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Self-Assembled Supramolecular Nanosystems from Engineered Block Copolymers for Targeted Therapy of Cancer and Brain Diseases

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Nanotechnology-based medicine (Nanomedicine) has received progressive interest for the treatment of intractable diseases, such as cancer, as well as for the non-invasive diagnosis through various imaging modalities. Engineered polymeric nanosystems with smart functions play a key role in nanomedicine as drug carriers, gene vectors, and imaging probes[1,2]. This presentation focuses present status and future trends of supramolecular nanosystems self-assembled from engineered block copolymers for therapy and non-invasive diagnosis of intractable diseases. Nanosystems with 10 to 100 nm in size can be prepared by programmed self-assembly of block copolymers in aqueous entity. Most typical example is polymeric micelle (PM) with distinctive core-shell architecture. PMs have several properties relevant for nanosystems, including controlled drug release, tissue penetrating ability, and reduced toxicity[3,4]. Furthermore, smart functionalities, such as pH- and/or redox potential responding properties, can be integrated into the PM structure[5]. These smart PMs loaded with various chemotherapy reagents were evidenced to have a significant utility in the treatment of intractable and metastatic cancers, including pancreatic cancer[6], glioblastoma[7,8], and tumors harboring recalcitrant cancer stem cells (CSCs)[9]. Eventually, five different formulations of the PMs developed in our group have already been in clinical trials world-wide, including Japan, Asia, USA and European countries[10].

Versatility in drug incorporation is another relevant feature of supramolecular nanosystems for drug delivery. Small nucleic acid (SNA)-based medicine can be assembled into nanosytstems through the ionic interaction with oppositely-charged polycationic block copolymers[11]. In this way, siRNA- or antisense oligo (ASO)-loaded micellar or vesicular nanosystems were prepared, and their utility in molecular therapy of cancer has been revealed[12-14]. Downsizing of polyion complex (PIC) assembly comparable to the size of antibody allowed it to crossing physiological barrier, including a thick fibrotic stroma in pancreatic cancer and blood-brain tumor barrier in glioblastoma, exerting significant antitumor activity[15,16]. Phase I clinical trial using this small-sized PIC nanocarrier loaded with siRNA has just been started in Japan for the treatment of HER2-negative breast cancer[17,18]. Furthermore, nanosysems hold promise for the treatment of intractable diseases other than cancer. Recently, we developed nanosystems decorated with glucose to crossing intact blood-brain barrier by recognizing glucose-transporter overexpressing on brain endothelial cells, indicating a novel route to deliver versatile drugs into brain for the treatment of neurodegenerative diseases, including Alzheimer's disease[19-21].

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