Supporting Information

Significant Accumulation of Polymyxin in Single Renal Tubular Cells: A Medicinal Chemistry and Triple Correlative Microscopy Approach

Mohammad A. K. Azad[†], Kade D. Roberts^{†‡}, Heidi H. Yu[†], Boyin. Liu[§], Alice V. Schofield[†], Simon A. James[∥], Daryl L. Howard[∥], Roger L. Nation[†], Kelly Rogers[⊥], Martin D. de Jonge[∥], Philip E. Thompson[‡], Jing Fu^{§¶}, Tony Velkov^{†¶}, Jian Li^{*†¶}

[†]Drug Delivery, Disposition and Dynamics, Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, Victoria 3052, Australia
[‡]Medicinal Chemistry, Monash Institute of Pharmaceutical Sciences, Monash University, Victoria 3052, Australia
[§]Department of Mechanical and Aerospace Engineering, Monash University, Clayton, Victoria 3800, Australia
^IAustralian Synchrotron, Clayton, Victoria 3168, Australia
^LCentre for Dynamic Imaging, Walter & Eliza Hall Institute of Medical Research, Parkville,

Victoria 3052, Australia

Joint senior authors.

*Corresponding Author E-mail: Colistin.Polymyxin@gmail.com

Contents

- 1. Figure S1
- 2. Figure S2

Figure S1: Fluorescence spectra illustrating the concentration-dependent enhancement of fluorescence emission of FADDI-096 in water.



Figure S2: Distribution of elements (Ca, Cl, Cu, Fe, K, P, S and Zn) in single NRK-52E and HK-2 cells determined with X-ray fluorescence microscopy (XFM). a) NRK-52E cells (i) without treatment, (ii) treated with 5 μ M FADDI-096 for 4 h, (iii) treated with 50 μ M FADDI-096 for 4 h, (iii) treated with 50 μ M FADDI-096 for 4 h; and HK-2 cells (v) without treatment, (vi) treated with 10 μ M FADDI-096 for 4 h. Signal intensities are scaled separately for each element shown from zero to the maximum value; the numbers at the top of the relevant panels note the maximum pixel value (μ g/cm²) in each sample. Scale: 10 μ m. Similar elemental distributions were observed previously.¹⁻⁴ (b) Accumulation of elements in single NRK-52E and HK-2 cells as described in panel a, measured using XFM (mean ± SD; n = 10).

Figure S2:



References:

(1) Dillon, C. T. Aust. J. Chem. 2012, 65, 204-217.

(2) Vogt, S.; Lai, B.; Finney, L.; Palmer, B.; Wu, L. E.; Harris, H.; Paunesku, T.; de Jonge, M.; Legnini, D.; Maser, J.; Glesne, D.; Lay, P.; Woloschak, G. *Microsc. Microanal.* **2007**, *13*, 40-41.

(3) Finney, L.; Mandava, S.; Ursos, L.; Zhang, W.; Rodi, D.; Vogt, S.; Legnini, D.; Maser, J.; Ikpatt, F.; Olopade, O. I.; Glesne, D. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 2247-2252.

(4) James, S. A.; Feltis, B. N.; de Jonge, M. D.; Sridhar, M.; Kimpton, J. A.; Altissimo, M.; Mayo, S.; Zheng, C. X.; Hastings, A.; Howard, D. L.; Paterson, D. J.; Wright, P. F. A.; Moorhead, G. F.; Turney, T. W.; Fu, J. *ACS Nano.* **2013**, *7*, 10621-10635.