

Electrochemical analysis of material permeability in 3-dimensional cultured cells

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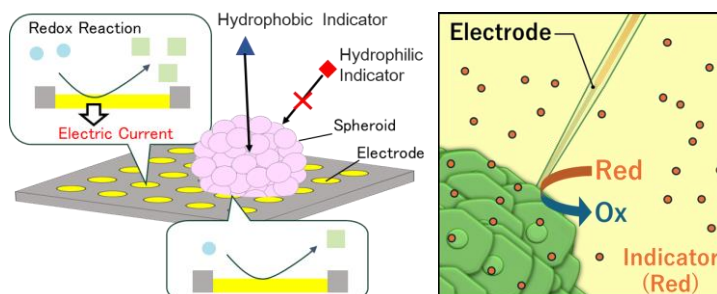
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Assessing drug efficacy and penetration into cancer tumors is important in drug design. In this study, the penetration of drug models into spheroids was analyzed using electrochemical techniques, which have advantages such as label-free and minimally invasive analysis. Microelectrode arrays (MEAs) and probe-type ultramicroelectrodes (UMEs) were employed to measure the redox drug models in the 3-dimensional cultured cells.

MEAs consisting of 25 electrodes of 10 μm -diameter with 40 μm -pitch were fabricated on a glass substrate by photolithography and sputtering techniques. A spheroid of human breast cancer cell line (MCF-7) was introduced onto the MEAs and incubated for 1 hour to attach to the substrate. Ferrocene methanol (FcCH_2OH) and ferrocyanide ion ($[\text{Fe}(\text{CN})_6]^{4-}$) were used as hydrophilic and hydrophobic indicators, respectively. The permeability of each redox indicator to the cells was evaluated by chronoamperometry. The current under the spheroid decreased due to the prevention of molecular diffusion to the electrodes through the spheroids. In addition, the decrease in the current of $[\text{Fe}(\text{CN})_6]^{4-}$ was clearer than that of FcCH_2OH .

For the analysis using the UMEs, the spheroid was incubated on the cell culture dish for 1 hour and the electrode was inserted into the spheroid incubated with each redox indicator. The decrease in current for FcCH_2OH was more distinct than for $[\text{Fe}(\text{CN})_6]^{4-}$, which was a similar trend with the MEAs. The decrease in current mainly depends on the concentration and diffusion coefficient of the redox indicators. For instance, the permeation coefficient of FcCH_2OH through cell membrane was higher than $[\text{Fe}(\text{CN})_6]^{4-}$ for redox indicators, resulting in an increase in current.¹

In summary, this study analyzed the penetration of redox indicators through the spheroid using MEAs and UMEs. These electrodes successfully clarified the differences in redox indicators, which will support the design of the drug.



1) T. Yasukawa *et al.* *Biochimica et Biophysica Acta* 1369 (1998) 152-158