Supplementary Table 1. Application of nanostructured metals in cancer diagnosis

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| --- | --- | --- | --- | --- | --- |
| Sample | Substrate | Algorithm | Clinical application | Year | Ref. |
| Serum | Ag NPs | PCA-LDA | Screening of nasopharyngeal cancer | 2019 | [13] |
| Au NPs | PC-DFA | Early detection of pancreatic cancer | 2019 | [14] |
|  | Ag NPs | - | Prediction of PCa presence and risk stratification | 2018 | [15] |
| Saliva | Ag NPs | PCA | Diagnosis of oral cancer | 2020 | [16] |
| Ag NPs | PCA-LDA | Diagnosis of Oral and oropharyngeal cancers | 2016 | [17] |
| Ag NPs: Silver nanoparticles; PCA-LDA: Principal components analysis-linear discriminant analysis; Au NPs: Gold nanoparticles; PC-DFA: Principal components differential function analysis; PCa: Prostate cancer. |

Supplementary Table 2. Label-free SERS detection of cancer based on colloidal metal nanoparticles

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| Sample | Substrate | Algorithm | Clinical application | Year | Ref. |
| Serum | Ag NPs | PCA-LDA | Identification of cancer patients and classification of cancer types | 2019 | [18] |
| Ag NPs | PLS-LDA | Discrimination between benign and malignant thyroid nodules | 2021 | [19] |
| Plasma | Ag NPs | PCA-LDA | Classification between different tumor stages in nasopharyngeal cancer | 2014 | [20] |
| Ag NPs | PCA-LDA | Detection and screening of esophageal cancer | 2014 | [21] |
| Urine | Au NPs | PCA-LDA | Diagnosis of prostate cancer | 2015 | [22] |
| Saliva | Au NPs | - | Diagnosis of breast cancer | 2017 | [23] |
| Ag NPs | PLS-DA | Differentiation of benign and malignant breast cancers | 2015 | [24] |
| Ag NPs: Silver nanoparticles; PCA-LDA: Principal components analysis-linear discriminant analysis; PLS-LDA: partial least square analysis and linear discriminant analysis; Au NPs: Gold nanoparticles; PLS-DA: Partial least squares–discriminant analysis. |

Supplementary Table 3. SERS detection of cancer based on colloidal metal nanoparticles with the help of Raman reporter and / recognition elements

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| --- | --- | --- | --- | --- | --- | --- |
| Sample | Target | Substrate | Raman reporter/ recognition elements | Clinical application | Year | Ref. |
| VOCs | Aldehydes | Dendritic Ag nanocrystal | 4-ATP | Recognition of lung malignancies | 2017 | [25] |
| MCF-7 cells and tissues | EREGFRPR | Au NPs | Alkyne- and nitrile- molecules/antibodies | Multicolor imaging of cancer cells and breast cancer tissues | 2019 | [26] |
| Serum saliva | MnSOD | Goldnanostructure | Thiolated aptamers | Sensitive detection of cancer biomarkers | 2015 | [27] |
| K562 cells | Telomerase | Au NP pyramids | Cyanine 5 | Recognition of cancer cells | 2016 | [28] |
| BloodCancer cells | CTCs Exosomes | Au NPs in triangular pyramid DNA | RecognitionDNA | Detection of CTCs and cancer cell-derived Exosomes | 2019 | [29] |
| Cancer cells derived exosomes | HER2EpCAM | Gold nanorods | QSY21 carboxylic acid-succinimidyl ester | Identification of HER2 and EpCAM biomarkers on breast cancer cells | 2018 | [30] |
| Melanoma cell | Metabolites | Multibranched Au NPs | Chemical groups | Recognition of metabolites produced by tumor cells | 2020 | [31] |
| Serum | PSAthrombin mucin-1 | Ag pyramids | 4-ATP/multiple aptamers | Quantitative detection of tumor markers at attomolar level | 2015 | [32] |
| CA 15-3CA 27-29CEA | Gold nanostar | Antibodies for tumor antigen | Early diagnosis and therapy response monitoring of cancer | 2015 | [33] |
| Exosomal miRNA | Head-flocked gold nanopillar | Locked nucleic acid | Early diagnosis and prognosis of cancer | 2019 | [34] |
| Transferrin | Ag microspheres | MIP | Early diagnosis and prognosis of cancer | 2016 | [35] |
| Blood | CTCs | AuNPsAu NRsAu NSs | 4-MBA | Diagnosis, prognosis and treatment monitoring of cancer | 2016 | [36] |
| Tumor tissues | PH | Au NRs | 4-NTP | Monitoring of pH under hypoxia in tumor tissues | 2016 | [37] |
| Blood | CTCs | Au NPs | 4-MBA/FA | Early diagnosis of cancer | 2015 | [38] |
| CTCs | AuNPs | pMBA/LHRH | Point-of-caretesting in cancer patients | 2019 | [39] |
| CTCs | AuNPs | 4-MBA, TFMBA, MNBA, MPY | Monitoring of cancer cells’ phenotypic evolution | 2018 | [40] |
| Extracellular vesicles | Glypican-1EpCAMsCD44V6 | AuNPs | MBA, DTNB, and TFMBA/ capture antibody (CD63) | Noninvasive cancer diagnosis | 2020 | [41] |
| HaCaTSK-Mel5 | PH | Au NPs | 4MBA | Discrimination between normal and cancer cells | 2019 | [42] |
| Colon-26 MDA-MB231MCF-7 | SA | Au NPs | Toluidine blue O | Detection of hypersialylated metastatic tumors | 2017 | [43] |
| VOCs: Volatile organic compounds; 4-ATP: p-aminothiophenol; ER: Estrogen receptor; EGFR: Epidermal growth factor receptor;PR: Progesterone receptor; Au NPs: Gold nanoparticles; MnSOD: Manganese super oxide dismutase; CTCs: Circulating tumor cells; HER2: Human epidermal growth factor receptor 2; EpCAM: epithelial cell adhesion molecule; MIP: Molecularly imprinted polymers; 4MBA: 4-mercaptobenzoic acid; 4-NTP: 4-Nitrothiophenol; FA: Folic acid; pMBA: 4-mercaptobenzoic acid; LHRH: luteinizing hormone releasing hormone; TFMBA: 2,3,5,6-tetrafluoro-4-mercaptobenzoic acid; MNBA: 4-Mercapto-3-nitro benzoic acid; MPY: 4-Mercaptopyridine; DTNB: 5,5′-dithiobis-(2-nitrobenzoic acid); SA: Sialic acid. |

Supplementary Table 4. SERS detection of cancer based on bimetallic composite substrate

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| Sample | Target | Substrate | LOD | Clinical application | Year | Ref. |
| Cancerous tissues | FRsSA | Au@AgNPs | - | Identification of metastatic cancer tissues | 2020 | [51] |
| lung normal cellslung cancer cells | Exosomes | Ag NCsAu NRs | - | Identification of exosomes derived from and cancer cells | 2017 | [52] |
| Raji cells | Cytokines | Au@AgNPs | 4.5 pg mL−1 | Identification of cytokines secreted from lymphoma cells  | 2019 | [53] |
| HCT 116 cells | CD44 receptor | Au@AgNPs | - | Identification and imaging of proteins overexpressed on the surface of cancer cells | 2016 | [54] |
| PCa cells  | miR-107 | Hollowed Au/Ag alloy nanocuboids | 0.7 fM | Early diagnosis of prostate cancer | 2019 | [55] |
| Blood | CTCsEBVDNA | Ag NPs coated Si NWs/MPs | - | Monitoring disease status and prognostication of NPC patients | 2019 | [56] |
| Serum | PSA | Au @Ag NPs | 1fg ml−1 | Ultra-low detection of tumor markers | 2018 | [57] |
| sPD-1sPD-L1 sEGFR | Au-Ag alloy  | 6.17 pg ml−10.68 pg ml−169.86 pg ml−1 | Multiplexed detection of soluble cancer protein biomarkers | 2018 | [58] |
| AFPmucin-1 | Au–Au–UCNP | 4.1 aM0.059 aM | Detection of multiplexed cancer biomarkers | 2017 | [59] |
| PSA | Si-core-Ag NPs- Si- shell | 3.4 fM | Sensitive detection of multiplexed cancer biomarkers | 2016 | [60] |
| Exosomes | Ag(shell)-Au(core) | 9×10-19mol L-1 | Early diagnosis, classification and metastasis monitoring ofpancreatic cancer | 2018 | [61] |
| Exosomes | Au-Ag-Ag core-shell-shell  | 26 particles µL-1 | Multiplex detection of cancer biomarkers | 2020 | [62] |
| LOD: Limit of detection; FRs: Folate receptors; SA: Sialic acid; Au@AgNPs: Au@Ag core@shell nanoparticles; Au NCs: Ag nanocubes; Au NRs: Au nanorods; PCa: Prostate cancer; CTCs: Circulating tumor cells; Si NWs: Si nanowires; MPs: Microscale pyramids; NPC: Nasopharyngeal carcinoma; sPD-1: Soluble programmed death 1; sPD-L1: Soluble programmed death-ligand 1; sEGFR: soluble epithermal growth factor receptor; UCNP: Upconversion nanoparticle. |

Supplementary Table 5 Application of nanoparticle-based SERS imaging in cancer diagnosis

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| Samples | SERS methods | Clinical application | Year | Ref. |
| Lumen of esophagus | Multiplexed cocktail of receptor-targeted SERS NPs | Visualization of tumor locations and the quantification of biomarkers | 2015 | [103] |
| Tissues | SERS NPs with a bare silica coating | Detection of invisible microscopic lesions | 2016 | [104] |
| Radiolabeled the SERS NPs with 64Cu | Early cancer detection | 2011 | [105] |
| SERS endoscopy combined with fluorescence | Multiple target detection of cancer lesions | 2015 | [106] |
| Fiber optic-based Raman spectroscopy device | Identification of the cancer lesions in an endoscopic procedure | 2013 | [107] |
| HeLa cells | SERS endoscopy using Plasmonic Nanowire Waveguides | Investigation of cellular processes of cancer cells | 2014 | [108] |
| Gastrointestinal tract | Luminal imaging of multiplexed SERS NPs | Quantitative molecular detection of small lesions | 2015 | [109] |
| Bladder tissue | Endoscope system combined with Au/Si SERS NPs | Detection and resection of nonmuscle invasive bladder cancer | 2018 | [110] |
| NPs: Nanoparticles; |