Insights from Correlations between Nanomaterials Design and Biological Response

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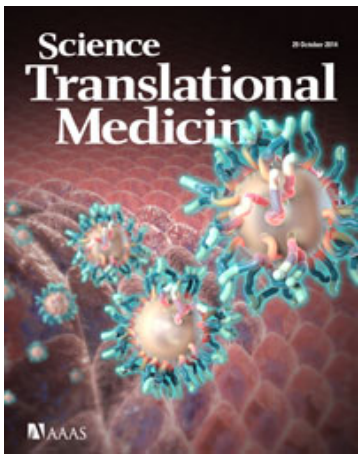
Despite significant promise of nanomaterials in medicine, few colloidal materials make the transition into the realm of human clinical applications. To a large extend this is due to a lack of fundamental understanding of how nanomaterials design modulates biological response. In turn, this can often be related to unresolved heterogeneities in composition, structure, and surface chemical properties in nanomaterials synthesis batches as compared to low molar mass compounds, the current paradigm in pharmaceutical treatments. In this presentation a novel class of ultrasmall multifunctional fluorescent core-shell polymer-silica hybrid nanoparticles will be introduced referred to as "Cornell dots" or simply "C dots". These particles have sizes below 10 nm, *i.e.* below the threshold for renal clearance, leading to favorable biodistributions and pharmacokinetics. Because of their small size that is of the order of a medium-size protein, high resolution chromatographic techniques can be applied to their characterization, opening up a new paradigm in establishing structure - biological response correlations. These smaller than 10 nm sized PEGylated probes for nanomedicine are the first dual-modality (optical/PET) hybrid nanoparticles of their class and properties receiving investigational new drug (IND) FDA approval for first in-human clinical trials in the US.[1] In this presentation, results on C dot synthesis and characterization will be reported with focus on materials properties that facilitate translation into clinical applications. This will include description of encouraging results of the characterization of C dots with high-resolution chromatographic techniques like GPC and HPLC. It will also include the use of C dots in unconventional therapeutic strategies against cancer involving the tumor microenvironment (TME), as well as the discovery of novel silica nanoparticle topologies.[2,3] The talk will finally discuss novel generation C dots as amorphous quantum nanomaterials enabling exquisite control of their quantum behavior under illumination leading to advanced materials for application in optical super-resolution microscopy (SRM) and photodynamic therapy.[4]



References:

1.) E. Phillips, O. Penate-Medina, P. B. Zanzonico, R. D. Carvajal, P. Mohan, Y. Ye, J. Humm, M. Gönen, H. Kaliagian, H. Schöder, H. W. Strauss, S. M. Larson, U. Wiesner, M. S. *Bradbury, Clinical translation of an ultrasmall inorganic optical-PET imaging nanoparticle probe,* Sci. Transl. Med. **6** (2014), 260ra149.

2.) S. Eun Kim, L. Zhang, K. Ma, M. Riegman, F. Chen, I. Ingold, M. Conrad, M. Z. Turker, M. Gao, X. Jiang, S. Monette, M. Pauliah, M. Gonen, P. Zanzonico, T. Quinn, U. Wiesner, M. S. Bradbury, M. Overholtzer, *Ultrasmall Nanoparticles Induce Ferroptosis in Nutrient-Deprived Cancer Cells and Suppress Tumor Growth*, Nat. Nanotech. **11** (2016), 977–985

3.) K. Ma, Y. Gong, T. Aubert, M. Z. Turker, T. Kao, P. C. Doerschuk, U. Wiesner, *Self-assembly of highly symmetrical, ultrasmall inorganic cages directed by surfactant micelles*, Nature **558** (2018), 577-580.

4.) F. F. E. Kohle, J. A. Hinckley, S. Li, N. Dhawan, W. P. Katt, J. A. Erstling, U. Werner-Zwanziger, J. Zwanziger, R. A. Cerione, U. B. Wiesner, *Amorphous Quantum Nanomaterials*, Adv. Mater. **31** (2019), 1806993.