Electronic Supplementary Information

Immuno-silent Polymer Capsules Encapsulating Nanoparticles for Bioimaging Applications

Jaishree Jeyaraman[$,†], Anna Malecka[§], Poonam Billimoria[§], Akansha Shukla[$,†], Barsha Marandi[$,†], Poulam M Patel[§], Andrew M Jackson[§,*], and Sri Sivakumar[$,†,‡,≠*]

[$]Department of Chemical Engineering, Indian Institute of Technology Kanpur, Kanpur, Uttar Pradesh-208016, India

[†]Centre for Environmental Sciences and Engineering, Indian Institute of Technology Kanpur, Kanpur, Uttar Pradesh-208016, India

[§]Host-Tumour Interactions Group, Department of Academic Oncology, Division of Cancer and Stem Cells, University of Nottingham, Nottingham, NG5 1PB, United Kingdom

[‡]Material Science Programme, Indian Institute of Technology Kanpur, Kanpur, Uttar Pradesh-208016, India

[≠]DST Thematic Unit of Excellence on Nanoscience and Soft Nanotechnology, Indian Institute of Technology Kanpur, Kanpur, Uttar Pradesh-208016, India

*Corresponding authors:

andrew.jackson@nottingham.ac.uk, Tel: 0115- 82 31860, Fax: 0115 82 31849,

srisiva@iitk.ac.in, Tel: +91-512-2597697, Fax: 91-512-2590104

S1. Synthesis of polymer capsules encapsulating YVO_4/$LaVO_4$/$GdVO_4$/Gd_2O_3:Tb^{3+} nanoparticles. Silica particles were prepared by base-catalyzed Stöber's process with the hydrolysis of tetraethylorthosilicate (4.7 mL) using ammonia (54.4 mL) in a solution of water (2 mL) and ethanol (50 mL). The particles were separated centrifugally by washing with deionized water followed by ethanol to remove the excess of reactants and heated at 80 °C overnight. For coating of lanthanide-doped nanoparticle shell over silica core, stoichiometric weights of $Y(NO_3)_3.4H_2O$/$La(NO_3).xH_2O$/$Gd(NO_3)_3.xH_2O$/$Gd_2O_3.xH_2O$, $Tb(NO_3)_3.5H_2O$ and $NaVO_3$ were added to a mixture of 1:7 ratio of water to ethanol and kept under magnetic stirring (protocol reported elsewhere for YVO_4:Eu^{3+}@silica).[1]Citric acid was used as chelating agent for metal ions with a molar ratio of 2:1 and polyethylene glycol (PEG) was added as a cross-linking agent with the concentrations of 0.08 g/mL. The solution was stirred for 1 h and silica particles were added. The suspension was further stirred for 3 h and the coated silica particles were separated by centrifugation. The samples were dried at 80 °C overnight and annealed at 500 °C for 3 h in air at a heating rate of 4 °C/min. Polymer coating on core-shell particles were done using layer-by-layer (LbL) assembly method.[2-10] PEI (1 mg/mL) was added to the particles and kept in rotospin for 15min. This adsorption step was followed by washing the samples with 0.5M NaCl and centrifuging it at 1000 rcf for 3 min for removal of the excess of polymer present in supernatant. Subsequently 7 polyelectrolyte layers were made with poly (sodium 4-styrene-sulfonate) (PSS) (1 mg/mL) and poly (allylamine hydrochloride) (PAH) (1 mg/mL) to form 8 layers with alternate positive and negative charge. LbL assembled core-shell particles with PSS as outer layer was incubated with bisamine-(PEG) (1mg/mL) for 24 h. Excess bisamine-(PEG) was removed by centrifugation and washing steps with de-ionized water. Finally, removal of silica core was done with buffer oxide etchant 0.75M HF: 4M HF.

S2. Synthesis of polymer capsules loaded with GdF_3 nanoparticles/iron oxide nanoparticles. Hollow polymer capsules were synthesized by LbL assembly of PSS and PAH as alternatively charged layers on aminated 1.1 μm silica. It was modified with PEG-bisamine as outer layer and removal of silica core was carried out using 5M HF leading to formation of hollow polymer capsules. These capsules acts as microreactors for synthesis of nanoparticles as precursor salts were added to them at appropriate growth conditions. For synthesizing GdF_3:Tb^{3+} nanoparticles, 0.26M citric acid was added to capsules (pH adjusted using ammonia) and mixed well for 15 min at 40 °C. It was followed by addition of $Gd(NO_3)_3.6H_20$ (0.5mM), $Tb(NO_3)_3.5H_2O$ (0.028mM) and NaF and mixed for 2 h at 40 °C. The capsules loaded with nanoparticles were separated out by centrifuging at 3000 rcf for 5 min and washed with deionized water. In case of iron oxide nanoparticles, the hollow polymer capsules were incubated with iron sulfate pentahydrate (0.02g/mL) for 12 h which aid in the adsorption of iron with sulfonate and carboxylate groups of polymer capsules.[11] Iron ions were further reduced using $NaBH_4$ (1mM) and hydrolyzed by NaOH, each for 30 min respectively. The iron oxide loaded capsules were separated by centrifugation and washing steps. For cell uptake experiments, RITC-PAH/FITC-PAH labeled capsules encapsulating iron oxide nanoparticles (protocol for FITC-PAH reported elsewhere was followed for preparation)[12] were prepared to visualize the capsules in confocal laser scanning microscope (CLSM).

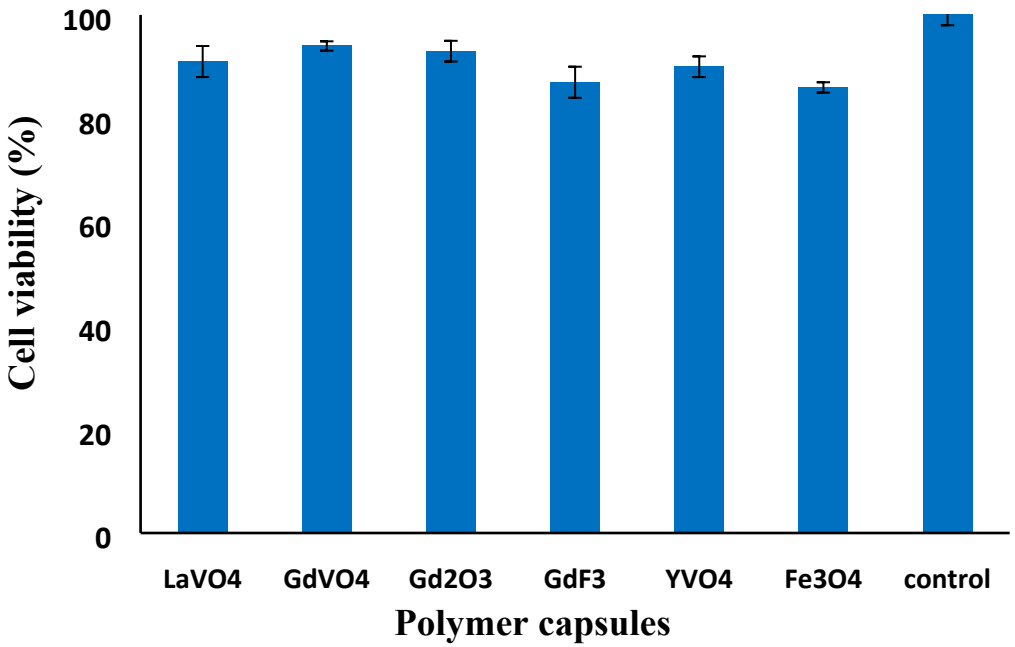

Figure S1. MTT assay plot of PEGylated polymer capsules encapsulating nanoparticles doped with terbium ions in IC-21 cell line (mouse peritoneal macrophages)

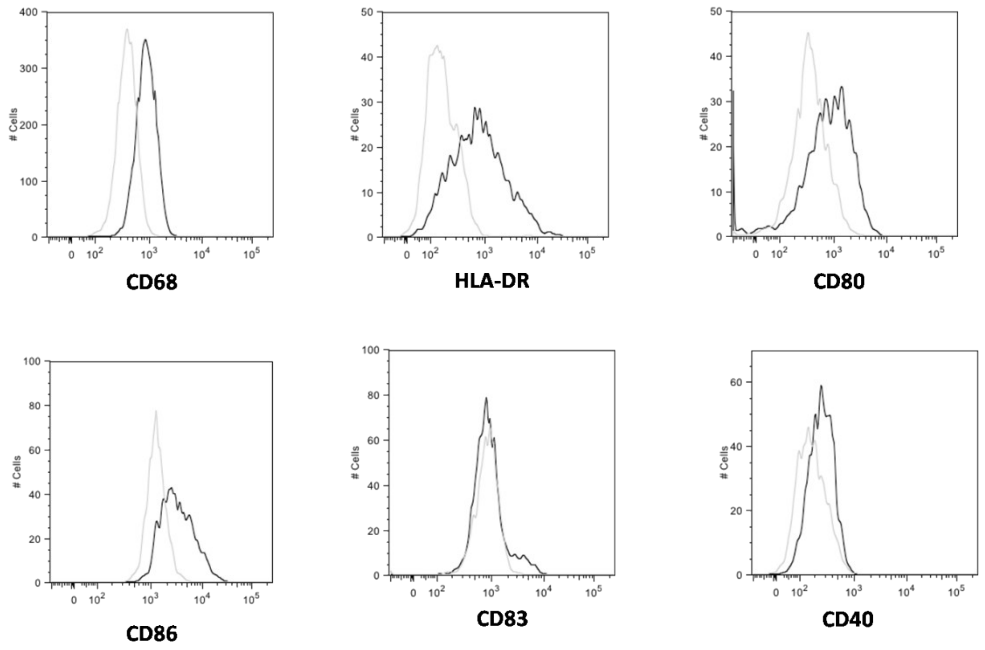

Figure S2a Phenotype of M1 macrophages analyzed by flow cytometry for expression of markers before activation (Faint line indicates isotype control and black line shows CD-marker).

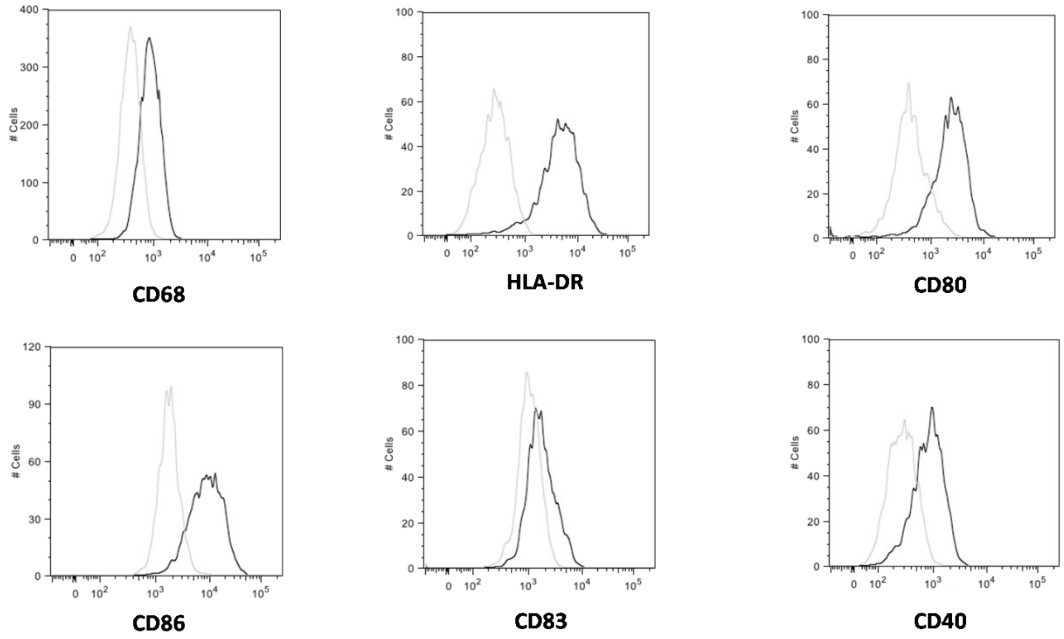

Figure S2b Phenotype of M1 macrophages analyzed by flow cytometry for expression of markers after activation with LPS/IFN-γ (Faint line indicates isotype control and black line shows CD-marker). Results shown for a representative donor out of 4.

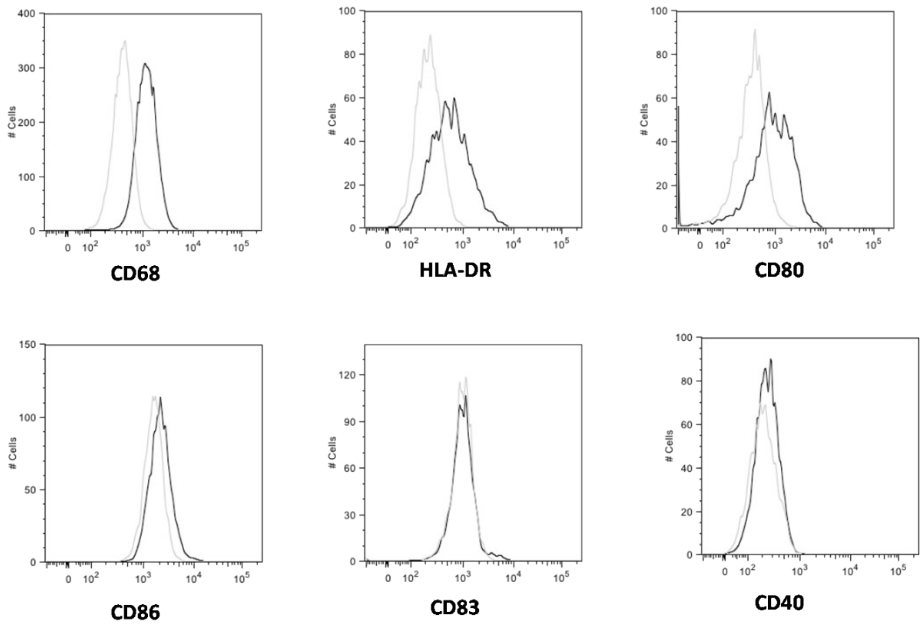

Figure S3a Phenotype of M2 macrophages analyzed for expression of markers before activation by flow cytometry (Faint line indicates isotype control and black line shows CD-marker).

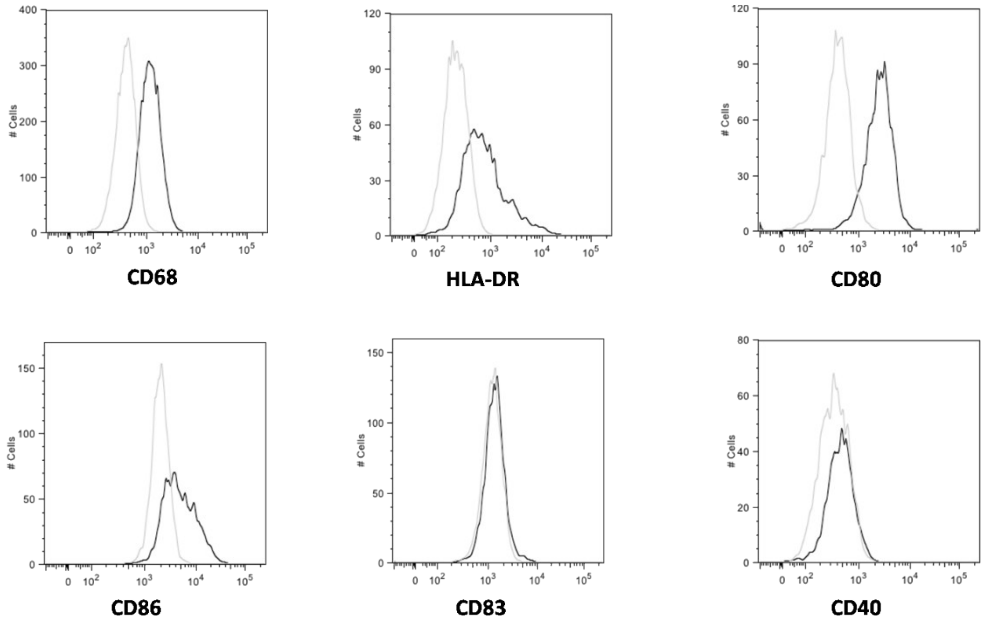

Figure S3b Phenotype of M2 macrophages analyzed for expression of markers after activation by flow cytometry (Faint line indicates isotype control and black line shows CD-marker).

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