

Mesenchymal stem cells differentiation into keratinocytes: what did we learn about calcium essentiality?

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Introduction. Epidermal differentiation is a complex process in which keratinocytes go through morphological and biochemical changes. Keratinocyte differentiation is in part mediated by a calcium gradient. High calcium concentration induces differentiation through genomic and non-genomic pathways such as desmosome formation. Abnormal keratinocyte differentiation is involved in the pathophysiology of skin diseases and different approaches have been proposed to study and treat these diseases. In this context, human Wharton's jelly mesenchymal stem cells (hWJSCs) emerged as a promising alternative to study skin biology. We have shown that hWJSCs are able to differentiate into keratinocytes; however, the role of calcium in this (trans)differentiation is not completely understood. **Objective:** The aim of this work was to study the effect of calcium on hWJSCs differentiation into keratinocytes. **Material and Methods:** hWJSCs were cultured in Dulbecco's modified Eagle's medium (DMEM), 10% fetal bovine serum until reached the spindle-shaped appearance. After characterization as mesenchymal stem cells, differentiation was induced by culturing cells in a medium for keratinocyte development (KSFM) supplemented with Epidermal Growth Factor, Insulin Growth Factor and 0.09 or 1.8 mM CaCl₂. Cells cultivated in DMEM containing 0.09 mM CaCl₂ were used as controls. Cultures were evaluated on days 1, 4, 7, 11, 14, 17 and 23, based on the activity of tissue kallikreins 5, 6 and 7 upon specific synthetic substrates. Cell morphology was also monitored in these time points. **Results and Discussion:** Data showed higher activity of these proteases in cell lysates of 17 and 23-day cultures independently of the calcium concentration in comparison to controls. In contrast, only cells cultivated in the presence of 1.8 mM CaCl₂ displayed morphological characteristics of keratinocytes. **Conclusion:** Our results show that calcium is not mandatory for the kallikreins activity appearance; however, it appears to be essential for the morphological changes during keratinocyte differentiation toward epidermal architecture.

Keywords: mesenchymal stem cells, keratinocyte differentiation, calcium.

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