

Supporting Information

Photon Correlation Spectroscopy

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	<i>HD (nm)</i>
SRPs	4.1 ± 1.2 nm
SRP-1	4.6 ± 1.3 nm
SRP-2	3.8 ± 1.0 nm
SRP-3	4.4 ± 1.3 nm

Table 1. Hydrodynamic diameters (HDs) of unfunctionalized SRPs and functionalized SRPs with melanin-targeting ligands **1**, **2** and **3** measured by PCS and performed at $[\text{Gd}^{3+}] = 10$ mM.

Mass Spectrometry

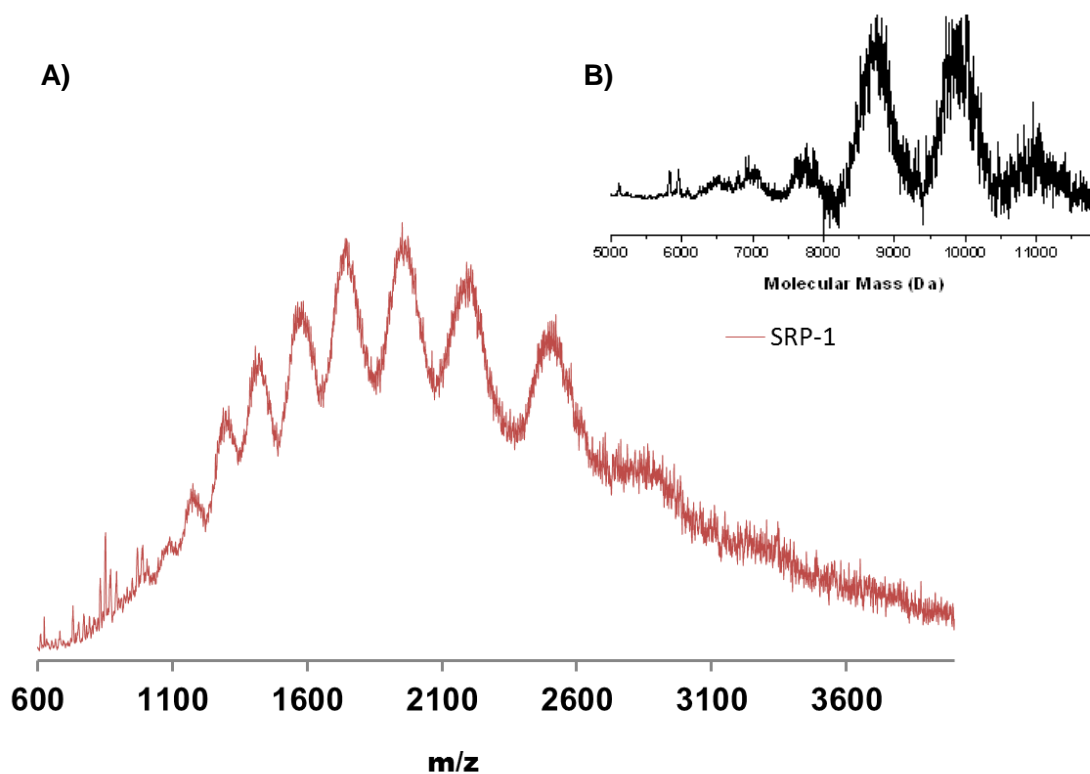


Figure 1. Mass spectrometry measurements of the functionalized SRPs with melanin-targeting ligand **1**: (A) Full m/z spectrum obtained after electrospraying the solution containing SRP-**1**, (B) Spectrum generated after deconvolution with the multiplicative correlation algorithm.

Infrared Spectroscopy

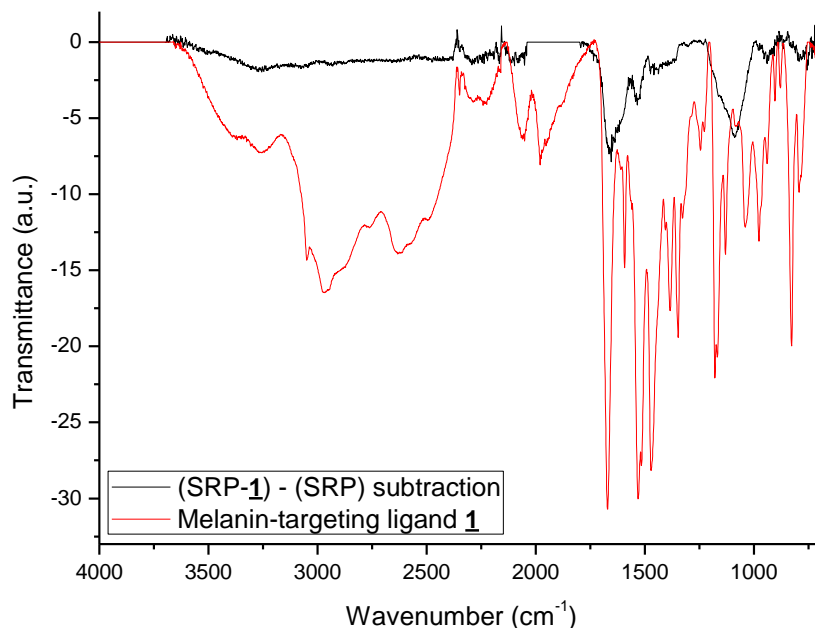


Figure 2. IR resulting spectrum of the subtraction of SRP-**1** to unfunctionalized SRP spectra and IR spectrum of the melanin-targeting ligand **1**.

IR melanin-targeting ligand **1**: cm^{-1} : 3050 (C-H, quinoxaline), 2968 and 2882 (C-H, $-\text{CH}_2-$ and $-\text{CH}_3$), 1671 (C=O, amide), 1592 (N-H, amide), 1510-1580 (C=C, quinoxaline), 1472 (C-H, $-\text{CH}_2-$), 1385 (C-H, $-\text{CH}_3$), 1180-1350 cm^{-1} (C-N, quinoxaline), 1030-1230 (C-N, amines) and 700-900 cm^{-1} (C-H, quinoxaline and N-H, primary amines)

IR Subtraction [SRP-**1**] – [SRP]: cm^{-1} : 1580-1720 (C=O and N-H, amide), 1500-1560 (C=C, quinoxaline), 1000-1360 (C-N, quinoxaline and tertiary amine)

IR melanin-targeting ligand **2**: cm^{-1} : 3393 (N-H, primary amide), 3067 (C-H, quinoxaline), 2923 and 2853 (C-H, $-\text{CH}_2-$), 1670 (C=O, amide), 1592 (N-H, amide), 1500-1580 (C=C, quinoxaline), 1474 (C-H, $-\text{CH}_2-$), 1388 (C-H, $-\text{CH}_3$), 1202-1354 cm^{-1} (C-N, quinoxaline), 1030-1230 (C-N, amines), 1127 (C-O, ether) and 700-900 cm^{-1} (C-H, quinoxaline and N-H, primary amines)

IR Subtraction [SRP-**2**] – [SRP]: cm^{-1} : 1667 (C=O, amide), 1602 (N-H, amide), 1532 (C=C, quinoxaline), 1475 (C-H, $-\text{CH}_2-$), 1389 (C-H, $-\text{CH}_3$), 1010-1360 (C-N, quinoxaline and tertiary amine, and C-O, ether)

IR melanin-targeting ligand **3**: cm^{-1} : 3380 (N-H, secondary amide), 2927 (C-H, $-\text{CH}_2-$), 1685 (C=O, secondary amide), 1635 (C=O, primary amide), 1581 (N-H, primary amide), 1521 (N-H, secondary

amide), 1500-1590 (C=C, quinoxaline), 1489 (C-H, -CH₂-), 1212-1351 cm⁻¹ (C-N, quinoxaline), 1030-1212 (C-N, amines), 1090-1134 (C-O, ether) and 700-900 cm⁻¹ (C-H, quinoxaline and N-H, primary amines)

IR Subtraction [SRP-**3**] – [SRP]: cm⁻¹: 1662 (C=O, amide), 1589 (N-H, primary amide), 1528 (N-H, secondary amide), 1500-1590 (C=C, quinoxaline), 1491 (C-H, -CH₂-), 1387 (C-H, -CH₃), 1000-1320 cm⁻¹ (C-N, quinoxaline and tertiary amine, and C-O, ether)

UV-visible absorption

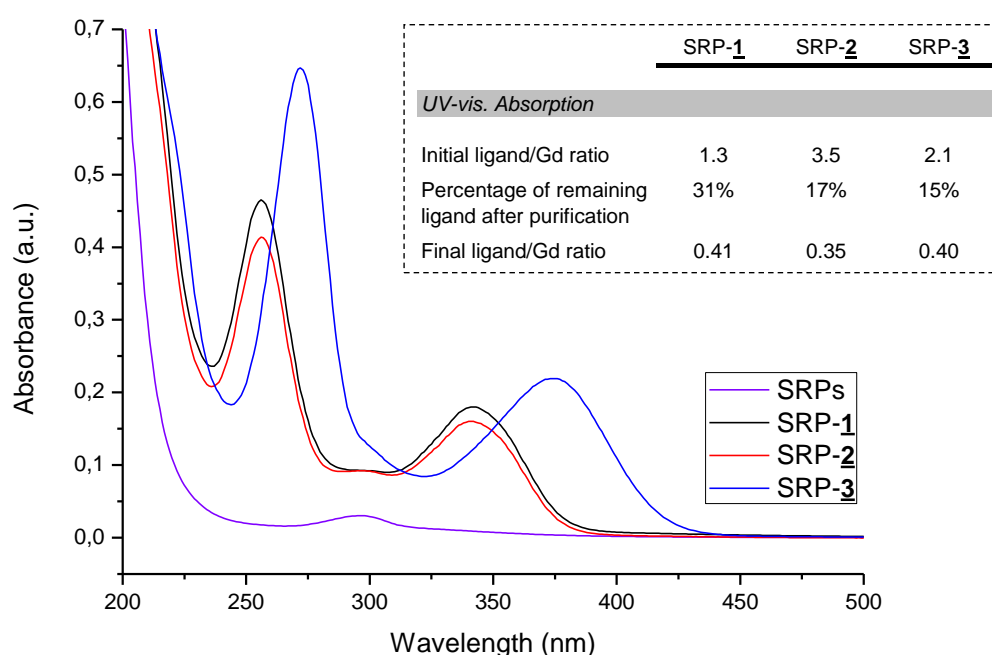


Figure 3. UV-visible Absorption Spectra of SRPs, SRP-**1**, SRP-**2**, SRP-**3** performed at 50 μ M Gd. In the box: initial and final melanin-targeting ligands/Gd molar ratios provided by UV-vis Absorption spectra, as well as the percentages of remaining melanin targeting ligands after purification.

Elemental Analyses

Elemental analyses were performed on unfunctionalized and functionalized SRPs. Two major hypotheses were made to estimate the SRP chemical compositions¹¹:

- each SRP displays 10 ± 1 DOTA molecules;
- the APTES/TEOS molar ratio of the polysiloxane network (1 Si = 0.6 APTES + 0.4 TEOS) remains constant during synthesis and purification steps.

Considering these two hypotheses and the molar ratios (*i.e.*, Si/Gd, C/Gd, N/Gd and I/Gd), an empirical method allowed tracing back to the approximate molecular formula of each SRP. Since only gadolinium, silicium, carbon, nitrogen and iodine weight percentages were measured, it was

appropriate to include any atom being different from the previously mentioned ones in our calculations. For example, water molecules and any counterion (e.g. Na⁺, OH⁻, etc.) were taken into account as well as solvent molecules. Indeed, since native SRP manufacturing was performed in diethylene glycol (DEG), some solvent molecules could have been trapped into the polysiloxane network during the synthesis.

	SRPs			SRP-1			SRP-2			SRP-3		
<i>Elemental Analysis - (Weight percent of each element)</i>												
	Exp.	Theo.	Error	Exp.	Theo.	Error	Exp.	Theo.	Error	Exp.	Theo.	Error
%Gd	9.96	9.96	0	8.23	8.20	0.03	8.37	8.29	0.08	8.67	8.13	0.54
%Si	9.18	9.18	0	8.42	8.39	0.03	8.53	8.45	0.08	9.78	9.17	0.61
%N	8.55	8.66	0.11	8.76	9.08	0.32	9.31	9.38	0.07	8.05	8.68	0.63
%C	31.65	31.16	0.49	32.06	31.62	0.44	32.97	32.78	0.19	29.85	29.76	0.09
%I	/	/	/	2.96	2.92	0.04	2.58	2.65	0.07	/	/	/

Table 2. Elemental analyses given in weight percent of element in the compound. For each sample, first the experimental weight percentages (carried out by the "Service Central d'Analyses de Solaize", CNRS), second the theoretical weight percentages deduced from the estimated molecular formulas and third the absolute error between the experimental and theoretical weight percentages are reported.

	SRPs	SRP-1	SRP-2	SRP-3
<i>Elemental Analysis</i> (Molar ratios)				
Si/Gd	5.16	5.51	5.71	6.32
N/Gd	9.64	11.96	12.49	10.43
C/Gd	41.64	51.05	51.62	45.12
I/Gd	/	0.45	0.38	/

Table 3. Molar ratios deduced from experimental weight percentages.

	SRPs	SRP-1	SRP-2	SRP-3
<i>Elemental Analysis - Number of ... molecules per SRP</i>				
Gd	6	5.9	5.8	6.1
DOTA	10	10	10	9
APTES	18.6	20.3	19.9	23.1
TEOS	12.4	13.5	13.2	15.4
Melanin-targeting ligands	/	2.6	2.3	2
H ₂ O (or counterions)	65	85	70	120
DEG	0	2	0	2
Estimated Molecular Mass (kDa)	9.5	11.3	11.0	11.8
<i>UV-visible Absorption - Number of melanin-targeting ligands per SRP</i>				
Melanin-targeting ligands	/	2.4	2	2.4

Table 4. Estimated molecular formulas of unfunctionalized SRPs and functionalized SRPs with melanin-targeting ligands, and their corresponding molecular mass deduced from weight percentages supplied by elemental analysis and considering the mentioned hypotheses (10 ± 1 DOTA per SRP and the APTES/TEOS molar ratio remains equals to 0.6 during any synthesis step or purification step). Ligand/SRP molar ratios deduced from Absorption UV-visible and considering the number of gadolinium atoms per SRP provided by Elemental Analysis.