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**Title:** Bone marrow stromal cell conditioned media reduces endoplasmic reticulum stress in alveolar epithelial cells in vitro

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**Body:** Introduction Idiopathic Pulmonary Fibrosis (IPF) is a chronic progressive lung disorder of unknown etiology. Evidence of endoplasmic reticulum (ER) stress has been found in lungs of IPF patients. In the present study we investigate possible effects of Bone Marrow Stromal Cell conditioned media (BMSC-cm) on ER stress response and wound healing in alveolar epithelial cells (AEC). Methods Wounded A549 were treated with 3µg of Tunicamycin for 24h to induce ER stress afterwards cells were treated with BMSC-cm or control media for 24h and 48h. qRT PCR was performed for analysis of ER stress markers: Grp78, XBP1 and CHOP and the wounds were measured at 0h, 24h and 48h. Results Gene expression level of Grp78 was reduced after BMSC-cm treatment at 24h compared to controls ( $3.03 \pm 0.36$  vs  $4.86 \pm 0.76$   $2\Delta\Delta\text{ct}$ ) and further reduced ( $1.71 \pm 0.28$   $2\Delta\Delta\text{ct}$ ) after 48h. Similarly, the spliced variant of XBP1 was reduced after BMSC-cm treatment compared to the control group ( $4.07 \pm 0.41$  vs  $5.42 \pm 0.51$   $2\Delta\Delta\text{ct}$ ) at 24h and at 48h ( $1.66 \pm 0.21$   $2\Delta\Delta\text{ct}$ ). Moreover, CHOP levels were diminished after BMSC-cm compared to controls ( $10.13 \pm 1.39$  vs  $1.74 \pm 1.07$   $2\Delta\Delta\text{ct}$ ) at 24h and at 48h ( $1.02 \pm 0.019$   $2\Delta\Delta\text{ct}$ ). Furthermore, the percentage of alveolar wound repair was increased in presence of BMSC-cm in ER stressed cells as compared to controls at 24h ( $48.50\% \pm 5.1$  vs  $20.34\% \pm 2.51$ ) and at 48h ( $60.1\% \pm 4.5$  vs  $22.45\% \pm 5.12$ ). Conclusions BMSC-cm increases alveolar epithelial wound healing, possibly by reducing ER stress in AEC. Since ER stress predisposes to AEC dysfunction and subsequent lung fibrosis, our study emphasize that ER stress inhibition may serve as important therapeutic target in IPF, perhaps by BMSC-cm.