Original Article



# Mitochondria-specific peptide amphiphiles induce mitochondrial dysfunction and peripheral T-cell lymphomas (PTCL) damage

**Qi Sun[1#], Ailing Gui[1#], Aihua Zou[2], Yichen Yan[1], Shi Qiu[1], Shun Zhu[1], Wen Liu[1], Ji Zuo[1], Qunling Zhang[3,4], Ling Yang[1]**

[1]Department of Cellular and Genetic Medicine, School of Basic Medical Sciences, Fudan University, Shanghai, China; [2]College of Chemistry and Materials Science, Shanghai Normal University, Shanghai, China; [3]Department of Lymphoma, Fudan University Shanghai Cancer Center, Shanghai, China; [4]Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China

*Contributions:* (I) Conception and design: L Yang, Q Zhang, A Zou; (II) Administrative support: L Yang, Q Zhang, J Zuo; (III) Provision of study materials or patients: L Yang, Q Zhang, W Liu; (IV) Collection and assembly of data: Q Sun, A Gui; (V) Data analysis and interpretation: Q Sun, A Gui, Y Yan, S Qiu, S Zhu; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

*Correspondence to:* Ling Yang. Department of Cellular and Genetic Medicine, School of Basic Medical Sciences, Fudan University, Shanghai, China. Email: yangling@fudan.edu.cn; Qunling Zhang. Department of Lymphoma, Fudan University Shanghai Cancer Center, Shanghai, China; Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China. Email: zhangqunling@fudan.edu.cn.

**Background:** Peripheral T-cell lymphomas (PTCL) are aggressive lymphomas with poor prognosis, and therefore, there is a pressing need to explore new targets or compounds. Mitochondria may serve as a potential therapeutic target for PTCL. A designed positively-charged segment (pKV) is anchored to the specific 15 amino acid sequence (MIASHLLAYFFTELN) to yield a cell-penetrating peptide (pHK-pKV) and a lipid chain (Pal) is conjugated to the N-terminus of pHK-pKV (Pal-pHK-pKV) are bioactive amphiphilic peptide assemblies targeting the interaction between mitochondrial voltage dependent anion channel 1 (VDAC1) and hexokinase II (HKII).

**Methods:** PTCL cell line H9 was treated with Pal-pHK-pKV and pHK-pKV, respectively. Cell proliferation in each group was measured by detecting cell viability and the corresponding marker Ki-67. Apoptosis was detected by immunofluorescence, flow cytometry and western blot. We also measured mitochondrial membrane potential, adenosine triphosphate (ATP) production, the cytochrome c distribution and the expression levels of B cell lymphoma 2 (*BCL-2*) and BCL-2 associated X protein (*BAX*). Western blot was used to detect the activation of the extracellular regulated protein kinases (ERK) signaling pathway.

**Results:** Pal-pHK-pKV and pHK-pKV with 20 μM blocked the interaction between VDAC1 and HKII, and detached HKII from mitochondria, which depolarized the mitochondrial membrane potential, induced mitochondria dysfunction, and decreased ATP production. The decreased ATP subsequently inhibited the activation of the ERK/BCL-2 pathway and increased the BAX/BCL-2 ratio. Cytochrome c was then released from the mitochondria and induced capase-3 activation and subsequently apoptosis. Additionally, decreased ATP induced the expression of *FAS* and then apoptosis.

**Conclusions:** Mitochondria specific peptide amphiphiles induce mitochondrial dysfunction and provide a new approach for the treatment of PTCL.

**Keywords:** Amphiphilic peptides; peripheral T-cell lymphoma (PTCL); mitochondrial dysfunction; apoptosis

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