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Authors: Eng-Soon Khor, Pooi-Fong Wong



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### ACCEPTED MANUSCRIPT

# Endothelial Replicative Senescence Delayed by the Inhibition of MTORC1 Signaling Involves MicroRNA-107

Eng-Soon Khor <sup>a</sup>, Pooi-Fong Wong <sup>a,\*</sup>

<sup>a</sup> Department of Pharmacology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia.

\* Corresponding author: Email address: wongpf@um.edu.my (P.F. Wong).

Other authors: Email address: darren khor@hotmail.my (E.S. Khor)

There are 6 figures and 2 supplementary figures in this paper.

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#### ABSTRACT

Accumulation of senescent endothelial cells can contribute to endothelium dysfunction. Suppression of MTOR signaling has been shown to delay senescence but the mechanism that underpins this effect, particularly one that involves miRNAs, remains to be further defined. This study sought to identify miRNAs involved in MTORC1-mediated inhibition of replicative senescence in endothelial cells. Pre-senescent HUVECs were prolonged treated with low dose rapamycin (1 nM), an MTOR inhibitor. Rapamycin treatment down-regulated the phosphorylated MTOR, RPS6 and 4EBP1 expressions, which confirmed MTORC1 suppression. Prolonged low dose rapamycin treatment has significantly reduced the percentage of senescence-associated beta galactosidase (SA- $\beta$  gal) positively stained

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