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Enabling nanomaterial, nanofabrication and cellular technologies for nanoneuromedicines

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Abstract

Nanoparticulate delivery systems represent an area of particular promise for nanoneuromedicines. They possess significant potential for desperately needed therapies designed to combat a range of disorders associated with aging. As such, the field was selected as the focus for the 2014 meeting of the American Society for Nanomedicine. Regenerative, protective, immune modulatory, anti-microbial and anti-inflammatory products, or imaging agents are readily encapsulated in or conjugated to nanoparticles and as such facilitate the delivery of drug payloads to specific action sites across the blood-brain barrier. Diagnostic imaging serves to precisely monitor disease onset and progression while neural stem cell replacement can regenerate damaged tissue through control of stem cell fates. These, taken together, can improve disease burden and limit systemic toxicities. Such enabling technologies serve to protect the nervous system against a broad range of degenerative, traumatic, metabolic, infectious and immune disorders.

Key words: Nanoneuromedicine; Nanotechnology; Nanoformulation; Drug development; Targeting

Introduction

Nanotechnology and nanomedicine approaches involving therapeutics and diagnostics have had a huge impact on medicine notably for cancer, developmental, infectious and immune disorders. However, until very recently, nanomedicine approaches have not been as deeply developed for the neurosciences. Nanoneuromedicines possess significant potential as opportunities abound in the development of desperately needed therapies and diagnostics to combat degenerative, inflammatory,

Abbreviations: AA, acrylic acid; Apo, apolipoprotein; BBB, blood-brain barrier; BCEC, brain capillary endothelial cells; BDNF, brain-derived neurotrophic factor; CNS, central nervous system; CNT, carbon nanotubes; FDA, U.S. Food and Drug Administration; GFAP, glial fibrillary acidic protein; HGF, hepatocyte growth factor; HIV-1, human immunodeficiency virus type 1; HL, hydrophilic; HP, hydrophobic; HAS, human serum albumin; LIF, leukemia inhibitory factor; MAP-2, microtubule-associated protein-2; MMA, methyl methacrylate; MWNT, multi-walled carbon nanotubes; NPC, neural progenitor cells; NSC, neural stem cell; P3HB4HB, copolymer of 3-hydroxybutyrate and 4-hydroxybutyrate; PANi, polyaniline; PBCA, poly(butyl cyanoacrylate); PD, Parkinson's disease; PEG, polyethylene glycol; PHA, polyhydroxyalkanoate; PHB, poly(3-hydroxybutyrate); PHBHHx, copolymer of 3-hydroxybutyrate and 3-hydroxyhexanoate; PHDCA, polyhexadecylcyanoacrylate; PLA, poly(lactic acid); PLO, poly-L-ornithine; PLGA, poly(lactic-co-glycolic acid); PLLA, poly-L-lactide; PMMAAA, copolymer of MMA and AA; PNS, peripheral nervous system; PPG, poly(propylene glycol); pVA, Poly(vinyl alcohol); RES, reticuloendothelial system; SWNT, single-walled carbon nanotubes

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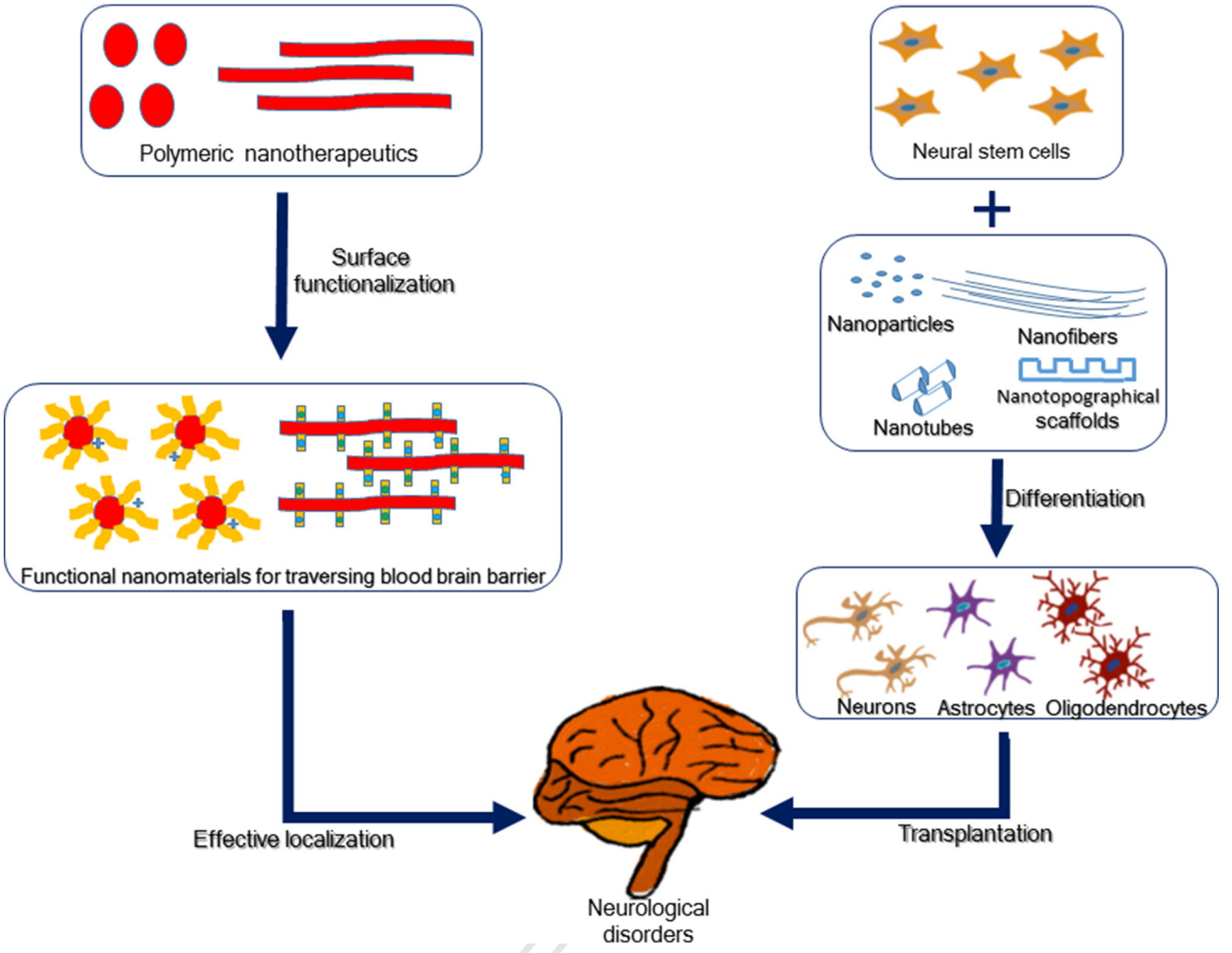

Figure 1. Nanotechnology approaches for targeted delivery of therapeutics and for control of stem cell behavior. These are outlined in box designations in their utilities to address neurological disorders.

infectious and genetic disorders associated with aging. This growing field was selected as the focus for the 2014 meeting of the American Society for Nanomedicine.[1]

A fundamental hurdle in developing effective therapies for nervous system disorders resides in an inherent inability of nerve cells to regenerate and/or even repair modest damage incurred to the brain and spinal cord.[2] Nervous system injury follows a variety of insults such as stroke, trauma, developmental disorders, aging, malignancy, chemical exposures or microbial infections.[3-7] Typical treatment options utilized, or in development, include therapeutic symptomatic management, stem cell implantation, neural tissue grafts or guidance strategies.[8-12] Another significant challenge associated with improving nervous system function includes transport of therapeutics across the blood-brain barrier (BBB). Typically, the therapies need to be delivered to the site of the nervous system malfunction and be available long-term. This could be overcome by surgical delivery of therapies to the affected brain and spinal cord sites. Alternative approaches are site-directed drug delivery. However, in contrast to other regions of the body, the nervous system poses unique challenges to site-specific drug delivery as the BBB moderates entry of substances into the brain.[13]

Nanotechnology approaches offer several opportunities to overcome these challenges, including the ability to circulate drug for extended times and to permit functionalization with targeting moieties to promote transport across cell membranes.[6,14] This could facilitate the use of multifunctional therapeutic, imaging and diagnostic devices, called theranostics.[15]

Drug targeting to specific locations is needed for enabling delivery across the BBB and for controlling the fate and behavior of the stem cells in stem cell-based therapies. This review surveys recent developments in delivery systems for nanomedicines that cross the BBB and those that affect stem cell repair or regeneration (Figure 1). These nanotechnology approaches serve as enabling technologies in the emerging field of nanoneuromedicine related to applications in diagnostics, imaging and therapeutics of relevance to the nervous system.

Advances in polymer chemistry and nanoparticle delivery for central nervous system (CNS) targeting

In many cases, nervous system targeted therapies include antioxidants, anti-inflammatory agents, immunomodulatory