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〈シンポジウム I〉

『次世代先端評価技術を駆使する』

将来のヒト影響評価体系のための理想的な生理学的培養組織モデル

酒 井 康 行*，篠原満利恵，小森喜久夫，竹 内 昌 治，藤 井 輝 夫

Ideal Physiologically-Relevant Cultured Tissue Models for Human Hazard Evaluation in the Future

Yasuyuki SAKAI*, Marie SHINOHARA, Kikuo KOMORI, Shoji TAKEUCHI, Teruo FUJII

Abstract

In this short review, we first described future direction of animal-free mechanism-based human hazard evaluation systems and pointed out the importance of physiologically-relevant *in vitro* cultured tissue models. Good examples of such tissue models can be seen in the latest studies by Wyss Institute, Harvard University, that is, breathing lung on-a-chip realized by *in vivo*-like mechanical movements based on advanced microfluidic technologies. This suggests that we will eventually be able to overcome *in vivo–in vitro* discrepancies that exist in using very convenient but unphysiological plastic culture wares and synthesized culture medium, when we continue the effort to understand the differences and successfully reconstitute *in vivo*-like microenvironments. In addition to reconstituting typical 3D hierarchical microstructure comprising of epithelium, stromal layers and endothelium, we pointed out one blind side issue, oxygen supply in the static culture; oxygen is transported by a simple diffusion process from the air-liquid interface at the surface of the culture medium to the cells cultured at the bottom of the plates, but this oxygen diffusion flux does not always meet the oxygen demand of the cell layers, resulting in forcing cell to take low efficient anaerobic respiration. To solve this issue completely, we used oxygen-permeable silicone rubber, poly（dimethylsiloxane）（PDMS）, as a culture surface at the bottom, so that oxygen can be supplied directly from the outer atmosphere to the cells. As the results, hepatic cells exhibited remarkable and spontaneous self-organizations; multilayer formation, spherical aggregate formation at very high cell densities, better development of bile canaliculi and good survival beneath Caco-2 cell layers formed on cell culture inserts. Through integration of such technologies enabling better mimicry of *in vivo* situation *in vitro*, physiologically-relevant tissue models can be realized and can be used in combination with advanced/comprehensive bioanalyses and numerical simulations for animal-free mechanism-based human hazard evaluation in the near future.

Key words: hazard evaluation, physiological tissue model, hierarchical tissue structure, spontaneous organization, aerobic respiration.