Supplementary Information

General and Mild Modification of Food-derived Extracellular Vesicles for Enhanced Cell Targeting

Chaoxiang Chen,[*a] *Mengdi Sun,*[a] *Xuan Liu,*[c] *Weijing Wu,*[d] *Liyun Su,*[b] *Yumei Li,*[a] *Gang Liu,*[*c] *and Xiaomei Yan,*[*b]

a. Department of Biological Engineering, College of Food and Biological Engineering, Jimei University, Xiamen, Fujian 361021, People's Republic of China.

b. Department of Chemical Biology, MOE Key Laboratory of Spectrochemical Analysis & Instrumentation, Key Laboratory for Chemical Biology of Fujian Province, Collaborative Innovation Center of Chemistry for Energy Materials, College of Chemistry and Chemical Engineering, Xiamen University, 361005, Xiamen, China.

c. State Key Laboratory of Molecular Vaccinology and Molecular Diagnostics, Center for Molecular Imaging and Translational Medicine, School of Public Health, Xiamen University, 361102, Xiamen, China.

d. Department of Public Health and Medical Technology, Xiamen Medical College, 361023, Xiamen, China. a Department of Biological Engineering, College of Food and Biological Engineering, Jimei University, Xiamen, Fujian 361021, People's Republic of China

* To whom correspondence should be addressed. E-mail: cxchen@jmu.edu.cn, gangliu.cmitm@xmu.edu.cn, xmyan@xmu.edu.cn.

Supplementary figures

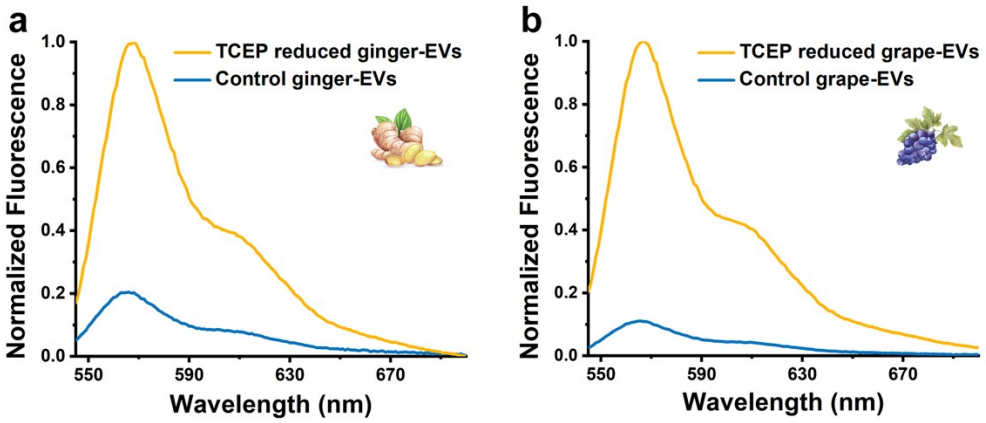

Fig. S1. Ligand conjugation of ginger- and grape-derived EVs via TCEP mediated modification method. (a) Fluorescence spectrometry measurement of AF555 conjugated ginger-derived mEVs with or without TCEP reduction. (b) Fluorescence spectrometry measurement of AF555 conjugated grape-derived mEVs with or without TCEP reduction.

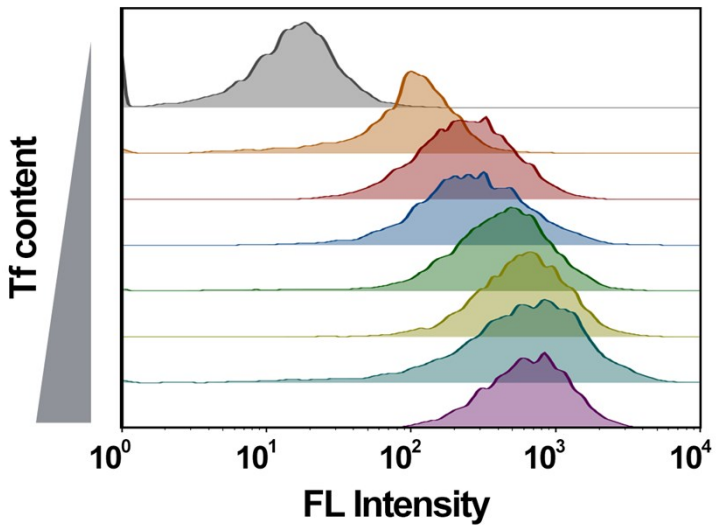

Fig. S2. HepG2 cellular uptake analysis of DiO-labeled mEVs conjugated with various concentration of transferrin by flow cytometry.

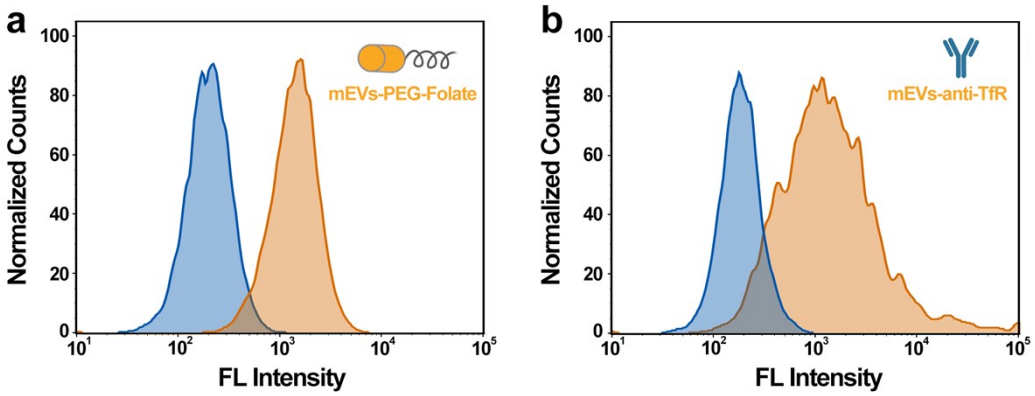

Fig. S3. (a) Cellular uptake analysis of HeLa cells incubated with DiO-labeled and folate-conjugated mEVs by flow cytometry. Here, a sulfhydryl reactive folate derivative, Folate-PEG-Mal, was attached to the surface of reduced mEVs through the thiol-maleimide click reaction. (b) Cellular uptake analysis of HepG2 cells incubated with DiO-labeled and antibody (anti-transferrin receptor) conjugated mEVs by flow cytometry. In this case, antibody against transferrin receptor (TfR) was derivatized with maleimide groups and conjugated to mEVs using the same approach.

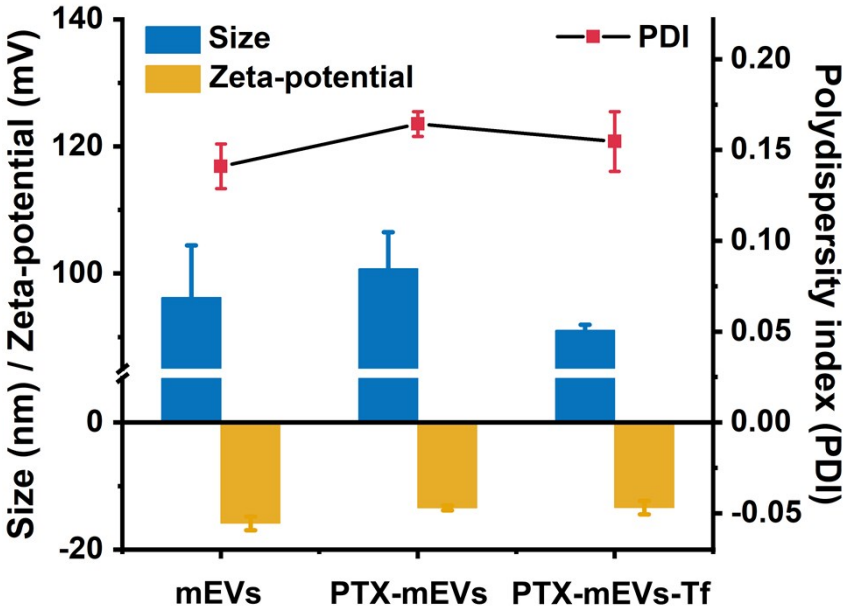

Fig. S4. Analysis of the particle size, PDI and zeta-potential of mEVs, PTX-mEVs and PTX-mEVs-Tf by DLS, respectively.

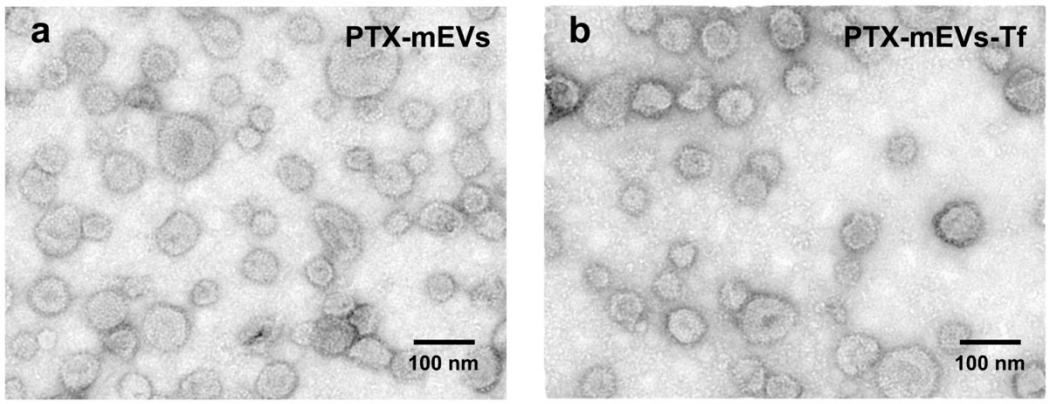

Fig. S5. The morphologies of PTX-mEVs (a) and PTX-mEVs-Tf (b) observed by TEM.