPs/4-ATP	Antibody			15 min	[35]
39.	CK-MB, cTnI, and Myo	Ag^{MB}@Au, Ag^{R6G}@Au NPs, Ag^{NBA}@Au	Antibody		0.93, 0.89, and 4.2 pg mL−1, respectively	9 min	[36]
40.	*Salmonella enteritidis*	Au@4-MBA@Ag NPs	Antibody		1×10^{5} CFU mL^{-1} and 1.36×102 CFU mL^{-1} for colorimetric and SERS signal, respectively	20 min	[37]
41.	WNV NS1 protein and inactivated WNV virions	Au/DTNB@Ag/ DTNB-MAb M4 NPs	Antibody	100-fold	0.1 ng/mL and 0.2×10^{2} copies/μL	15 min	[38]
42.	Cardiac troponin I	Nonspherical gap-enhanced Raman tags	Antibody	30 times	0.1 ng/mL	11 min	[39]

Table S2. Commonly used Raman reporting molecules in SERS-LFIA-based in vitro diagnostics.

No	Reporting Molecule	Molecular weight	Structure	Peak (cm^{-1})	Ref.
1	4-MBA	154.19		1080,1066,1587,1078,1588	13, 23, 24, 27, 30, 33, 37, 40-45
2	DTNB	396.35		1331,1334,1560	1, 3, 10, 21, 26, 27, 29-31, 34, 38, 46-54
3	4- MPBA	153.99		1060, 495	11, 21, 55

4	4-ATP	125.19		1095, 1140,1078,1588	25, 35, 56
5	MGITC	421.98		1 613， 1615	19, 57-63
6	HITC	536.49		928	20

7	R6G	479.01		1513	36
8	CV	407.98		918，1621	64
9	NBA	353.85		590	22, 36, 45, 65
10	4-MBN	135.18		2 225，1073	28, 66

11	MB	319.85		1624，1550	22, 36, 64
12	BDT	142.234			67
13	4-NBT	155.174		1300	39, 32
14	MMTAA	189.28		1288	23

Note：4-MBA：4-mercaptobenzoic acid, DTNB: 5,5'-Dithiobis-(2-nitrobenzoic acid),4-MBPA: 4-Mercaptophenylboronic acid, 4-ATP: 4-aminothiophenol, MGITC: Malachite green isothiocyanate, HITC: 1,1',3,3,3',3'-hexamethyl-2,2'indotricarbocyanine iodide, R6G:Rhodamine 6G, CV: Crystal violet, NBA: Nile blue A, 4-MBN: 4-Mercaptobenzonitrile; MB: Methylene blue; BDT: 1,4-Benzenedithiol；NBT: 4-

nitrobenzenthiol；MMTAA：2-mercapto-4-methyl-5-thiazoleacetic acid.

Table S3. Application of SERS-LFIA for multiplex detection in diagnostics.

NO.	Target	Sample type	Detection format	Number of T-lines	Sensing Signal	Detection Limit	Ref.
1.	*S. aureus, S. typhi, and P. aeruginosa*	Urine sample	Multiplex detection	3	Colorimetric and SERS mode	10 cells mL^{-1}	21
2.	H1N1, SARSCoV-2 and RSV,	Throat swab	Sandwich, Multiplex detection	3	Colorimetric and SERS mode	85 copies mL^{-1}, 8 pg mL^{-1}, and 8 pg mL^{-1}	1
3.	SARS-CoV-2 IgM/IgG	Serum samples	Multiplex detection	2	Colorimetric and SERS mode		3
4.	SARS-CoV-2 and influenza a virus	Nasopharyngeal samples	Sandwich, Multiplex detection	2	Colorimetric and SERS mode	5.2 PFU/mL and 23 HAU/mL,	19
5.	*E. coli*	Urine sample	Capture-antibody independent, Multiplex detection	1	Raman&Colorimetric& Photothermal mode	10^3 cfu/mL in colorimetric mode, 10^2 cfu/mL in Raman mode	24

						and 10^2 cfu/mL in photothermal mode	
6.	Cardiac troponin I, N-terminal natriuretic peptide precursor	Serum samples	Multiplex detection	2	Colorimetric and SERS mode	1 pg/mL and 10 pg/mL	25
7.	Amyloid A and C-reactive protein	Unprocessed blood sample	Multiplex detection	2	Raman&Colorimetric mode	0.1 and 0.01 ng/mL	26
8.	Alzheimer's disease biomarkers (Aβ42 and Aβ40)	Serum samples	Multiplex detection	1	Colorimetric and SERS mode	15.3 and 16.8 fg mL^{-1}	27
9.	SARS-CoV-2 S and NP antigens	Throat swab	Multiplex detection	2	Colorimetric and SERS mode	23 pg mL^{-1} and 2 pg mL^{-1}	10
10.	*Staphylococcus aureus*	Blood samples	Multiplex detection	3	Colorimetric-SERS-photothermal-catalytic mode	CFU/mL for SERSLFIA, 27 CFU/mL for PT-LFIA, and 18 CFU/mL for CL-LFIA	11

11.	H1N1 and *S. pneumoniae*	Saliva, throat swab	Sandwich	1	Colorimetric and SERS mode	29 pfu/mL and 16 cells/mL	30
12.	Dehydroepiandrosterone		Sandwich, Multimodal Detection		Colorimetric, SERS and photothermal mode	1.0 ng mL^{-1} for CM-LFIA, 0.42 ng mL^{-1} 1 for PT-LFIA, and 0.013 ng mL^{-1} for SERS-LFIA	31
13.	SARS-CoV-2 N protein antibody	Clinical serum samples	Multimodal Detection	1	Colorimetric and SERS mode	The visual limit of 10^{-8}mg/mL, the SERS LOD of 0.08 pg/mL	13
14.	Anti-SARS-CoV-2 IgM and IgG antibodies		Sandwich, Multiplex detection	2	Colorimetric and SERS mode	1 ng/mL and 0.1 ng/mL	32
15.	Matrix etalloproteinase-9 (MMP-9), S100 calcium-binding protein B protein	Clinical blood samples	Sandwich, Multiplex detection	3	Colorimetric and SERS mode	0.01 pg/mL	33

	(S100-β), and neuro-specific enolase (NSE)						
16.	Protein S1 of SARS-CoV-2	Saliva samples	Multimodal Detection	1	Colorimetric and SERS mode	91.24 pg/mL	[20]
17.	Mycoplasma pneumoniae	Serum samples	Sandwich, Multimodal Detection	1	Colorimetric and SERS mode	0.1 ng mL^{-1}	[29]
18.	Prostate specific antigen, alpha-fetoprotein, carcinoembryonic antigen	Serum samples	Sandwich, Multimodal Detection, Multiplex detection	3	Colorimetric and SERS mode	1.43, 1.92, and 3.84 pg mL^{-1}	[34]
19.	Free and total prostate-specific antigens	Serum samples	Multimodal Detection	1	SERS and temperature mode		[35]
20.	CK-MB, cTnI, and Myo	Serum samples	Sandwich, Multimodal Detection	1	Colorimetric and SERS mode	0.93, 0.89, and 4.2 pg mL^{-1}, respectively,	[36]
21.	WNV NS1 protein and inactivated WNV virions		Sandwich, Multimodal Detection	1	Colorimetric and SERS mode	0.1 ng/mL and 0.2×10^2	[38]

						copies/μL	

Table S4. Some Patents of SERS-LFIA in recent years.

NO	Publish number	Patent name	Applicants
1	CN 116908436 A	SERS (Surface Enhanced Raman Scattering) immune probe for detecting zearalenone as well as preparation method and application of SERS immune probe	Univ Soochow
2	WO 2023/049490 A1	Label-Free Food Analysis and Molecular Detection	Purdue Reserach Found
3	CN 115524484 A	Three-mode double-color lateral flow immunochromatography test paper based on phenylboronic acid gold nanoflowers and detection method	Univ China Pharma
4	US 2014/0287526 A1	Nanotube Based Lateral Flow Device for Biomarker Detection	Biomedomics Inc
5	US 2024/0003877 A1	Devices, Systems, and Methods for the Detection of a Target Analyte Using Magnetic Focus Lateral Flow Immunoassay Techniques	Purdue Research Foundation
6	US 2023/0103404 A1	Detection System and a Portable Detection Device	Academia Sinica
7	WO 2023/149966 A2	Methods of Fabricating a Multianalyte Detection Device and Devices Thereof	The Trustees of Boston College
8	US 2017/0336398 A1	Compositions and Methods for Antigen Detection Incorporating Inorganic Nanostructures to Amplify Detection Signals	Univ Washington State
9	WO 2022/038374 A1	Improvements in or Relating to a Device for Analysing a Sample	Vidya Holdings Ltd
10	WO 2019/199999 A1	Superparamagnetic Particle Imaging and Its Applications in Quantitative Multiplex Stationary Phase Diagnostic Assays	Ge Yu,Mars Sciences Ltd
11	WO 2023/102062 A1	Multi-Targeted, Modular Virus Sensing Platform	Univ Texas
12	US 2022/0074929 A1	Quantification, Isolation, and Characterization of Exosomes Using Droplet-Based and Well-Based Microfluidic Systems	Univ Hong Kong Science & Tech

13	US 10562863 B2	Heterobifunctional linker	Univ Alberta
14	WO 2021/202495 A2	Anti-Acinetobacter Baumannii Polyclonal Antibody (Ab-Pab), and Uses Thereof	Univ California
15	WO 2023/131961 A1	Electrochemical Detection of a Viral Infection	Univ Ramot
16	EP 3771908 A1	Lateral-Electrophoretic Bioassay	Fundacio Inst Catala De Nanociencia I Nanotecnologia Icn2
17	WO 2023/275876 A1	Method and System for Analyzing Biological Data	Memed Diagnostics Ltd

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