3rd International Conference on
AGING & GERONTOLOGY
July 18-19, 2018 | Atlanta, USA

Ping Song
Georgia State University, USA

β-Hydroxybutyrate prevents vascular cell senescence through heterogeneous nuclear ribonucleoprotein A1 (hnRNP A1)-upregulated octamer-binding transcriptional factor 4

Statement of the Problem: Vascular aging is considered as a main risk factor for cardiovascular diseases. β-hydroxybutyrate (β-HB), one of three human ketone bodies, usually functions as an alternative source of energy during nutrient deprivation. Elevation of ketone bodies, including β-HB, during fasting or caloric restriction is believed to induce anti-inflammation effects and alleviate aging-related neurodegeneration. However, whether β-HB regulates molecular signaling in the aging process, specifically the senescence pathway in vascular cells, has not been previously studied. The objective of this study is to investigate the effect of β-HB on vascular cell senescence and the underlying molecular mechanisms.

Methodology and Results: Vascular cells treated with β-HB and a ligand fishing pull-down approach were employed as an *in vitro* model. Mouse treated with β-HB was used as an *in vivo* animal model. β-HB stimulates cellular quiescence in vascular cells, which significantly inhibits both replicative senescence and stress-induced premature senescence via p53-independent mechanisms. Further, we identified heterogeneous nuclear ribonucleoprotein A1 (hnRNP A1) as a direct binding target of β-HB. The binding of β-HB with hnRNP A1 profoundly enforces hnRNP A1 binding to Octamer-binding transcriptional factor (Oct) 4 mRNA. The binding of hnRNP A1 with Oct4 mRNA stabilizes Oct 4 mRNA and Oct4 expression. Moreover, Oct4 increases Lamin B1, a key factor in maintaining chromosome stability against DNA damage-induced senescence. Finally, either fasting or intraperitoneal injection of β-HB *in vivo* elevates Oct4 and Lamin B1 in both endothelial and vascular smooth muscle cells in mice *in vivo*.

Conclusions: Ketone body β-HB exerts anti-aging function in vascular cells by upregulating an hnRNP A1-controlled Oct4-mediated Lamin B1 pathway.

Biography

Ping Song has a broad background in cell biology and biochemistry with specific training and expertise in both vascular biology and metabolism. By developing effective cell and mouse animal models, His researches are focused on vascular biology and remodeling under aging, diabetic, or tobacco smoking/and e-cigarette condition. Recently, His lab reported that activation of adenosine monophosphate-activated protein kinase (AMPK), an energy gauge and redox sensor, delays aging process by reduction of cyclin-dependent kinase (CDK) inhibitor p16 that is mediated by HMG box-containing protein 1 (HBP1). AMPKα2 isoform plays a fundamental role in anti-oxidant stress and anti-senescence. AMPKα also plays an important role in maintaining chromosome integrity and reduction of DNA damage, which is highly associated with cellular senescence. Ketone body β-hydroxybutyrate exerts anti-aging effects in both endothelial and vascular smooth muscle cells by upregulating a heterogeneous nuclear ribonucleoprotein A1-controlled Oct4-mediated Lamin B1 signaling pathway.

pingsong2007@gmail.com

Notes: