

Micropatterned substrates to accelerate pathological smooth muscle cells aging

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Abstract

Hutchinson-Gilford Progeria Syndrome (HGPS) is a rare genetic disorder that causes accelerated aging in children leading to premature death. Smooth muscle cells (SMCs) are the most affected cells in HGPS patients. In this work, we studied whether SMCs, derived from induced pluripotent stem cells with and without HGPS phenotype, responded differentially to ECM, in particular to its topography. Moreover, we studied whether ECM could accelerate SMC aging. Human SMCs with and without HGPS phenotype showed differential cell alignment, nuclear shape and cell apoptosis but not cell cycle or SMCs markers expression when cultured in substrates with different topography. Our results further showed that substrate topography accelerated significantly the aging of SMCs with HGPS during 15 days of cell culture, as confirmed by the increase of progerin and other senescent markers. The aged SMCs showed an over-expression of nuclear envelope proteins SUN1 and Nesprin2, at both nuclear and cytoplasmatic regions. Our results unraveled new possible mechanisms to understand the aging process in SMCs.

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