

2nd International Conference on

TUMOR & CANCER IMMUNOLOGY AND IMMUNOTHERAPY

July 17-18, 2017 Chicago, USA

A Novel Mechanism Regulating Polyamine Homeostasis through an Antizyme Citrullination Pathway

Hui-Chih Hung^{1,3}, Chien-Yun Lee^{1,2,3} and Guang-Yaw Liu^{4,5}

¹Department of Life Sciences, National Chung Hsing University, Taichung, Taiwan

²Graduate Institute of Biotechnology, National Chung Hsing University, Taichung, Taiwan

³Molecular and Biological Agricultural Sciences Program, Taiwan International Graduate Program, Academia Sinica, Taipei, Taiwan

⁴Institute of Biochemistry, Microbiology and Immunology, Chung Shan Medical University, Taichung, Taiwan

⁵Division of Allergy, Immunology and Rheumatology, Chung Shan Medical University Hospital, Taichung, Taiwan

This study reveals a novel mechanism for the regulation of polyamine homeostasis through protein arginyl citrullination of antizyme (AZ), a natural inhibitor of ornithine decarboxylase (ODC). ODC is a tumor promoter and is critical for cellular polyamine production. AZ binds to ODC dimers and promotes the degradation of ODC via the 26S proteasome. This study demonstrates the protein citrullination of AZ catalyzed by peptidylarginine deiminase type 4 (PAD4) both in vitro and in cells. Higher levels of putrescine and citrullinated AZ proteins were observed in cells with PAD4 activation. The levels of ODC enzyme activity and protein increased with the level of citrullinated AZ proteins in PAD4-overexpressing cells. Our data also indicated that citrullinated AZ proteins have weaker binding affinities with ODC, greatly reducing the ability of citrullinated AZ protein to bind, inhibit, and promote the degradation of ODC. Based on LC-MS/MS analysis, eight citrullination sites of AZ were identified; Arg180 and Arg183 were identified as the critical citrullinated residues in AZ that impair the binding, inhibition, and degradation of ODC. This study is the first paper, to our knowledge, to demonstrate the post-translational modification of AZ by arginyl citrullination and reveals that AZ citrullination is involved in the up-regulation of cellular ODC and polyamines, strongly implying an association with cancer development.

Biography

Hui-Chih Hung, Department of Life Sciences, National Chung Hsing University, Taichung, Taiwan, Tel. 886 4 2284-0416; Fax. 886 4 2285-1856

hchung@dragon.nchu.edu.tw

Notes: