

Crossing the blood-brain barrier with carbon dots: uptake mechanism and *in vivo* cargo delivery

Elif S. Seven¹, Yasin B. Seven^{2,3}, Yiqun Zhou¹, Sijan Poudel-Sharma⁴, Juan J. Diaz-Rucco¹, Emel Kirbas Cilingir¹, Gordon M. Mitchell^{2,3}, J. David Van Dyken⁴, Roger M. Leblanc^{1*}

¹ Department of Chemistry, University of Miami, 1301 Memorial Dr., Coral Gables, FL, USA 33146

² Department of Physical Therapy, University of Florida, 101 Newell Dr, Gainesville, FL, USA 32603

³ McKnight Brain Institute, University of Florida, 1149 Newell Dr, Gainesville, FL, USA 32610

⁴ Department of Biology, University of Miami, 1301 Memorial Dr., Coral Gables, FL, USA 33146

*Corresponding Author

rml@miami.edu

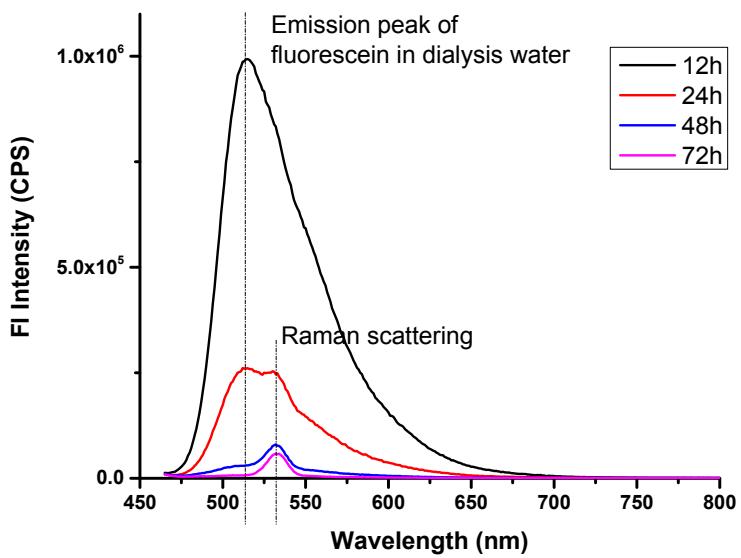


Figure S-1. Intensity of the fluorescence emission peak of fluorescein present in dialysis water decreased during purification every time dialysis water changed. After 3 days of dialysis, there was no fluorescence emission peak in the dialysis water showing the elimination of the free fluorescein in the GluCD-F dispersed in water.

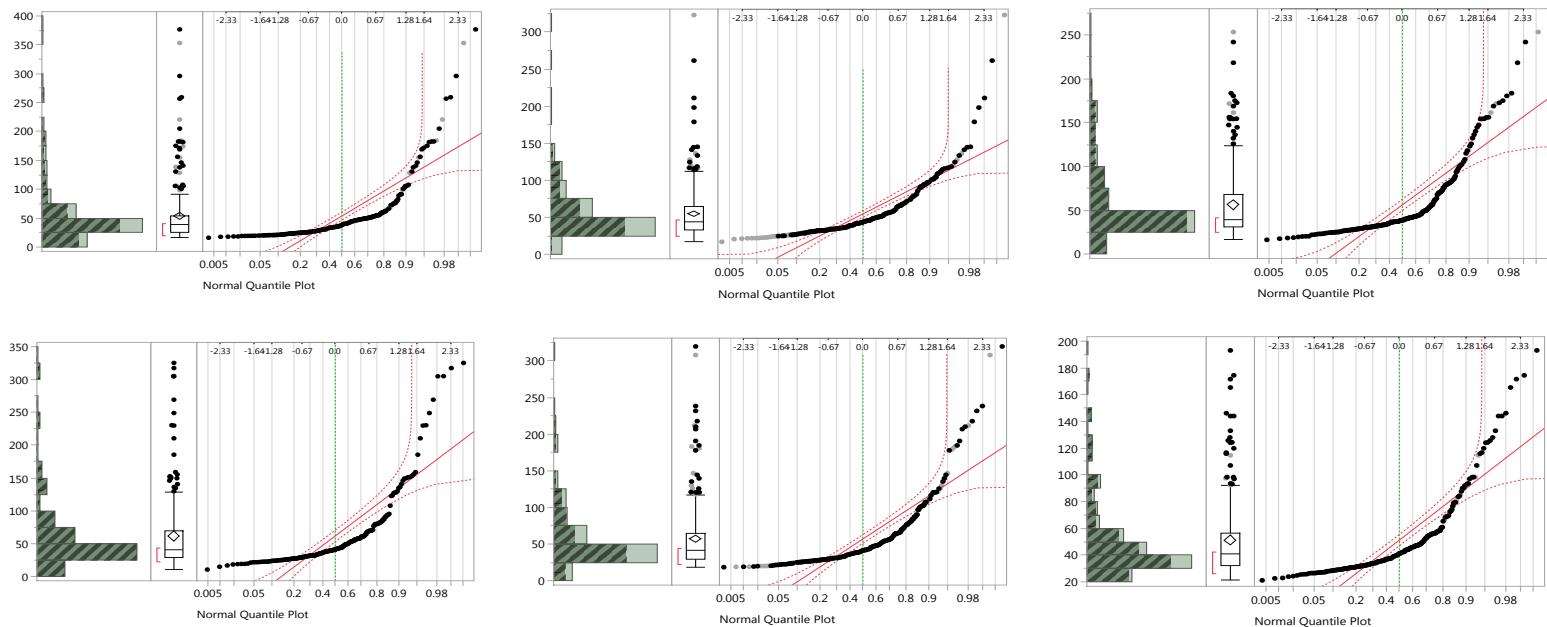


Figure S-2. Area distributions of EBY.VW 5000-C (Hex-) (top three, for three replicates) and EBY.VW 5000-T (Hex-) (bottom three, for three replicates)

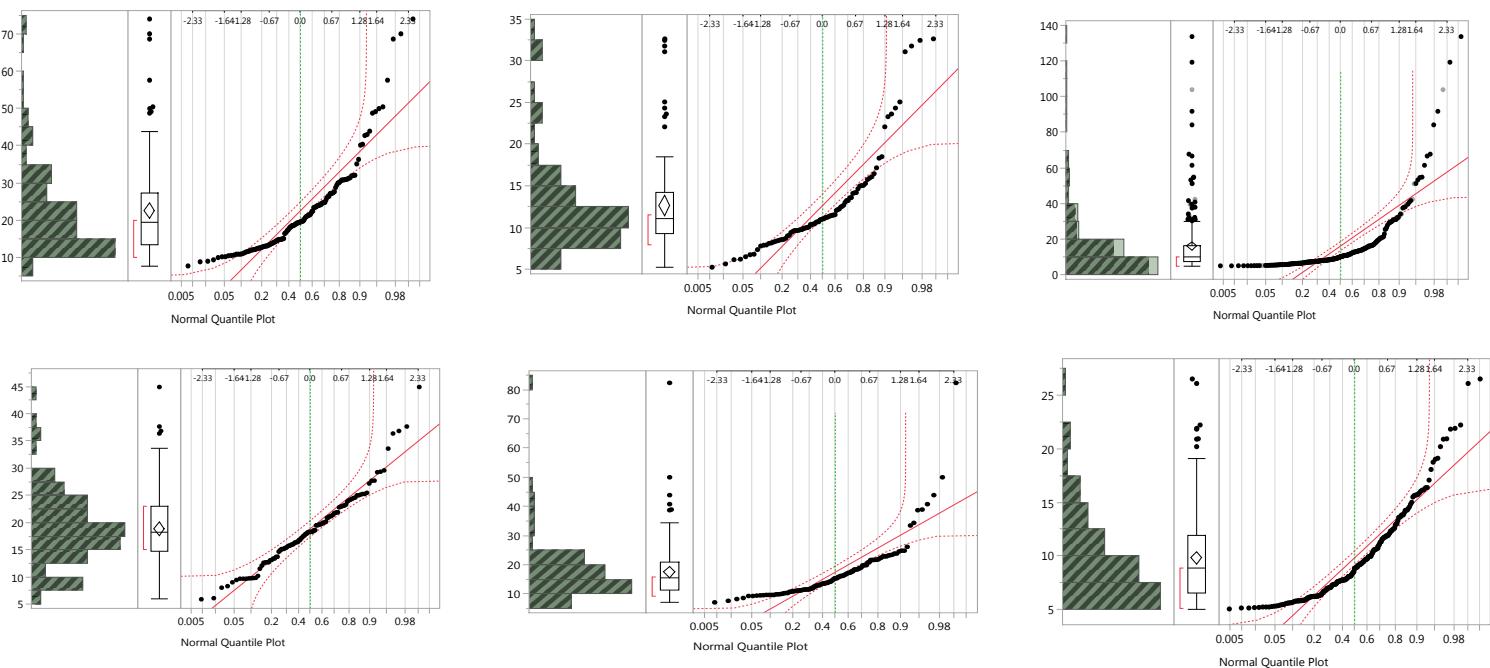


Figure S-3. Area distributions of BC-C (Hex+) (top three, for three replicates) and BC-T (Hex+) (bottom three, for three replicates)

Table S-1. The mean areas of ROIs for each group

	EBY.VW 5000	BC
Control 1	62.05	22.55
Control 2	54.17	12.67
Control 3	54.78	16.20
Treatment 1	56.27	18.87
Treatment 2	51.36	17.48
Treatment 3	57.07	9.83

Table S-2. Comparison between the mean area of ROIs for each group

Level	-Level	p-value
EBY.VW 5000-C	BC-T	<0.0001*
EBY.VW 5000-C	BC-C	<0.0001*
EBY.VW 5000-T	BC-T	<0.0001*
EBY.VW 5000-T	BC-C	<0.0001*
EBY.VW 5000-C	EBY.VW 5000-T	0.5759
BC-C	BC-T	0.6408

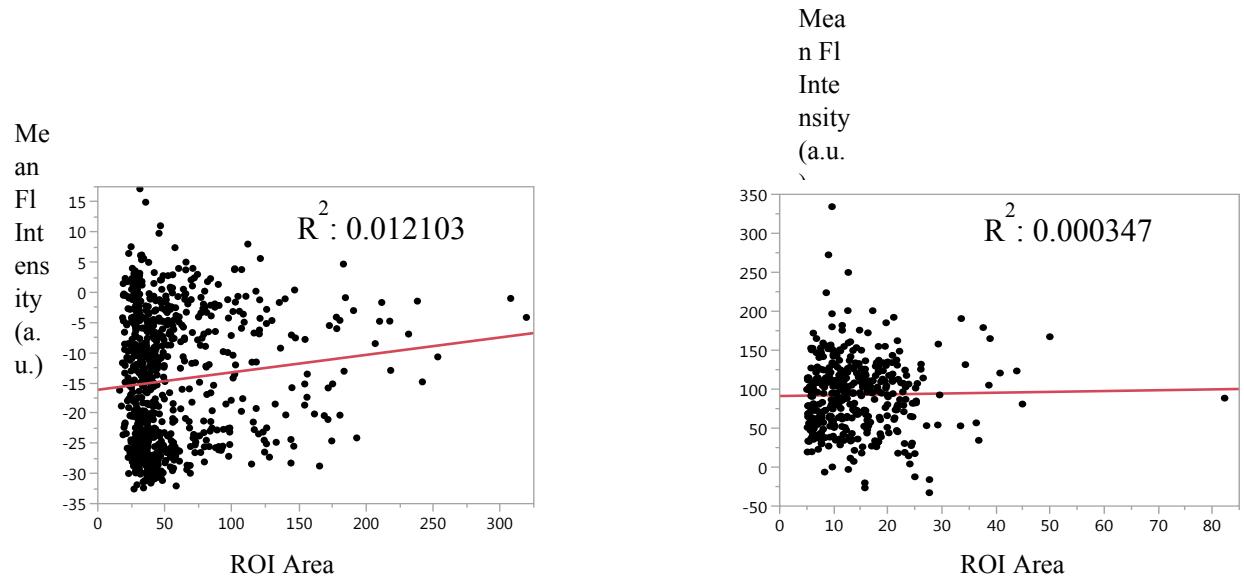


Figure S-4. Bi-variate analysis of Fl intensity vs ROI area for EBY.VW 5000 (Hex-) (left) and BC (Hex+) (right) strains

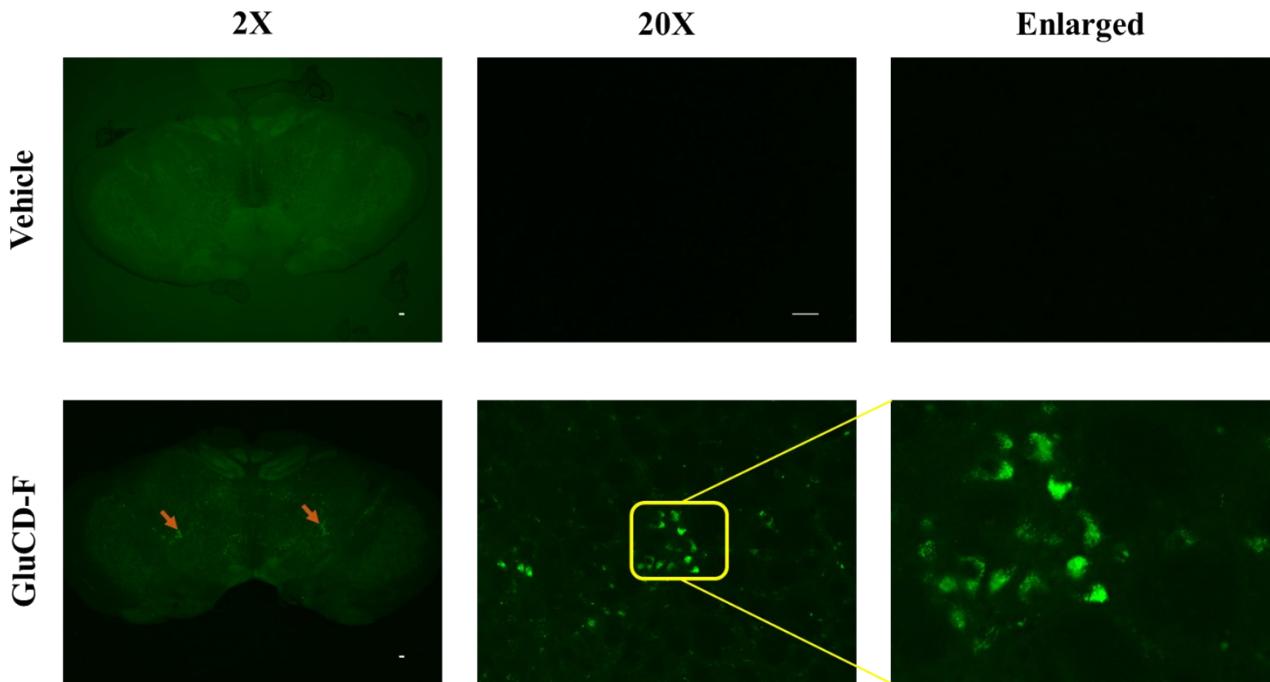


Figure S-5. Representative brainstem fluorescence images from vehicle and glucose carbon dot-fluorescein conjugate (GluCD-F) treated rats. Scale bar (2X): 100 μm , Scale bar (20X): 50 μm