**Supporting Information**

# Facile PEG-Based Isolation and Classification of Cancer Extracellular Vesicles and Particles with Label-Free Surface-Enhanced Raman Scattering and Pattern Recognition Algorithm

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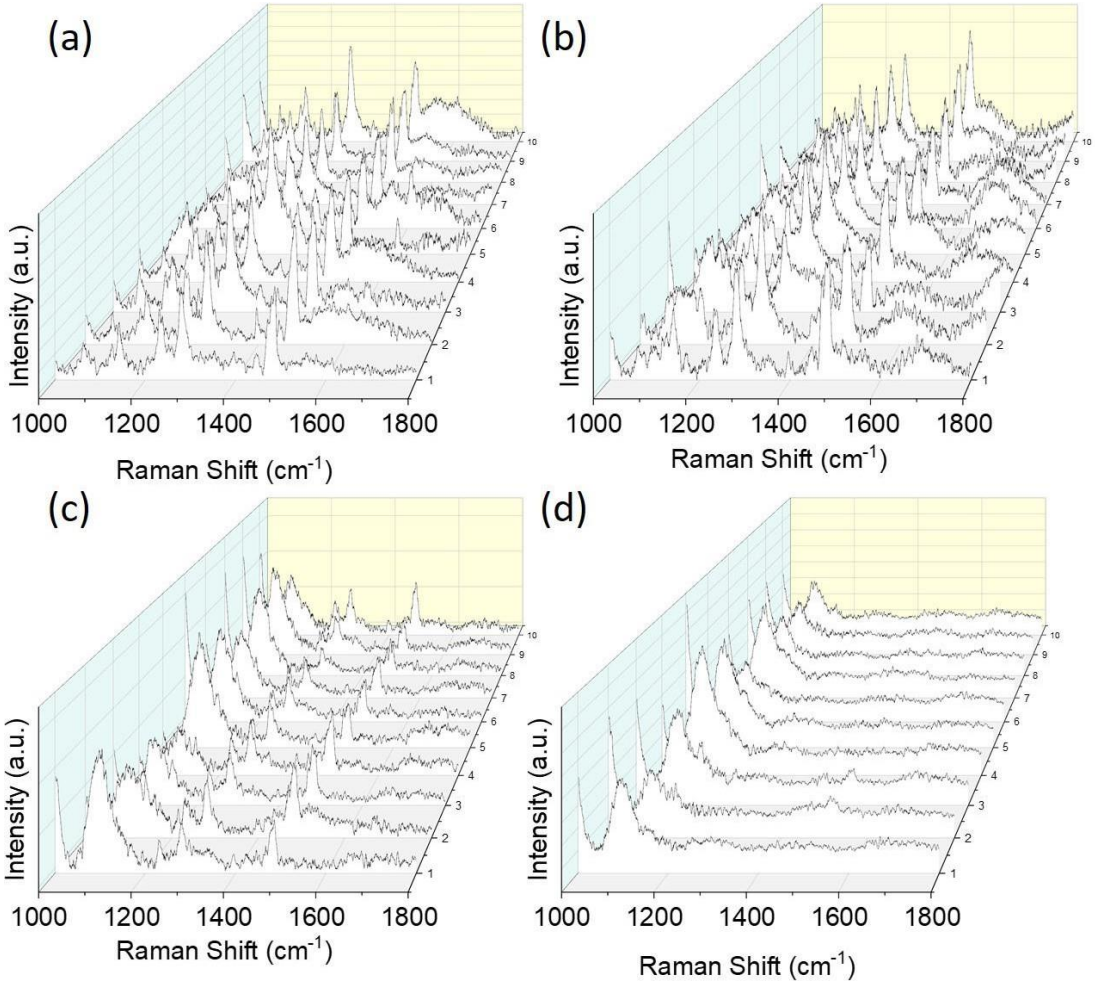


**Figure S1.** The Raman spectra of cancer EVPs and normal EVPs. (a) Raman spectra of THP-1 cancer EVPs. (b) Raman spectrum of DU145 cancer EVPs. (c) Raman spectra of COLO cancer EVPs. (d) Raman spectrum of normal EVPs.

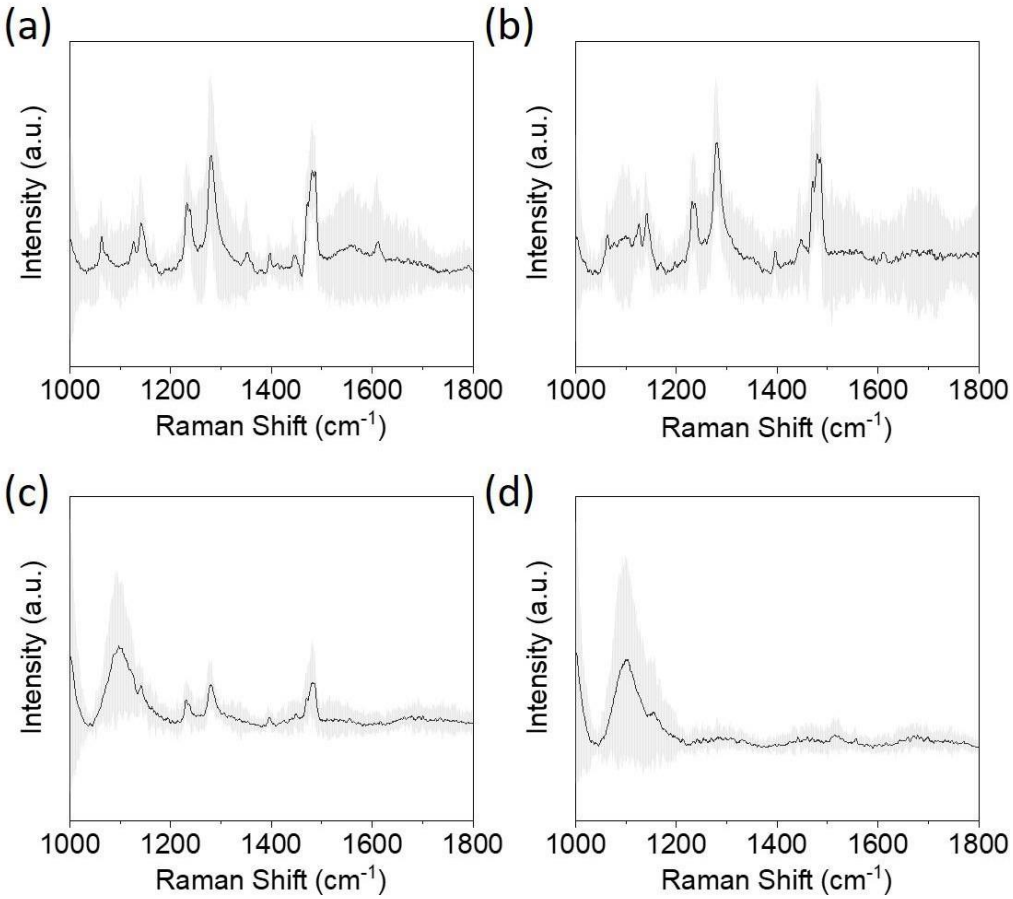


**Figure S2.** The average Raman spectra of cancer EVPs and normal EVPs (a) The average spectra of THP-1 cancer EVPs. (b) The average spectra of DU-145 cancer EVPs. (c) The average spectra of COLO-205 cancer EVPs. (d) The average spectra of normal EVPs.

**Table S1.** The peak area of RhB only and RhB with AMO in the 1649 $cm^{-1}$ and 625 $cm^{-1}$ Raman shift positions.

| | Raman Shift ($cm^{-1}$) | Peak Area (a.u.) |
|---|---|---|
| RhB | 1649 (Peak1) | 1739.75 |
| | 625(Peak2) | 460.90 |
| RhB and AMO | 1649 (Peak1) | 6465.79 |
| | 625 (Peak2) | 1144.94 |

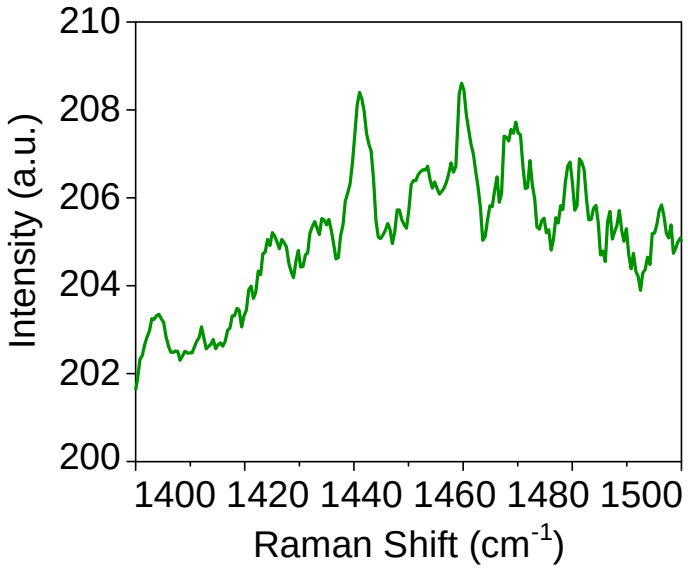


**Figure S3.** The partially enlarged average Raman spectra of EVPs derived from normal between 1400-1500 $cm^{-1}$ in Figure 3.

**Table S2.** The peak positions and major assignments of SERS observed in EVPs samples.

| **Peak positions ($cm^{-1}$)** | **Major assignments** | **References** |
|---|---|---|
| **1074** | C-N stretching vibration in collagen | 1 |
| **1084** | C-C stretching in phospholipids | |
| **1094-1095, 1134** | C-N stretching in D-Mannos | 1 |
| **1140** | Carotenoids | |
| **1261-1264** | CH bending in phospholipids | 2, 3 |
| **1400-1500** | CH2, CH3 stretching in proteins, lipids and collagen | 1 |
| **1541-1551** | C-N stretching in amide II | |
| **1580** | C=C stretching in phenylalanine, acetoacetate and riboflavin | |
| **1654** | C=O bending in α-helix and collagen | 1, 4 |

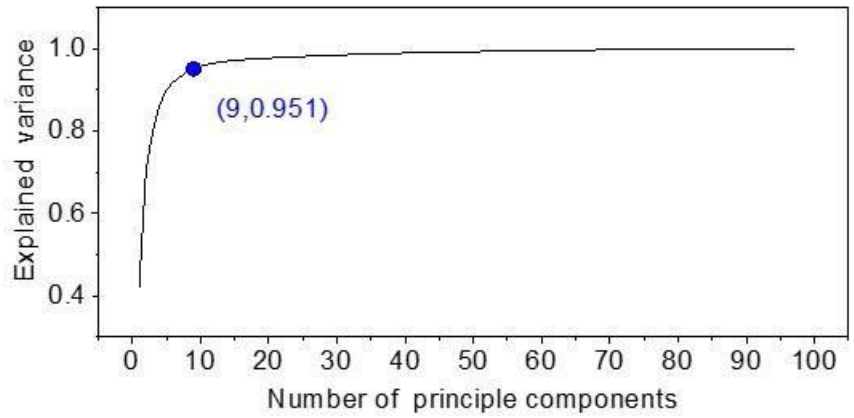


**Figure S4**. Explained variance as a function of the number of dimensions

**Table S3**. Explained variance contained in each principle component.

| Principle component | PC1 | PC2 | PC3 | PC4 | PC5 | PC6 | PC7 | PC8 | PC9 |
|---|---|---|---|---|---|---|---|---|---|
| Explained variance (%) | 42.23 | 28.24 | 9.64 | 6.25 | 3.77 | 1.78 | 1.30 | 1.17 | 0.77 |

**Table S4**. The parameters of the PCA-SVM algorithm classification of the Raman spectra among cancer EVPs by PC1 and PC2.

| | **THP-1** | **DU-145** | **COLO-205** |
|---|---|---|---|
| **Accuracy** | 76.7% | 56.7% | 93.3% |
| **Precision** | 72.7% | 50.0% | 71.4% |
| **Sensitivity** | 66.7% | 30.8% | 100% |

**References**


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2. B. Yan, B. Li, Z. Wen, X. Luo, L. Xue and L. Li, BMC Cancer, 2015, 15, 650.
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4. D. Lin, S. Feng, J. Pan, Y. Chen, J. Lin, G. Chen, S. Xie, H. Zeng and R. Chen, Opt. Express, 2011, 19, 13565-13577.