Gas-liquid interfacial plasmas for novel gene transfer systems

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Gas-liquid interfacial atmospheric-pressure plasmas are medically utilized for highly-efficient and minimally-invasive gene transfer systems, where the various kinds of plasma-induced stimulations could affect the transfer efficiency. In an attempt to identify the dominant factors for enhancing the gene transfer, we focus on reactive species and measure the concentration and distribution of the plasma-produced reactive species in liquid using two types of plasmas; "plasma jet in contact with liquid" and "micro plasma in liquid (in-liquid plasma)". We have revealed a positive correlation between the transfer efficiency and concentration of the short-lived reactive species such as $^{\bullet}OH_{aq}$. Furthermore, it is found that the duration of $^{\bullet}OH_{aq}$ production by the in-liquid plasma is longer than that by the plasma jet, and accordingly, the higher transfer efficiency is realized by the in-liquid plasma compared with the plasma jet irradiation.

1. Introduction

Non-equilibrium atmospheric-pressure plasmas (APPs) in liquid or in contact with liquid, i.e., gas-liquid interfacial atmospheric-pressure plasmas (GLI-APPs), have attracted much attention as a novel technology, which provides new physical and chemical effects on the surface of the liquid and the exotic reactions are expected in the liquid. Using the GLI-APPs, several applications have been developed in material science such as nanoparticle synthesis, surface treatment of nanomaterials, while in life science such as medicine, agriculture, and biology.

Recently, GLI-APPs are medically utilized for highly-efficient and minimally-invasive gene transfer systems [1-3], where the various kinds of plasma-induced stimulations could affect the transfer efficiency. In an attempt to identify the dominant factors for enhancing the gene transfer, we focus on reactive species, which are classified into three categories in terms of the life-span: long-lived (e.g. H_2O_2) and short-lived (e.g. $^{\bullet}OH$, $O_2^{\bullet -}$) reactive species, and investigate the functions of the plasma-produced reactive species in liquid on the cell activity such as cell-membrane permeability [4,5] using two types of plasmas; "plasma jet in contact with liquid" and "micro plasma in liquid (in-liquid plasma)".

2. Experimental Results and Discussion

First, we developed a plasma jet whose plume is in contact liquid using low frequency (frequency: 8-10 kHz, voltage: 5-12 kV) with Helium gas flow, which was exposed to the biological buffer at a controlled thickness. To evaluate the spatial mapping of liquid phase OH radicals ($^{\bullet}OH_{aq}$) and plasma-induced effect on the gene transfer, the gelling reagent containing terephtalic acid (TA) and adherent cells with gene-simulated fluorescent dye (YOYO-1) are prepared, respectively. It is found that $^{\bullet}OH_{aq}$ which reaches to gelling reagent decreases with an increase in liquid thickness (<1 mm), and the plasma-induced YOYO-1 transfer is found to decay markedly with liquid thickness. Furthermore, the center-localized distribution of $^{\bullet}OH_{aq}$, which is resulting from the center-peaked $^{\bullet}OH$ distribution in the gas phase region, corresponds with the distribution of the transferred cells by plasma irradiation.

Second, we generated in-liquid plasma by applying a pulse power (voltage: 1.5 kV, pulse width: 10-100 μs, current:0.2-2.8 A) to micro-scale thin electrode in the biological buffer. Here, indirect plasma irradiation (IPI) method was employed to eliminate factors except for products in liquid for a clarification of cell response mechanism. The transfer efficiency using in-liquid plasma is found to be much higher than that using plasma jet. Furthermore, it is observed that the duration of $^{\bullet}OH_{aq}$ production by the in-liquid plasma is longer than that by the plasma jet.

These results suggest that short-lived reactive species such as $^{\bullet}OH_{aq}$ is likely one of the dominant factors responsible for the plasma-induced YOYO-1 transfer, and the higher transfer efficiency is relevant to the longer duration of $^{\bullet}OH_{aq}$ production using the in-liquid plasma compared with the plasma jet irradiation.

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