

## Supplementary Materials for

### Molecular phenotyping and image-guided surgical treatment of melanoma using spectrally distinct ultrasmall core-shell silica nanoparticles

Feng Chen, Brian Madajewski, Kai Ma, Daniella Karassawa Zanoni, Hilda Stambuk, Melik Z. Turker, Sébastien Monette, Li Zhang, Barney Yoo, Peiming Chen, Richard J. C. Meester, Sander de Jonge, Pablo Montero, Evan Phillips, Thomas P. Quinn, Mithat Gönen, Sonia Sequeira, Elisa de Stanchina, Pat Zanzonico, Ulrich Wiesner\*, Snehal G. Patel\*, Michelle S. Bradbury\*

\*Corresponding author. Email: bradburm@mskcc.org (M.S.B.); ubw1@cornell.edu (U.W.); patels@mskcc.org (S.G.P.)

Published 4 December 2019, *Sci. Adv.* **5**, eaax5208 (2019)  
DOI: 10.1126/sciadv.aax5208

#### The PDF file includes:

- Fig. S1. Clinical trial SLN mapping case in a patient with head and neck melanoma using cRGDY-Cy5.5-PEG-C' dots (NCT02106598).
- Fig. S2. Development of 700- and 800-nm emitting NIR fluorescent C' dots.
- Fig. S3. Morphology and purity characterization of  $\alpha$ MSH-PEG-Cy5.5-C' dots and cRGDY-PEG-CW800-C' dots.
- Fig. S4. The relationship between probe concentration and signal intensity of different probes.
- Fig. S5. The bleed-through of  $\alpha$ MSH-PEG-Cy5.5-C' dot probes to the 800-nm channel under the excitation of a 700-nm laser (particle concentration range, 0 to 125 nM).
- Fig. S6. The bleed-through of cRGDY-PEG-CW800-C' dot probes to the 700-nm channel under the excitation of a 800-nm laser (concentration range, 0 to 250 nM).
- Fig. S7. The bleed-through of cocktail C' dots ( $\alpha$ MSH-PEG-Cy5.5-C' dot probes and cRGDY-PEG-CW800-C' dot) probes to the 700- or 800-nm channels under the combined excitation of 700- and 800-nm lasers (concentration range, 0 to 250 nM).
- Fig. S8. Summary of MIP PET images of all seven spontaneous melanoma miniswines (the related MIP short videos are also provided as movies S1 to S7).
- Fig. S9. The marking of the expected SLN locations.
- Fig. S10. A representative example of multiplexing optical data analysis using the software (Architector Image Viewer, version 1.9.0) from Quest Spectrum.
- Fig. S11. Whole-body PET/CT imaging of pig #1.
- Fig. S12. Whole-body PET/CT imaging and histological analysis of pig #2.
- Fig. S13. Whole-body PET/CT imaging and histological analysis of pig #3.
- Fig. S14. Whole-body PET/CT imaging and histological analysis of pig #4.
- Fig. S15. Whole-body PET/CT imaging and histological analysis of pig #6.
- Fig. S16. Whole-body PET/CT imaging and histological analysis of pig #7.
- Fig. S17. IVIS imaging to identify nanoparticles at the tumor site.

Fig. S18. Average body weight of all male mice from the microdose toxicology study.

Fig. S19. Average body weight of all female mice from the microdose toxicology study.

Table S1. Optimization of 800-nm emitted NIR fluorescent C' dots.

Table S2. In vivo signal intensity and bleed-through percentage of cocktail C' dots excited with a 700-nm laser.

Table S3. Summary of the injection information of all seven spontaneous melanoma miniswines.

Table S4. Summary of PET SUV numbers of all nodes from seven spontaneous melanoma miniswines (~0.5-mm tumor burden was highlighted in green; NA means tumor burden diameter was not available).

Table S5. Microdose toxicology study animal group.

Table S6. Mortality and morbidity summary table of the microdose toxicology study.

Table S7. Hematology parameters in the microdose toxicology study.

Table S8. Clinical chemistry parameters in the microdose toxicology study.

Table S9. Tissues examined microscopically in the microdose toxicology study.

Table S10. Hematology parameters, group 5, male, tumor, vehicle control (saline), day 2.

Table S11. Hematology parameters, group 6, female, tumor, vehicle control (saline), day 2.

Table S12. Hematology parameters, group 7, male, tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 2.

Table S13. Hematology parameters, group 8, female, tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 2.

Table S14. Hematology parameters, group 9, male, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 2.

Table S15. Hematology parameters, group 10, female, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 2.

Table S16. Hematology parameters, group 11, male, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 2.

Table S17. Hematology parameters, group 12, female, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 2.

Table S18. Hematology parameters, group 13, male, no tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 2.

Table S19. Hematology parameters, group 14, female, no tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 2.

Table S20. Hematology parameters, group 15, male, tumor, vehicle control (saline), day 14.

Table S21. Hematology parameters, group 16, female, tumor, vehicle control (saline), day 14.

Table S22. Hematology parameters, group 17, male, tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S23. Hematology parameters, group 18, female, tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S24. Hematology parameters, group 19, male, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 14.

Table S25. Hematology parameters, group 20, female, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 14.

Table S26. Hematology parameters, group 21, male, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S27. Hematology parameters, group 22, female, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S28. Hematology parameters, group 23, male, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S29. Hematology parameters, group 24, female, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S30. Hematology parameters, group 5, male, tumor, vehicle control (saline), day 2.

Table S31. Hematology parameters, group 6, female, tumor, vehicle control (saline), day 2.

Table S32. Hematology parameters, group 7, male, tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 2.

Table S33. Hematology parameters, group 8, female, tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 2.

Table S34. Hematology parameters, group 9, male, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 2.

Table S35. Hematology parameters, group 10, female, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 2.

Table S36. Hematology parameters, group 11, male, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 2.

Table S37. Hematology parameters, group 12, female, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 2.

Table S38. Hematology parameters, group 13, male, no tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 2.

Table S39. Hematology parameters, group 14, female, no tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 2.

Table S40. Hematology parameters, group 15, male, tumor, vehicle control (saline), day 14.

Table S41. Hematology parameters, group 16, female, tumor, vehicle control (saline), day 14.

Table S42. Hematology parameters, group 17, male, tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S43. Hematology parameters, group 18, female, tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S44. Hematology parameters, group 19, male, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 14.

Table S45. Hematology parameters, group 20, female, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 14.

Table S46. Hematology parameters, group 21, male, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S47. Hematology parameters, group 22, female, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S48. Hematology parameters, group 23, male, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

Table S49. Hematology parameters, group 24, female, no tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.

**Other Supplementary Material for this manuscript includes the following:**

(available at [advances.sciencemag.org/cgi/content/full/5/12/eaax5208/DC1](http://advances.sciencemag.org/cgi/content/full/5/12/eaax5208/DC1))

Movie S1 (.mov format). MIP video of pig #1.  
Movie S2 (.mov format). MIP video of pig #2.  
Movie S3 (.mov format). MIP video of pig #3.  
Movie S4 (.mov format). MIP video of pig #4.  
Movie S5 (.mov format). MIP video of pig #5.  
Movie S6 (.mov format). MIP video of pig #6.

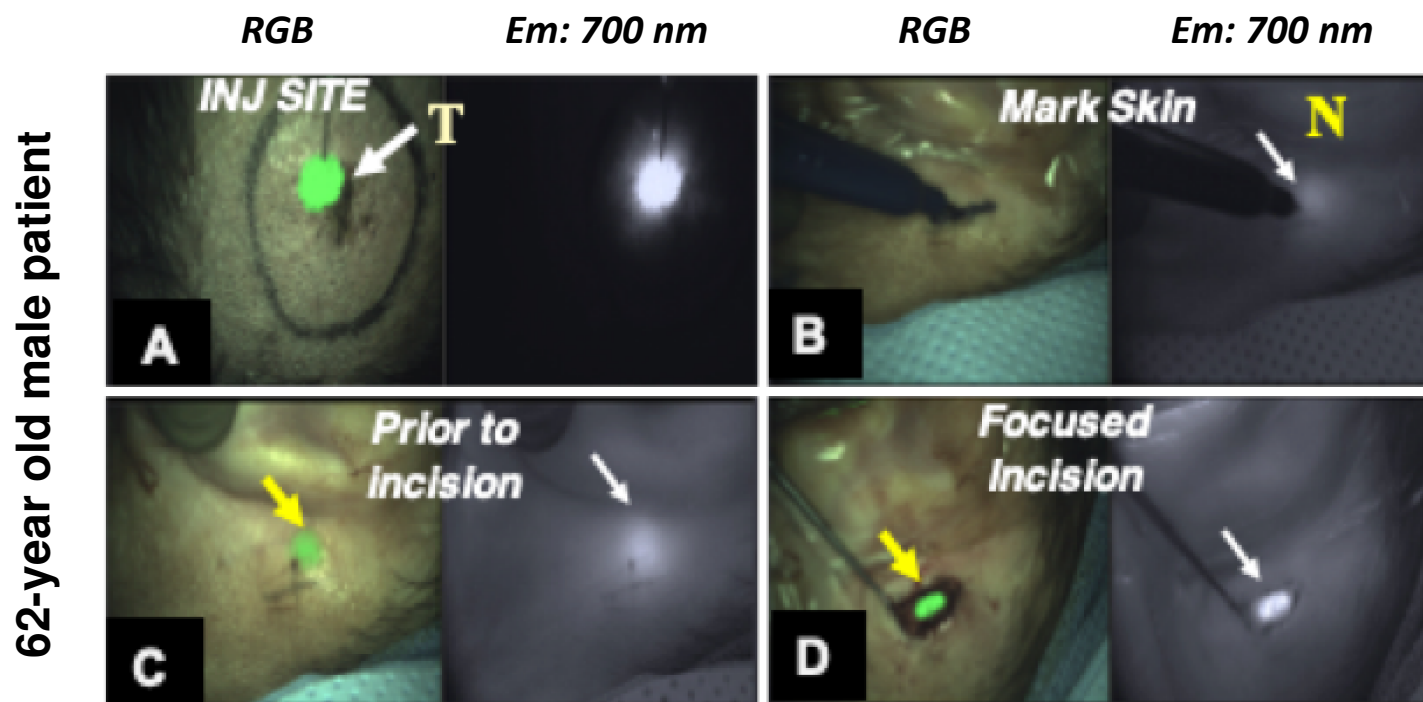
Movie S7 (.mov format). MIP video of pig #7.

Movie S8 (.mp4 format). Image-guided multiplexing, pig #5.

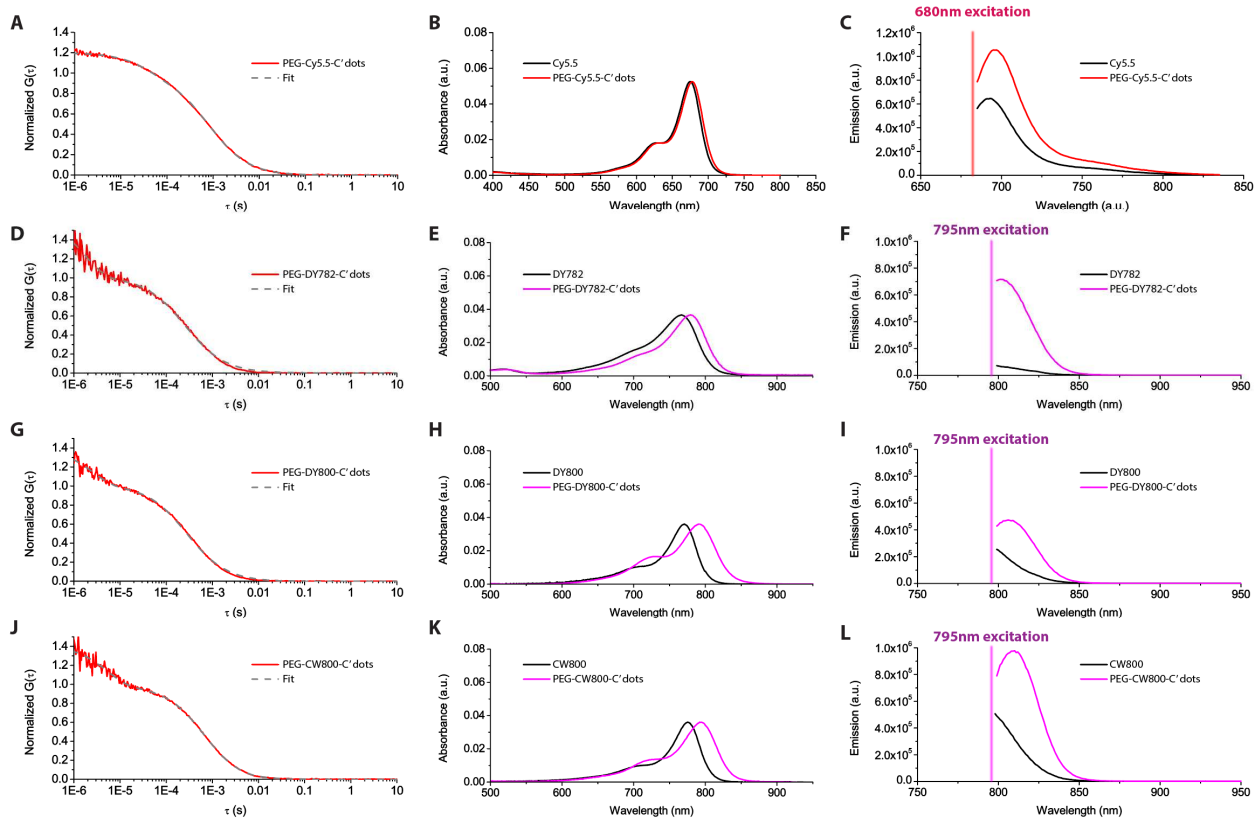
Movie S9 (.mov format). Image-guided multiplexing, pig #3.



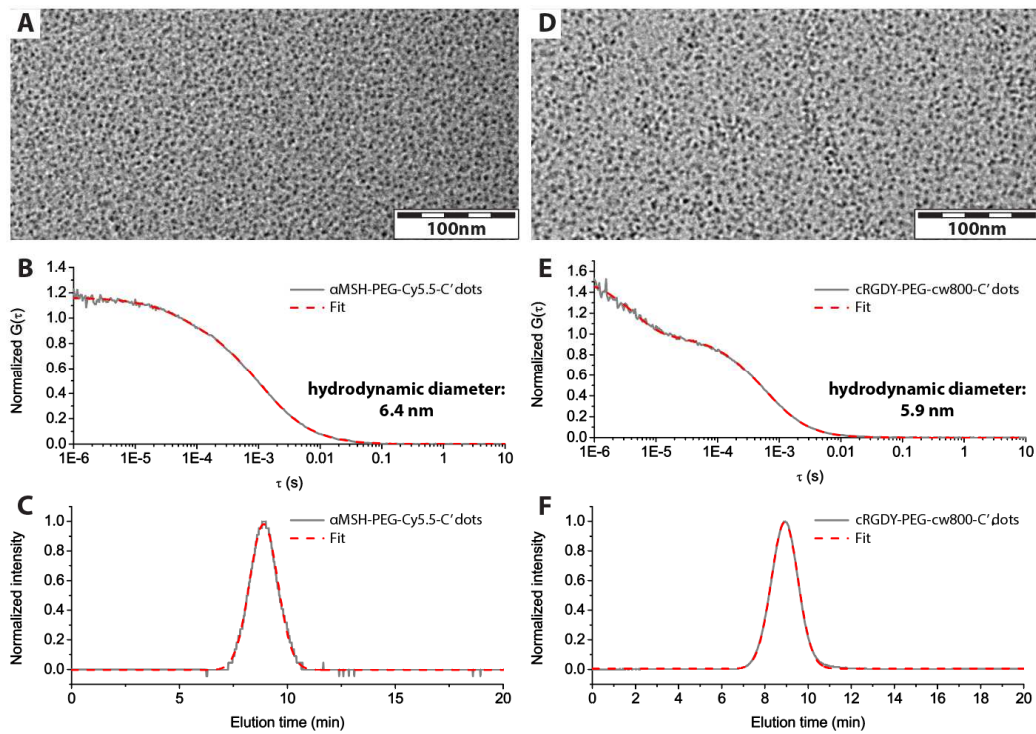
## 1. SUPPLEMENTARY FIGURES



**Fig. S1. Clinical trial SLN mapping case in a patient with head and neck melanoma using cRGDY-Cy5.5-PEG-C' dots (NCT02106598).** The results showed a 62-year old male patient with a scalp melanoma (**T**) and fluorescence signal (arrows) overlying the site of a metastatic post-auricular SLN (**N**) through the intact skin. The patient was injected peritumorally with a single injection of ultrabright cRGDY-PEG-Cy5.5-C' dots about a primary lesion (**T**) of the scalp (**A**). Focal fluorescence was seen through the intact skin overlying the post-auricular SLNs (**N**) in the surgical suite using real-time optical imaging guidance of Quest Spectrum® camera system (**B&C**). This approach allows the operating surgeon to limit the extent of surgical dissection (short black line in **B**) and the subsequent size of the resection cavity, in addition to accurately identifying the metastatic SLN in real-time (**D**). (Photo Credit: Snehal G. Patel, Memorial Sloan Kettering Cancer Center).



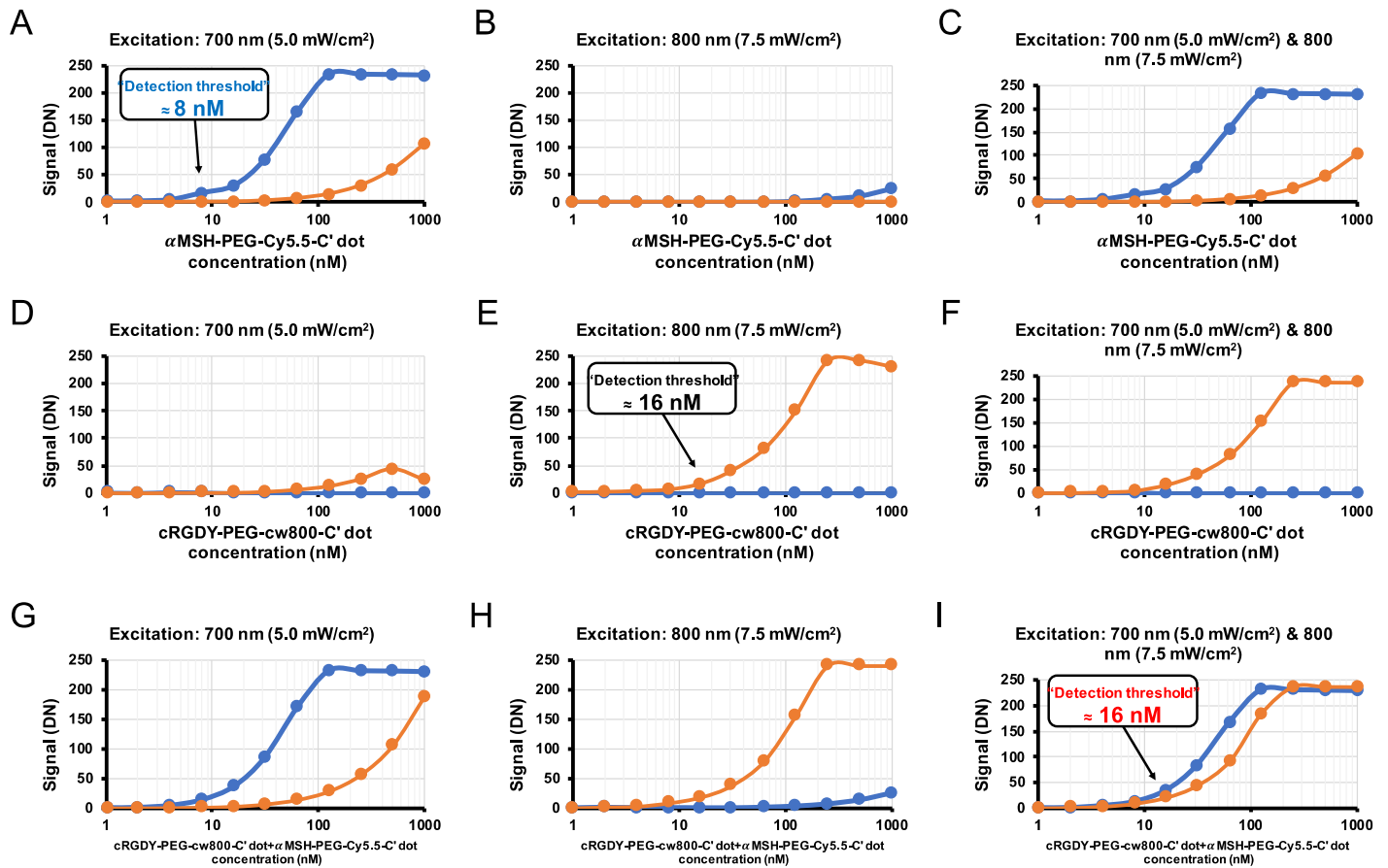
**Fig. S2. Development of 700- and 800-nm emitting NIR fluorescent C' dots.** (A to C) FCS correlation curve with fit (A), UV-Vis absorbance comparison to free dye (B), and emission spectrum comparison to free dye (C) of PEG-Cy5.5-C' dots. (D to F) FCS correlation curve with fit (D), UV-Vis absorbance comparison to free dye (E), and emission spectrum comparison to free dye (F) of PEG-DY782-C' dots. (G to I) FCS correlation curve with fit (G), UV-Vis absorbance comparison to free dye (H), and emission spectrum comparison to free dye (I) of PEG-DY800-C' dots. (J to L) FCS correlation curve with fit (J), UV-Vis absorbance comparison to free dye (K), and emission spectrum comparison to free dye (L) of PEG-CW800-C' dots. The maximum intensity of the absorbance of different samples was matched by adjusting sample concentration (B, E, H, and K) before the measurement of emission spectra under the excitation conditions mimicking the camera system (C, F, I, and L). The area under curve of individual emission spectra over the range of wavelengths corresponding to the two NIR windows of the camera system was determined (C, F, I and L) in order to estimate the fluorescence brightness detectable by the camera system (table S1). (Photo Credit: Kai Ma, Cornell University).



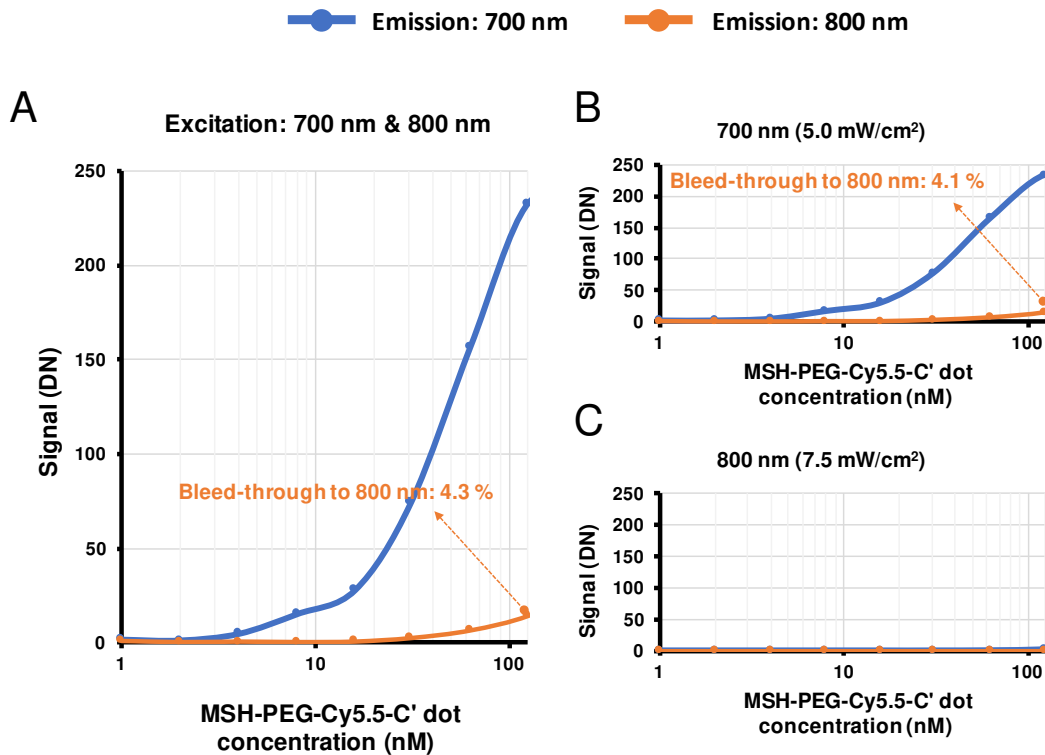
**Fig. S3. Morphology and purity characterization of  $\alpha$ MSH-PEG-Cy5.5-C' dots and cRGDY-PEG-CW800-C' dots.** (A to C) Representative TEM image (A), FCS correlation curve with fit (B), and GPC elugram with fit (C) of  $\alpha$ MSH-PEG-Cy5.5-C' dots. (D to F) Representative TEM image (A), FCS correlation curve with fit (B), and GPC elugram with fit (C) of cRGDY-PEG-CW800-C' dots. (Photo Credit: Kai Ma, Cornell University).

—●— Emission: 700 nm

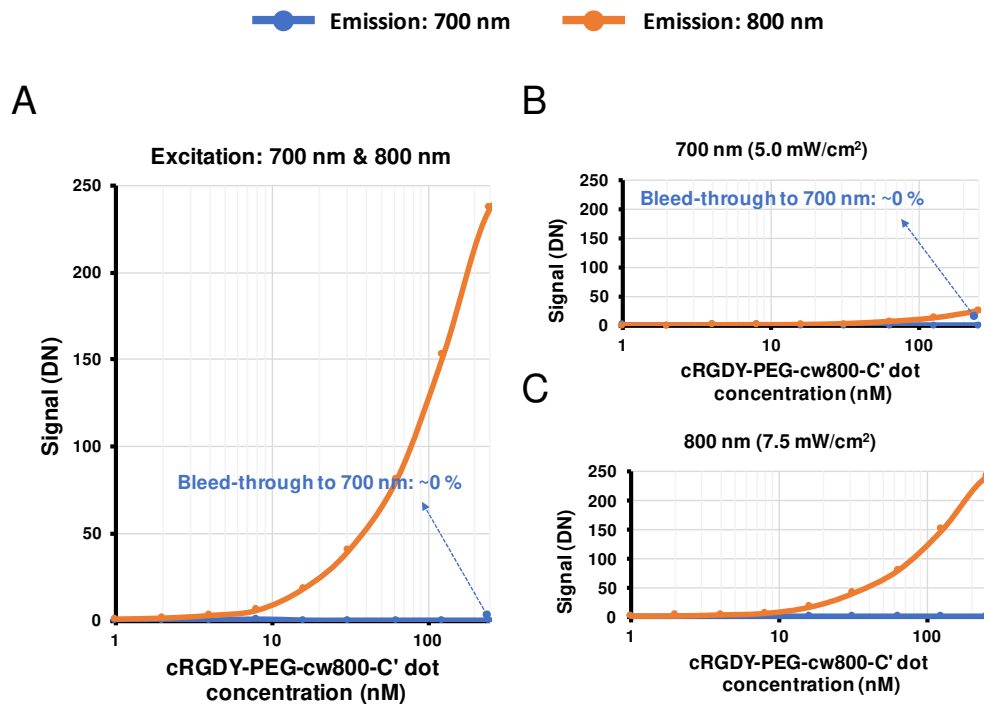
—●— Emission: 800 nm



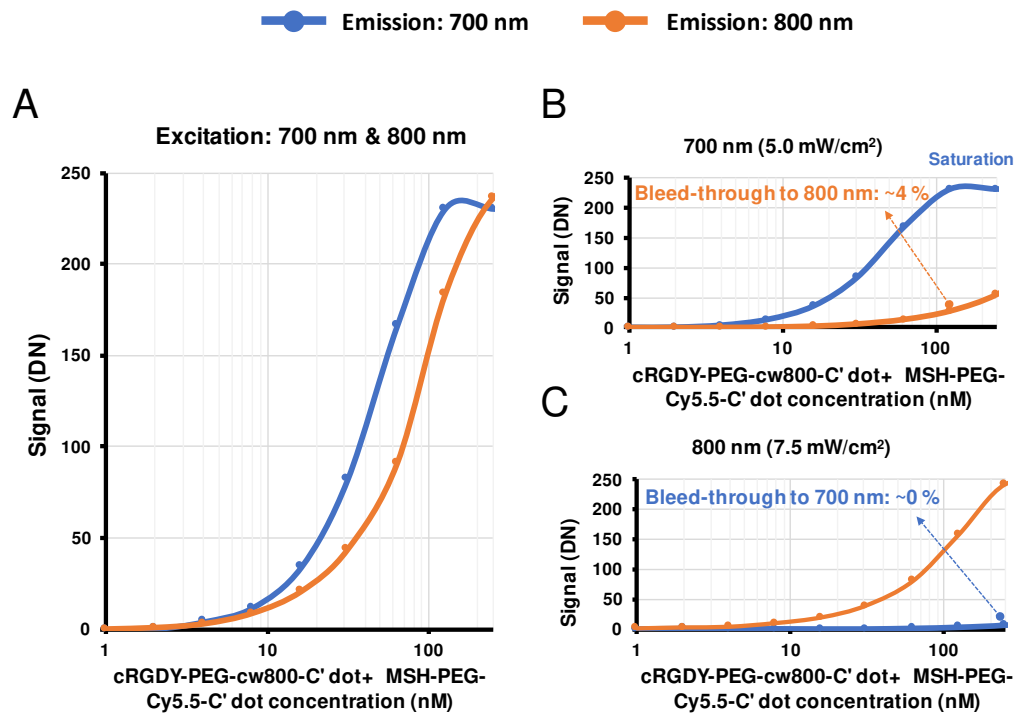
**Fig. S4. The relationship between probe concentration and signal intensity of different probes.** The relationship between probe concentration and signal intensity of different probes of (A-C)  $\alpha$ MSH-PEG-Cy5.5-C' dots, (D-F) cRGDY-PEG-CW800-C' dots, (G-I) mixed probes, under varied excitation conditions of 700-nm laser (A, D, G), 800-nm laser (B, E, H) and 700-nm+800-nm (C, F, I). (Photo Credit: Feng Chen, Memorial Sloan Kettering Cancer Center).



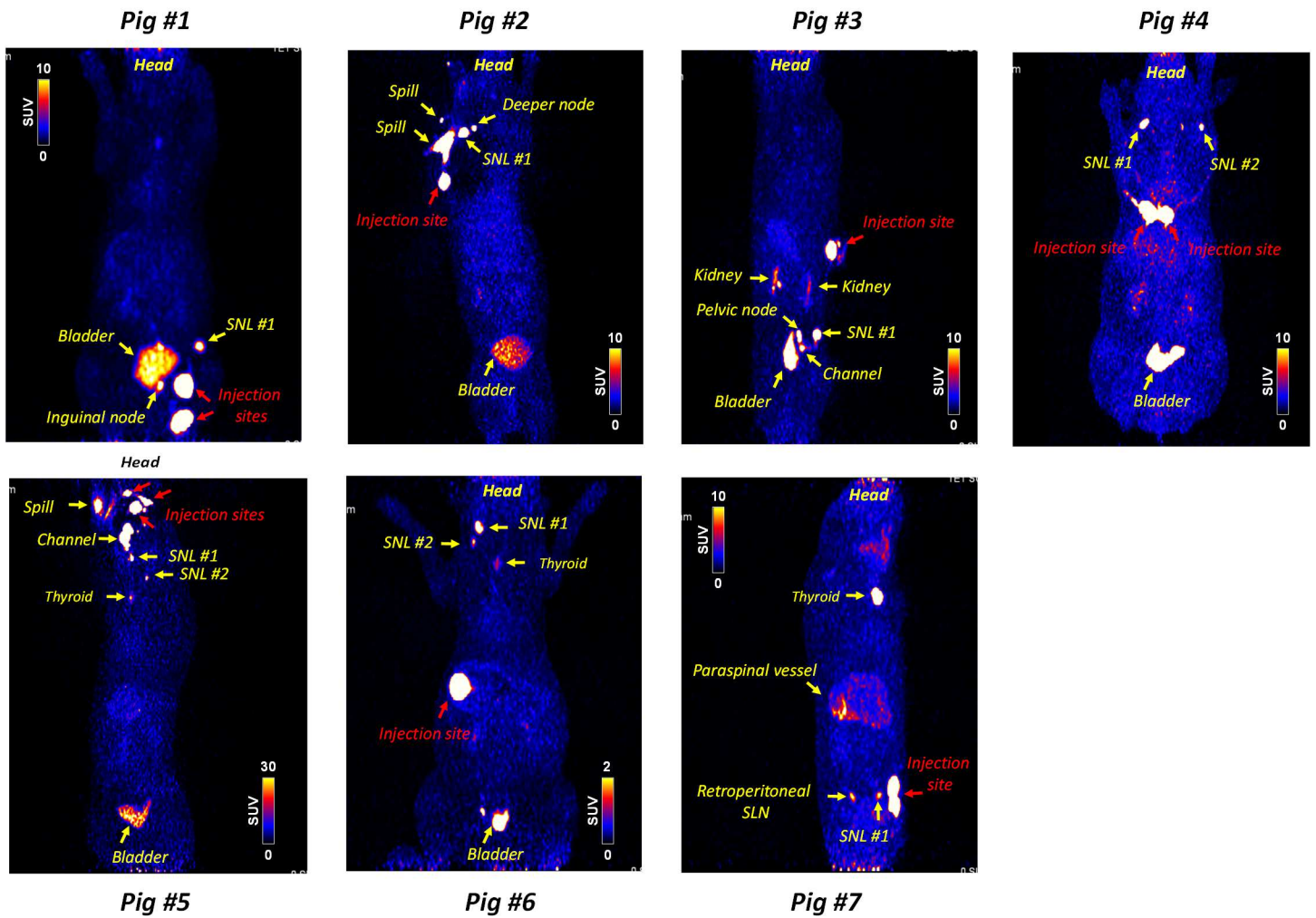
**Fig. S5. The bleed-through of  $\alpha$ MSH-PEG-Cy5.5-C' dot probes to the 800-nm channel under the excitation of a 700-nm laser (particle concentration range, 0 to 125 nM).** (Photo Credit: Feng Chen, Memorial Sloan Kettering Cancer Center).



**Fig. S6. The bleed-through of cRGDY-PEG-cw800-C' dot probes to the 700-nm channel under the excitation of a 800-nm laser (concentration range, 0 to 250 nM).** (Photo Credit: Feng Chen, Memorial Sloan Kettering Cancer Center).

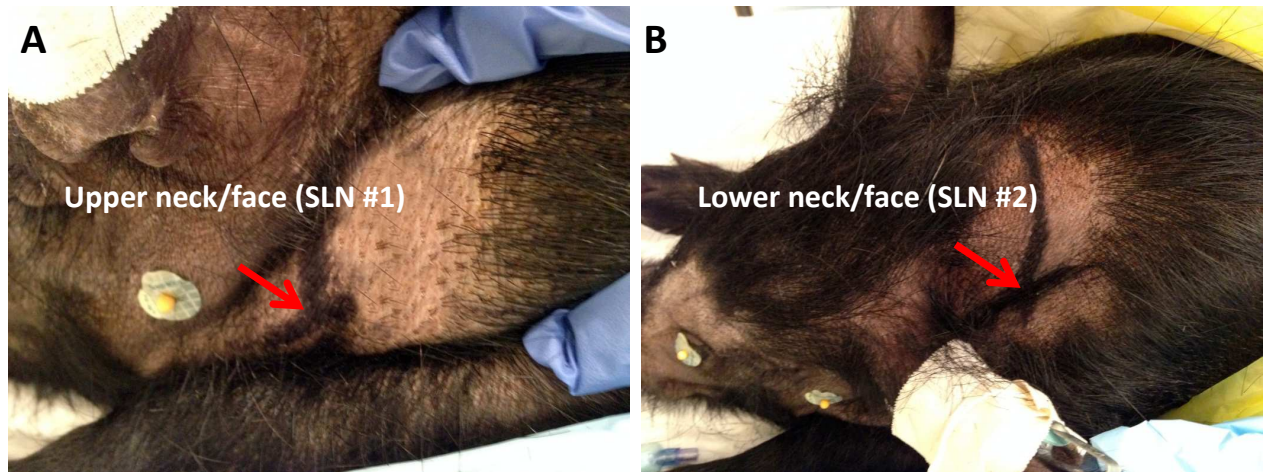


**Fig. S7. The bleed-through of cocktail C' dots ( $\alpha$ MSH-PEG-Cy5.5-C' dot probes and cRGDY-PEG-CW800-C' dot) probes to the 700- or 800-nm channels under the combined excitation of 700- and 800-nm lasers (concentration range, 0 to 250 nM). (Photo Credit: Feng Chen, Memorial Sloan Kettering Cancer Center).**

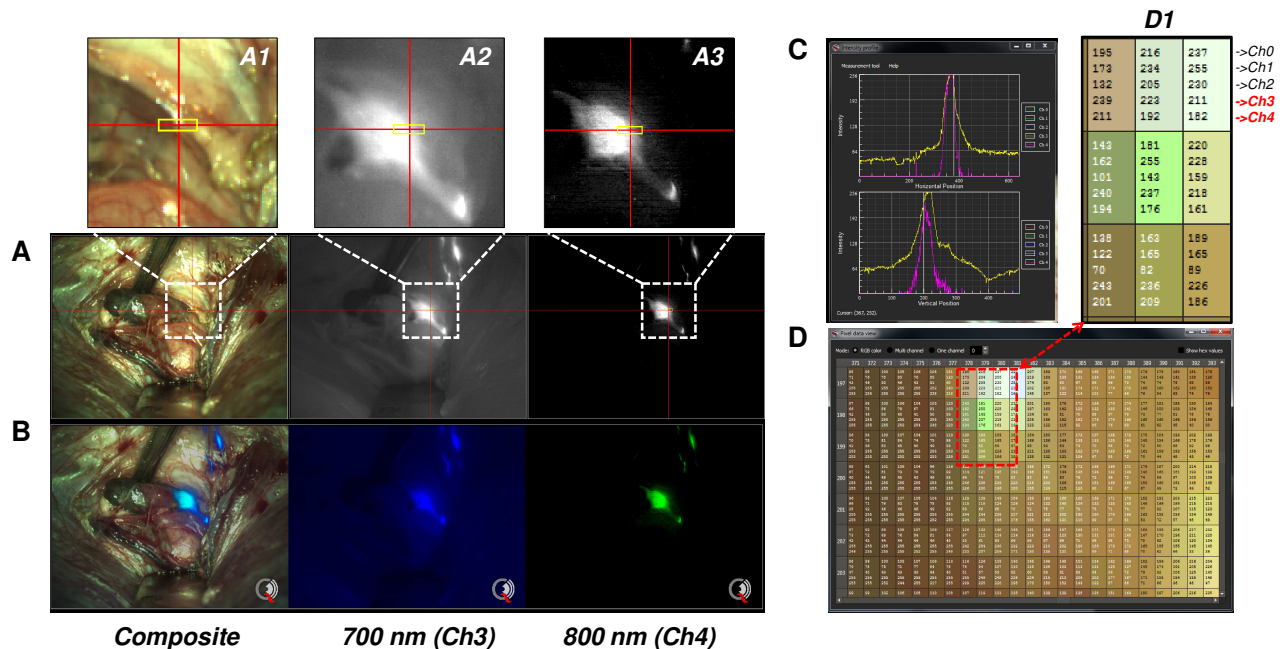


**Fig. S8. Summary of MIP PET images of all seven spontaneous melanoma miniswine (the related MIP short videos are also provided as movies S1 to S7).** (Photo Credit: Feng Chen, Memorial Sloan Kettering Cancer Center).





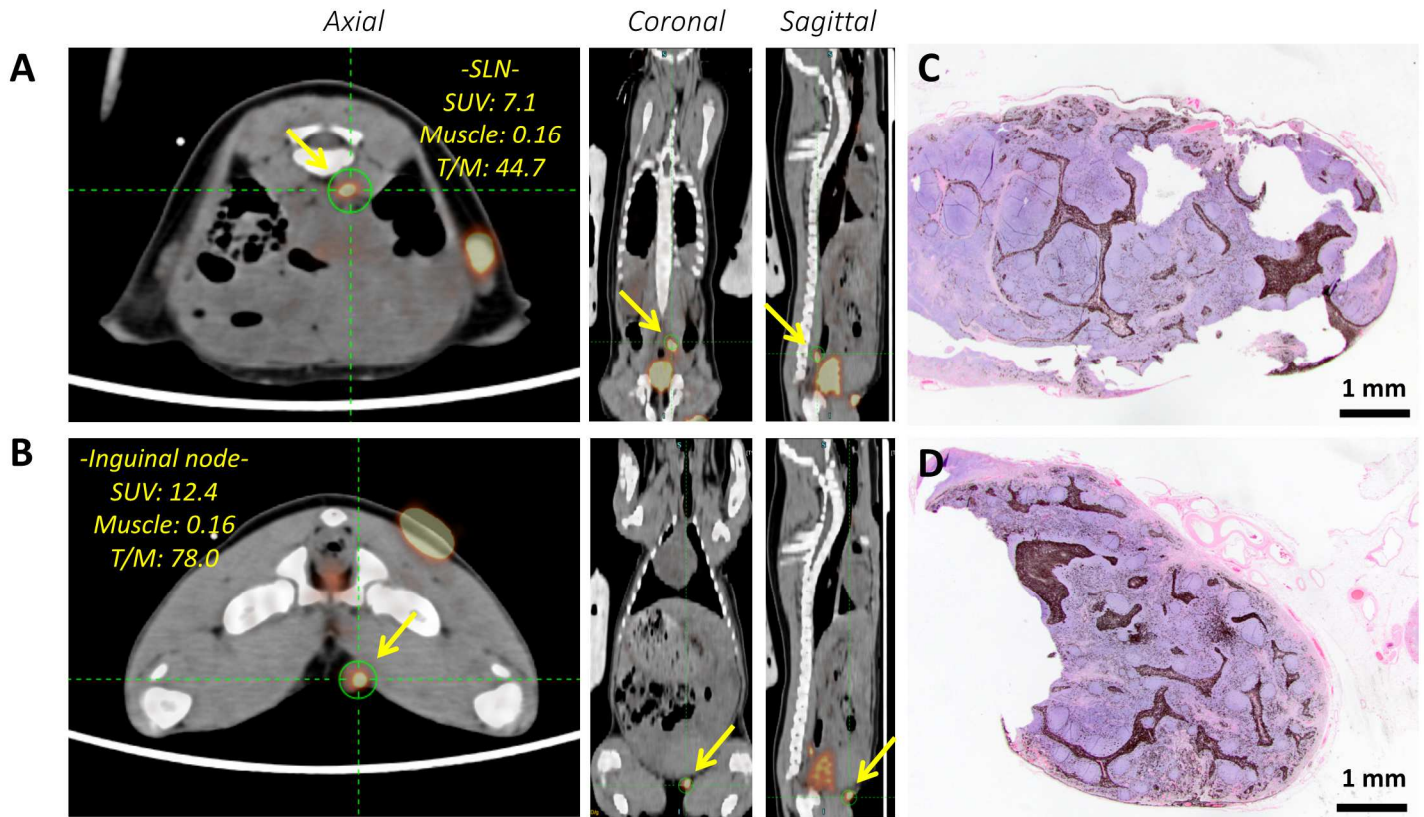
**Fig. S9. The marking of the expected SLN locations. (A) SLN #1, (B) SLN #2, based on the corresponding whole-body PET/CT imaging (shown in Figs. 4A, B). (Photo Credit: Hilda Stambuk, Memorial Sloan Kettering Cancer Center).**



**Fig. S10. A representative example of multiplexing optical data analysis using the software (Architector Image Viewer, version 1.9.0) from Quest Spectrum. (A) From left to right, bright field image, grayscale 700-nm channel (Ch3) image, grayscale 800-nm channel (Ch4) image. A1-A3 images are corresponding enlarged areas in (A). (B) From left to right, composite image of two NIR fluorescence images of Cy5.5 and CW800, blue “pseudo-color” image of 700-nm channel, green “pseudo-color” image of 800-nm channel. (C) Optical signal intensity for each pixel from 700-nm (Ch3, yellow) and 800-nm (Ch4, pink) channels. For each channel (Ch3 and Ch4 separately) 6 values are used and averaged to derive a final intensity value (D) Pixel data of the highlighted area in (A). (Photo Credit: Snehal G. Patel, Michelle S. Bradbury, Memorial Sloan Kettering Cancer Center & Richard J. C. Meester, Quest Medical Imaging).**

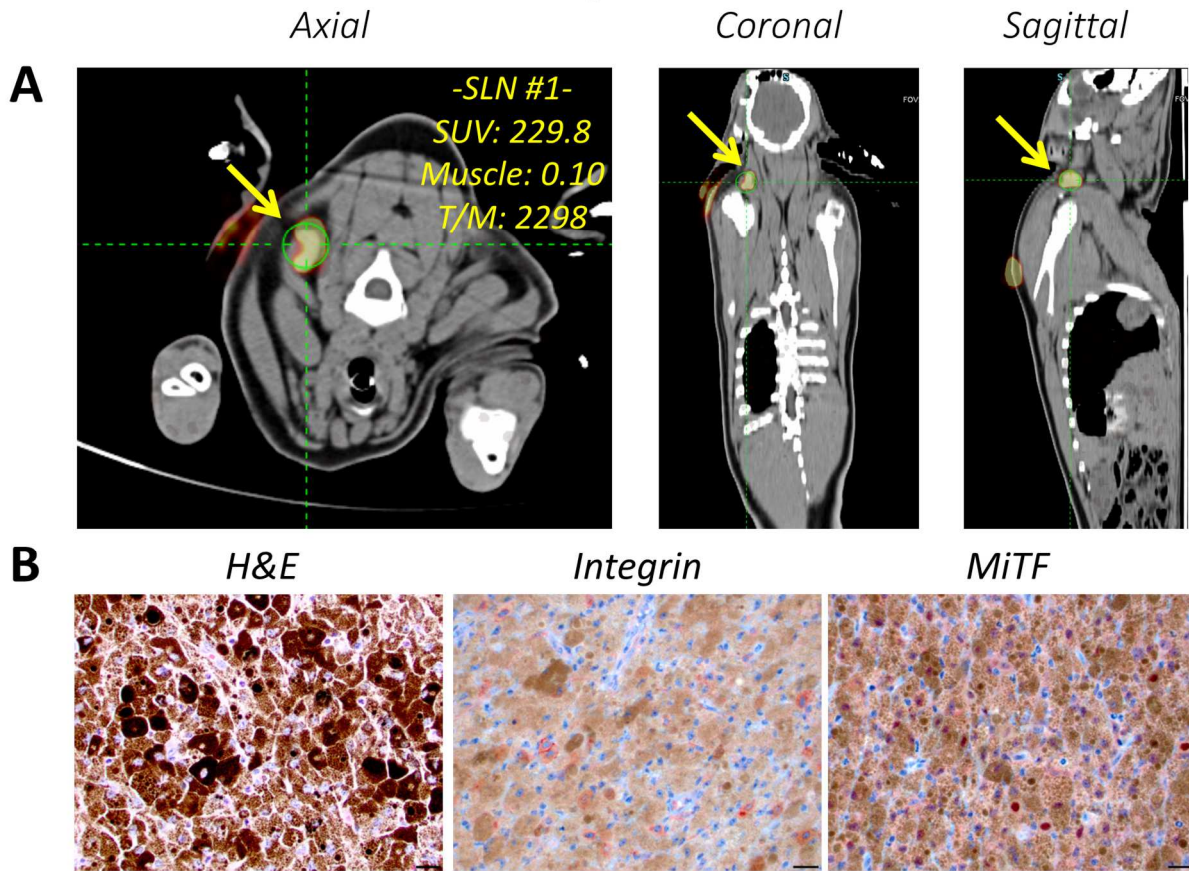


## Pig #1



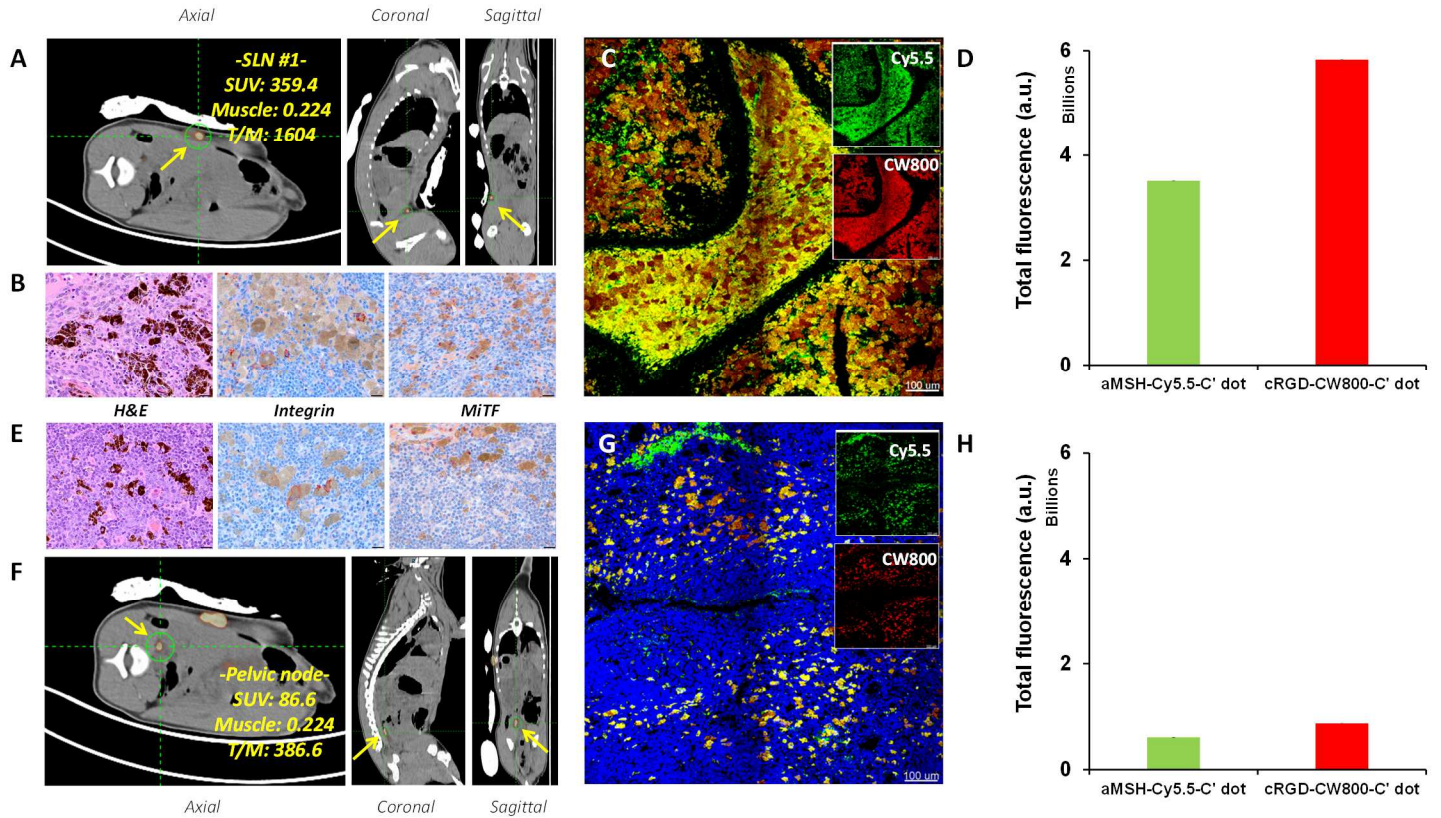
**Fig. S11. Whole-body PET/CT imaging of pig #1. (A) SNL, (B) Inguinal node.** Left: axial view. Middle: coronal view. Right: sagittal view. H&E staining of (C) SNL, and (D) Inguinal node. Scale bar: 1 mm. (Photo Credit: Feng Chen, Brian Madajewski & Sébastien Monette, Memorial Sloan Kettering Cancer Center).

## Pig #2



**Fig. S12. Whole-body PET/CT imaging and histological analysis of pig #2.** (A) Preoperative whole-body PET/CT imaging of spontaneous melanoma miniswine (pig #2). Left: axial view. Middle: coronal view. Right: sagittal view. (B) *Ex vivo* histological analysis of SLN #1. Left: H&E staining. Middle: integrin staining. Right: MiTF staining. Scale bar: 20  $\mu$ m. (Photo Credit: Feng Chen, Brian Madajewski & Sébastien Monette, Memorial Sloan Kettering Cancer Center).

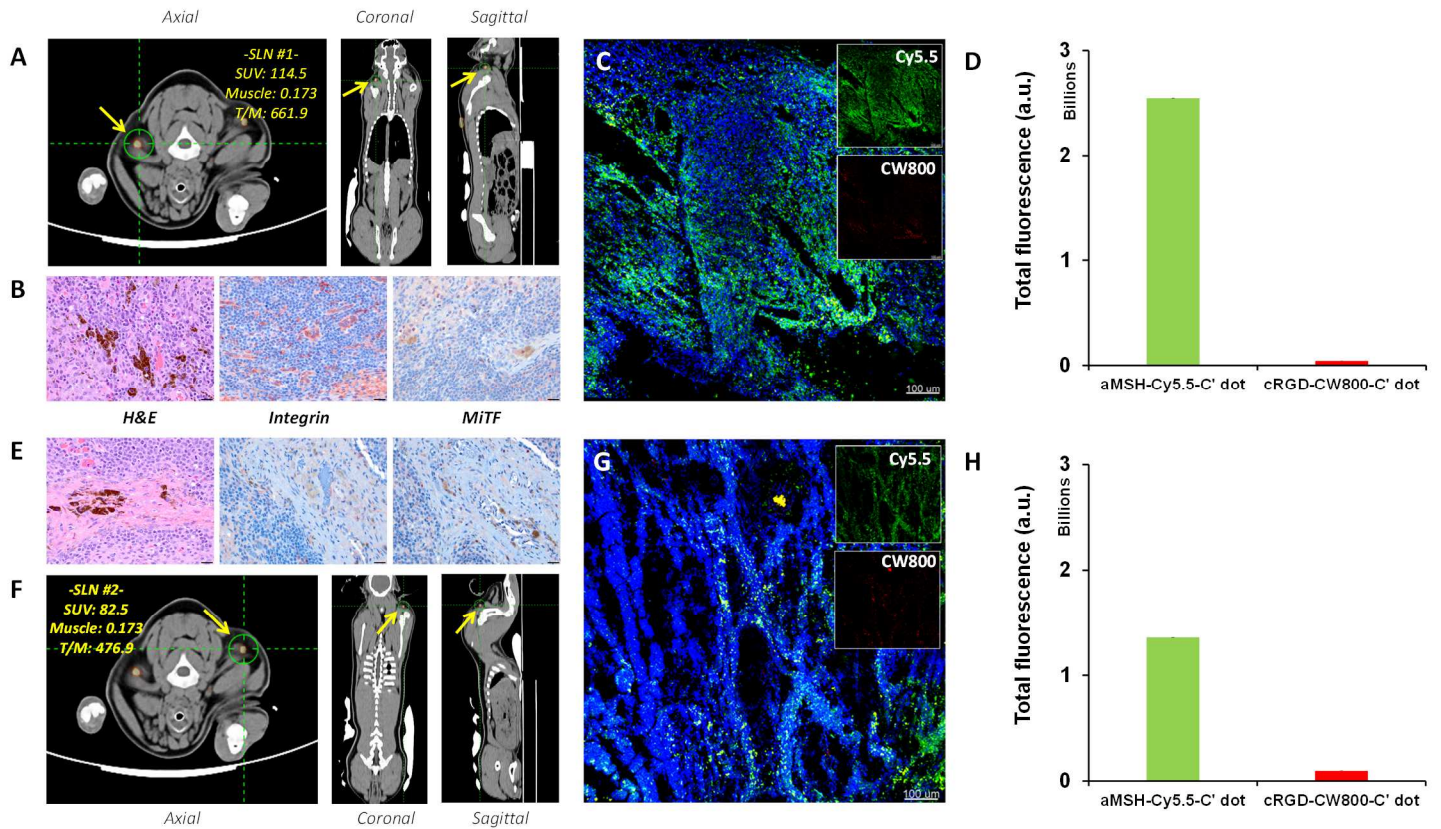
### Pig #3



**Fig. S13. Whole-body PET/CT imaging and histological analysis of pig #3.** Preoperative whole-body PET/CT imaging of spontaneous melanoma miniswine (pig #3). (A) SLN #1, (F) pelvic node. Left: axial view. Middle: coronal view. Right: sagittal view. *Ex vivo* histological analysis of (B) SLN #1 and (E) pelvic node. Left: H&E staining. Middle: integrin staining. Right: MiTF staining. Scale bar: 20  $\mu$ m. High resolution confocal fluorescence microscopy of (C) SLN #1 and (G) pelvic node with DAPI nuclear stain (scale bar = 100  $\mu$ m). Inset shows the corresponding Cy5.5 and CW800 channels. Quantification of Cy5.5 and CW800 signals' total fluorescence intensities of (D) SLN #1 and (H) pelvic node. (Real-time video footage of pig #3 was also provided as **Video S9**). (Photo Credit: Feng Chen, Brian Madajewski & Sébastien Monette, Memorial Sloan Kettering Cancer Center).

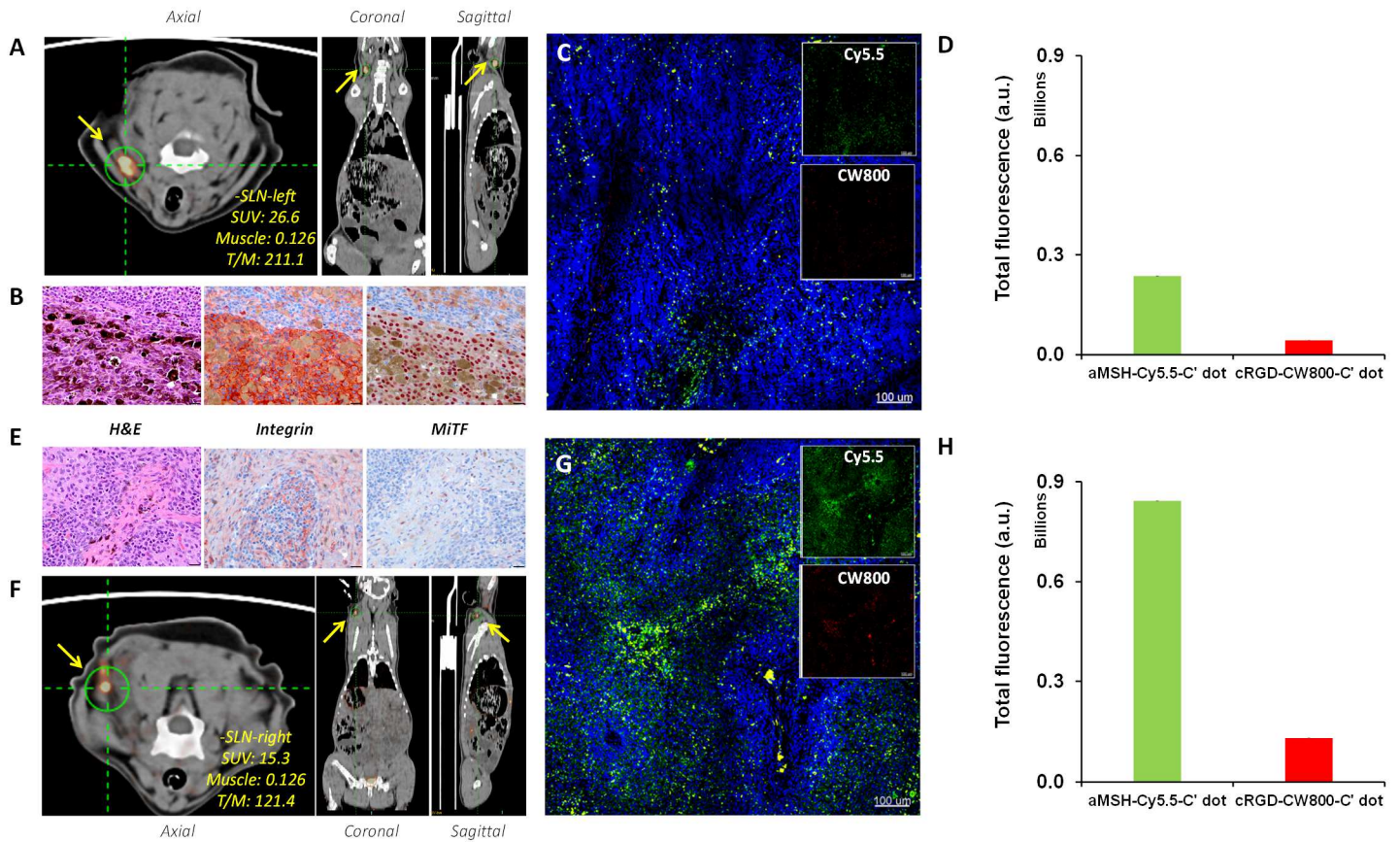


## Pig #4



**Fig. S14. Whole-body PET/CT imaging and histological analysis of pig #4.** Preoperative whole-body PET/CT imaging of spontaneous melanoma miniswine (pig #4). (A) SLN #1, (F) SLN #2. Left: axial view. Middle: coronal view. Right: sagittal view. *Ex vivo* histological analysis of (B) SLN #1 and (E) SLN #2. Left: H&E staining. Middle: integrin staining. Right: MiTF staining. Scale bar: 20  $\mu\text{m}$ . High resolution confocal fluorescence microscopy of (C) SLN #1 and (G) SLN #2 with DAPI nuclear stain (scale bar = 100  $\mu\text{m}$ ). Inset shows the corresponding Cy5.5 and CW800 channels. Quantification of Cy5.5 and CW800 signals' total fluorescence intensities of (D) SLN #1 and (H) SLN #2. (Photo Credit: Feng Chen, Brian Madajewski & Sébastien Monette, Memorial Sloan Kettering Cancer Center).

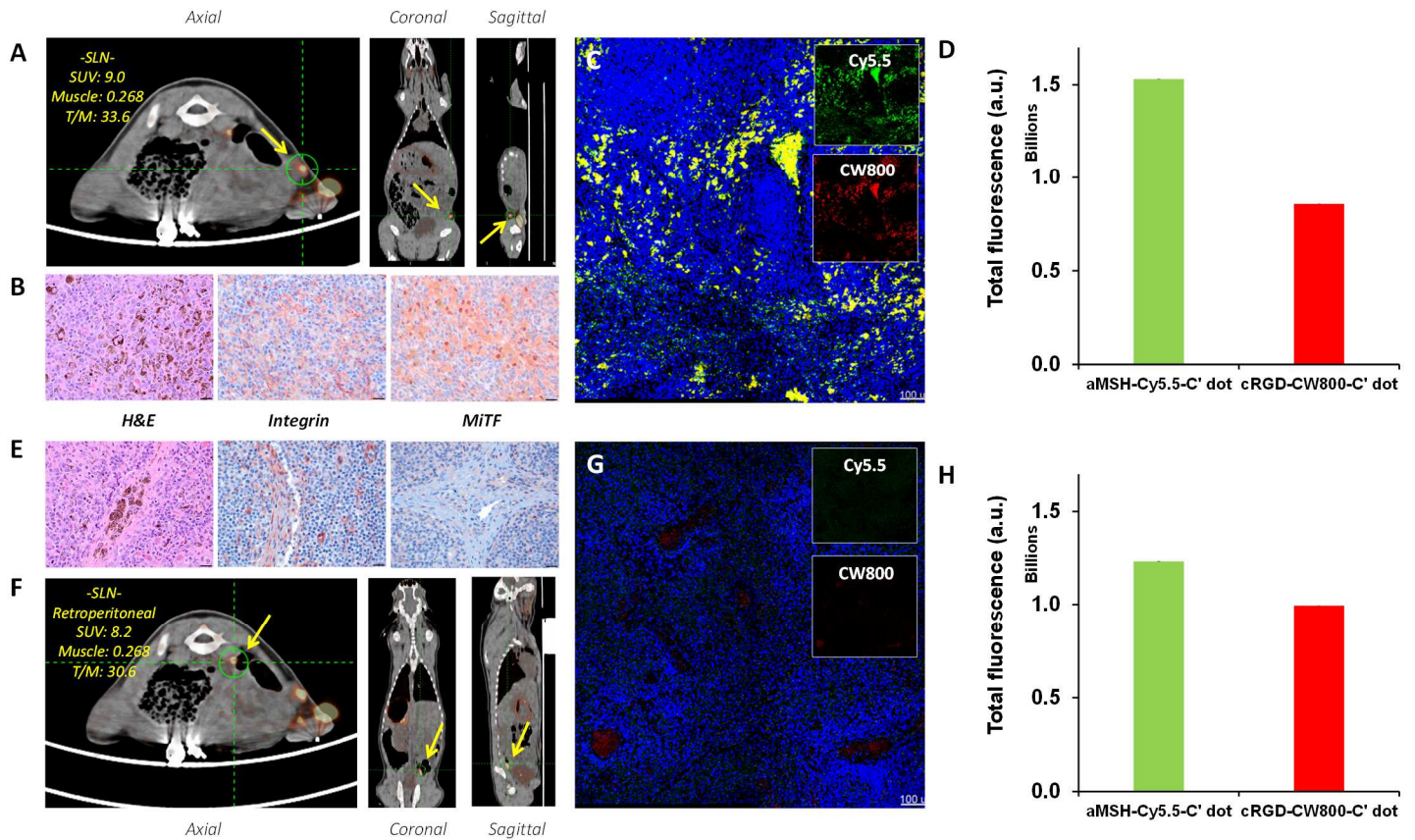
**Pig #6**



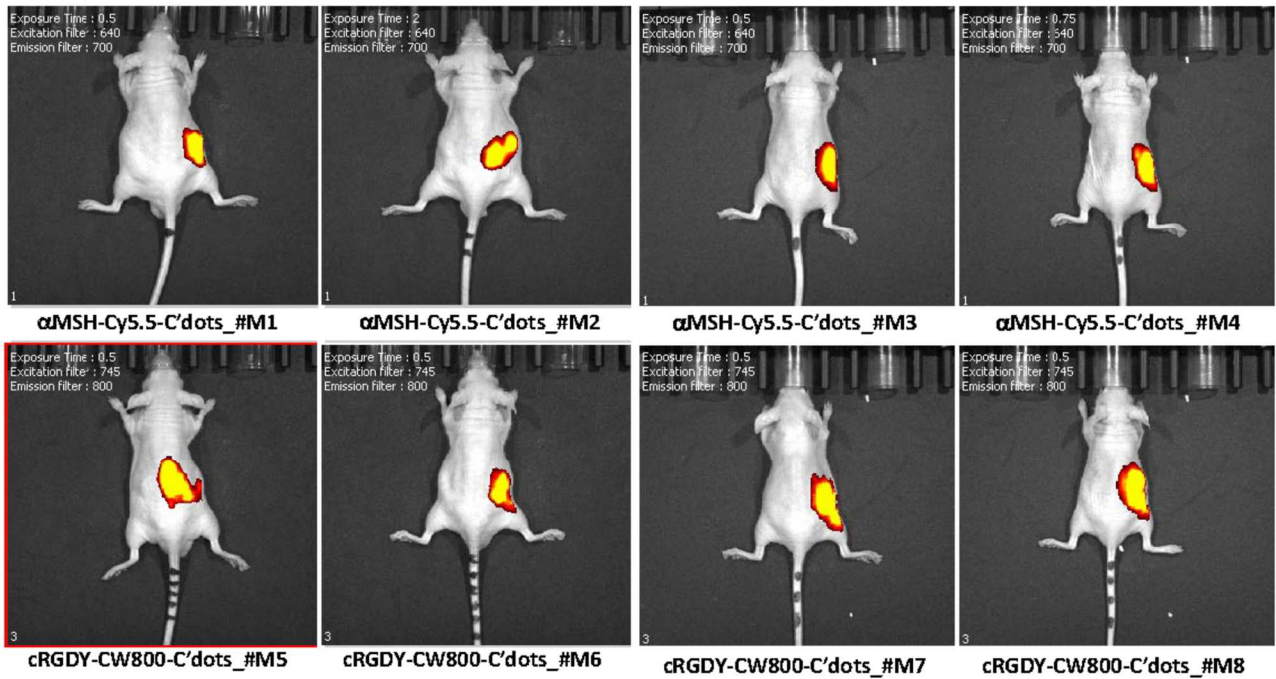
**Fig. S15. Whole-body PET/CT imaging and histological analysis of pig #6.** Preoperative whole-body PET/CT imaging of spontaneous melanoma miniswine (pig #6). (A) SLN #1, (F) SLN #2. Left: axial view. Middle: coronal view. Right: sagittal view. *Ex vivo* histological analysis of (B) SLN #1 and (E) SLN #2. Left: H&E staining. Middle: integrin staining. Right: MiTF staining. Scale bar: 20  $\mu$ m. High resolution confocal fluorescence microscopy of (C) SLN #1 and (G) SLN #2 with DAPI nuclear stain (scale bar = 100  $\mu$ m). Inset shows the corresponding Cy5.5 and CW800 channels. Quantification of Cy5.5 and CW800 signals' total fluorescence intensities of (D) SLN #1 and (H) SLN #2. (Photo Credit: Feng Chen, Brian Madajewski & S ebastien Monette, Memorial Sloan Kettering Cancer Center).



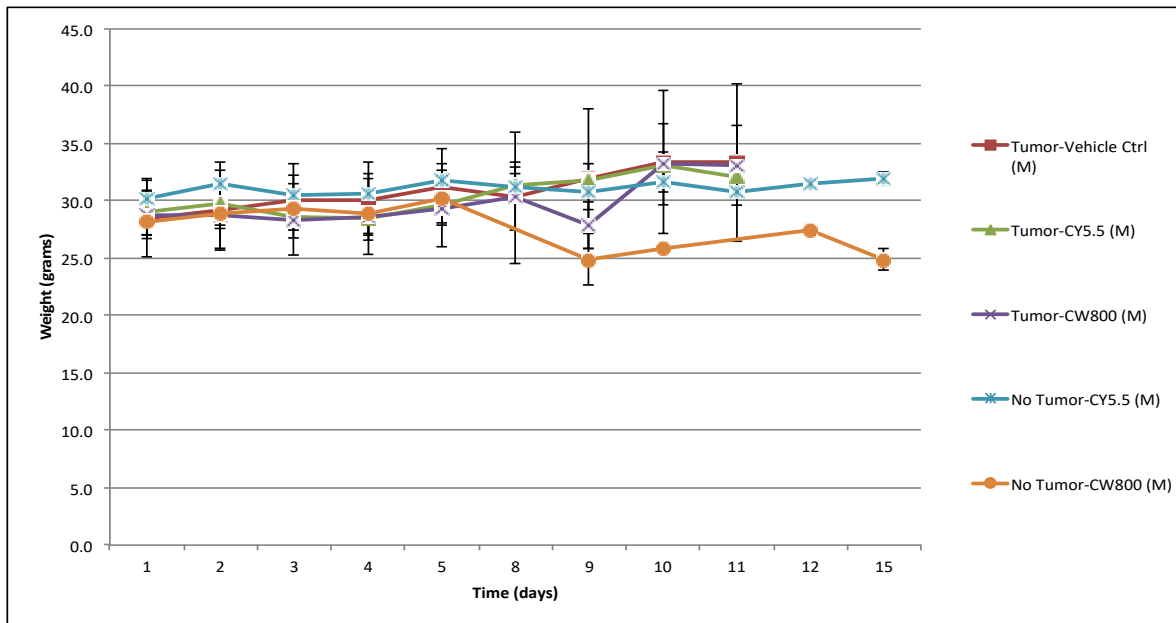
**Pig #7**



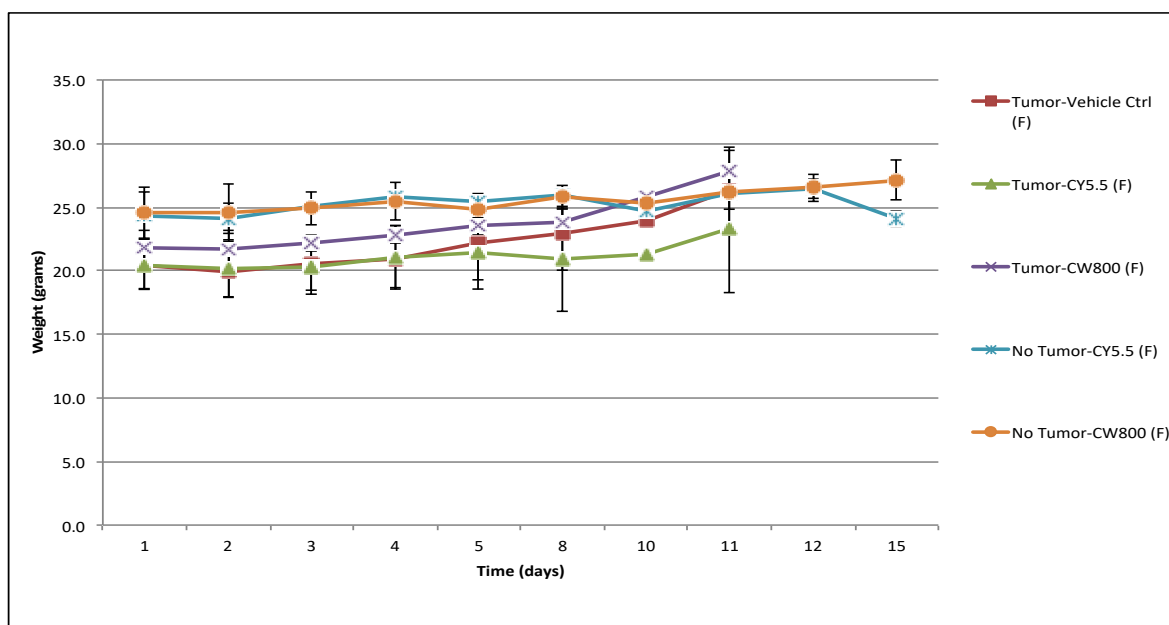
**Fig. S16. Whole-body PET/CT imaging and histological analysis of pig #7.** Preoperative whole-body PET/CT imaging of spontaneous melanoma miniswine (pig #7). (A) SLN, (F) Retroperitoneal SLN. Left: axial view. Middle: coronal view. Right: sagittal view. *Ex vivo* histological analysis of (B) SLN and (E) Retroperitoneal SLN. Left: H&E staining. Middle: integrin staining. Right: MiTF staining. Scale bar: 20  $\mu$ m. High resolution confocal fluorescence microscopy of (C) SLN and (G) Retroperitoneal SLN with DAPI nuclear stain (scale bar = 100  $\mu$ m). Inset shows the corresponding Cy5.5 and CW800 channels. Quantification of Cy5.5 and CW800 signals' total fluorescence intensities of (D) SLN and (H) Retroperitoneal SLN. (Photo Credit: Feng Chen, Brian Madajewski & Sébastien Monette, Memorial Sloan Kettering Cancer Center).



**Fig. S17. IVIS imaging to identify nanoparticles at the tumor site.** Mice in Groups 1-4 were anesthetized using isoflurane and whole-body optical fluorescence imaging was acquired to identify nanoparticle fluorescence at the tumor site (subcutaneous injection) on Study Day 1, 15 minutes post-injection. Mice were scanned using the IVIS Spectrum photon-counting device optical imaging system (Xenogen, Alameda, CA) with the blocks and filters for Cy5.5 fluorescence (Ex: 684 nm; Em: 710 nm) and CW800 fluorescence (Excitation: 778 nm, Emission: 794 nm). (Photo Credit: Elisa de Stanchina, Memorial Sloan Kettering Cancer Center).



**Fig. S18. Average body weight of all male mice from the microdose toxicology study.** (Photo Credit: Elisa de Stanchina, Memorial Sloan Kettering Cancer Center).



**Fig. S19. Average body weight of all female mice from the microdose toxicology study.** (Photo Credit: Elisa de Stanchina, Memorial Sloan Kettering Cancer Center).

## 2. SUPPLEMENTARY TABLES

**Table S1. Optimization of 800-nm emitted NIR fluorescent C' dots.**

	Sample	Diameter	Measured Absorbance Peak	Measured Emission Peak	# of dyes per C' dot	Relative Brightness	
						Single dye	C' dot
First NIR window	Cy5.5 dye	1.4 nm	675 nm	693 nm	-	1 (reference)	-
	PEG-Cy5.5-C' dot	6.4 nm	678 nm	697 nm	1.7	1.5	2.6
Second NIR window	DY782 dye	1.9 nm	768 nm	792 nm	-	1 (reference)	-
	DY800 dye	2.1 nm	771 nm	790 nm	-	2.8	-
	CW800 dye	1.7 nm	775 nm	792 nm	-	5.9	-
	PEG-DY782-C' dot	5.9 nm	780 nm	802 nm	1.7	11.3	19.2
	PEG-DY800-C' dot	5.0 nm	791 nm	806 nm	2.3	8.3	19.1
	PEG-CW800-C' dot	6.2 nm	795 nm	810 nm	3.0	17.1	51.2



**Table S2. In vivo signal intensity and bleed-through percentage of cocktail C' dots excited with a 700-nm laser. (800 signal/700 signal)\*100 = bleed %.**

Cocktail C' dots concentration	Signal in 700 nm channel	Signal in 800 nm channel	Bleed percentage
15 $\mu$ M	210.3 (saturated)	36.6	17.4
1.5 $\mu$ M	210.3 (saturated)	14.9	7.1
0.15 $\mu$ M	101.0	1.1	1.1

**Table S3. Summary of the injection information of all seven spontaneous melanoma miniswines. Each miniswine was injected with 19-28 MBq of <sup>124</sup>I-cRGDY-PEG-CW800-C' dots.**

Pig #	Injection time	Imaging time	Post-injection time	Weight (kg)	Total injected dose (MBq)
Pig #1	2014/07/09, 10:29 AM	2014/07/09, 11:22 AM	~ 1 h	3.88	24.4
Pig #2	2014/08/06, 10:38 AM	2014/08/06, 11:41 AM	~ 1 h	14.5	28.1
Pig #3	2015/04/08, 10:09 AM	2015/04/08, 11:08 AM	~ 1 h	12.5	23.2
Pig #4	2015/04/13, 09:48 AM	2015/04/13, 10:42 AM	~ 1 h	13.1	24.5
Pig #5	2015/06/23, 10:27 AM	2015/06/23, 11:23 AM	~ 1 h	16.3	20.5
Pig #6	2015/10/13, 11:20 AM	2015/10/13, 12:20 AM	~ 1 h	6.3	22.2
Pig #7	2016/02/23, 10:26 AM	2016/02/23, 11:25 AM	~ 1 h	4.68	19.4

**Table S4. Summary of PET SUV numbers of all nodes from seven spontaneous melanoma miniswines (~0.5-mm tumor burden was highlighted in green; NA means tumor burden diameter was not available).**

Miniswine ID	Name of the node	SUV (Mean)	SD	SUV (Min.)	SUV (Max.)	Muscle (Mean SUV)	Target to background ratio	SD	Tumor burden Diameter (mm)
#1	Right SLN	7.1	1.0	5.3	8.9	0.159	44.65	6.29	2.50
	Right inguinal node	12.4	1.2	11.5	13.9		77.99	7.55	2.10
#2	Left: SLN #1	229.8	13.5	207.7	251.4	0.0995	2309.55	135.68	13.20
	Right: SLN #1	359.4	30.5	301.6	410.2		1604.46	136.16	8.20
#3	Pelvic node	86.6	11.7	73.7	101.2	0.224	386.61	52.23	2.10
	Left: SLN	114.5	14.6	89.4	142.1		661.85	84.39	NA
	Right: SLN	82.5	4.9	76.6	89.0		476.88	28.32	NA
#5	Left: SLN #1	73.3	29.2	66.1	80.4	0.129	568.22	226.36	5.70
	Left: SLN #2	26.5	7.2	22.5	29.8		205.43	55.81	0.50
	Left: SLN #1	26.6	2.6	22.4	31.7		211.11	20.63	3.70
#6	Left: SLN #2	15.3	0.7	14.5	16.2	0.126	121.43	5.56	NA
	Right SLN	9.0	1.0	6.7	10.5		33.58	3.73	1.60
	Retroperitoneal SLN	8.2	1.0	6.2	9.7		30.60	3.73	NA

**Table S5. Microdose toxicology study animal group.**

Group	Mice/group	Sex	Mice ID #	Sac. day	Tumors	Necropsy
<b>Imaging samples</b>						
1. αMSH-PEG-Cy5.5-C'dots (1.2 nmol)	2	M	1-2	Day 1	No	No
2. αMSH-PEG-Cy5.5-C'dots (1.2 nmol)	2	F	3-4	Day 1	No	No
3. cRGDY-PEG-CW800-C'dots (1.2 nmol)	2	M	5-6	Day 1	No	No
4. cRGDY-PEG-CW800-C'dots (1.2 nmol)	2	F	7-8	Day 1	No	No
<b>Interim sacrifice on day 2</b>						
5. M21 Tumor- Saline Control	10	M	9-18	Day 2	Yes	Gross and histology
6. M21 Tumor- Saline Control	10	F	19-28	Day 2	Yes	Gross and histology
7. M21 Tumor- αMSH-PEG-Cy5.5-C'dots (1.2 nmol)	10	M	29-38	Day 2	Yes	Gross and histology
8. M21 Tumor- αMSH-PEG-Cy5.5-C'dots (1.2 nmol)	10	F	39-48	Day 2	Yes	Gross and histology
9. M21 Tumor- cRGDY-PEG-CW800-C'dots (1.2 nmol)	10	M	49-58	Day 2	Yes	Gross and histology
10. M21 Tumor- cRGDY-PEG-CW800-C'dots (1.2 nmol)	10	F	59-68	Day 2	Yes	Gross and histology
11. No Tumor- αMSH-PEG-Cy5.5-C'dots (1.2 nmol)	3	M	69-71	Day 2	No	Gross
12. No Tumor - αMSH-PEG-Cy5.5-C'dots (1.2 nmol)	3	F	72-74	Day 2	No	Gross
13. No Tumor- cRGDY-PEG-CW800-C'dots (1.2 nmol)	3	M	75-77	Day 2	No	Gross
14. No Tumor- cRGDY-PEG-CW800-C'dots (1.2 nmol)	3	F	78-80	Day 2	No	Gross
<b>Final sacrifice on day 14</b>						
15. M21 Tumor- Saline Control	5	M	81-85	Day 14	Yes	Gross and histology
16. M21 Tumor- Saline Control	5	F	86-90	Day 14	Yes	Gross and histology
17. M21 Tumor- αMSH-PEG-Cy5.5-C'dots (1.2 nmol)	5	M	91-95	Day 14	Yes	Gross and histology
18. M21 Tumor- αMSH-PEG-Cy5.5-C'dots (1.2 nmol)	5	F	96-100	Day 14	Yes	Gross and histology
19. M21 Tumor- cRGDY-PEG-CW800-C'dots (1.2 nmol)	5	M	111-105	Day 14	Yes	Gross and histology
20. M21 Tumor- cRGDY-PEG-CW800-C'dots (1.2 nmol)	5	F	106-110	Day 14	Yes	Gross and histology
21. No Tumor- αMSH-PEG-Cy5.5-C'dots (1.2 nmol)	3	M	111-113	Day 14	No	Gross
22. No Tumor - αMSH-PEG-Cy5.5-C'dots (1.2 nmol)	3	F	114-116	Day 14	No	Gross
23. No Tumor- cRGDY-PEG-CW800-C'dots (1.2 nmol)	3	M	117-119	Day 14	No	Gross
24. No Tumor- cRGDY-PEG-CW800-C'dots (1.2 nmol)	3	F	120-122	Day 14	No	Gross

**Table S6. Mortality and morbidity summary table of the microdose toxicology study.**

Group #	Sex	Animal ID#	Study day Found dead	Possible cause of death	Test article related
18. Tumor Test Article αMSH-PEG-Cy5.5-C'dots at 1.2 nmol	F	99, 100	11	Large Tumor burden	Unlikely
19. Tumor Test Article cRGDY-PEG-CW800-C'dots at 1.2 nmol	M	103	9	Large Tumor burden	Unlikely
20. Tumor Test Article cRGDY-PEG-CW800-C'dots at 1.2 nmol	F	108	11	Large Tumor burden	Unlikely
23. No Tumor Test Article cRGDY-PEG-CW800-C'dots at 1.2 nmol	M	118	8	Skin infection	No

**Table S7. Hematology parameters in the microdose toxicology study.**

Hematology Parameter
Total Leukocyte count (WBC)
% Neutrophils
% Lymphocyte
% Monocytes
% Basophils
% Eosinophils
Erythrocyte count (RBC)
Hemoglobin (HB)
Hematocrit (HCT)
Mean Corpuscular Volume (MCV)
Mean Corpuscular Hemoglobin (MCH)
Mean Corpuscular Hemoglobin Concentration (MCHC)
Platelet count
Mean Platelet Volume (MPV)
Red Blood Cell Distribution Width (RDW)

**Table S8. Clinical chemistry parameters in the microdose toxicology study.**

<b>Clinical Chemistry Parameter</b>
Alkaline Phosphatase (ALP)
Alanine Aminotransferase (ALT)
Serum Aspartate Aminotransferase (AST)
Albumin
Total Protein
Globulin
Total Bilirubin
Blood Urea Nitrogen (BUN)
Creatinine
Cholesterol
Glucose
Calcium
Phosphorus
Chloride
Potassium
Sodium
Sodium/Potassium ratio (Na/K ratio)
Albumin/Globulin ratio (A/G ratio)

**Table S9. Tissues examined microscopically in the microdose toxicology study.**

<b>Tissues</b>	
Adrenals	Ovaries
Bone marrow	Oviducts
Bones/joints	Pancreas
Brain	Pituitary gland
Cecum	Prostate
Cervix	Salivary glands
Colon	Skeletal muscle
Epididymis	Seminal Vesicles
Esophagus	Small intestine
Eyes	Spinal cord
Gall bladder	Spleen
Haired skin	Stomach
Heart	Testes
Kidneys	Thyroids
Liver	Trachea
Lungs	Tongue
Mandibular lymph nodes	Urinary Bladder
Mesenteric lymph nodes	Uterus
Nasal cavity	Vagina
Oral cavity	



**Table S13. Hematology parameters, group 8, female, tumor, test article αMSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 2.**

Animal No	WBC	NEU	LYM	MONO	EOS	BAS	NEU %	LYM %	MONO %	EOS %	BAS %	RBC	HGB	HCT	MCV	MCH	MCHC	RDW%	PLT	MPV	
	K/ul	K/ul	K/ul	K/ul	K/ul	K/ul	%	%	%	%	%	M/ul	g/dL	%	fL	Pg	g/dL	%	K/ul	fL	
	6.95-9.95	3.58-5.48	1.75-3.03	0-3.24	0-1.86	0-0.20	53.7-77.7	11.8-25.8	0-18.4	0-10.6	0-2.0	4.8-5.4	15.6-17.2	43.5-51.5	87.1-99.1	29.7-34.7	31.5-37.5	13.9-19.9	443-563	6.7-12.7	
39	8.3	1.6	6.3	0.3	0.2	0	18.7	75.7	3.6	2	0	7	14.2	38.2	54.3	20.2	37.1	10.8	1056	5.1	
40	9.3	1.8	7	0.2	0.3	0	19.6	74.8	2.4	3	0.2	7.4	13.9	38.6	52.6	19	36.1	10.9	1124	4.7	
41	11	3.4	6.8	0.4	0.4	0	30.8	62	3.3	3.8	0.1	7.3	13.9	38	52.3	19.1	36.6	11.2	1263	4.5	
42	7.4	1.4	5.5	0.3	0.2	0	18.8	75.1	3.6	2.5	0	7.1	13.7	37.3	52.3	19.2	36.7	11	1308	4.4	
43	7.8	1.4	6.1	0.2	0.2	0	18	77.5	2	2.2	0.3	7.8	14.6	41.6	53.3	18.8	35.2	12.1	1106	4.4	
44	14.8	3.4	10.4	0.4	0.7	0	22.9	70.3	2.5	4.5	0.1	7.9	15	41.2	52.6	19.2	36.5	11.5	1212	4.4	
45	6.5	2	4.2	0.2	0.2	0	30.6	63.8	3.1	2.3	0.2	7.8	15.1	41.3	52.7	19.2	36.5	11.5	211	5.8	
46	5.3	1.5	3.3	0.2	0.2	0	28.3	63.4	4.3	3.7	0.3	7.9	14.8	41.4	52.9	18.8	35.7	10.9	951	4.6	
47	6.6	1.6	4.7	0.2	0.2	0	24.5	70.3	2.4	2.7	0.1	7.2	14	39	54	19.4	36	11.2	709	5.2	
48	5.6	1.6	3.7	0.2	0.2	0	28.4	64.6	3	3.8	0.2	7.1	13	36.7	51.6	18.3	35.5	11.7	1062	4.7	
Mean	8.3	2	5.8	0.2	0.3	0	24	69.8	3	3.1	0.2	7.4	14.2	38.3	52.8	19.1	36.2	11.3	1000.2	4.8	
SD	2.9	0.8	2.1	0.1	0.2	0	6.2	5.9	0.7	0.8	0.1	0.3	0.7	1.9	0.8	0.5	0.6	0.4	325.3	0.5	
SEM	0.9	0.2	0.7	0	0.1	0	1.6	1.9	0.2	0.3	0	0.1	0.2	0.6	0.3	0.2	0.2	0.1	102.9	0.1	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

**Table S14. Hematology parameters, group 9, male, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 2.**

Animal No	WBC	NEU	LYM	MONO	EOS	BAS	NEU %	LYM %	MONO %	EOS %	BAS %	RBC	HGB	HCT	MCV	MCH	MCHC	RDW%	PLT	MPV	
	K/ul	K/ul	K/ul	K/ul	K/ul	K/ul	%	%	%	%	%	M/ul	g/dL	%	fL	Pg	g/dL	%	K/ul	fL	
	6.95-9.95	3.58-5.48	1.75-3.03	0-3.24	0-1.86	0-0.20	53.7-77.7	11.8-25.8	0-18.4	0-10.6	0-2.0	4.8-5.4	15.6-17.2	43.5-51.5	87.1-99.1	29.7-34.7	31.5-37.5	13.9-19.9	443-563	6.7-12.7	
49	7.7	4.2	3	0.3	0.2	0	54.4	39.3	3.6	2.3	0.4	7.3	14.6	39.5	54.1	20	36.9	11.1	1023	4.6	
50	7.9	3.6	4	0.2	0.2	0	45.1	50.3	2.3	2	0.3	8.6	16.2	44.5	51.9	18.9	36.4	11.5	1129	4.9	
51	6.6	3.5	2.7	0.2	0.2	0	53.1	41.2	2.7	2.9	0.1	7.8	14.8	40.5	51.9	19	36.6	10.7	1209	4.9	
52	5.4	2.6	2.5	0.1	0.1	0	48.3	46.9	2.5	1.9	0.4	8	15.8	43.6	54.4	19.7	36.3	11.3	954	4.8	
53	8	1.3	6.3	0.3	0.2	0	16.9	78.9	3.5	1.9	0.2	8.1	15.2	42.4	52.9	18.9	36.9	11.5	1394	4.3	
54	11.6	1.7	9.5	0.2	0.2	0	15	81.5	1.9	1.5	0.1	7.7	14.3	40.5	52.7	18.7	35.4	11.4	1427	4.6	
55	11.1	2.2	8.2	0.4	0.2	0	20	74.2	3.9	1.8	0.1	8.1	15	40.6	50.4	18.6	36.9	11.2	1164	4.7	
56	7.2	1.5	5.5	0.1	0.1	0	20.4	76	1.8	1.7	0.1	7.7	14.1	40.7	53.1	18.4	34.7	11.7	656	5.3	
57	6.7	2.5	3.7	0.3	0.2	0	37.6	56	3.8	2.6	0	7.8	15.1	41.6	53.3	19.3	36.2	12.3	1032	4.5	
58	8.6	4	3.7	0.6	0.3	0	46.5	42.4	7.1	3.6	0.4	8.1	16	43.3	53.5	19.7	36.9	10.9	907	4.9	
Mean	8.1	2.7	4.9	0.3	0.2	0	35.6	58.6	3.3	2.2	0.2	7.9	15.1	41.7	52.8	19.1	36.2	11.4	1087.5	4.8	
SD	2	1.1	2.4	0.1	0.1	0	16.1	17.1	1.5	0.6	0.2	0.3	0.7	1.6	1.2	0.5	0.7	0.4	234.9	0.3	
SEM	0.6	0.3	0.8	0	0	0	5.1	5.4	0.5	0.2	0	0.1	0.2	0.5	0.4	0.2	0.2	0.1	71.1	0.1	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

**Table S15. Hematology parameters, group 10, female, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 2.**

Animal No	WBC	NEU	LYM	MONO	EOS	BAS	NEU %	LYM %	MONO %	EOS %	BAS %	RBC	HGB	HCT	MCV	MCH	MCHC	RDW%	PLT	MPV	
	K/ul	K/ul	K/ul	K/ul	K/ul	K/ul	%	%	%	%	%	M/ul	g/dL	%	fL	Pg	g/dL	%	K/ul	fL	
	6.95-9.95	3.58-5.48	1.75-3.03	0-3.24	0-1.86	0-0.20	53.7-77.7	11.8-25.8	0-18.4	0-10.6	0-2.0	4.8-5.4	15.6-17.2	43.5-51.5	87.1-99.1	29.7-34.7	31.5-37.5	13.9-19.9	443-563	6.7-12.7	
59	8	1.6	4	0.2	0.2	0	26.9	65.9	3.8	3.3	0.1	7.4	13.4	37.6	50.7	18.1	35.6	11.6	1056	4.3	
60	8.9	1.9	6.5	0.3	0.2	0	21.3	73.4	3.2	1.9	0.2	9	16.3	45.1	50.2	19.2	36.2	11	1040	5	
61	12.4	2.8	9	0.5	0.2	0	22.1	72.2	4	1.6	0.1	8.1	15.4	42.4	52.2	18.9	36.3	11.6	974	4.9	
62	4.2	1.2	2.7	0.2	0.1	0	28.4	64.6	4.3	2.6	0.1	8.3	15.1	41.6	50	18.2	36.3	11.8	623	4.6	
63	3.2	0.9	2.2	0.1	0.1	0	26.6	67.4	1.8	4	0.2	7.5	14.3	39.9	53.1	19.1	35.9	12	1022	4.6	
64	7.4	2.9	4.1	0.3	0.1	0	38.7	55	4.4	1.8	0.1	7.8	14.9	38.8	50.9	19	37.3	11.7	1027	4.9	
65	5.3	1.8	3.3	0.2	0.1	0	33.2	62	3.4	1.4	0	7.6	14	38.5	50.5	18.4	36.4	11.5	969	4.7	
66	8.3	1.6	6.4	0.2	0.2	0	18.9	76.7	2.2	2	0.2	8	14.9	40.9	51.2	18.7	36.4	11.3	994	4.7	
67	5.9	1.7	4	0.1	0.1	0	29.3	66.9	2.4	1.4	0	8.4	15.4	42.6	50.4	19.2	36.1	11.2	1281	4.5	
68	7.3	2.6	4.2	0.4	0.1	0	35.3	58.1	5.2	1.3	0.1	8	15	41.9	52.1	18.7	35.8	11.9	999	4.7	
Mean	6.9	1.9	4.6	0.2	0.1	0	28.1	66.2	3.5	2.1	0.1	8	14.9	41	51.1	18.6	36.2	11.6	986.4	4.7	
SD	2.6	0.7	2.1	0.1	0	0	6.3	6.8	1.1	0.9	0.1	0.5	0.8	2.2	1	0.4	0.5	0.3	155.4	0.2	
SEM	0.8	0.2	0.7	0	0	0	2	2.1	0.3	0.3	0	0.2	0.3	0.7	0.3	0.1	0.1	0.1	50.4	0.1	
N	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10

**Table S16. Hematology parameters, group 11, male, no tumor, test article αMSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 2.**

Animal No	WBC	NEU	LYM	MONO	EOS	BAS	NEU %	LYM %	MONO %	EOS %	BAS %	RBC	HGB	HCT	MCV	MCH	MCHC	RDW%	PLT	MPV
	K/ul	K/ul	K/ul	K/ul	K/ul	K/ul	%	%	%	%	%	M/ul	g/dL	%	fL	Pg	g/dL	%	K/ul	fL
	6.95-9.95	3.58-5.48	1.75-3.03	0-3.24	0-1.86	0-0.20	53.7-77.7	11.8-25.8	0-18.4	0-10.6	0-2.0	4.8-5.4	15.6-17.2	43.5-51.5	87.1-99.1	29.7-34.7	31.5-37.5	13.9-19.9	443-563	6.7-12.7
69	12.5	2.2	9.6	0.5	0.2	0	17.3	76.9	4.1	1.8	0	8.1	14.9	41.7	51.7	18.5	35.8	11.7	1386	4.4
70	7	1.3	5.3	0.3	0.1	0	19.2	75.9	3.6	1.3	0	7.4	13.7	37.3	50.8	18.7	36.8	11.5	1142	4.8
71	8	1.9	5.6	0.3	0.2	0	23.3	70.5	3.8	2.4	0	7	13.4	37	53.1	19.2	36.2	11.3	1123	5
Mean	9.1	1.8	6.8	0.4	0.2	0	19.9	74.4	3.8	1.8	0	7.5	14	38.7	51.9	18.8	36.3	11.5	1210.3	4.7
SD	2.9	0.4	2.4	0.1	0.1	0	3.1	3.4	0.3	0.6	0	0.6	0.8	2.6	1.2	0.4	0.5	0.2	135.1	0.3
SEM	1.7	0.2	1.4	0.1	0	0	1.8	2	0.1	0.3	0	0.3	0.5	1.5	0.7	0.2	0.3	0.1	78	0.2















**Table S42. Hematology parameters, group 17, male, tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.**

Animal No	BUN	Creatinine	Phosphorus	Calcium	Total Protein	Albumin	Globulin	Alb/Glob Ratio	Glucose	Cholesterol	ALT (GPT)	AST (GOT)	ALP	Total Bilirubin	Sodium	Potassium	Chloride	Na/K Ratio
	mg/dl	mg/dl	mg/dl	mg/dl	g/dl	g/dl	g/dl	--	mg/dl	mg/dl	U/L	U/L	U/L	mg/dl	mEq/L	mEq/L	mEq/L	--
41.3-53.3	3.9-5.5	6.2-8.2	10.9-13.9	2.9-4.1	3.3-4.5	223-279	87-121	66-96	157-207	228-334	2.8-4.4	114-140	5.1-6.5	75-95				
91	21.6	0.4	6.4	8.6	4.7	2	2.7	0.7	97	86	39	>1000	44	0.1	155	4	119	39
92	24.2	0.3	6.3	7.6	4.6	2	2.6	0.8	131	100	40	982	45	0.1	153	3.3	117	46
93	20.2	0.2	6.8	8.4	4.5	2	2.5	0.8	151	100	48	945	52	0.1	153	4.3	117	36
94	21.1	0.3	5	8.7	4.5	2	2.5	0.8	149	88	39	>1000	37	0.1	154	4	118	39
95	26.7	0.4	8	8.8	4.6	2.1	2.5	0.8	167	98	43	574	61	0.1	155	3.3	120	47
Mean	22.9	0.3	6.5	8.4	4.6	2	2.6	0.8	139	94.4	41.8	833.7	47.8	0.1	154	3.8	118.2	41.4
SD	2.7	0.1	1.1	0.5	0.1	0	0.1	0	26.7	6.8	3.8	225.6	9.1	0	1	0.5	1.3	4.8
SEM	1.2	0	0.5	0.2	0	0	0	0	11.9	3.1	1.7	130.3	4.1	0	0.4	0.2	0.6	2.2
N	5	5	5	5	5	5	5	5	5	5	5	3	5	5	5	5	5	5

**Table S43. Hematology parameters, group 18, female, tumor, test article  $\alpha$ MSH-PEG-Cy5.5-C' dots at 1.2 nmol, day 14.**

Animal No	BUN	Creatinine	Phosphorus	Calcium	Total Protein	Albumin	Globulin	Alb/Glob Ratio	Glucose	Cholesterol	ALT (GPT)	AST (GOT)	ALP	Total Bilirubin	Sodium	Potassium	Chloride	Na/K Ratio
	mg/dl	mg/dl	mg/dl	mg/dl	g/dl	g/dl	g/dl	--	mg/dl	mg/dl	U/L	U/L	U/L	mg/dl	mEq/L	mEq/L	mEq/L	--
41.3-53.3	3.9-5.5	6.2-8.2	10.9-13.9	2.9-4.1	3.3-4.5	223-279	87-121	66-96	157-207	228-334	2.8-4.4	114-140	5.1-6.5	75-95				
96	27.3	0.2	10.9	9.2	4.7	2.1	2.6	0.8	95	95	43	100	49	0.2	155	4.5	122	34
97	35.5	0.2	8.5	9.1	4.4	1.9	2.5	0.8	213	98	45	>1000	41	0.1	154	4	120	39
98	26.6	<0.2	8.3	9.2	4.3	1.9	2.4	0.8	182	117	57	>1000	41	0.1	152	3.7	115	41
99	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD
100	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD
Mean	29.8	0.2	9.2	9.2	4.5	2	2.5	0.8	163.3	103.3	48.3	Not calculated	42.7	0.1	153.7	4.1	119	38
SD	4.9	0	1.4	0.1	0.2	0.1	0.1	0	61.2	11.9	7.6	Not calculated	4.6	0.1	1.5	0.4	3.6	3.6
SEM	2.9	0	0.8	0	0.1	0.1	0.1	0	35.3	6.9	4.4	Not calculated	2.7	0	0.9	0.2	2.1	2.1
N	3	2	3	3	3	3	3	3	3	3	3	3.0	3	3	3	3	3	3

**Table S44. Hematology parameters, group 19, male, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 14.**

Animal No	BUN	Creatinine	Phosphorus	Calcium	Total Protein	Albumin	Globulin	Alb/Glob Ratio	Glucose	Cholesterol	ALT (GPT)	AST (GOT)	ALP	Total Bilirubin	Sodium	Potassium	Chloride	Na/K Ratio
	mg/dl	mg/dl	mg/dl	mg/dl	g/dl	g/dl	g/dl	--	mg/dl	mg/dl	U/L	U/L	U/L	mg/dl	mEq/L	mEq/L	mEq/L	--
41.3-53.3	3.9-5.5	6.2-8.2	10.9-13.9	2.9-4.1	3.3-4.5	223-279	87-121	66-96	157-207	228-334	2.8-4.4	114-140	5.1-6.5	75-95				
101	23.1	0.4	6.4	8.1	4.4	2	2.4	0.8	163	82	37	>1000	44	0.1	154	4.3	121	36
102	26.2	0.2	9.7	8.9	4.2	1.7	2.5	0.7	143	81	29	>1000	43	0.1	156	4	122	39
103	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD
104	24.7	0.6	>15.0	11.5	5.1	2.3	2.8	0.8	170	110	66	842	63	0.1	156	11.8	123	13
105	21.8	0.2	7	8.5	3.9	1.7	2.2	0.8	143	72	40	>1000	39	0.1	154	3.5	118	44
Mean	24	0.4	7.7	9.3	4.4	1.9	2.5	0.8	154.8	86.3	43	842	47.3	0.1	155	5.9	121	33
SD	1.9	0.2	1.8	1.5	0.5	0.3	0.3	0.1	13.9	16.5	16	Not calculated	10.7	0	1.2	3.9	2.2	13.7
SEM	1	0.1	1	0.8	0.3	0.1	0.1	0	6.9	8.2	8	Not calculated	5.4	0	0.6	2	1.1	6.9
N	4	4	3	4	4	4	4	4	4	4	4	4	4	4	4	4	4	4

**Table S45. Hematology parameters, group 20, female, tumor, test article cRGDY-PEG-cw800-C' dots at 1.2 nmol, day 14.**

Animal No	BUN	Creatinine	Phosphorus	Calcium	Total Protein	Albumin	Globulin	Alb/Glob Ratio	Glucose	Cholesterol	ALT (GPT)	AST (GOT)	ALP	Total Bilirubin	Sodium	Potassium	Chloride	Na/K Ratio
	mg/dl	mg/dl	mg/dl	mg/dl	g/dl	g/dl	g/dl	--	mg/dl	mg/dl	U/L	U/L	U/L	mg/dl	mEq/L	mEq/L	mEq/L	--
41.3-53.3	3.9-5.5	6.2-8.2	10.9-13.9	2.9-4.1	3.3-4.5	223-279	87-121	66-96	157-207	228-334	2.8-4.4	114-140	5.1-6.5	75-95				
106	21.9	0.2	4.7	8.5	4.4	1.9	2.5	0.8	126	70	46	>1000	46	0.5	154	4.6	121	33
107	23.1	0.2	7	7	4.1	1.9	2.2	0.8	217	117	51	>1000	42	0.1	151	4.1	116	37
108	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD
109	23.7	0.2	10.3	8.7	4.6	1.9	2.7	0.7	194	87	51	>1000	40	0.1	154	4.2	120	37
110	25.7	0.2	10.9	7.9	4.2	1.8	2.4	0.8	173	94	61	>1000	43	0.1	151	4.1	120	37
Mean	23.6	0.2	8.2	8	4.3	1.9	2.5	0.8	177.5	92	52.3	Not calculated	42.6	0.2	152.5	4.3	119.3	36
SD	1.6	0	2.9	0.8	0.2	0	0.2	0.1	38.8	19.5	6.3	Not calculated	2.5	0.2	1.7	0.2	2.2	2
SEM	0.8	0	1.5	0.4	0.1	0	0.1	0	19.4	9.7	3.1	Not calculated	1.3	0.1	0.9	0.1	1.1	1
N	4	4	4	4	4	4	4	4	4	4	4	4.0	4	4	4	4	4	4

