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Activation of Endoplasmic Reticulum Stress Response by Applying of Nanosecond Pulsed Electric Fields for Medical Application

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Utilization of nanosecond pulsed electric fields (nsPEFs) has been widely studied as a novel approach to induce cellular stress for biological and medical applications. Endoplasmic reticulum (ER) stress has become to be considered as a cause of diseases as diabetes mellitus, Parkinson's disease, and so on. The objective of this study is to activate the ER stress response, which is a built-in function in cell to avoid ER stress, by applying pulsed high electric fields. Eventually, we aim to establish therapy and prevention methods for the diseases. When we previously applied nsPEFs on skeletal muscle of mice, a little of ER stress response was induced. Therefore, nsPEFs were applied on suspended solution of cultured cells to investigate adequate condition to activate stress response in this study. The nsPEFs of 14-ns and 70-ns pulse-width were applied on suspended solution of HeLa and MEF cells. The applied pulse electric field strength was changed with the charging voltage of Blumlein pulse forming network and selection of a cuvette with electrodes. The number of applied 14-ns and 70-ns PEFs changed from 10 to 30 and from 10 to 500, respectively. It is well known that eIF2α phosphorylation is induced by various cellular stress, especially ER stress. Western blotting was used to analyze the nsPEFs-induced eIF2α phosphorylation. The cell viability after nsPEFs exposure was measured with WST-8 assay (water soluble tetrazolium salts). It was confirmed that 14-ns and 70-ns pulses activated ER stress response. The 14-ns pulses activated a little response. The 70-ns pulses activated stress response as large as thapsigargin treatment (enzyme inhibitor inducing ER stress). In addition, the viable cells decreased with increase of the number of applied pulses by 70-ns pulse application. However, it was confirmed that 70-ns pulses could activate sufficiently large stress response even when most cells survived.

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