## Three-dimensional spheroid formation of adipose-derived stem cells improves the survival of fat transplantation by enhance their therapeutic effect

Yucang He<sup>1</sup>, Zikai Zhang<sup>1</sup>, Zihao Li<sup>1</sup>, Min Lin<sup>2</sup>, Siqi Ding<sup>3</sup>, Hanwen Wu<sup>1</sup>, Fangfang Yang<sup>1</sup>, Zhongming Cai<sup>1</sup>, Tian Li<sup>1</sup>, Jingping Wang<sup>1</sup>, Chen Ke<sup>1</sup>, Shengsheng Pan<sup>1</sup>, and Liqun Li<sup>1</sup>

<sup>1</sup>The First Affiliated Hospital of Wenzhou Medical University <sup>2</sup>The Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University <sup>3</sup>Yiwu Central Hospital

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## Abstract

Adipose-derived stem cells (ADSCs) have important applications in basic research, especially in fat transplantation. Some studies have found that three-dimensional (3D) spheroids formed by mesenchymal stem cells have enhanced therapeutic potential. However, the fundamental basics of this effect are still being discussed. In this study, ADSCs were harvested from subcutaneous adipose tissues and 3D spheroids were formed by the automatic aggregation of ADSCs in a non-adhesive 6-well plate. Oxygen glucose deprivation (OGD) was used to simulate the transplantation microenvironment. We found that 3D culture of ADSCs triggered cell autophagy. After inhibiting autophagy by Chloroquine, the rates of apoptosis were increased. When the 3D ADSC-spheroids were re-planked, the number of senescent ADSCs decreased, and the proliferation ability was promoted. In addition, there were more cytokines secreted by 3D ADSC-spheroids including VEGF, IGF-1 and TGF- $\beta$ . After adding the conditioned medium with human umbilical vein endothelial cells (HUVECs), 3D ADSC-spheroids were more likely to promote migration, and tube formation, stimulating the formation of new blood vessels. Fat grafting experiments in nude mice also showed that 3D ADSC-spheroids enhanced survival and neovascularization of fat grafts. These results suggested that 3D spheroids culturing of ADSCs can increase the therapeutic potential in fat transplantation.

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