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Potential Therapeutic Effect of Human Adipose-Derived Stem Cells on hypoxia in vitro and in vivo

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Peripheral arterial disease (PAD) is a chronic circulatory disease characterized by narrowed arteries and reduced blood flow to the extremities.
The beneficial effects of adipose stem cells (ASCs) have been used in multiple clinical trials as a therapeutic intervention for PAD. To further explore the therapeutic mechanism of stem cells for PAD, we designed this study in ECs under hypoxic conditions.
First, to mimic the pathological mechanism of PAD in vitro, we used CoCl2 to create a hypoxic environment in Endothelial cells（ECs）, and simultaneously using co-culture of ECs and ASCs, we found that under hypoxic conditions, ECs angiogenesis was attenuated, while stem cells promoted the angiogenic capacity of endothelial cells. Next, we found that hypoxia causes calcium homeostasis in endothelial cells, and stem cells promote calcium homeostasis. Finally, we used western blotting to observe the UPR pathway, and found that mimic hypoxia will cause endoplasmic reticulum stress, and stem cells can reduce endoplasmic reticulum stress, thereby ensuring cell survival.
In the in vivo test section, we found that ASC was shown to ameliorate the effects of ischemia on muscle tissue in ApoE-/- mice hindlimb ischemia model. Animals showed less muscle necrosis, less inflammation, and lover levels of muscle enzymes after ASCs injection.
In general, these data suggest that ASCs may be a meaningful treatment option for patients with PAD, who do not have traditional revascularization options.