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Polyacrylate-based vaccine delivery system

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Classical vaccines incorporating live or attenuated microorganisms possess several disadvantages and cannot be applied against cancer and some pathogens. Modern vaccines utilizing immunogenic subunits derived from a particular pathogen are able to overcome these obstacles but need a specific delivery system for their efficacy. Nanotechnology has opened a new window into these delivery methodologies. Particles-based subunit vaccine formulations have been proven to be very effective in inducing cellular and humoral immune responses. We synthesized polymeric constructs consisting of polyacrylate cores and peptide epitopes derived from bacterial or cancer antigens. The peptide epitopes were synthesized using solid phase peptide synthesis, whereas polymeric cores were synthesized by successive atom transfer radical polymerization. Unprotected peptide epitopes containing an N-terminus azide moiety were conjugated to core structures via copper-catalyzed alkyne-azide 1,3-dipolar cyclo-addition "click" reaction. The self-adjuvanting vaccine particles were formed under aqueous conditions and purified by dialysis. The particles were characterized by dynamic light scattering, transmission electron microscopy and elemental analysis to determine size and conjugation efficacy between polymer and peptides. Ability of nanoparticles to induce humoral immune responses against Group A *Streptococcus* was examined in mice. To test the efficacy of polymer-peptide conjugates as a therapeutic vaccine against established tumors, *in vivo* tumor treatment experiments were performed based on well-established procedures with C57BL/6 mice using TC-1 tumor model. The designed new delivery system based on the polyacrylate polymer with self-assembled properties induced humoral immune responses which were dependent on the particle size. The strong immune responses were observed even after single subcutaneous immunization. The produced antibodies were able to recognize and kill clinical isolated bacterial strains. The polymer-peptide conjugates were also used for the design of therapeutic vaccine against cervical cancer. Treatment with these conjugates led to significantly better survival compared to treatment with any other immunogens including IFA-adjuvanted positive control. Our findings suggested that this delivery system is a promising strategy for the design of prophylactic vaccines to induce humoral immunity as well as therapeutic peptide-based vaccines that induce adequate cellular immunity against a target disease. This delivery system also removes the use of incompletely defined and ordinarily toxic immune adjuvants, producing a safe and effective for potential vaccines for human use.

Biography

Mariusz Skwarczynski has completed his PhD in Chemistry. In 2004 he was awarded with Japan Society for the Promotion of Science Fellowship to conduct research on Paclitaxel in Kyoto Pharmaceutical University. Among others, he has developed epimerization-free method for the synthesis of isodipeptides, which have been commercialized by Merck-Novabiochem. In 2008 he joined Professor Istvan Toth group at University of Queensland, Australia. Since then his research is focused on nanotechnology-based peptide vaccine delivery approaches. In 2010 he was awarded with University of Queensland Strategic Fund Research Fellowship. He has published over 100 peer-reviewed publications, including several book chapters and one book.

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