FEATURES

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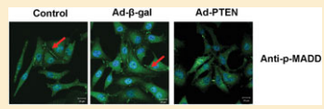

Mitogen-activated kinase activating death domain containing protein (MADD) is abundantly expressed in cancer cells and necessary for maintaining cancer cell survival. However, this survival function of MADD is dependent upon its phosphorylation by protein kinase B (Akt). The tumour suppressor PTEN (phosphatase and tensin homolog deleted on chromosome 10) is a lipid phosphatase that negatively regulates the phosphatidylinositol 3-kinase (PI3K)-Akt signalling pathway. The downstream targets of PTEN in triggering apoptosis have not yet been completely identified. The authors report that MADD can act as a pro-apoptotic factor to initiate apoptosis when its phosphorylation is attenuated by PTEN. The data shows that tumor necrosis factor α-related apoptosis-inducing ligand (TRAIL) induces a reduction in MADD phosphorylation with a concomitant up-regulation of PTEN. Knock down of PTEN using a specific siRNA prevents TRAIL-induced reduction in pMADD levels. Surprisingly, Akt non-phopshorylated MADD translocates from the plasma membrane to cytoplasm where it is bound to 14-3-3 and displaces 14-3-3 associated Bax, which translocates to mitochondria resulting in cytochrome-C release. Taken together, the data reveals that PTEN can convey the death signal by preventing MADD phosphorylation by Akt.

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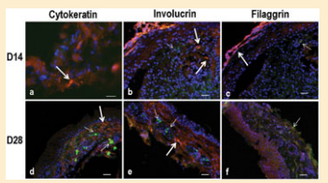

Wound healing is a major problem in diabetic patients and current treatments have met with limited success. The following evaluates the treatment of excisional and diabetic wounds using a stem cell isolated from the human umbilical cord Wharton's jelly (hWJSC) that shares unique properties with embryonic and adult mesenchymal stem cells. hWJSCs are non-controversial, available in abundance, hypo-immunogenic, non-tumorigenic, differentiate into keratinocytes and secrete important molecules for tissue repair. When human skin fibroblasts (CCD) in conventional scratch-wound assays were exposed to hWJSC-conditioned medium (hWJSC-CM) the fibroblasts at the wound edges migrated and completely covered the spaces by day 2 compared to controls. The number of invaded cells, cell viability, total collagen, elastin and fibronectin levels were significantly greater in the hWJSC-CM treatment arm compared to controls ($p < 0.05$). When a single application of green fluorescent protein (GFP)-labelled hWJSCs (GFP-hWJSCs) or hWJSC-CM was administered to full-thickness murine excisional and diabetic wounds, healing rates were significantly greater compared to controls ($p < 0.05$). Wound biopsies collected at various time points showed the presence of green GFP-labelled hWJSCs, positive human keratinocyte markers (cytokeratin, involucrin, filaggrin) and expression of ICAM-1, TIMP-1 and VEGF-A. On histology, the GFP-hWJSCs and hWJSC-CM treated wounds showed reepithelialization, increased vascularity and cellular density and increased sebaceous gland and hair follicle numbers compared to controls. hWJSCs showed increased expression of several miRNAs associated with wound healing compared to CCDs. The studies demonstrate that hWJSCs enhance healing of excisional and diabetic wounds via differentiation into keratinocytes and release important molecules.