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Electrical Equivalent Circuit Network-Based Study of Programmed Cell Death Induced by Plasma-Injected Electric Energy

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1. Introduction

We have been studying the plasma molecular/gene introduction method [1]. In this study, we investigate the relationship between cell death and the energy injected into a cell by the electric current by using the electrical equivalent circuit network (EECN) analysis [2].

2. Experimental Setup

Mouse-derived fibroblasts (L-929) were cultured adherently in 96-well plates. The culture medium was replaced with a GFP plasmid solution, followed by plasma irradiation. Each well plate was placed on a grounded electrode, and a sinusoidal voltage of 20 kVpp at 20 kHz was applied for 2 to 100 ms using a fine electrode positioned 0.5 mm above the liquid surface at the center of each well. After 24 hours of incubation, GFP fluorescence was observed to evaluate transfection, and the radius r of the circular region of dead cells—referred to as the "cell death circle"—and centered directly beneath the electrode, was measured.

3. Assumptions for EECN Calculation

We constructed the entire EECN system—including the cells, DNA solution, and 96-well plate—and calculated the electric power injected into the cells. In our model, we assumed that the instantaneous power per unit volume becomes effective in cell death if it exceeds a specific threshold, P_{th} . Furthermore, we assumed that cell death is caused by the electrical energy injected into a single cell, which is obtained by integrating the effective power over time. This energy must also exceed a specific threshold, W_{th}, to induce cell death. Based on these assumptions, we calculated the dependence of the cell death radius r on the duration of plasma treatment.

4. Results and Discussion

When P_{th} and W_{th} were appropriately set, the relationship between plasma treatment time and the radius r of the cell death circle showed good agreement between experimental results and calculations based on an electrical equivalent circuit model. This suggests that cell death is induced by current—i.e., by energy injection—and supports the assumption that cell death occurs when the energy, defined as the time-integrated instantaneous power exceeding the threshold P_{th} , exceeds the threshold W_{th}. The presence of these two thresholds suggests that the observed cell death may be due to apoptosis, rather than necrosis caused by physical damage from energy accumulation.

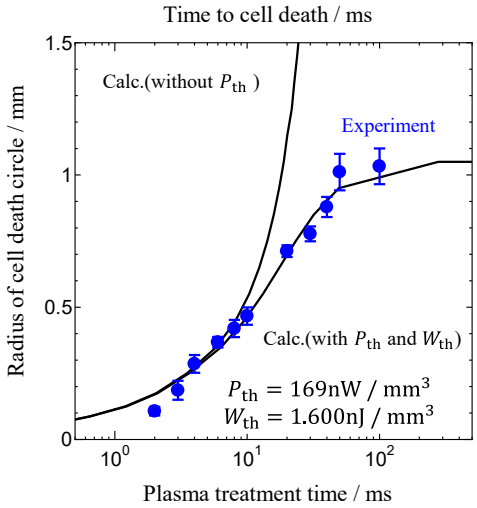

Figure 1. The relationship between the increasing radius r of the cell death circle and plasma treatment time was reproduced by appropriately setting P_{th} and W_{th}.

5. Conclusion

EECN analysis suggests that the electric current supplied by plasma is the primary factor inducing cell death. Although a long-term plasma exposure increases the total electric power injection to the cells, the radius of the cell death circle does not expand beyond a certain point. This observation implies that the cell death is not due to necrosis but rather results from a regulated process, specifically programmed cell death. The two-step threshold model successfully reproduces the experimental results, supporting the conclusion that this model effectively captures the current-induced programmed cell death mechanism.

Acknowledgments

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References

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[2] Yugo Kido et al, PLoS ONE, 16(1): e0245654, 2021.