Effects of Sirtuin 1 on the proliferation and osteoblastic differentiation of periodontal ligament stem cells and stem cells from apical papilla

Q.-B. Zhang\textsuperscript{1,2*}, W. Cao\textsuperscript{1*}, Y.-R. Liu\textsuperscript{3}, S.-M. Cui\textsuperscript{2} and Y.-Y. Yan\textsuperscript{1}

\textsuperscript{1}Key Laboratory of Stomatology, Guangzhou Medical University, Guangzhou City, Guangdong Province, China
\textsuperscript{2}Department of Temporo-Mandibular Joint Surgery, Hospital of Stomatology, Guangzhou Medical University, Guangzhou, Guangdong Province, China
\textsuperscript{3}Department of Pediatric Dentistry, Hospital of Stomatology, Guangzhou Medical University, Guangzhou, Guangdong Province, China

\*These authors contributed equally to this study.

Corresponding author: Q.-B. Zhang
E-mail: doctorqingbin@hotmail.com

Received August 7, 2015
Accepted October 19, 2015
Published March 24, 2016
DOI http://dx.doi.org/10.4238/gmr.15015234

ABSTRACT. The function of SIRT1 in the proliferation and osteoblastic differentiation of dental stem cells is unclear. The aim of this study was to assess the roles of SIRT1 in these processes using periodontal ligament stem cells (PDLSCs) and stem cells from apical papilla (SCAPs). A defined concentration of resveratrol, an SIRT1 activator, or nicotinamide, an SIRT1 inhibitor, was administered to PDLSCs, SCAPs, and a mixed group of the two cell lines, and their effects on these processes analyzed. Cell proliferation was tested using microtitration with a tetrazolium dye (MTT). Alkaline phosphatase (ALP) activity, mineralization ability, and the expression of osteoblastic differentiation-associated genes were assessed as well. These studies demonstrated that resveratrol could
promote cell proliferation of all three groups in a gradually increasing trend over time. In contrast, nicotinamide suppressed the proliferation of the three cell lines. The results also showed that the markers of osteoblastic differentiation: ALP activity, mineralization ability, and the expression levels of the osteoblastic genes ALP, osteopontin, osteocalcin, and bone sialoprotein, were enhanced in the groups with resveratrol treatment. In contrast, following addition of nicotinamide, ALP activity, mineralization ability, and the expression levels of the osteoblastic genes were down-regulated in the cells. Together, these results suggest that the SIRT1 activator and inhibitor compounds, resveratrol and nicotinamide, function at high efficiency in adjusting cell proliferation, and that SIRT1 is a powerful regulator of osteoblastic differentiation of PDLSCs and SCAPs. In addition, co-culture of the two cell lines could promote their abilities of proliferation and osteogenic differentiation.

**Key words:** Sirtuin1; Cell culture; Periodontal ligament stem cells; Stem cells from apical papilla; Proliferation; Osteoblastic differentiation