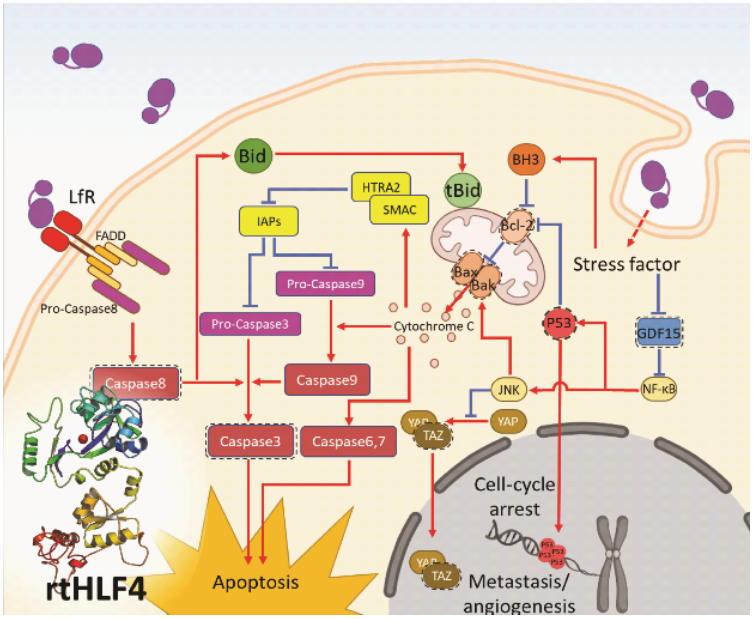
Engineering of human lactoferrin for improved anticancer activity

Yu Pan [1], Niying Chua [2], Kaisheng Lim[1] and Chun Loong Ho[1,*]

[1] Department of Biomedical Engineering, Southern University of Science and Technology (SUSTech), Shenzhen, China; e-mail: 11930397@mail.sustech.edu.cn and limkaisheng.work@gmail.com.
[2] School of Biological Sciences, Nanyang Technological University, 60 Nanyang Driver 637551; Niying001@e.ntu.edu.sg.
* Correspondence: e-mail: hejl@sustech.edu.cn; Tel.:18576699774

Abstract: Peptides resulting from protease-digested lactoferrin often exhibit improved therapeutic properties, including anti-microbial, anti-fungal, and anti-parasitic activities. However, there are limited studies that investigate the digested lactoferrin fragments for anticancer activities. Protease-digested lactoferrin fragments that have improved anticancer activities can be an attractive alternative to chemotherapeutic drugs that are often accompanied by severe side effects. Herein we report the isolation and characterization of recombinant engineered-lactoferrin (rtHLF4) that exhibit up to 100-fold improved anti-cancer activity compared to the full-length lactoferrin (flHLF) against various human cancer cell lines. Further, rtHLF4 was able to exert the anticancer effect within 24 hours of treatment, compared to the flHLF. Through transcriptomic analysis of various cancer biomarkers, rtHLF4 was found to upregulate various pro-apoptotic markers and downregulate signaling proteins involved in angiogenesis and metastasis. We further determined that rtHLF4 showed no hemolytic activity at high concentrations. We believe that this anticancer protein has the potential to be further developed as an adjuvant therapy or preventive therapy for cancer patients.

Graphical abstract:



Keywords: Lactoferrin; Anti-cancer; Tryptic-digestion.

Funding: This research was funded by the Shenzhen Institutes of Advanced Technology External Funds, grant number DWKF20190001, National Natural Science Foundation of China's Research Fund for International Young Scientists, grant number 22050410270, Guangdong Innovative Projects for the Characteristics of General Colleges and Universities, grant number 2018KTSCX200, and Guangdong Innovative and Entrepreneurial Research Team Program, grant number 2019ZT08Y191. Check carefully that the details given are accurate and use the standard spelling of funding agency names at https://search.crossref.org/funding. Any errors may affect your future funding.

Acknowledgments: The authors wish to thank Xinyi CHEN and Jun CHEN for their comments on the manuscript. The authors also wish to thank the advice provided by Professor Dai Lei and Assistant Professor Tan Yang from the Shenzhen Institute of Advanced Technology (SIAT). The authors recognize Zeyang QU, Jingyu XIAO and Juliana RIZAL for their help in the experimental designs.