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Carboxyl-functionalized polyurethane nanoparticles exhibit immunosuppressive properties via autophagy activation

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Surface functionalization of nanoparticles (NPs) plays the dominant roles in biomedical applications. However, NPs may induce oxidative stress and inflammation to reduce the application efficiency and injure the biological system, but the mechanisms are not completely understood. In the recent years, biodegradable polyurethane (PU) has gained attention in many biomedical fields because of its unique structure of microphase separation, excellent elasticity, and blood compatibility. Here, we demonstrate that the polyurethane nanoparticles (PU NPs) with distinct surface COO- contents modulate the immune responses in macrophages. We observed that macrophages dramatically reduced response to LPS for the mRNA expressions of IL-1β, IL-6, and TNF-α with carboxyl-modified PU NPs, not with amino-modified PU NPs, suggesting a robust anti-proinflammatory response occurred after PU NP treatment. PU NPs with more carboxyl-modification adsorbed more extracellular calcium and transported into cells. The cytosolic calcium plays a key role in autophagy activation. The increased intracellular calcium induced LC3-II protein activation and up-regulation of autophagy related genes, such as autophagy related 5 (ATG5), beclin 1, and cathelicidin. We also observed clear co-localization of autophagosomes and pNF-κB. Furthermore, the immune suppression of PU NPs was attenuated by incubation with EGTA or Bafilomycin A1. These evidences suggested that PU NPs reduced the NF-κB-related inflammation via autophagy pathways. The engineered PU NPs with particular surface modifications may be a platform to realize the biological performance of nanomaterials and to understand how the surface chemistry of NPs regulates immune responses. Moreover, PU NPs may further be regarded as a promising carrier with drugs for therapeutic applications of immune-related diseases.

Biography

Yen-Jang Huang has completed his PhD from National Cheng Kung University, Taiwan and Postdoctoral studies from National Taiwan University, Taiwan. He specializes in molecular biology, biomaterials and nanomedicine.

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