

In Vitro Artificial Skin Model with Appendages for Drug Discovery

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The skin has a complex tissue architecture composed of a large variety of cell types of ectodermal and mesodermal origins. Most of these cells are produced from corresponding progenitor/stem cells by tightly regulated mechanisms. In our previous studies, we have demonstrated the utility of in vivo skin reconstitution assay. The characteristics of this assay system we used are that the cells in a mixed suspension segregate from each other and actively form tissue architecture through cell-cell and cell-environment interactions.

However, few studies have succeeded in generating a three-dimensional (3D) tissue-like structure. During embryogenesis, the cells accumulate and form complicated organ structure. Cellular interactions of epithelial, mesenchymal and endothelial progenitors are very important steps of this early organogenesis.

In this study, we have generated a 3D tissue-like structure in vitro using mouse skin epidermal and dermal cells mixed with human umbilical vein endothelial cells and mesenchymal stem cells. These cells formed a 3D spheroid within 72 hours after inoculation on a Matrigel-coated dish. Epidermal keratinocytes were mainly located at the surface of the spheroids and endothelial cells were positioned inside of the spheroids. Mixed cell spheroids formed hair follicles 3 weeks after subcutaneous transplantation into the back skin of nude mice.