

## Supplementary Material

### **A Targeted Nanoglobular Manganese(II) Chelate Conjugate for Magnetic Resonance Molecular Imaging of Tumor Stroma**

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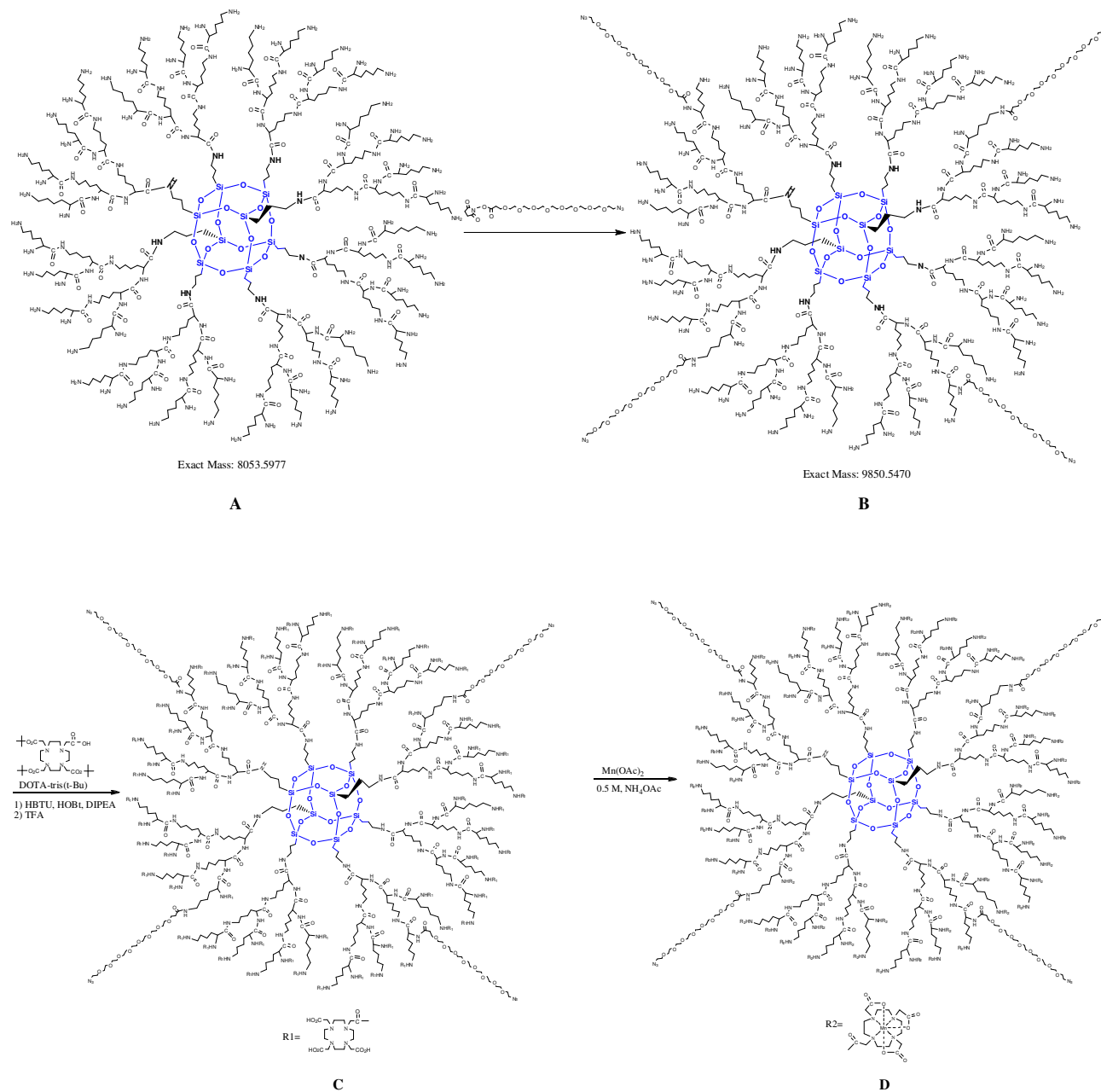
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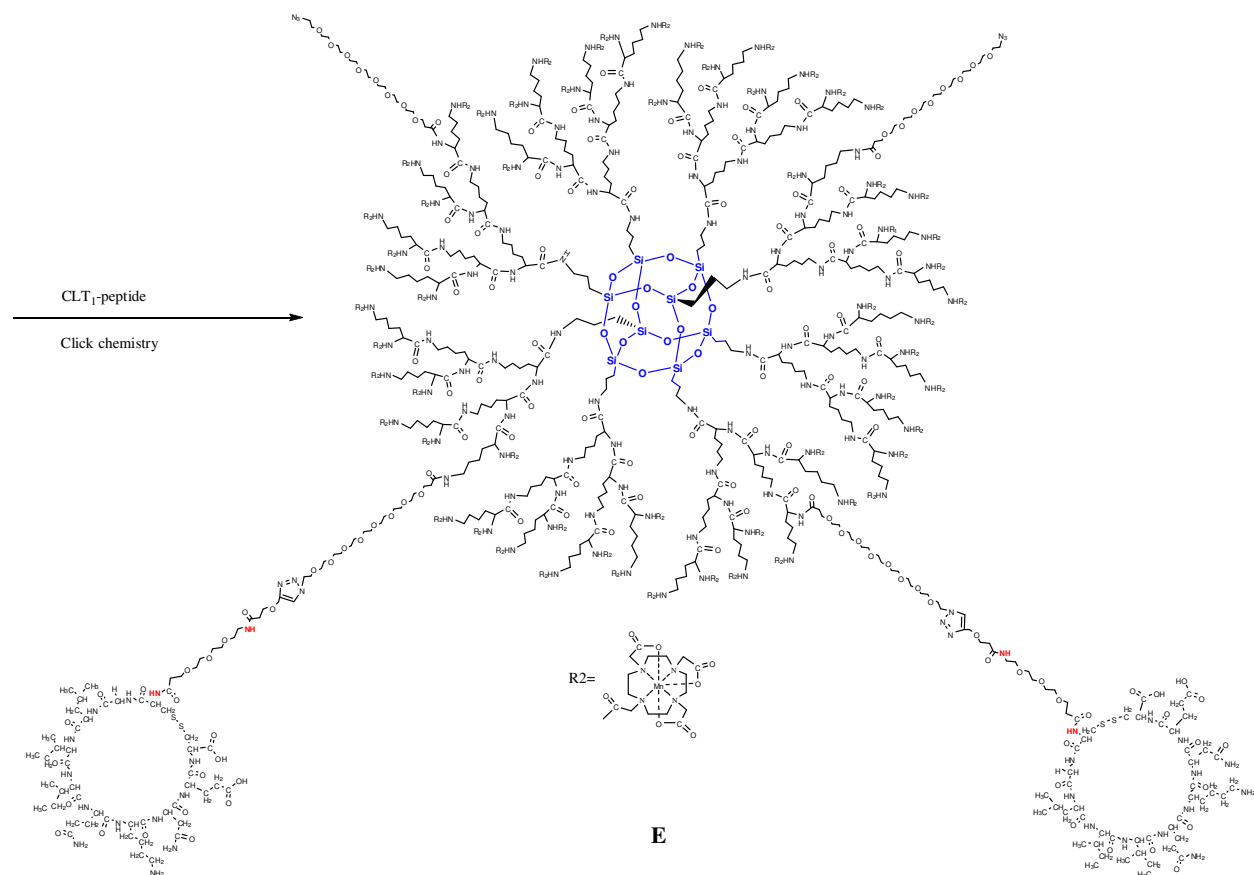
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## Experimental Section

### Scheme S1: Synthesis of CLT1 peptide targeted nanoglobular Mn(II) chelate (P-G3-Mn)

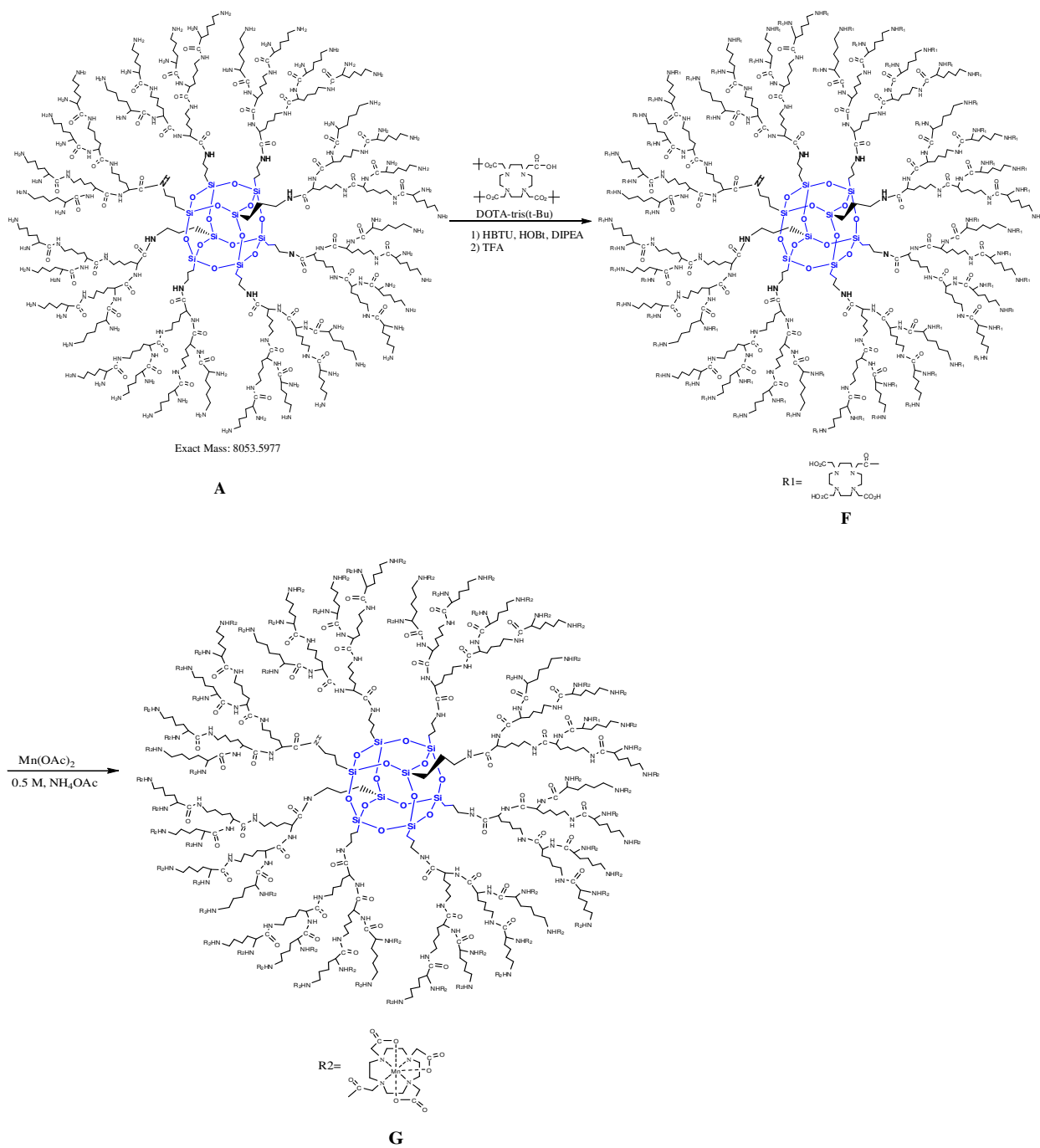


- A:** Generation 3 (G3) nanoglobule with an OAS core
- B:** G3 nanoglobule-PEG-azido conjugate
- C:** G3 nanoglobule-DOTA-PEG-azido conjugate
- D:** G3 nanoglobule-Mn-DOTA-PEG-azido conjugate

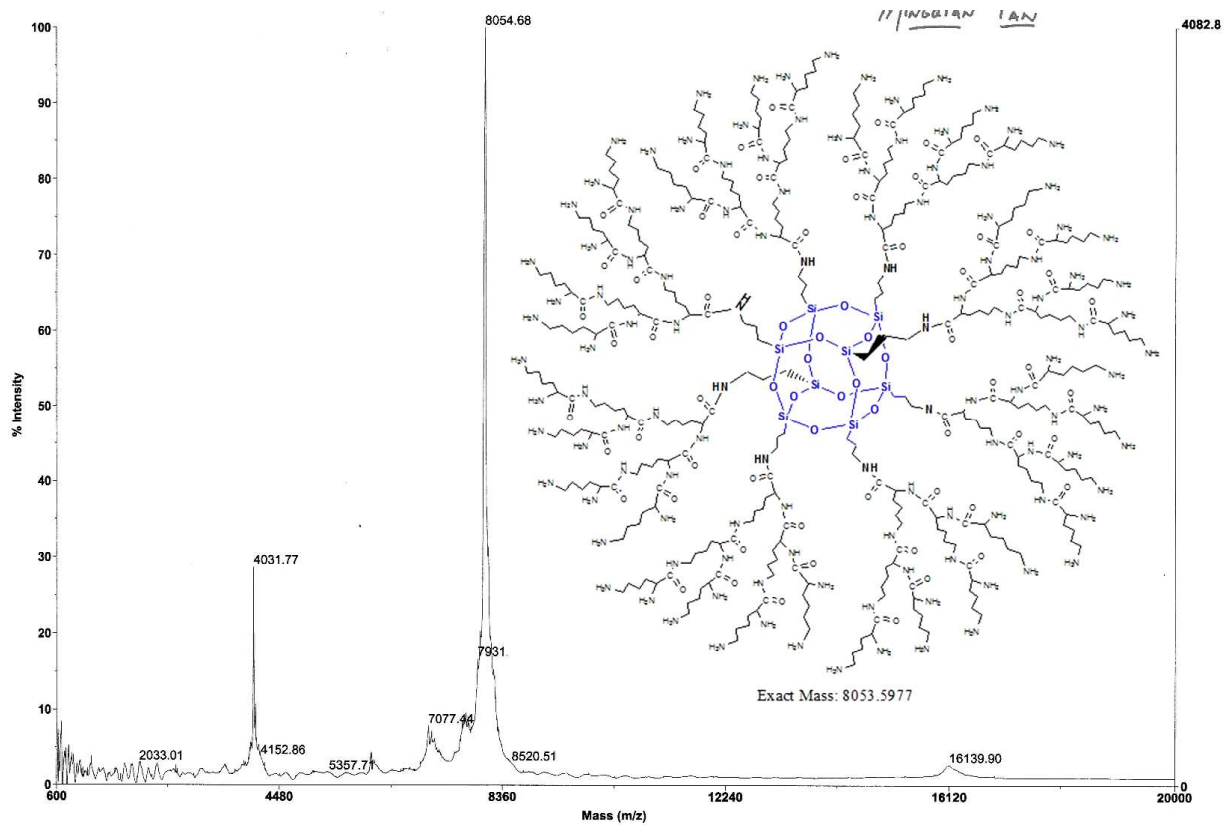


**E:** CLT<sub>1</sub> peptide targeted nanoglobular Mn(II) chelate contrast agent (P-G3-Mn)

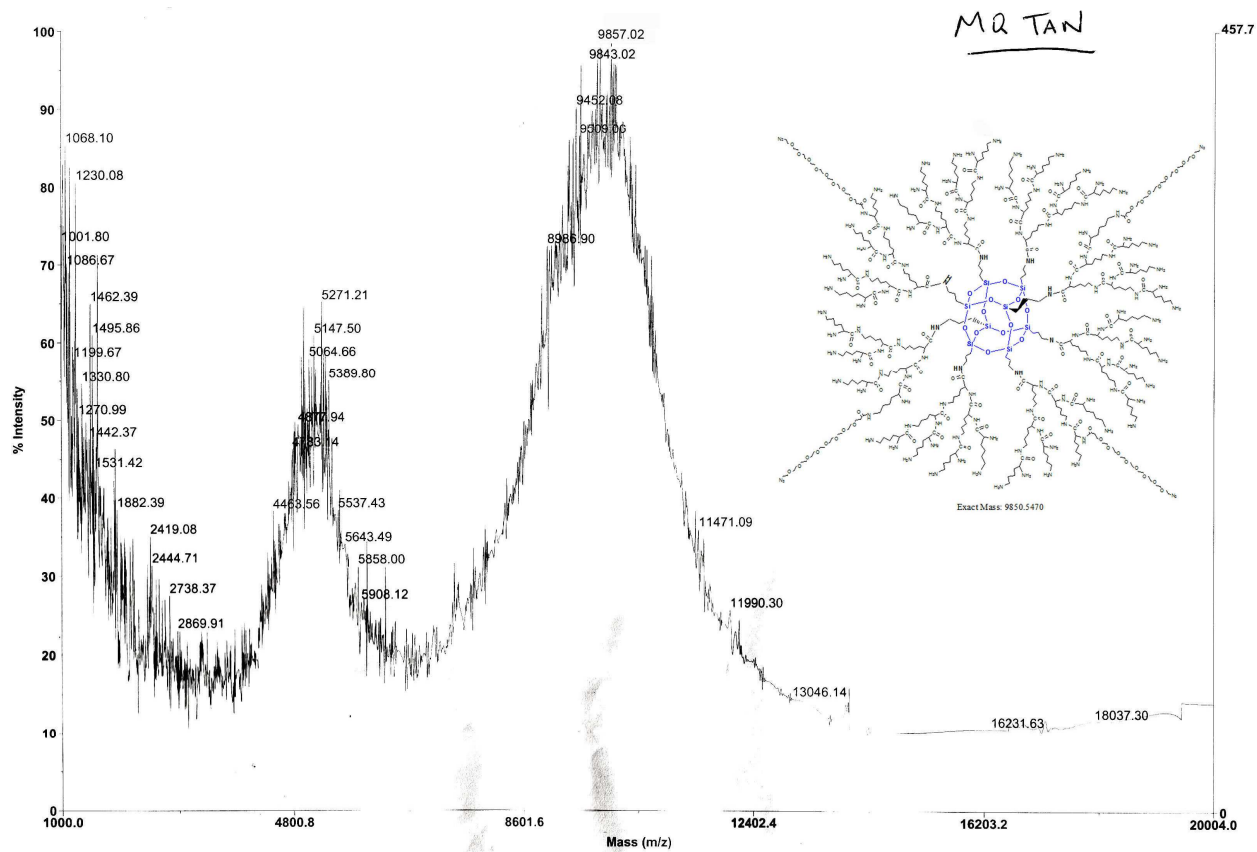
**Scheme S2: Synthesis of non-targeted nanoglobular Mn(II) chelate (G3-Mn)**



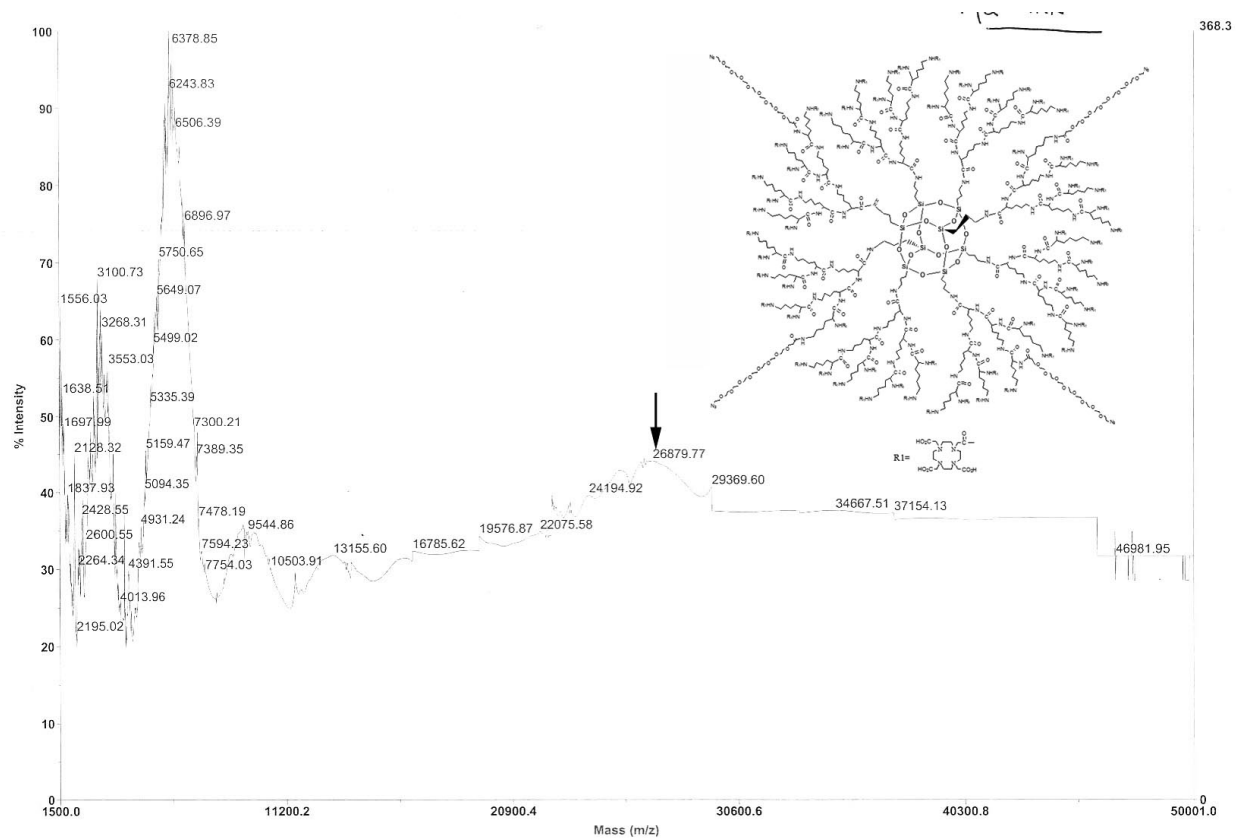
- A:** G3 nanoglobule with an OAS core  
**F:** G3 nanoglobule-DOTA conjugate  
**G:** Non-targeted nanoglobular Mn(II) chelate contrast agent



**Figure S1.** MALDI-TOF mass spectrum of G3 nanoglobule. Insert shows its structure.

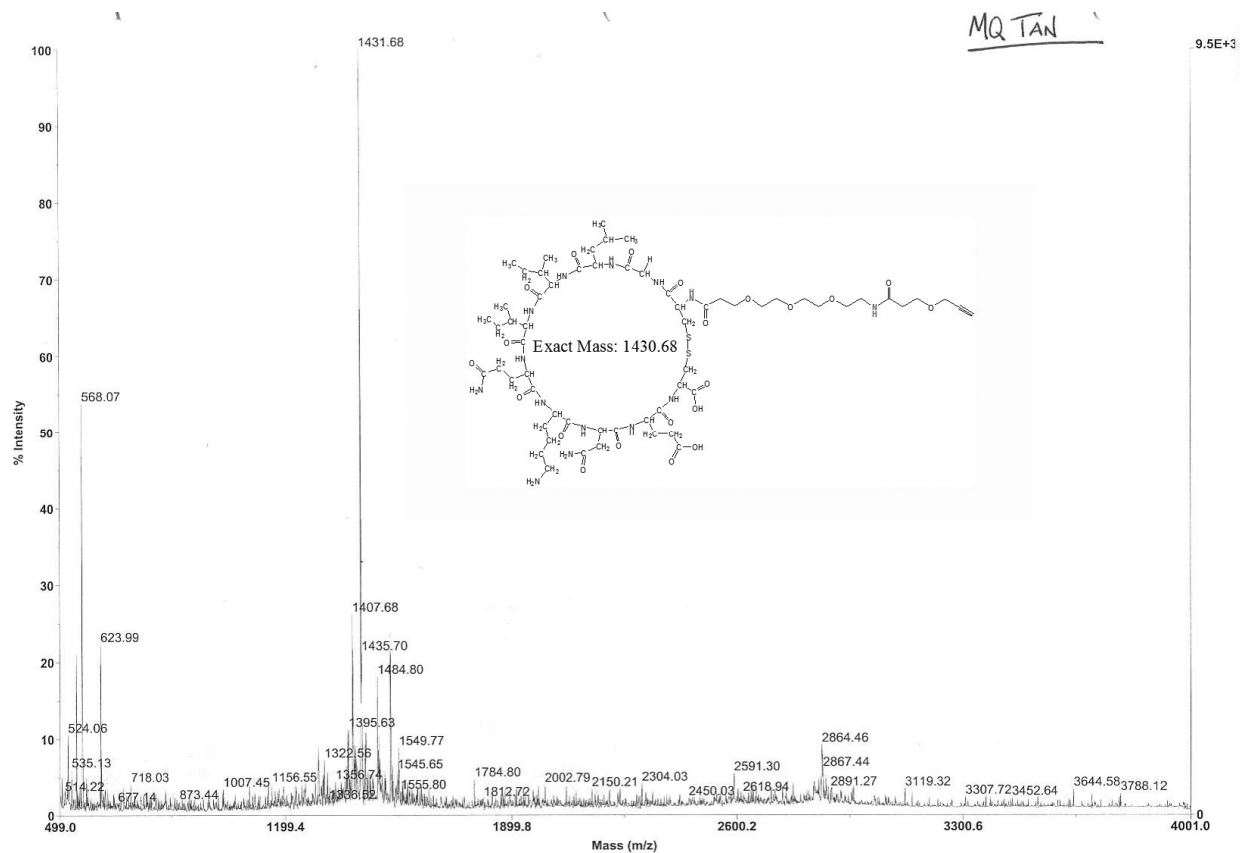


**Figure S2.** MALDI-TOF mass spectrum of G3 nanoglobule-PEG-azido conjugate. Insert shows its structure.



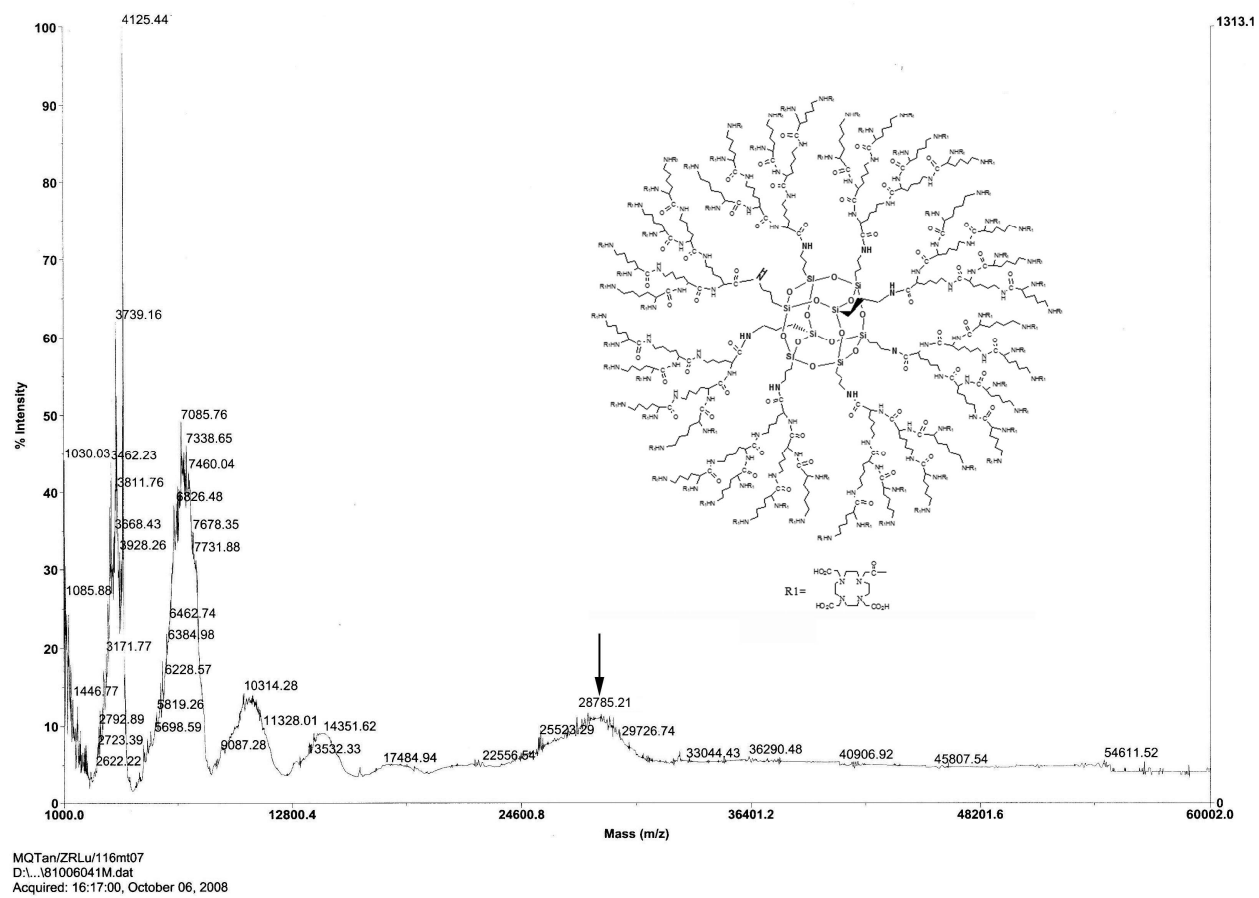
**Figure S3.** MALDI-TOF mass spectrum of the G3 nanoglobule-DOTA-PEG-azido conjugate.

Insert shows its structure.

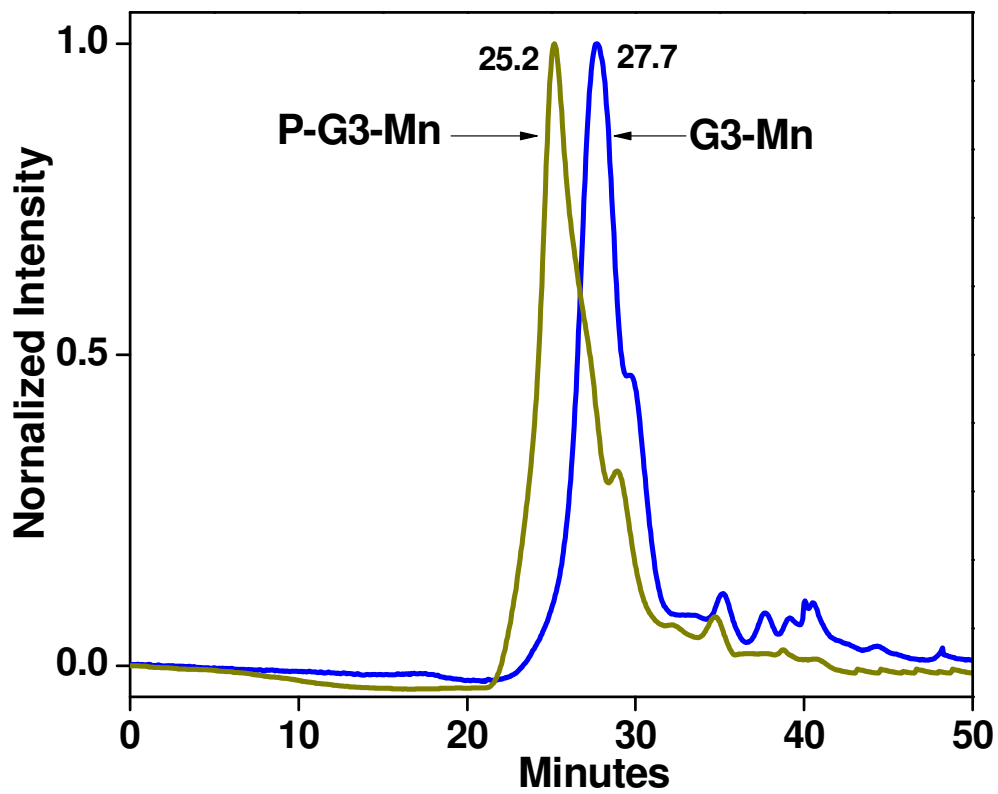


**Figure S4.** MALDI-TOF mass spectrum of CLT1 peptide PEG-propargyl conjugate. Insert shows its structure.

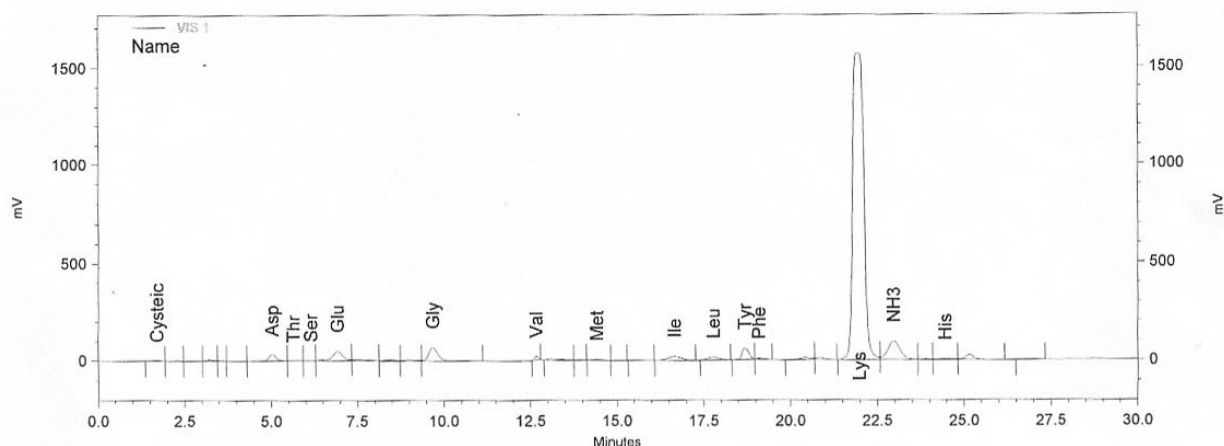




**Figure S5.** MALDI-TOF mass spectrum of G3 nanoglobule-DOTA conjugate. Insert shows its structure.



**Figure S6.** Size-exclusion HPLC chromatograms of targeted (P-G3-Mn) and non-targeted (G3-Mn) nanoglobular Mn(II) chelate contrast agent



**Figure S7.** Amino acid analysis of targeted nanoglobular Mn(II) chelate contrast agent (P-G3-Mn)

**Table S1.** Amino acid analysis of targeted nanoglobular Mn(II) chelate contrast agent (P-G3-Mn)

Peak	Retention time (min)	Amino acid Name	Area	Total nmol per sample
1	1.703	Cys (C)	191594	0.409
2	5.023	Asp (D)	1874065	4.782
3	6.923	Glu (E)	4212284	11.514
4	9.683	Gly (G)	5017285	11.234
5	12.663	Val (V)	564905	4.533
6	16.673	Ile (I)	2137764	5.526
7	17.787	Leu (L)	1382040	3.582
8	18.683	Tyr (Y)	3004913	7.451
9	21.973	Lys(K)	138658768	303.245
10	22.973	NH <sub>3</sub>	9369929	44.902

**Peptide CLT1: CGLIIQKNEC**

**Table S2.** Elemental analysis results of nanoglobular agents with inductively coupled plasma-optical emission spectroscopy (ICP-OES)

	Amount of sample (mg)	solution (g)	Mn (ppm)	S (ppm)	Cu (ppm)	Mn (wt.%)	S (wt.%)	Cu (wt.%)
P-G3-Mn	0.70	5.004	9.99	0.505	0.27	7.14	0.361	0.19
P-G3-Mn	1.42	7.972	12.90	0.643	0.37	7.29	0.360	0.21
Average						7.20	0.3605	0.20
G3-Mn	1.38	9.223	13.49			9.01		
G3-Mn	2.54	11.236	21.31			9.77		
Average						9.39		