

# Author's Accepted Manuscript

Proteasome activation enhances stemness and lifespan of human mesenchymal stem cells

Marianna Kapetanou, Niki Chondrogianni, Spyros Petrakis, George Koliakos, Efstathios S. Gonos



www.elsevier.com

PII: S0891-5849(16)31136-4  
DOI: <http://dx.doi.org/10.1016/j.freeradbiomed.2016.12.035>  
Reference: FRB13141

To appear in: *Free Radical Biology and Medicine*

Received date: 5 September 2016  
Revised date: 7 December 2016  
Accepted date: 24 December 2016

Cite this article as: Marianna Kapetanou, Niki Chondrogianni, Spyros Petrakis, George Koliakos and Efstathios S. Gonos, Proteasome activation enhance stemness and lifespan of human mesenchymal stem cells, *Free Radical Biology and Medicine*, <http://dx.doi.org/10.1016/j.freeradbiomed.2016.12.035>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and a review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain

Proteasome activation enhances stemness and lifespan of human mesenchymal stem cells.

**Marianna Kapetanou<sup>1,2</sup>, Niki Chondrogianni<sup>1\*</sup>, Spyros Petrakis<sup>3</sup>, George Koliakos<sup>3,4</sup> and Efstathios S. Gonos<sup>1\*</sup>**

<sup>1</sup>National Hellenic Research Foundation, Institute of Biology, Medicinal Chemistry & Biotechnology, 48 Vas. Constantinou Ave., Athens, 116 35, Greece

<sup>2</sup>Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Athens, Panepistimiopolis, 15701 Athens, Greece

<sup>3</sup>Biohellenika Biotechnology Company, 57001, Thessaloniki, Greece

<sup>4</sup>Department of Biological Chemistry, Medical School, Aristotle University of Thessaloniki, 54124 Thessaloniki, Greece

sgonos@eie.gr

nikichon@eie.gr

\*Corresponding author: Efstathios S. Gonos. National Hellenic Research Foundation, Institute of Biology Medicinal Chemistry & Biotechnology, 48 Vas. Constantinou Ave., Athens, 116 35, Greece, tel: +30-210-7273756 (ESG), +30-210-7273768 (NC), FAX: +30-210-7273677

\*Corresponding author: Niki Chondrogianni, National Hellenic Research Foundation, Institute of Biology Medicinal Chemistry & Biotechnology, 48 Vas. Constantinou Ave., Athens, 116 35, Greece. tel: +30-210-7273768 (NC), FAX: +30-210-7273677

## ABSTRACT

The age-associated decline of adult stem cell function contributes to the physiological failure of homeostasis during aging. The proteasome plays a key role in the maintenance of proteostasis and its failure is associated with various biological phenomena including senescence and aging. Although stem cell biology has attracted intense attention, the role of proteasome in stemness and its age-dependent deterioration remains largely unclear. By employing both Wharton's-Jelly- and Adipose-derived human adult mesenchymal stem cells (hMSCs), we reveal a significant age-related decline in proteasome content and peptidase activities, accompanied by alterations of proteasomal complexes. Additionally, we show that senescence and the concomitant failure of proteostasis negatively affects stemness. Remarkably, the loss of proliferative capacity and stemness of hMSCs can be counteracted through proteasome activation. At the mechanistic level, we demonstrate for the first time that Oct4 binds at the promoter region of  $\beta 2$  and  $\beta 5$  proteasome subunits and thus possibly regulates their expression. A firm understanding of the mechanisms regulating proteostasis in stem cells will pave the way to innovative stem cell-based interventions to improve healthspan and lifespan.

## Abbreviations:

MSC: Mesenchymal Stem Cell; hMSC: human Mesenchymal Stem Cell; WJ: Wharton's Jelly; ASC: Adipose Stem Cell; CPDs: Cumulative Population Doublings; CT-L: Chymotrypsin-Like; T-L: Trypsin Like; PGPH: Peptidylglutamyl-peptide hydrolyzing; ROS: Reactive Oxygen Species; RNAi: RNA interference; siRNA: short interfering RNA; ChIP: Chromatin Immune Precipitation; Oe: overexpression

**Keywords:** stem cells, pluripotency, differentiation, stemness, senescence, aging, proteasome, proteostasis

## INTRODUCTION

Download English Version:

<https://daneshyari.com/en/article/5502221>

Download Persian Version:

<https://daneshyari.com/article/5502221>

[Daneshyari.com](https://daneshyari.com)