Extracellular nanovesicle-based therapeutics

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Exosomes contain various proteins, DNAs, and RNAs that originate from the parent cells. Exosomes are involved in cell-to-cell communication in the physiological processes, and transmit specific information from parent cells to recipient cells, thereby influencing the genotype or phenotype of recipient cells. Based on therapeutic effects of mesenchymal stem cells (MSCs), MSC-derived exosomes have recently emerged as a new therapeutic platform for cell-free therapeutics and are currently being tested in animal studies and human clinical trials for treatment of various diseases. Poor organ-targeting ability and insufficient therapeutic efficacy of systemically injected MSC-derived exosomes were identified as critical limitations for their further applications. In the first part of this presentation, I present on therapeutic efficacy-potentiated, organ-targeting, exosome-mimetic, extracellular nanovesicles and demonstrate their feasibility for repairing injured spinal cord and myocardium. Iron oxide nanoparticle (IONP)–incorporated extracellular nanovesicles (NV-IONP) were fabricated from IONP-treated hMSCs. Their therapeutic efficacy was demonstrated in animal models for spinal cord injury and myocardial infarction. In the second part of this presentation, exosome-mimetic extracellular nanovesicles derived from M1 macrophages (M1NVs) are introduced to stimulate antitumor immune responses. Immune checkpoint inhibitors, such as anti–PD–L1 antibody (aPD–L1), can allow cytotoxic T cells to attack tumors. However, the cytotoxic T cells' activity even in the presence of immune checkpoint inhibitors is still suppressed by immune-suppressing cells such as M2 tumor-associated macrophages (TAMs) and Treg in the tumor microenvironment. I demonstrate that the macrophage repolarization using M1NVs can promote the antitumoral activity of cytotoxic T cells by polarizing M2 TAMs to M1 macrophages and removing regulatory T cells, and potentiate the anticancer efficacy of the immune checkpoint blockade therapy.