Correlative light and electron microscopy to detect neuron cells in stem cell differentiated tissue cultures

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In the study of tissues differentiated from stem cells, many types of cells could exist in a culture. The mixtures of multiple cell types, such as neuronal cells, the myotubes and endothelial cells, are usually difficult to be distinguished by regular optical microscopy without labeling. In addition to the limitation of resolution, depth of field is another dilemma when we analyze these tissue samples. The combination of optical and electron microscopy become the unavoidable issue[1]. When we check out the neuronal cells, we usually observe the morphology with long cellular extensions and detailed features. Some of the tiny structures, such as synapse or vesicles, require different microscopy for observation. For this purpose, scanning electron microscopy (SEM) provides higher resolution and thicker depth of field than optical microscopy; ultrastructure can be revealed by transmission electron microscopy (TEM). Fluorescent microscopy (FM) label specific cell types by antibodies conjugated with fluorescent dyes. Combination of images from different microscopy is essential for multiple cell types of tissue cultures[2].

In this study, we used fluorescent labeling to detect neuron filament in the culture differentiated from induced pluripotent stem cells (iPSCs) then perform electron microscopy by SEM or TEM. Compare to the topography of samples, we could trace the images between optical and electron microscopy. The correlation of different microscopies was linked by surface features of sample itself. We also correlated images labeled the neuron by antibodies conjugated with nano-gold in SEM images. Through comparing and aligning images captured by different microscopy, we distinguished the neurons from the tissue with multiple types of cells.

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