

Cell-to-cell transmission of HSV-1 in differentiated keratinocytes promotes multinucleated giant cell formation

Herpes simplex virus (HSV) infection in the skin causes small grouped vesicles characterized by acantholytic cells and multinucleated giant cells (MGCs). Little is known how the differentiation status of keratinocytes is involved in the formation of MGCs by HSV-1 infection. As the human epidermis is composed of several layers of keratinocytes that undergo terminal differentiation, Yamamoto Y et al elucidated whether the differentiation status of keratinocytes affects viral entry, propagation, cell-to-cell transmission of HSV-1, and MGC formation. Keratinocytes in high-Ca²⁺ medium formed MGCs, but those in low-Ca²⁺ medium formed single nuclear round cells in response to HSV-1 infection. HSV-1 entered the keratinocytes more effectively in low-Ca²⁺ than in high-Ca²⁺ medium, although transcripts of HSV receptors were comparable in both conditions. A cell-to-cell fusion assay showed that HSV-1-infected and adjacent-uninfected keratinocytes were involved in MGCs. These data suggested that differentiated keratinocytes promote MGC formation by cell-to-cell fusion with resolution of cell membrane and cell-to-cell transmission of HSV-1 from infected keratinocytes to neighboring uninfected keratinocytes.

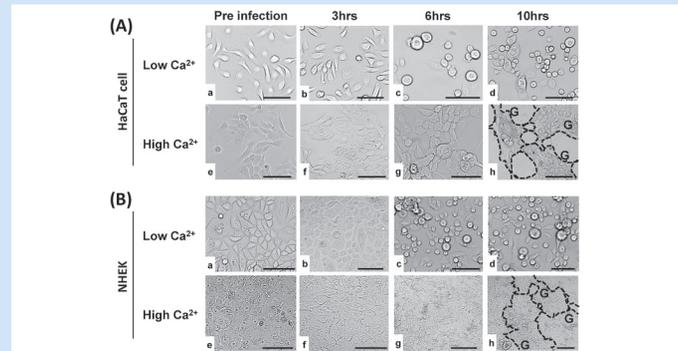


Fig. 1. Morphological change of KCs with HSV-1 infection by bright-field microscopy. The form of KCs changed from unicellular spindle or round shape in low-Ca²⁺ medium to polygonal shape and sheet-like formation in high-Ca²⁺ medium. MGCs is formed with HSV-1 infected KCs cultured in high-Ca²⁺ but not in low-Ca²⁺ medium. A: HaCat cells; B: NHEKs; a-d: cultured in low-Ca²⁺ medium; e-h: cultured in high-Ca²⁺ medium. a, e: before HSV-1 infection; b, f: 3 h poi; c, g: 6 h poi; d, h: 10 h poi. G: multinucleated giant cell; Bar = 100µm.

Nanoparticle-mediated local delivery of pioglitazone attenuates bleomycin-induced skin fibrosis

Poly(lactico-glycolic acid) (PLGA) is one of the most successful biodegradable polymers for biomedical applications. Peroxisome proliferator-activated receptor-γ (PPAR-γ) plays an important role in endogenous anti-fibrotic defense mechanisms. Recent studies have suggested that pioglitazone, a synthetic PPAR-γ activator, has effects beyond reducing blood sugar and it can reduce fibrosis and inflammation when used systemically. Kanemaru M et al aimed to assess the effects of local injections of pioglitazone-loaded PLGA nanoparticles (PGN-NP) on an experimental sclerosis and to demonstrate the *in vivo* pharmacokinetics of subcutaneously administered PLGA nanoparticles. Subcutaneous injections of PGN-NP attenuated skin fibrosis in BLM-induced scleroderma model mice. Pioglitazone significantly suppressed migration ability and TGF-β-mediated myofibroblast differentiation in cultured fibroblasts. Subcutaneously injected NIR-NP remained in the vicinity of the injection site more than non-particulate silicon naphthalocyanine. These results provided a basis for the development of new treatments for dermal fibrosis and a better understanding of the potential of PLGA nanoparticles in dermatology.

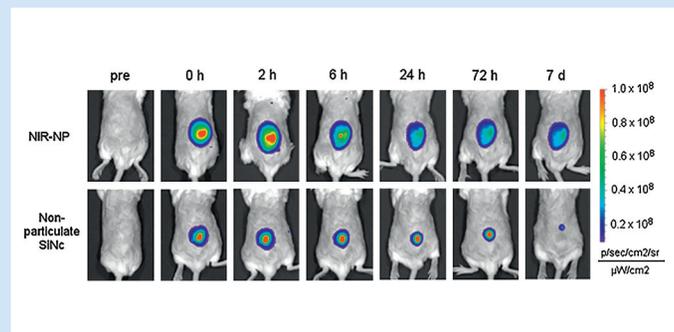


Fig. 6 (A). *In vivo* pharmacokinetics of nanoparticles. (A) *In vivo* images of NIR-NP and non-particulate silicon naphthalocyanine (SINC) at several different time points after subcutaneous injection into the dorsal skin.