

# Design principles for precision nanomedicine

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## ABSTRACT

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Getting across biological barriers and deliver therapeutic cargo to the right site is indeed a very challenging task that requires the judicious combination of physiological information with carrier engineering. In the last decade, we have approached this problem, applying a constructionist approach where we mimic biological complexity in the form of design principles to produce functional bionic units from simple building blocks and their interactions. We combine synthetic and supramolecular chemistry to tune inter/intramolecular interactions and self-assembly processes to form dynamic soft materials. Among the different bionic efforts, we have focussed our attention to possibly one of the few that encompasses polymerisation, compartmentalisation and positional self-assembly in the same unit; Polymersomes. These are vesicles formed by the self-assembly of amphiphilic block copolymers in water. We have equipped polymersomes with the critical elements to address the challenges for getting across biological barriers. They have surface engineered to control both attractive (binding) and repulsive (anti-fouling) interaction with proteins and receptors to create systems that can avoid opsonisation and yet target specific cell populations. We have engineered their mechanical properties so as to be flexible and able to penetrate dense tissues exploiting size-exclusion percolation patterns. We have equipped them with both asymmetric topology and enzymes to control their fluid-dynamics and diffusion so as to create chemotactic and active propulsion toward endogenous signalling molecules. Finally, we have engineered their shape and size to guide cellular endocytosis as well as to escape the endocytic sorting accessing and delivering cargo within the cell interior. I will present our design efforts discussing each structural and functional elements as a function of the respective biological challenge, I will conclude presenting applications where these precision systems are being applied to address challenges in oncology, immunology and neurology.

**References:** Joseph *et al.* *Science Adv.* 2017, in the press; Robertson *et al.* *J. Immunol.* 2017, 198, 3596; Messenger *et al.* *Angew. Chem. Int. Ed.* 2016, 37, 11272-11275; Simón-Gracia *et al.* *Biomaterials* 2016, 104, 247-257; Ruiz Perez *et al.* *Science Adv.* 2016, e1500948; Tian *et al.* *Sci. Rep.* 2015, 5, 11990; Robertson *et al.* *ACS Nano*, 2014, 8, 4650-4661; Madsen *et al.* *J. Am. Chem. Soc.* 2013, 135, 14863-14870; Wang *et al.* *Angew. Chem. Int. Ed.* 2012, 51, 11122-11125; LoPresti *et al.* *ACS Nano* 2011, 5 (3), 1775-1784; Murdoch *et al.* *Nanomedicine* 2010, 5, 1025-1036; Gill *et al.* *Nature Chem.* 2009, 1, 662 - 667; T. Smart *et al.* *NanoToday* 2008, 3, (3-4), 38-4; Lomas *et al.* *Adv. Mater.* 2007, 19, 4238-4243; Battaglia *et al.* *Angew. Chem. Int. Ed.* 2006, 45, 2052-2056; Battaglia *et al.* *Nature Mater.* 2005, 4, 869-876.

## BIOGRAPHY

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Giuseppe Battaglia holds the Chair in Molecular Bionics in the Department of Chemistry at the University College London. Giuseppe is also a EPSRC Established Career Fellow, the Director of the EPSRC/Jeol Centre for Liquid-phase electron microscopy at UCL and Honorary Professor of Chemical Engineering at the Department of Chemical Engineering also at UCL. Prior to joining UCL, Giuseppe held positions as Lecturer -2006, Senior Lecturer -2009 and Professor -2011 in the Departments of Materials Sci. Eng. (2006-2009) and Biomedical Science (2009-2013) at the University of Sheffield. Giuseppe has published over 100 research articles, reviews and book chapters and he is named inventor in 9 patents. He was awarded the 2009 HFSP Young Investigator Award jointly with Prof A. Engler from UCSD, the 2011 APS/IoP Polymer Physics Exchange Award Lecture, the 2011 GSK Emerging Scientist Award, the 2012 Award for special contribution to Polymer Therapeutics, the 2014 RSC Thomas Graham Award Lecture, 2015 SCI/RSC McBain Medal for Colloid Science and the 2017 Anhui Province 100 Foreign Talent Award.

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