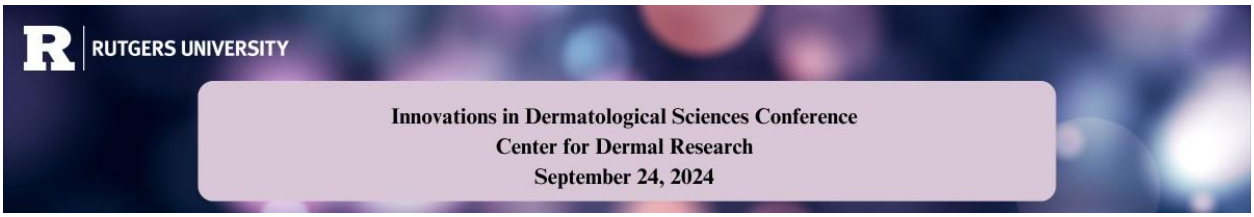

"Non-surgical skin cancer treatment using bioadhesive nanoparticles"

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ABSTRACT: The development of biomaterials continues to evolve. We have focused on strategies to enhance drug delivery to the skin, using poly(D,L-lactic acid)-hyperbranched polyglycerol to develop complimentary "sticky" biodegradable nanoparticles (BNPs) and "stealthy" non-adhesive nanoparticles (NNPs), which are tunable for different applications. This synthesis approach ensures the stability and efficacy of the encapsulated agents and minimizes systemic exposure and toxicity. In the realm of skin cancer prevention, we demonstrated the advantages of BNPs in sunscreen formulations. Traditional sunscreens often suffer from issues like unwanted skin penetration and photodegradation, which can lead to systemic absorption of actives and decreased efficacy. BNPs address these challenges by providing a stable platform for the encapsulation of UV filters such as avobenzone and octocrylene. The BNPs enhance the photostability and water resistance of the sunscreen, ensuring long-lasting protection against ultraviolet radiation. Clinical studies have demonstrated that BNP-based sunscreens offer comparable protection to FDA standards while reducing the risk of skin absorption and related side effects. Further, BNPs have shown promise in the treatment of cutaneous squamous cell carcinomas (SCCs). By encapsulating therapeutic agents within BNPs, we have achieved localized drug delivery that enhances uptake by tumor cells and prolongs retention within the tumor microenvironment. This approach improves the efficacy of the treatment and minimizes systemic exposure. In vivo studies have demonstrated that BNPs loaded with chemotherapeutic agents such as topoisomerase inhibitors significantly enhance tumor matrix retention, tumor cell uptake, and survival rates in SCC models. For locally invasive melanoma treatment, we have explored NNPs as a delivery system for immunostimulatory agents. Encapsulating agents such as monophosphoryl lipid A (MPLA) within NNPs allows for enhanced intratumoral delivery, promoting a robust anti-tumor immune response. This method leverages the non-adhesive properties of NNPs, which allows efficient lymphatic transport to draining lymph nodes and sustained release of the therapeutic agents. We have shown that NNPs can effectively modulate the tumor microenvironment, tumor draining lymph node, and systemic immune response, thereby improving the efficacy of immunotherapy in clinically relevant animal models of melanoma. The combination of NNPs with low-dose chemotherapy further augments the anti-tumor response, offering a promising strategy for melanoma treatment.