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学 位 (博 士) 論 文 要 旨
(Doctoral thesis abstract)

論文提出者 Ph. D. Candidate	生物システム応用科学府 生物機能システム科学 専攻 博士後期課程 第一 専修グループ(Department Course) 平成 31 年度入学 (Your Entrance Fiscal Year) 氏名 曹鳳強 (Your Name (Family, First) and Seal)				
主指導教員 氏 名 Chief Advisor's Name	荻野賢司	副指導教員 氏 名 Vice Advisor's Name	赤井伸行	副指導教員 氏 名 Vice Advisor's Name	
論文題目 Title	Engineered soft particles as the delivery system for advanced biomedical applications				
<p>論文要旨 (和文要旨(2000 字程度)または英文要旨(500words)) ※欧文・和文どちらでもよい。但し、和文の場合は英訳を付すこと。 Write a summary in Japanese (2000 characters) or in English (500words). If the abstract is written in Japanese, needed to translate into English.</p> <p>With the development of advanced technologies in drugs, engineering safe and efficient drug delivery systems has become the focus of medical research. Current study stemmed from solid nano/micro-particles delivery system with various charge, size and shapes, but seldomly realize the essential role of softness in cellular recognition. Therefore, the thesis proposed the bio-mimetic drug delivery platforms based on natural and engineered soft particles and incorporate functional molecules, which enable them to interact with cells dynamically and improve drug delivery efficiency. We use natural soft particles, milk-derived exosomes, to load chemotherapeutic drugs and modify peptides targeting lung cancer cells externally to achieve a high anti-tumor efficacy and low systemic toxicity. On the other hand, particle-stable emulsions with softy and deformability were established to increase the affinity with cells, promoting immune recognition and enhancing the immune response of vaccines.</p> <p>The dissertation studies were unfolded as follow</p> <p>1. A soft exosome-based biocompatible drug delivery system was used to deliver paclitaxel to adenocarcinomas of the lung. As membrane structure vesicles, exosome was soft extracellular vesicle. In this part, the milk-derived exosomes were modified with a tumor-targeting peptide to efficiently target lung adenocarcinoma cells. Then, iRGD modified exosomes were loaded with chemotherapeutic drug for enhanced tumorthrapy.</p> <p>2. Poly-lactic-co-glycolic acid nanoparticle-stabilized Pickering emulsion (PNPE) was designed to improve the cellular affinity of the delivery system to antigen-presenting cells and induce efficient internalization of antigens. Due to softness, the PNPE overcame the disadvantage of rigid forms and simulated the flexibility and fluidity of pathogens. In this part, a method was set up to test the affinity of PNPE to cell surfaces and elaborate on the subsequent internalization by immune cells. As a result of enhanced cellular affinity to the immunocytes through dynamic curvature changes and lateral diffusions, antigen uptake was subsequently boosted.</p> <p>3. Particulate alum was constructed via microgel-stabilized squalene-in-water Pickering emulsion</p>					

for enhanced vaccination. Owing to its oil core, the PAPE exhibited soft and flexible, which changed contact area for multivalent interactions with cells. Additionally, PAPE with higher hydrophobicity and specific surface area increased the cellular affinity for enhanced dendritic cell (DC) uptake. Consequently, internalized PAPE dictated the intracellular fate of delivered SARS-CoV-2 antigens, which escaped from the lysosomes and were presented to T cells, inducing potent humoral and cellular immune responses. Hence, PAPE may offer potential insights for the development of a safe and efficient COVID-19 vaccine adjuvant.

4. Immunization strategies of aluminum hydrogel-stabilized Pickering emulsion (ASPE) were optimized to intensity the magnitude and quality of immunity. Immunization strategies of ASPE based vaccine were optimized from the antigen assembly pattern, dosage of adjuvant and antigen, the number of immunizations and intervals to intensify immune response. Intriguingly, antigens directly adsorbing to the surface of emulsion droplets induced a stronger antigen-specific antibody response. Additionally, mice were administered twice, 4 weeks apart, with 50 µg/dose of ASPE and 1µg/dose of antigen promoted long-term antigen specific antibody immune responses and increased memory B cells proliferation significantly.

(英訳) ※和文要旨の場合(300 words)

If the abstract is written in Japanese, needed to translate into English.(300 words)