Versatile Dendritic Nanoparticles for Enhanced Cancer Immunotherapy and Liquid Biopsy

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Abstract
Dendritic polymers have drawn considerable attention to be used as a nanoscale platform for various biomedical applications over the past few decades. In this presentation, our recent efforts on engineered poly(amidoamine) (PAMAM) dendrimers will be summarized, focusing on their applications to immunotherapy and liquid biopsy. For immunotherapy, generation 7 (G7) PAMAM dendrimers were employed as a platform to accommodate multiple antibody molecules against PD-L1 (aPD-L1) or PD-L1-binding peptides, followed by characterization, binding kinetics measurements, in vitro cell assays, and in vivo tests. The three independent binding measurements using surface plasmon resonance (SPR), bio-layer interferometry (BLI), and atomic force microscopy (AFM) all revealed that the dendrimer conjugates exhibited a significantly greater binding kinetics than their free counterparts (either aPD-L1 or PD-L1-binding peptides), by up to five orders of magnitude. Such enhancement was likely achieved through the multivalent binding effect mediated by dendrimers and surface stabilization of the peptide structure, which was translated into significantly improved in vitro efficiency and in vivo selectivity/efficacy. For liquid biopsy, we have developed a novel detection/isolation method for circulating tumor cells (CTCs) from blood using a biomimetic approach combined with nanotechnology. The biomimetic combination of dynamic rolling and multivalent binding via dendrimers significantly enhanced the surface capture efficiency of tumor cells by up to ~150 fold, compared to a conventional method relying on a single cancer cell marker, such as epithelial cell adhesion molecule. Following a series of in vitro and in vivo validation on our CTC device, recent clinical data obtained using our device exhibited the strong correlation between kinetic CTC profiles and clinical outcomes. Furthermore, the harvested CTCs from patients' blood were used as the subject of post-capture analysis, such as immunostaining against various cancer markers and single cell RNA sequencing. More recently, the similar surface configuration was engineered to effectively detect another circulating biomarker, tumor-derived exosomes, which will be also discussed. All in all, our results collectively demonstrate the versatile potential of the engineered dendrimers to be used in various applications, such as immunotherapy and liquid biopsy.

Bio

Dr. Seungpyo Hong is Milton J. Henrichs Chair and Professor of Pharmaceutical Sciences and Director of Wisconsin Center for NanoBioSystems (WisCNano) at University of Wisconsin-Madison (UW-Madison). He holds appointments as Adjunct Professor at the University of Illinois at Chicago (UIC) and Yonsei University, Seoul, Korea, while serving as Associate Editor for Nanomedicine: Nanotechnology, Biology and Medicine of Elsevier. Dr. Hong is also active in entrepreneurship, co-founding a biotech startup called Capio Biosciences where he serves as President and CEO. He graduated from Hanyang University in Seoul, Korea with B.S. and M.S. degrees in polymer engineering in 1999 and 2001, respectively. He then received his PhD in Macromolecular Science and Engineering from University of Michigan in 2006 and joined MIT as a postdoctoral associate in the laboratory of Prof. Robert Langer. From 2008 to 2014, he was an Assistant Professor at UIC where he was promoted to Associate Professor with tenure in 2014, and subsequently joined the UW-Madison faculty as Full Professor in 2016. To date, Prof. Hong's research has culminated in well over 100 peer-reviewed articles that have accumulated a total of over 17,000 citations, 1 co-edited book, 8 book chapters, and 22 issued or pending patents, while delivering over 200 invited talks worldwide. His scientific contributions have been recognized, resulting in him receiving honors, including 2022 Inducted Fellow of American Institute for Medical and Biological Engineering (AIMBE), 2012 New Investigator Award from American Association of Pharmaceutical Scientists (AAPS), and 2012 Rising Star Award from the University of Illinois at Chicago.