A new technology for cultured skin formation using developmental molecular mechanism

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Sonic hedgehog (Shh) regulates the principal processes in many developmental stages including the epithelial-mesenchymal interaction. The extraordinary acceleration of signaling by Shh is responsible for the development of human basal cell carcinomas and trichoepitheliomas; they might originate from the very immature keratinocytes including the stem cells. We tried to utilize the mitogenic effect of Shh to accelerate the formation of cultured epithelium, which is already used in the medical field practically. To this end, we transfected shh cDNA into a Swiss-3T3 cell line, widely used as a feeder for keratinocytes, and established a Shh expressing cell line. The lethally irradiated Shh expressing feeder cells remarkably accelerated the growth of keratinocyte colonies obtained from the human neonatal foreskin, and the formation of well-stratified cultured epithelium, which is rich in immature small keratinocytes, expressing cytokeratin 14. This acceleration was suppressed by the addition of cyclopamine, a specific inhibitor of Shh signaling. These data indicate that the Shh is a promising mitogen to improve the technology for cultured epithelium formation.