Title:

High concentration of glucose activates migration and proliferation of human skin keratinocytes through inducing active release of HMGB1.

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Abstract:

High-mobility group box 1 (HMGB1) is a nuclear factor and a secreted protein. During inflammation, HMGB1 is secreted into the extracellular space where it can interact with the receptor for advanced glycation end products (RAGE) and trigger proinflammatory signals. This protein has also been shown to function as a cytokine and to promote keratinocyte scratch wound healing. In the present study, we investigated the effect of a high glucose concentration on secretion of HMGB1 in cultured human skin keratinocytes. A high concentration (10 mM) of glucose induced HMGB1 release in human skin keratinocytes and promoted phosphorylation of ERK1/2 but not that of p38 or JNK. The MEK1/2 inhibitor PD98059 also suppressed HMGB1 release induced by 10 mM glucose. The high concentration of glucose activated migration and proliferation of human skin keratinocytes, and antibodies to HMGB1 inhibited these glucose-induced phenomena in vitro. These results suggest that a high glucose concentration induces HMGB1 release from skin keratinocytes and may enhance wound healing in the skin.