**Versatile Dendritic Nanoparticles for Immunotherapy, Gene Delivery, and Controlled Tumor Penetration**

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Dendritic polymers have drawn considerable attention to be used as a nanocarrier platform for various therapeutic agents over the past few decades. Major advantages of the macromolecules include: i) the ability to mediate strong multivalent binding; ii) efficient, controlled tumor penetration due to their sub 10 nm size and deformability; and iii) facile multifunctionalization through various conjugation chemistries. In this presentation, our recent efforts on using poly(amidoamine) (PAMAM) dendrimers for immunotherapy and miRNA delivery will be summarized. For immunotherapy, a few of antibody molecules against PD-L1 (aPD-L1) were conjugated to a generation 7 (G7) PAMAM dendrimer, followed by characterization, binding kinetics measurements, and in vitro cell assays. The three independent binding measurements using surface plasmon resonance (SPR), bio-layer interferometry (BLI), and atomic force microscopy (AFM) revealed that the dendrimer-aPD-L1 conjugates exhibited a significantly greater binding kinetics than free aPD-L1, by two orders of magnitude. Such enhancement was likely achieved through the multivalent binding effect mediated by dendrimers, which was translated into an improved killing of cancer cells (786-O and MCF-7) when co-treated with activated Jurkat cells and doxorubicin upon treatment with the dendrimer-aPD-L1 conjugates. For miRNA delivery, we prepared dendriplexes between G7 PAMAM dendrimers conjugated with Cy5.5 and miR-22 or miR-150 that are frequently found impaired among acute myeloid leukemia (AML) patients. Particularly, the G7-miR-150 dendriplexes were further functionalized with FLT-3 ligands (FLT-3L) that target *FLT3* overexpressed by AML cells. The both *in vitro* and *in vivo* results demonstrated that the dendrimers successfully delivered miR-22 and miR-150 to AML cells, of which specificity was further improved through conjugation with FLT-3L. Additionally, we have found that tumor penetration and intratrumoral location of PAMAM dendrimers could be controlled through engineering size, surface charge, and attached targeting agents, as shown in a series of studies using multicellular tumor spheroid (MCTS) models. All in all, the results that will be presented indicate the versatility of dendrimers to be used as a nanoscale delivery platform, demonstrating great potential to change the paradigm of currently available cancer treatments.

BIO

Dr. Seungpyo Hong is Professor of Pharmaceutical Sciences and Biomedical Engineering, and serves as Director of Wisconsin Center for NanoBioSystems (WisCNano) at the University of Wisconsin-Madison (UW-Madison). He also holds an appointment as Adjunct Professor in the Colleges of Pharmacy at the University of Illinois at Chicago (UIC) and at Yonsei University, Seoul, Korea, He graduated from Hanyang University in Seoul, Korea with B.S. and M.S. degrees in polymer engineering in 1999 and 2001, respectively. After working as a researcher at Korea Institute Science and Technology (KIST), he started his Ph.D. study at the University of Michigan working with his advisors Profs. Mark Banaszak Holl and James Baker, Jr. Dr. Hong graduated with his PhD in Macromolecular Science and Engineering in 2006 and joined MIT as a postdoctoral associate in the laboratory of Prof. Robert Langer. From 2008 to 2014, he was 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. Since 2008, he has led a research group under the major research theme of “Biomimetic Nanotechnology” for cancer treatment. To date, Prof. Hong’s research has culminated in ~80 peer-reviewed articles that have a combined total number of ~12,000 citations, 7 book chapters, and 17 issued or pending patents, while delivering over 130 invited talks worldwide and over 170 conference proceedings. His academic/research achievements have been recognized by the related scientific communities, resulting in him receiving a number of awards including 2012 AAPS New Investigator Award in Pharmaceutics and Pharmaceutical Technologies and 2012 UIC Researcher of the Year - Rising Star Award.