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CELL CULTURE APPARATUS AND DOSE RESPONSE MEASURING METHOD

Field of the Invention

The present invention relates to a cell culture apparatus, for cultivating the cells in the medium, and a dose response measuring method.

Description of the Prior Art

In general, in order to measure the dose response of given cells to the DC current or the induced current, it is a common practice to let the electric currents differing in capacity flow in the cells or to apply different electric fields to the cells for letting the induced electric currents differing in capacity flow in the cells thereby measuring the difference in the dose response of the cells. The dose response of the cells reflects the change in the number of cells, change in the genes of the cells, change in the chromosomes of the cells, change in the functions of the cells, change in the components of the cells or the like. The cell holding system designed for measuring the response of the cell comprises the culture vessels, culture cages and culture membranes each having equal area. Normally, the cells are cultivated in the culture vessels or the like, and the cultivated cells are taken out of the vessel, diluted, divided into a

predetermined quantity and put into the cell holding system. More specifically, different sets of cells are put into the cell holding system for different dose experiments. Then, different electric currents are made to flow at different times to measure the variation of the current.

In the above-mentioned method, the time period for experiment is divided into different time periods for different doses. The nature of the cells and the number of cells to be compared in terms of the dose cannot be determined on 100% basis unless being compared simultaneously. This is because there is the possibility that the cultivated cells propagates with time and changes in nature depending on ambient condition. Thus, if such points are not taken into consideration, the dose responses of the cells in different conditions will be measured to obtain inaccurate results of measurements. Conventionally, therefore, in order to overcome such shortcomings, it has been necessary to increase the number of experiment apparatus so that a number of identical cells held in a number of holding systems can simultaneously undergo the experiments by using a number of experiment apparatuses.

The present invention was made in consideration of the above-mentioned problems of the prior art, and an object of the present invention is to provide a cell culture apparatus and a dose response measuring method capable of accurately measuring

the dose responses of the cells to different values of electric current regardless of the timing of the experiment, the natures and the numbers of the divided cells to be placed in the culture vessels.

Summary of the Invention

The cell culture apparatus comprises the vessels, for cultivating the cells deposited in the culture media by flowing the electric current between a pair of electrodes disposed at opposing two ends, and the current density controlling means, for providing at least two different current densities for the cells in the culture media placed in the culture vessels, wherein the current density control means is connected in series with the electric current circuit system.

The cell culture apparatus comprises the culture vessel, for cultivating the cells deposited in the culture medium by applying a predetermined voltage between the pair of electrodes provided at the two ends of the opposing electrodes to flow the electric current between the electrodes, and the electric current density control means, for supplying at least two currents differing in the current density to the cells in the culture medium placed in the culture vessel, wherein an electricity transmitting barrier member is provided between said electric current density control

means and said electrodes.

In the cell culture apparatus, the electric current density control means is composed of a permeable membrane having an extremely fine structure exceeding the order of micron which will not permit the entry of the cell, and a plurality of said membranes, differing in area, are held in the holders arranged at predetermined intervals.

The dose response measuring method comprises the process, for flowing an electric current between said electrodes by applying the predetermined voltage across a pair of electrodes provided at opposing two ends, and the process, for simultaneously supplying at least two different current densities to the cells in the same culture medium.

Brief Description of the Drawings

Fig.1 is a schematic diagram illustrating the cell culture apparatus according to the present invention.

Detailed Description of the Preferred Embodiments

The cell culture apparatus, as one of the embodiments of the present invention, will be described in the following with reference to the accompanying drawings. Fig. 1 is a schematic view of the cell culture apparatus. Reference numeral 10

represents the cell culture apparatus. The cell culture apparatus is provided with an electric current controller 14 which is for controlling the electric current supplied from the power source 12 and is connected in series with the electrodes of the cell culture apparatus in order to supply a predetermined value of electric current through a closed circuit.

The cell culture apparatus 10 has a rectangular form with internal space having a predetermined cubic volume and is provided with a vessel 16 designed for being capable of holding the fluid. The vessel is provided with electrodes (18, 18') at two opposing ends (on the insides of the opposing walls) thereof. Each culture medium, through which the response of the cell is measured, is placed in the vessel. A plurality (e.g., 3) of the holders (22, 24, 26) are arranged at predetermined intervals between the two electrodes. A plurality of holders are installed in series to the electric current circuit system.

The holders (22, 24, 26) are respectively provided with permeable membranes (23, 25, 27), each having an extremely fine structure exceeding the order of the micron. Each of the permeable membranes has a mesh diameter of about 0.3mm, thickness of several microns to 10 microns.

The electricity transmitting barriers (28, 28') such as the agarose barriers are provided between the vessel and each holder.

The agarose may be applied to the surface of each electrode. The provision of the agarose reduces the influence of chemical reaction near the surfaces of the electrodes on the cells.

Each of the holders (22, 24, 26) is provided with the permeable membrane only at its portion through which the electric current flows. In other words, substantially circular permeable membranes (23, 25, 27) are provided only at the predetermined places through which the electric current occurring between the electrodes flows. The areas of the permeable membranes are set to d1, d2 and d3, varying among the three holders. For instance, when the ratios of areas among the three circular membranes are set to 1 : 2 : 3, the corresponding electric current densities become 3, 2 and 1.

The culture media, each containing the cells, are respectively placed among the holders arranged at the predetermined intervals. Then, the electric current is made to flow by applying the predetermined voltage between the two electrodes. The electric current density in the culture medium can be obtained by dividing the value of the flowing electric current by the area of the membrane. Then, the dose response is measured by simultaneously supplying at least two electric currents, differing in the electric current density, to the cells in the same culture medium by applying the predetermined voltage across a pair of electrodes provided at

opposing two ends.

In the above-mentioned embodiment, a pair of electrodes is arranged laterally so that the electric current flows in a horizontal direction, but the electric current may be set to flow in vertical direction by arranging the electrodes vertically. The electric current can be made to flow in the cells more stably and uniformly when the electric current is made to flow in vertical direction.

After applying the electric current for a given length of time, the holders are raised and the cells are used to measure the response. Thus, responses of the cell for different current densities are obtained in the same cell at the same time. A membrane shape may not be limited to circular but rectangular. The cells are deposited on the permeable membrane. The cell includes absorbent cells, such as endothelial cell or fibroblast.

When the cell culture apparatus and the dose response measuring method according to the present invention are employed, the dose responses to different values of electric current can be measured accurately even where the natures and the numbers of the cells vary depending on the timing of the measurement resulting from the division of the timing of the measurement.

Industrial Applicability

This invention provides a cell culture apparatus, for cultivating the cells in the medium, and a dose response measuring method.

WHAT IS CLAIMED IS:

1. A cell culture apparatus, comprising a vessel, for cultivating the cells in a medium by applying a predetermined voltage between a pair of electrodes disposed at opposing two ends for letting an electric current flow between said electrodes to cultivate the cells in the medium, and a current density control means for supplying at least two currents differing in the current density to the cells of the medium placed in said vessel, wherein the current density control means is connected in series with said current circuit system.

2. A cell culture apparatus, comprising a vessel for cultivating the cells in the medium by applying a predetermined voltage between a pair of electrodes disposed at opposing two ends for letting an electric current between said electrodes to cultivate the cells in the medium, and a current density control means for supplying at least two currents differing in the current density to the cells in the medium placed in the vessel, wherein said current density control means is connected in series with said current circuit system, the current density control means also being provided with an electricity transmitting barrier member and being provided between said current density control means and said electrodes.

3. The cell culture apparatus according to claim 1 or claim

2, wherein said current density control means is composed of a permeable membrane having a structure exceeding the order of micron, and a plurality of the membranes differing in area are installed in holding members arranged at predetermined intervals.

4. A dose response measuring method comprising a process for applying a predetermined voltage between a pair of opposing electrodes disposed at two opposing ends for letting an electric current flow between said electrodes and a process for simultaneously supplying at least two electric currents differing in the current density to the cells in the medium.