

Cardio-Therapeutic Potential of Recombinant Human Anti-Protease Protein and Its Nanomedical Application

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Abstract

Protease enzymes cause significant damage to cardiac tissue during and during myocardial ischemia/reperfusion (I/R) injury. They also contribute to myocardial remodeling and hypertrophy. Inhibiting protease activity is an effective strategy to impede the proliferation of injured tissue and the progression of heart remodeling and hypertrophy. Although many small-molecule protease inhibitors are in development, a major concern is the "off-target effect" demonstrated by these therapeutic agents. Alternatively, employing a comprehensive endogenous anti-protease peptide may produce more reliable results and guarantee safety.

Secretory leukocyte protease inhibitor (SLPI) is an 11.7 kDa cationic protein that is released into the extracellular environment and has demonstrated the ability to block the activity of many inflammatory serine proteases. Our previous study demonstrated that giving recombinant human secretory leukocyte protease inhibitor (rhSLPI) by means of overexpression of rhSLPI gene or treatment with recombinant protein of human SLPI provided cytoprotective effect against I/R injury both in an in vitro, ex vivo, and in vivo study model. Interestingly, although the beneficial effects of SLPI are believed to be due to the anti-protease activity, few studies showed that those effects of SLPI might be independent on its anti-protease activity. Our recent unpublished data showed that recombinant protein of anti-protease deficient mutant SLPI also provided cardio protection against I/R injury. Therefore, the therapeutic potential of SLPI is believed to be in part by the direct effect of SLPI.

One of the clinical limitations of using recombinant human SLPI as therapeutic agent is a short half-life in circulation. The pre-clinical studies in animal models revealed the short half-life of recombinant human SLPI in circulation. Therefore, any strategies to improve stability and extend the half-life of SLPI in system, could provide greater therapeutic benefit. The application of nanomedicine, especially for SLPI delivery and specifically to cardiac target still be a challenging research question of our team. This could provide the novel approach for targeted drug delivery for cardiovascular diseases.

Keywords: Serine protease, Protease inhibitor, Secretory leukocyte protease inhibitor, Ischemic heart disease, Cardio protection, Nanomedicine

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Education History

[Doctorate]	2009	(Medicine- Cardiovascular Medicine Research), King's College London- British Heart Foundation Centre, Cardiovascular Division, The Rayne Institute-St. Thomas' hospital London, United Kingdom
[Master]	2002	(Biochemistry), Faculty of Science, Mahidol University, Bangkok, Thailand
[Bachelor]	1998	(Medical Technology), Faculty of Medical Technology, Mahidol University, Bangkok, Thailand



Professional Background

2020 - Present	Associate Professor, Biomedical Engineering Institute, Chiang Mai University, Chiang Mai, Thailand
2020 – 2020	Director- Integrative Biomedical Research Unit (IBRU), Faculty of Allied Health Sciences, Naresuan University, Phitsanulok, Thailand
2018 – 2020	Associate Professor, Department of Medical Technology, Faculty of Allied Health Sciences, Naresuan University, Phitsanulok, Thailand
2013 – 2017	Deputy Dean for Research Affairs, Graduate Study, and International Relations Faculty of Allied Health Sciences, Naresuan University Phitsanulok, Thailand
2010 – 2020	Director- Biomedical Research Unit in Cardiovascular Sciences, Faculty of Allied Health Sciences, Naresuan University, Phitsanulok, Thailand
2011- 2018	Assistant Professor, Department of Medical Technology, Faculty of Allied Health Sciences, Naresuan University, Phitsanulok, Thailand
2003 – 2005	Deputy Dean for Administrative Affairs, Faculty of Allied Health Sciences, Naresuan University Phitsanulok, Thailand



Selected Awards and Honors

1.	2018	Best Researcher Faculty of Allied Health Sciences, Naresuan University – Publications Best Researcher Faculty of Allied Health Sciences, Naresuan University - Citations
2.	2017	Best Research Work award, Higher Education Research Promotion Congress
3.	2016	Best Researcher Faculty of Allied Health Sciences, Naresuan University
4.	2015	Best Researcher Faculty of Allied Health Sciences, Naresuan University
5.	2012	Research of Outstanding Research Award “Cardiac Electro Physiology and Pathophysiology” Thailand Research Fund
6.	2012	Best Researcher Faculty of Allied Health Sciences, Naresuan University (International Publication)



Selected Publications

1. Mongkolpathumrat P., Chouyratchakarn W., Pikwong F., Phutiyothin C., Kumphune S. Roles of secretory leukocyte protease inhibitor (SLPI) in non-communicable diseases and study models. Heliyon. 2024 10(2):e24550.
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4. Mongkolpathumrat P, Kijawornrat A, Prompant E, Panya A, Chattipakorn N, Barrère-Lemaire S, Kumphune S. Post-Ischemic Treatment of Recombinant Human Secretory Leukocyte Protease Inhibitor (rhSLPI) Reduced Myocardial Ischemia/Reperfusion Injury. Biomedicines. 2021 Apr 13;9(4):422.
5. Prompant E., Sanit J., Barrère-Lemaire S., Nargeot J., Noordali H., Madhani M., Kumphune S. Cardio-protective Effects of Secretory Leukocyte Protease Inhibitor (SLPI) Against Myocardial Ischemia/Reperfusion Injury. Exp. Ther. Med. 2018; 15:5231-5242