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TERT and GDF11 cooperate in rejuvenating senescent endothelial progenitor cells and predict the prognosis of elderly patients with acute myocardial infarction

Shaoheng Zhang[1,2], Zhao Lan[1,3], Wei Jiarui[1], Wang Jiahong[2], Chen Nannan[2], Gong Qunlin[2], Su Feng[2] and **Yan Jian[3]**
[1]GuangZhou Red Cross Hospital - Jinan University, China
[2]Yangpu Hospital - Tongji University School of Medicine, China
[3]Dahua Hospital, China

Background: Endothelial progenitor cells (EPCs) play a key role in cardiovascular regeneration following acute myocardial infarction (AMI); however, in older patients, EPCs appear to lose their regenerative capacity.

Objectives: This study aimed to evaluate the role of two potential anti-aging factors, TERT (the catalytic subunit of telomerase) and growth differentiation factor 11 (GDF11), in rejuvenating senescent EPCs in elderly patients with AMI.

Methods: We compared the quantity and capabilities of EPCs from old-aged (>60 years), middle-aged (45–60 years), and young-aged (<45 years) AMI patients. The role of TERT and GDF11 in young and old-aged EPCs were examined *in vitro*. Finally, we validated our finding by comparing GDF11/TERT expression in AMI patients with poor/good prognosis.

Results: Circulating count and survival of EPCs, and TERT and GDF11 expression levels, decline with age among patients with AMI. Meanwhile, upregulation of TERT and GDF11 can rejuvenate old-aged EPCs *in vitro* by renewing their survival and angiogenic abilities through activation of the eNOS- and pro-survival signaling pathways. Depletion of TERT causes senescence in vascular endothelial function and angiogenesis of young EPCs. An independent cohort of patients confirmed the predictive power of TERT and GDF11 expression as indicators of clinical outcomes post-AMI.

Conclusions: TERT cooperates with GDF11 to enhance regenerative capabilities of older EPCs. When combined with GDF11, TERT may represent a potential therapeutic target for the treatment of elderly patients with AMI.

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