Electronic Supplementary Material (ESI) for Analytical Methods.

Recent progress in surface-enhanced Raman spectroscopy-based biosensors for the detection of extracellular vesicles

Hong Zheng[#a], Qin Ding[#b], Chen Li[a], Wei Chen[a], Xiaoqiang Chen[a], Qin Lin[a], Desheng Wang[*a], Youliang Weng[*b] and Duo Lin[*b]

[a] *Department of Otolaryngology Head and Neck Surgery, Fujian Medical University Union Hospital, Fuzhou, China*

[b] *Clinical Oncology School of Fujian Medical University, Fujian Cancer Hospital, Fuzhou, Fujian, China*

[c] *Key Laboratory of OptoElectronic Science and Technology for Medicine, Ministry of Education, Fujian Provincial Key Laboratory for Photonics Technology, Fujian Normal University, Fuzhou, China*

Table S1. peak assignments of surface-enhanced Raman spectroscopy of cell-derived EVs

Peak (cm−1)	Origin	EVs source	Substrates
406	cholesterol	RBC	EVs with Au@AgNPs[1]
486,487	Polysaccharide	B16F10(melanoma cell), RBC normal cell(alveolar cell)	EVs coated with AuNP[2] GNP substrates[3]
505,521	S-S stretching(proteins)	H1975(lung cancer cell)	Ag NCs on Au NR array substrate[4]
		B16F10(melanoma cell), RBC	EVs with Au@AgNPs[1] EVs coated with AuNP[2]
537	Cholesterol ester, Adenosine, S-S difulfide dridge in cysteine	normal cell(alveolar cell) Lung cancer cell HPAEpiC(normal cell)	GNP substrates[3, 5]
546	cholesterol	B16F10(melanoma cell), RBC	EVs with Au@AgNPs[1] EVs coated with AuNP[2]
570	Carbohydrate present in cell membrane	H1299, H522(lung cancer cells)	GNP substrates[3]
602	CCO	H1299, H522(lung cancer cells)	GNP substrates[3]
615,625,630	C – C twisting(proteins)	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform [6]
		NL-20, BEAS-20, L929(lung normal cells) PC-9(lung cancer cell)	Ag NCs on Au NR array substrate[4]
643,645,647,648	C – C twisting(Tyr)	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates [7]
		B16F10(melanoma cell), RBC	3D plasmonic nanobowl platform[6]
		Lung cancer cell, HPAEpiC(normal cell)	EVs with Au@AgNPs[1] GNP substrates[5]
650	C−S stretching	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
667	N – type sugar pucker	PANC1(Pancreatic cancer cell)	EVs with nanostars[8]
668	T, G (DNA/RNA)	B16F10(melanoma cell), RBC	EVs with Au@AgNPs[1]
700	Cholesterol, cholesterol ester, C-S stretching mode	normal cell(alveolar cell)	GNP substrates[3]

707	Aminoacid, lipid band due to cholesterol	SKOV-3(ovarian cancer cell) B16F10(melanoma cell), RBC MDA-MB-231(breast cancer cell)	3D plasmonic nanobowl platform[6] EVs with Au@AgNPs[1] GO-GNS mixed-dimensional substrate[9]
714,725,727, 729,732	Met, Adenine, Ser	normal cell SKOV-3(ovarian cancer cell) PANC1(Pancreatic cancer cell) H1299, H522(lung cancer cells)	GNP substrates[3] 3D plasmonic nanobowl platform[6] EVs with nanostars[8]
735	C−S stretching	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
754,760	Trp	PANC1(Pancreatic cancer cell) SKOV-3(ovarian cancer cell)	EVs with nanostars[8] 3D plasmonic nanobowl platform[6]
781,786,788	Cytosine ring breathing mode, DNA backbone phosphodiester symmetric stretch	H1299, H522(lung cancer cells) SKOV-3(ovarian cancer cell) B16F10(melanoma cell), RBC PANC1(Pancreatic cancer cell) normal cell	GNP substrates[3] 3D plasmonic nanobowl platform[6] EVs with Au@AgNPs[1] EVs with nanostars[8]
789-795	vibrations in nucleic acid	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
805	Si−O stretching, predominantly silicon motion	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
813,819	Ribose	Lung cancer cell HPAEpiC(normal cell)	GNP substrates[5]
830,831	Tyr	SKOV-3(ovarian cancer cell) Lung cancer cell	3D plasmonic nanobowl platform[6] GNP substrates[5]
838	Amine group	H1299, H522(lung cancer cells)	GNP substrates[3]
843	Glucose	H1299, H522(lung cancer cells)	GNP substrates[3]

847.4	Monosaccharides(α -glucose, (C-O-C) skeletal mode	H1975(lung cancer cell)	Au nanopyramid hybrid substrate[10]
850	lipids,t(C – C) vibration	CCD841-CoNnormal cell) HCT116(Colon cancer cell)	Super-hydrophobic substrate[11]
852,854.4	Ring breathing Tyr (proteins)	SKOV-3(ovarian cancer cell) HCC827(lung cancer cell)	3D plasmonic nanobowl platform[6] Au nanopyramid hybrid substrate[10]
869	Pro	H1299, H522(lung cancer cells)	GNP substrates[3]
871	Tyr	Lung cancer cell HPAEpiC(normal cell)	GNP substrates[5]
879	Trp	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform[6]
883	ρ (CH2)(protein)	B16F10(melanoma cell)	EVs coated with AuNP[2]
903	carbohydrate-related SERS vibrations	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
911	Glucose, Ring breathing mode	H1299, H522(lung cancer cells)	GNP substrates[3]
920	Protein	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform[6]
925,927,931	Pro, Val	Lung cancer cell HPAEpiC(normal cell) SKOV-3(ovarian cancer cell)	GNP substrates[5] biosilica/AgNP composite substrates[7]
937	Protein	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform[6]
942,944,948,960	C – C – N stretching (e.g. α -helix backbone in protein)	Lung cancer cell HPAEpiC(normal cell) PANC1(Pancreatic cancer cell) SKOV-3(ovarian cancer cell)	GNP substrates[5] EVs with nanostars[8] biosilica/AgNP composite substrates[7]
970	lipid band due to Phosphate monoester groups	MDA-MB-231(breast cancer cell)	GO-GNS mixed-dimensional substrate[9]
1000,1003	Phe	SKOV-3(ovarian cancer cell) H1975(lung cancer	3D plasmonic nanobowl platform[6] Ag NCs on Au NR array

		cell)	substrate[4]
		PANC1(Pancreatic cancer cell)	EVs with nanostars[8]
		RBC	EVs with Au@AgNPs[1]
1010,1050, 1090	Si−O stretching; oxygen vibrating between silicon in the Si−O−Si bond	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1014	tryptophan band due to the ring breathing	SK-BR3(breast cancer cell)	GO-GNS mixed-dimensional substrate[9]
1015	C−C stretching vibration possibly coupled to C−N stretching vibration	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1016,1017	Phe	Lung cancer cell HPAEpiC(normal cell)	GNP substrates[5]
1032,1033, 1034.3,1038	CH2 CH 3 bending,t(C‐C) vibration, Pro	B16F10(melanoma cell), RBC	EVs coated with AuNP[2]
		CCD841-CoN, HPAEpiC(normal cells)	GNP substrates[5] Au nanopyramid hybrid substrate[10]
		HCC827(lung cancer cell)	Super-hydrophobic substrate[11]
		HCT116(Colon cancer cell)	
1050	Lipid	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform[6]
1056	lipid band is due to C• •O stretch	MDA-MB-231(breast cancer cell)	GO-GNS mixed-dimensional substrate[9]
1058,1059	DNA bases	Lung cancer cell, HPAEpiC(normal cells)	GNP substrates[5]
1072	Mannose, C-N stretching mode	H1299, H522(lung cancer cells)	GNP substrates[3]
1095,1101	PO2− stretching, C−C stretching, C−O−C stretching, glycosidic link in	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
		SK-BR3(breast cancer cell)	GO-GNS mixed-dimensional substrate[9]

	DNA/RNA		
1110,1113.6,1115, 1120,1120.3	The strong C-O band of ribose (serves as a marker band for RNA in solutions),Nucleic acid	SKOV-3(ovarian cancer cell) H1975, HCC827(lung cancer cell) B16F10(melanoma cell), RBC	biosilica/AgNP composite substrates[7] Au nanopyramid hybrid substrate[10] EVs coated with AuNP[2] 3D plasmonic nanobowl platform[6]
1124,1134	t(C – C) inphase aliphatic C – C stretch of lipids	CCD841-CoN(normal cell) HCT116(Colon cancer cell) B16F10(melanoma cell), RBC	EVs coated with AuNP[2] Super-hydrophobic substrate[11] EVs coated with AuNP[2]
1145	CH2, CH3 deformations in proteins and lipids	H1299, H522(lung cancer cells)	GNP substrates[3]
1150	Deoxyribose phosphate backbone (C-C stretching mode), Adenosine, Thymine, Glycogen	normal cell(alveolar cell)	GNP substrates[3]
1160-1170	carbohydrate-related SERS vibrations	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1172	δ (C H) (e.g., protein)	B16F10(melanoma cell), RBC	EVs coated with AuNP[2]
1175	Tyr, Phe	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform[6]
1175	nucleic acid vibrations in DNA/RNA, phenylalanine, or tyrosine vibrations in proteins	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1179	ν (C–C) and ν (C–O) (phospholipids)	B16F10(melanoma cell), RBC	EVs with Au@AgNPs[1] EVs coated with AuNP[2]

1198,1207, 1211,1213.5	Tyr, Phe ν (C-C6H6) mode, Stretching of C-N	SK-BR3(breast cancer cell) SKOV-3(ovarian cancer cell) B16F10(melanoma cell), RBC HCC827, H1975(lung cancer cells) normal cell(alveolar cell)	GO-GNS mixed-dimensional substrate[9] 3D plasmonic nanobowl platform[6] EVs with Au@AgNP[1] Au nanopyramid hybrid substrate[10] GNP substrates[3]
1217,1222, 1238.4	Amide III	HPAEpiC(normal cell) HCC827(lung cancer cell)	GNP substrates[5] Au nanopyramid hybrid substrate[10]
1235	ribonucleic acid from Uraci	CCD841-CoN(normal cell) HCT116(Colon cancer cell)	Super-hydrophobic substrate[11]
1240	C−N stretching + N−H deformation, amide III in proteins	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1243,1253.5,1254,1256, 1260,1271	amide III (proteins)/ asymmetric phosphate stretching (nucleic acids), CH2 in-plane deformation (lipids), Triglycerides (fatty acids)	B16F10(melanoma cell), RBC PC-9, H1975, HCC827(lung cancer cells) NL-20, BEAS-20, L929(lung normal cells) SKOV-3(ovarian cancer cell) MDA-MB-231(breast cancer cell)	EVs with Au@AgNPs[1] EVs coated with AuNP[2] Au nanopyramid hybrid substrate[10] Ag NCs on Au NR array substrate[4] 3D plasmonic nanobowl platform[6] GO-GNS mixed-dimensional substrate[9]
1278	ribonucleic acid from Cytosine	CCD841-CoN(normal cell), HCT116(Colon cancer cell)	Super-hydrophobic substrate[11]
1287,1290,1293,1295	CH2,CH3 deformation/C−N stretching + N−H deformation; amide III in proteins	SKOV-3(ovarian cancer cell) B16F10(melanoma cell) PANC1(Pancreatic cancer cell)	biosilica/AgNP composite substrates[7] EVs coated with AuNP[2] EVs with nanostars[8]

1303,1307, 1309.3	C−N asymmetric stretching (protein)/CH3CH2 twisting (lipid)	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform[6]
		B16F10(melanoma cell), RBC	EVs with Au@AgNPs[1]
		H1975(lung cancer cell)	EVs coated with AuNP[2]
			Au nanopyramid hybrid substrate[10]
1310-1340	carbohydrate-related SERS vibrations	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1310,1313	Trp, Cα-H	Lung cancer cell, HPAEpiC(normal cells)	GNP substrates[5]
1326	ω CH3CH2 twisting (nucleic acids)	B16F10(melanoma cell), RBC	EVs with Au@AgNPs[1]
			EVs coated with AuNP[2]
1330	Phospholipid	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform[6]
1334	Ring breathing of adenine	PANC1(Pancreatic cancer cell)	EVs with nanostars[8]
1336	backbone deformation Cα−H/Cα−C stretching/CH2,CH3 twisting or wagging in proteins	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1354	Guanine (nucleic acid)	B16F10(melanoma cell)	EVs coated with AuNP[2]
1360,1367, 1369.6	CH3/CH2 twisting or bending mode of lipid/collagen	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
		B16F10(melanoma cell), RBC	EVs coated with AuNP[2]
		HCC827(lung cancer cell)	Au nanopyramid hybrid substrate[10]
1370,1378	Carbohydrate	B16F10(melanoma cell), RBC	EVs coated with AuNP[2]
		HCC827(lung cancer cell)	Ag NCs on Au NR array substrate[4]
1375,1376	Amide III	Lung cancer cell, HPAEpiC(normal cells)	GNP substrates[5]
1378	Lipid	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform[6]
1381	δ CH3 symmetric (lipids)	B16F10(melanoma cell), RBC	EVs with Au@AgNPs[1]
			EVs coated with AuNP[2]

1381	C=O symmetric stretching, CH2 deformation, N – H in plane deformation (e.g. protein)	PANC1(Pancreatic cancer cell)	EVs with nanostars[8]
1386-1390	symmetrical CH3 deformation in DNA/RNA, proteins, or lipids	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1388	DNA peak due to NH in-plane deformation	SK-BR3(breast cancer cell)	GO-GNS mixed-dimensional substrate[9]
1394,1404	CH rocking	SKOV-3(ovarian cancer cell) NL-20, BEAS-20, L929(lung normal cells)	3D plasmonic nanobowl platform[6] Ag NCs on Au NR array substrate[4]
1400	protein vibrational modes, e.g., CH2 deformations	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1416,1422	DNA bases	HPAEpiC(normal cell) H1975(lung cancer cell)	GNP substrates[5] Au nanopyramid hybrid substrate[10]
1440	Lipid	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform[6]
1443,1445,1460, 1448,1449	CH2, CH3 deformation (e.g. protein backbone, acyl chain in lipids)	B16F10(melanoma cell), RBC SKOV-3(ovarian cancer cell) HCC827(lung cancer cell) PANC1(Pancreatic cancer cell)	EVs coated with AuNP[2] biosilica/AgNP composite substrates[7] Ag NCs on Au NR array substrate[4] EVs with nanostars[8]
1465,1466	lipids	B16F10(melanoma cell), RBC SKOV-3(ovarian cancer cell)	EVs with Au@AgNPs[1] EVs coated with AuNP[2] 3D plasmonic nanobowl platform[6]
1466,1470,1480	overlapping of the CH deformation occurring in both lipids and proteins	Lung cancer cell CCD841-CoN, HPAEpiC(normal cells) HCT116(Colon cancer cell)	GNP substrates[5] Super-hydrophobic substrate[11]
1474.8,1481	Amide II (largely due to coupling of CN	H1975, HCC827(lung cancer cells)	Au nanopyramid hybrid substrate[10]

	stretching & in-plane bending of N-H group		
1477	DMAP + δ (C H) (e.g., lipid, protein)	B16F10(melanoma cell), RBC	EVs coated with AuNP[2]
1490	DNA	B16F10(melanoma cell), RBC	EVs with Au@AgNPs[1]
1500	conjugated −C=C− vibrations in nucleic acids	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1506.6	N=H bending, Cytosine	HCC827(lung cancer cell)	Au nanopyramid hybrid substrate[10]
1510	DNA peak due to purine A, G ring	MDA-MB-231(breast cancer cell)	GO-GNS mixed-dimensional substrate[9]
1528	ν (C C) conjugated	B16F10(melanoma cell), RBC	EVs coated with AuNP[2]
1539	Cytosine	H1299, H522(lung cancer cells)	GNP substrates[3]
1542,1545	amide II (proteins)	B16F10(melanoma cell), RBC SKOV-3(ovarian cancer cell)	EVs with Au@AgNPs[1] biosilica/AgNP composite substrates[7]
1545	lipid band due to δ (CH3,CH2) in acyl chain	MDA-MB-231(breast cancer cell)	GO-GNS mixed-dimensional substrate[9]
1552,1563,1588	Trp	SKOV-3(ovarian cancer cell) B16F10(melanoma cell), RBC Lung cancer cell HPAEpiC(normal cell)	3D plasmonic nanobowl platform[6] EVs with Au@AgNPs[1] EVs coated with AuNP[2] GNP substrates[5]
1576	Guanine (nucleic acid)	B16F10(melanoma cell), RBC	EVs coated with AuNP[2]
1584.8	Hydroxyproline	HCC827(lung cancer cell)	Au nanopyramid hybrid substrate[10]
1590,1590.9	C−C ring vibration in aromatic groups	SKOV-3(ovarian cancer cell) H1975(lung cancer cell)	biosilica/AgNP composite substrates[7] Au nanopyramid hybrid substrate[10]
1595	nucleic acid	H1975(lung cancer cell) SKOV-3(ovarian cancer cell)	Ag NCs on Au NR array substrate[4] biosilica/AgNP composite substrates[7]

1600	Phe	SKOV-3(ovarian cancer cell)	3D plasmonic nanobowl platform[6]
1605	lipid band due to the ergostero	MDA-MB-231(breast cancer cell)	GO-GNS mixed-dimensional substrate[9]
1605.9,1608,1614, 1618,	Cytosine (NH2), Ring C-C stretch of phenyl	H1975, HCC827(lung cancer cells)	Au nanopyramid hybrid substrate[10]
1620	(1), Phenylalanine, tyrosine, vibration of C = C (protein)	B16F10(melanoma cell), RBC SKOV-3(ovarian cancer cell)	EVs coated with AuNP[2] Ag NCs on Au NR array substrate[4] EVs with Au@AgNPs[1] biosilica/AgNP composite substrates[7]
1622	Amide I, Tyr, Trp, Phe	Lung cancer cell HPAEpiC(normal cell)	GNP substrates[5]
1630	tryptophan due to −C 伸 O stretch	SK-BR3(breast cancer cell)	GO-GNS mixed-dimensional substrate[9]
1630	amide I C=O stretching vibrations in proteins	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1630	Amide I (random coils of proteins)	normal cell(alveolar cell)	GNP substrates[3]
1632	amide I α-helix and β structure (proteins)	B16F10(melanoma cell), RBC	EVs with Au@AgNPs[1]
1650	amide I vibrations in proteins or C=C stretching in lipids	SKOV-3(ovarian cancer cell)	biosilica/AgNP composite substrates[7]
1664	amide I (proteins)/DNA	B16F10(melanoma cell), RBC	EVs with Au@AgNPs[1]
1687	Amide I	Lung cancer cell	GNP substrates[5]

Table S2. peak assignments of surface-enhanced Raman spectroscopy of plasma/serum-derived EVs

Peak(cm−1)	Origin	EVs source	Substrates
502,504	S-S difulfide dridge in cysteine	Lung cancer patients, healthy volunteers	GNP substrates[5]
651	Tyr	Lung cancer patients, healthy volunteers	GNP substrates[5]
734	Met, Adenine	Lung cancer patients, healthy volunteers	GNP substrates[5]
787	Nucleic Acids	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
830	C-O-O	healthy volunteers, pancreatic cancer patients	APS-mica[13]
850-860	Polysaccharide Structure	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
864.1	Ribose vibration, one of the distinct RNA modes	healthy volunteers	Au nanopyramid hybrid substrate[10]
1003,1008, 1047	Phe	healthy volunteers Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients Lung cancer patients	Microstructured arrays containing AuNPs[12] GNP substrates[5]
1032	Phospholipid and/or Polysaccharide	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
1051,1063.9, 1077,1124	C-C skeletal stretching	healthy volunteers, pancreatic cancer patients Lung cancer patients	APS-mica[13] Au nanopyramid hybrid substrate[10] GNP substrates[5]
1128	Proteins and/or Ceramides	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance	Microstructured arrays containing AuNPs[12]

		(MGUS) patients	
1135	C-N	healthy volunteers	GNP substrates[5]
1151	Lipids and nucleic acids (cytosine, guanine, adenine)	Lung cancer patients	GNP substrates[5]
1157	β -Carotene Accumulation	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
1170.4	C-H in-plane bending mode of tyrosine	healthy volunteers	Au nanopyramid hybrid substrate[10]
1173	Lipids and nucleic acids (cytosine, guanine, adenine)	healthy volunteers	GNP substrates[5]
1209	Tryptophan and/or Phenylalanine	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
1255.6	Lipids	healthy volunteers	Au nanopyramid hybrid substrate[10]
1302.9	Amide III (protein)	healthy volunteers	Au nanopyramid hybrid substrate[10]
1316,1316.1	Nucleic Acids and/or Collagen and/or Guanine	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients healthy volunteers	Microstructured arrays containing AuNPs[12] Au nanopyramid hybrid substrate[10]
1345.7	CH3, CH2 wagging	healthy volunteers	Au nanopyramid hybrid substrate[10]
1373.3	T, A, G (ring breathing modes of the DNA/RNA bases)	healthy volunteers	Au nanopyramid hybrid substrate[10]
1376	Amide III	Lung cancer patients	GNP substrates[5]
1378	Carbohydrate and/or Nucleic Acids	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
1386.2,1402	CH3 band	healthy volunteers	Au nanopyramid hybrid substrate[10]

			GNP substrates[5]
1420	DNA bases	Lung cancer patients	GNP substrates[5]
1427.2	Deoxyribose (B,Z-marker)	healthy volunteers	Au nanopyramid hybrid substrate[10]
1450	CH2 bending	healthy volunteers, pancreatic cancer patients	APS-mica[13]
1457	Deoxyribose	healthy volunteers	Au nanopyramid hybrid substrate[10]
1459	C-H	Lung cancer patients, healthy volunteers	GNP substrates[5]
1479.6	Amide II	healthy volunteers	Au nanopyramid hybrid substrate[10]
1515.8	Cytosine	healthy volunteers	Au nanopyramid hybrid substrate[10]
1539	Nucleic Acids	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
1589	Phenylalanine, hydroxyproline	healthy volunteers	Au nanopyramid hybrid substrate[10]
1655.2	Amide I of proteins	healthy volunteers	Au nanopyramid hybrid substrate[10]
1672	Ceramide	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
869,872	Tyr	Lung cancer patients, healthy volunteers	GNP substrates[5]
980,981	Trp, Val	Lung cancer patients, healthy volunteers	GNP substrates[5]
1235-1285	Proteins and/or Nucleic Acids and/or Lipids	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
1296,1301	Amide III—collagen	Lung cancer patients, healthy volunteerss	GNP substrates[5]
1300-1400	CH2 twisting	healthy volunteers,	APS-mica[13]

		pancreatic cancer patients	
1335-1345	Nucleic Acids (Purine Bases) and/or Tryptophan and/or Glycine Backbone and/or Proline Side Chain	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
1440-1450	Proteins and/or Lipids	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
1490-1500	Nucleic Acids	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
1560-1580	Tryptophan and/or Nucleic Acids and/or Proteins and/or Carbohydrates	Multiple myeloma(MM)patients, monoclonal gammopathy of uncertain significance (MGUS) patients	Microstructured arrays containing AuNPs[12]
1593,1596	Phe	Lung cancer patients, healthy volunteers	GNP substrates[5]

Table3. Statistical classification method of the Raman spectra

Method	Samples	Sensitivity	Specificity	Ref.
PCA	Normal cell and lung cancer cell	95.3%, 91.67%	97.3%, 100%	[3]
	Breast cancer cell	100%	100%	[14]
	Ovarian cell and endometrial cancer cell	100%	99.2%	[7]
	6 volunteers and 14 breast cancer patients	91.67%	100%	[14]
PCA-LDA	Pancreatic cancer cell and prostate cancer cell and colorectal cancer cell	100%.	100%.	[8]
PC-DFA	Normal cell and lung cancer cell	90.6%	97.1%	[13]
PLS-DA	Normal cell and melanoma cell	92.0%, 95.1%	96.9%, 100%	[2]
	Red blood cell and melanoma cell	91.7%, 96.9%	96.9%, 91.7%	[1]
	10 volunteers and 10 osteosarcoma patients	86%,	100%	[15]
Deep learning	10 volunteers and 43 Lung cancer patients	84%	85%	[5]

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