Supporting Information

Human Umbilical Cord Wharton's Jelly-Derived Mesenchymal Stem Cells Labeled with Mn^{2+} and Gd^{3+} Co-Doped $CuInS_2$−ZnS Nanocrystals for Multimodality Imaging in a Tumor Mice Model

Shashank Shankar Chetty[a], Selvarasu Praneetha[a], Arumugam Vadivel Murugan[a], Kavitha Govarthanan[b], Rama Shanker Verma[b]**

[a]*Advanced Functional Nanostructured Materials Laboratory, Centre for Nanoscience and Technology, Madanjeet School of Green Energy Technologies, Pondicherry University (A Central University), Puducherry-605014, India.*

[b]*Stem Cell and Molecular Biology Laboratory, Bhupat and Jyoti Mehta School of Biosciences, Department of Biotechnology, Indian Institute of Technology-Madras (IIT-M), Chennai-600036, India.*

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Corresponding Author *E-mail:avmrajeshwar@gmail.com, avmurugan.nst@pondiuni.edu.in. Tel. +91-413-2654975.

*E-mail: vermars@iitm.ac.in, Tel. + 91-44-2257-4109

S1. Phase transformation protocol *via* ligand exchange

Briefly, 50 mg of MUA was dissolved in 0.5 mL of methanol and pH was adjusted to 12 using TMAH under continuous stirring. The transparent MUA-methanol mixture was added dropwise to 5 mL of MW-R synthesized DDT-functionalized NCs in chloroform and stirred at 70 °C for 30 min. Subsequently, 5 mL of PBS buffer was added and stirred for 20 min. The resultant solution separated into two phases, upper phase containing water soluble MUA-functionalized NCs in PBS and lower phase containing DDT ligands in chloroform. The MUA-functionalized NCs in PBS was stored at room temperature for further characterizations.

S2. Induced differentiation of WJ-MSCs and histological staining

Adipocyte differentiation: The CIS-ZMGS NCs labeled WJ-MSCs were supplemented with the induction medium comprising dexamethasone (1 μM), isobutylmethylxanthine (0.5 mM), insulin (10 μg/mL), indomethacin (200 μM) for 14 days and examined by labeling lipid droplets using Oil Red O.

Osteocyte differentiation: The CIS-ZMGS NCs labeled WJ-MSCs were supplemented with the induction medium comprising of L-ascorbic acid 2-phosphate (0.2 mM), dexamethasone (1 μM), and β-glycerol phosphate (10 mM) for 14 days and visualized by staining mineral depositions using alizarin red.

Chondrocyte differentiation: The CIS-ZMGS NCs labeled WJ-MSCs were supplemented with the induction medium comprising of BSA (1.25 mg/mL), insulin (6.25 μg/mL), transferrin (6.25 g/mL), transforming growth factor (10 ng/mL), selenous acid (6.25 g/mL), dexamethasome (100 nM), L-ascorbic acid (0.1 mM), proline (0.35 mM), linolenic acid (5.33 mg/mL) and sodium pyruvate (1mM) for 28 days and imaged by staining glycosaminoglycan using toluidine blue.

S3. Histopathology, ICP-MS, immuno-fluorescence and hematology analysis

After 6 h post-transplantation of CIS-ZMGS NCs labeled WJ-MSCs, all the major organs (liver, lungs, spleen, heart and kidney) were excised from tumor-bearing C57BL/6 mice and embedded in paraffin for developing thin sections. The sections were stained with haematoxylin and eosin for histopathological studies. For ICP-MS analysis, tissue organs were pre-digested using nitric acid method and the concentrations of Cu (copper) was determined by Teledyne Leeman, Prodigy XP. For immuno-fluorescence assay, the thin section of excised tumor was fixed with 2% PFA and blocked using 3% BSA at room temperature for 1 h.[59] The sections were primarily conjugated using anti-human nuclei (1:100, HuNu; Millipore, US) for 12 h at 4 °C and secondary labeled with goat anti-mouse IgG conjugated with fluorescent Cy3 (1:500, Invitrogen, US) in dark for 2 h. The tumor sections were gently rinsed with DPBSA after staining using Hoechst (1 μM) for 5 min and imaged under fluorescence microscope (Nikon Ti-E, Japan). For hematology investigation, blood samples were harvested and analysed for whole blood count, lipid profiles, bio-chemical levels, liver and kidney function tests by automated analyzer (Mindray, China).

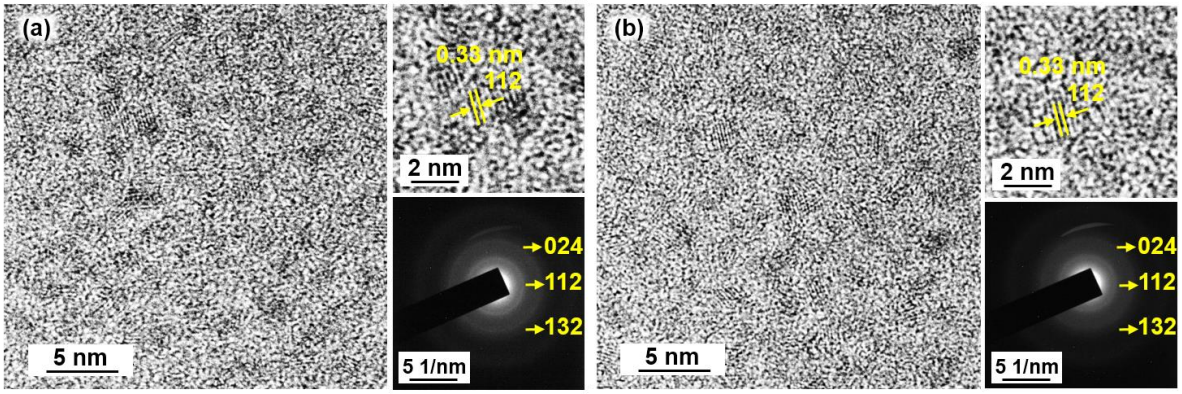

Figure S1. HR-TEM images of (a) Mn^{2+} and (b) Gd^{3+} doped $CuInS_2$-ZnS NCs. [Inset: Higher magnification and SAED pattern, respectively]

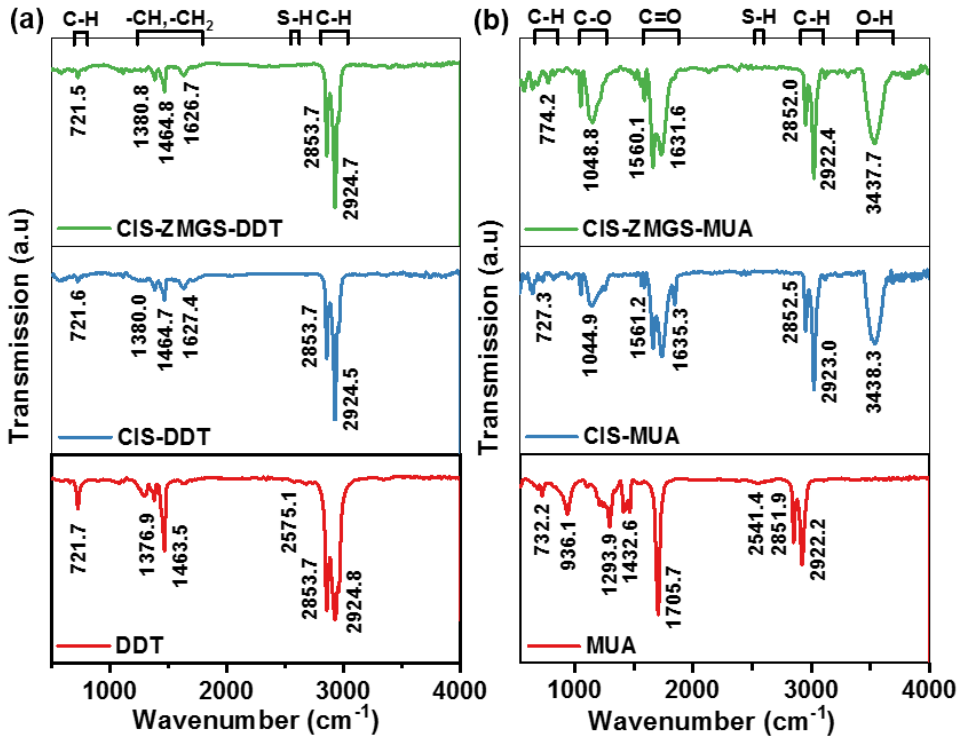

Figure S2. FT-IR spectra of (a) DDT- and (b) MUA-functionalized NCs before and after phase transformation, respectively.

Functionalization of ligands on the surface of NCs play crucial role reinforcing structural defects and optical properties of synthesized NCs. The FT-IR spectra DDT-fucntionalized NCs exhibited characteristics peaks around 2853.7 and 2924.8 cm^{-1}, assigned to symmetric and asymmetric CH_2 and CH_3 stretching modes, respectively. The vibrational peak at 1464.7, 1463.5 cm^{-1} and a feeble peak at ~1380.0 cm^{-1} are ascribed to deformed vibration of $–CH_2$ and C-H stretching, respectively. In particular, the absence of characteristic peak at 2575.1 cm^{-1} due to S-H stretching clearly corroborated the coordination of DDT ligands on NCs surface during MW-R synthesis. After phase transformation, the MUA-functionalized NCs in water exhibited vibrational peaks around 2852.0 and 2922.4 cm^{-1}, assigned to symmetric and asymmetric CH_2 and CH_3 stretching modes, respectively. The characteristics peak around 1048.4, 1560.1, 1631.6 cm^{-1} are ascribed to carboxyl (-COOH) group. In addition, the absence of vibration peak 2541.4 cm^{-1} due to S-H

stretching confirmed the substitutive ligand exchange of DDT over MUA ligand on NCs surface. Interestingly, ligand exchange mechanism using MUA involves two functional groups *i.e.* thiols (S-H) and carboxyl (-COOH). During phase transformation process in alkaline pH, the functional groups are deprotonated and thus, cations (Cu^{+}, Zn^{2+}) on NCs surface exhibit enhance binging affinity with thiols than carboxyl group that spatially orient outward to adjust the pH of solution above pKa, thereby dispersing NCs in water.

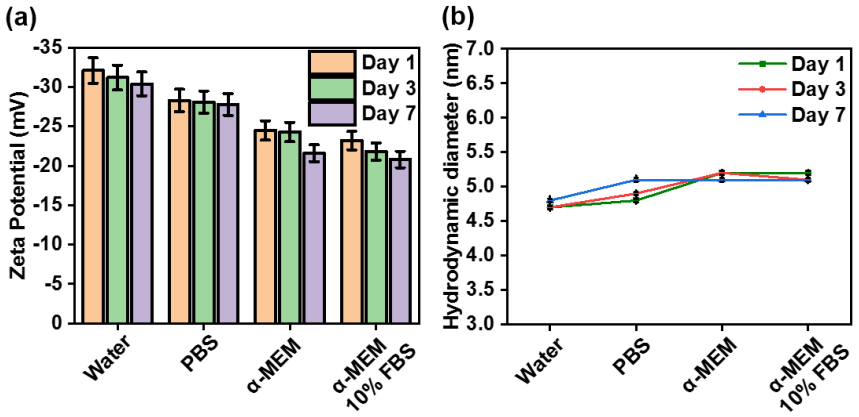

Figure S3. Time-dependent changes (a) Zeta potential and (b) hydrodynamic diameter of MUA-functionalized CIS-ZMGS NCs in different physiological conditions.

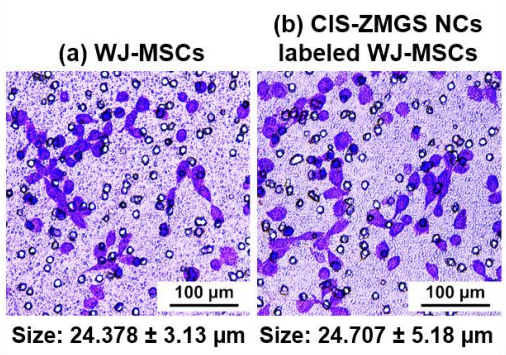

Figure S4. Crystal violet staining of (a) WJ-MSCs and (b) CIS-ZMGS NCs labeled WJ-MSCs for cell size measurement.

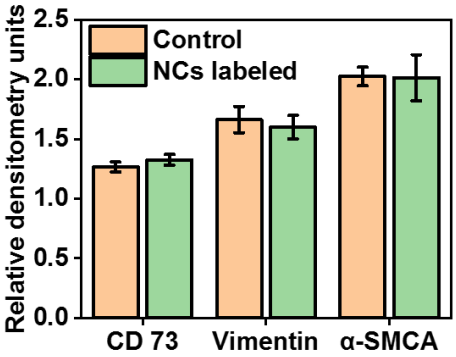

Figure S5. Quantitative analysis of proteins (CD73, Vimentin, α-SMCA) expression by western blot technique.

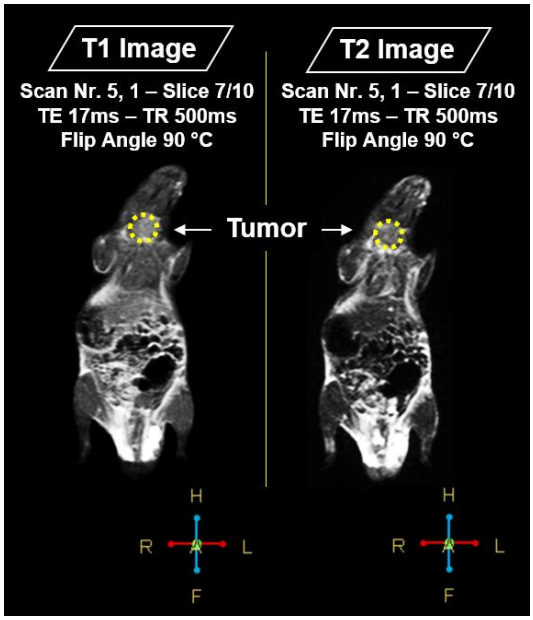

Figure S6. *In vivo* T_1-weighted (left) and T_2-weighted (right) MR imaging of control B16F10 tumor-bearing C57BL/6 mice.

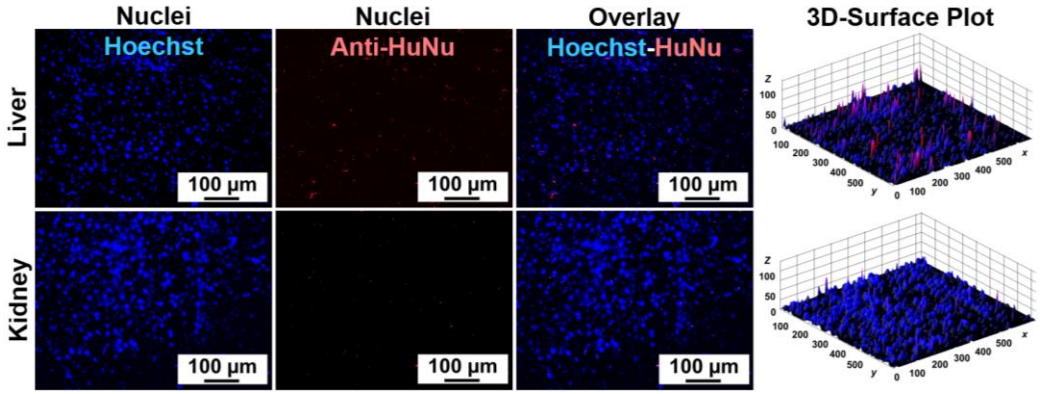

Figure S7. Immuno-fluorescence labeling of excised liver (above) and kidney (below) tissues with Hoechst dye (blue) and anti-HuNu antibody (red).

Table S1. Elemental quantification of MW-R synthesized CIS-ZMGS NCs by XPS analysis

Peak	Cu 2p	In 3d	S 2p	Zn 2p	Mn 2p	Gd 3d	C 1s	O 1s
Atomic Concentration (%)	1.21	4.92	20.35	8.03	1.69	1.07	56.92	5.82

Table S2. List of primer sequences for RT-PCR analysis of differentiated MSCs.

Gene Name	Primer Detail
CEBP A	FP-5' AAGAAGTCGGTGGACAAGAACAG 3' RP-5' TGCGCACCGCGATGT 3'
CEBP B	FP- 5' GCAAGAGCCGCGACAAG 3' RP- 5' GGCTCGGGCAGCTGCTT 3'
PPAR G	FP- 5' AGGCGAGGGCGATCTTGACAG 3' RP- 5' GATGCGGATGGCCACCTCTTT 3'
FABP 4	FP-5' GCTTTGCCACCAGGAAAGTG 3' RP-5' ATGGACGCATTCCACCACCA 3'
Collagen I	FP-5' GGCCATCCAGCTGACCTTCC 3' RP-5' CGTGCAGCCATCGACAGTGAC 3'
Collagen II	FP-5' TGAACGAGGTTTCCCAGGTG 3' RP-5' CCAGGCATTCCCTGAAGACC 3'
Runx2	FP-5' GCGGTGCAAACTTTCTCCAG3' RP-5' TCACTGTGCTGAAGAGGCTG 3'
Opn	FP-5' TTGCAGCCTTCTCAGCCAA 3' RP- 5' GGAGGCAAAAGCAAATCACTG 3'
Sox9	FP-5' AGCACTCATAATATGGCATCCTTCA 3' RP- 5' AGGTAAGTTTCACGGAGAGAACAA 3'