Opinion

Pharmacological properties of natural rubber latex nanoparticles and their application to tissue engineering

Keywords: natural rubber latex, nanoparticles, tissue engineering, cytotoxicity, biocomposites

Abbreviations: NRL; natural rubber latex, MC3T3-E1; mouse osteoblast progenitor cells, A549; human alveolar basal epithelial adenocarcinoma cells, A2780; human ovarian cancer cells, MDA-MB-231; human mammary adenocarcinoma cells, hMSCs; human mesenchymal stem cells

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Biomaterials with various functions are important not only for applications in the fields of regenerative medicine and tissue engineering, but also for the elucidation of pharmacology. The development and discovery of new biomaterials is constantly being driven by researchers around the world. Natural rubber latex (NRL) is derived from the lactiferous sap of the *Hevea brasiliensis* (para rubber tree) and has been used in traditional medicine as vegetal-origin functional biomaterials.[1] Since NRL particles are substances that occur in nature, such as those collected from rubber trees and Russian dandelions, biocompatibility can be fully expected. For example, latex has already established itself as a folk medicine and is used to suppress comedones, diabetes, gastritis, and inflammation.[2–6] However, although latex has high potential as a pharmacological application, the cytotoxicity of NRL particles has not been well understood.

This opinion highlights the current development of natural rubber latex in tissue engineering, and importance for investigation on cytotoxicity of NRL nanoparticles. Promising results regarding the current challenges and perspectives of natural rubber latex-based tissue engineering is described.[7–9] Biocompatibility is an important property of biomaterials in tissue engineering, and in vitro cell proliferation studies on the surface of various biomaterials are essential. Very recently the potential use of NRL nanoparticles in regenerative medicine was evaluated by Furaya et al.[10] Mouse osteoblast progenitor cells (MC3T3-E1) were used as normal cells and human alveolar basal epithelial adenocarcinoma cells (A549) were used as cancer cells to study NRL particle cytotoxicity in vitro. It was found that MC3T3-E1 cells showed no cytotoxic to NRL particles up to 1.0 mg/mL, and that NRL particles at low concentrations grew MC3T3-E1 cells stably and efficiently. By ultracentrifugation at $10^5 g$, the NRL particles were separated into three components, and it was discovered that the water-soluble components consisting of protein components and phospholipids are involved in cell proliferation and cancer cell death. Cytotoxicity to A549 cells was demonstrated at NRL particle concentrations of 0.01 mg/mL or more, and A549 cells were selectively induced apoptotic cell death. The efficacy of NRL particles alone was weaker than that of the clinically used anticancer prodrug (cisplatin), but it was clarified that it had target selectivity for tumor cells and had weak side effects. In addition, human ovarian cancer cells (A2780) and human mammary adenocarcinoma cells (MDA-MB-231) were studied in detail from the viewpoints of cell cycle and programmed cell death (apoptosis). This report contributes to the advancement of research on NRL nanoparticles, which are promising bio-nanoparticles with potential as anticancer agents to induce apoptotic cell death. The researchers hope that using NRL as an anticancer agent can reduce serious side effects on healthy human cells.

In addition, genetic analysis revealed that NRL particles also induce cartilage differentiation of human mesenchymal stem cells (hMSCs). Okamoto's group concluded that NRL particles are biomaterials that can be applied to bio-engineering.[11] They succeeded in fabricating cartilage/NRL biocomposite materials by forming hMSC spheroids for the first time. It is important to note the interface between the NRL-based implant and its host tissue is particularly susceptible to stress. A mismatch of any of the biomechanical factors leads to deterioration of the interface and transformation from normal cells to tumor cells, resulting in an excessive response to matrix elasticity. Further efforts are required to investigate the mechanical properties of bio-composite materials and long-term toxicity in a preclinical environment. In tissue engineering, the complex interactions between cellular and surface structures, as well as the underlying NRL regulatory signaling and gene expression during processes such as tissue development and cancer invasion, will be the focus of future research.

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Conflicts of interest

The author declare that there are no conflicts of interest.

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