CURRICULUM VITAE

김효수

서울의대 순환기내과

[Education]

1987-1994	Ph.D. in Medical Science, Postgraduate School, Seoul National University
1985-1987	Master of Medical Science, Postgraduate School, Seoul National University
1980-1984	M.D., Seoul National University College of Medicine
1978-1980	Premedical Course, College of Liberal Arts & Science, Seoul National University

[Research Interests]

Basic research field: "stem cell biology & its application"

[Recent 5 major papers (with impact factor 〉 10) as the first or corresponding author]

1. Dasom Shin, Soungchan Kim, Hwan Lee, Hyun-Chae Lee, Jaewon Lee, Hyun-woo Park, Mina Fukai, EunByule Choi, Subin Choi, Bon-Jun Koo, Ji-Hoon Yu, Gyurae No, Sungyoon Cho, Chan Woo Kim, Dohyun Han, Hyun-Duk Jang, and Hyo-Soo Kim (corresponding). PCSK9 stimulates Syk, PKCδ, and NF-κB, leading to atherosclerosis progression independently of LDL receptor. Nature Communications 2024 (in press).[IF=16.6]
2. Han-Mo Yang, Joonoh Kim, Baek-Kyung Kim, Hyun Ju Seo, Ju-Young Kim, Joo-Eun Lee, Jaewon Lee, Jihye You, Sooryeonhwa Jin, Sahmin Lee, Yoo-Wook Kwon, Hyun-Duk Jang, Hyo-Soo Kim (corresponding). Resistin Regulates Inflammation and Insulin Resistance in Humans via the Endocannabinoid System. Research 2024 (in press). [IF=11.0]
3. Han-Mo Yang; Joonoh Kim; Hyun-Duk Jang; Dasom Shin; Ju-Young Kim; Jihye You; Hyun-Chae Lee; Sahmin Lee; Hyo-Soo Kim (corresponding). Resistin Impairs Mitochondrial Homeostasis via Cyclase-associated Protein 1-mediated Fission, Leading to Obesity-induced Metabolic Diseases. Metabolism 2023 Jan;138:155343. [IF=13.9]
4. Yoo-Wook Kwon, Jeong-Hwan Chae, Hyo-Soo Kim (corresponding). A subset of macrophages and monocytes in the mouse bone marrow express atypical chemokine receptor-1. Cell Stem Cell, Volume 29, Issue 7, 7 July 2022, Pages 1016-1017. [IF=25.7]
5. Jin-Woo Lee; Jin Hur; Yoo-Wook Kwon; Cheong-Whan Chae; Jae-Il Choi; Injoo Hwang; Ji-Yeon Yun; Jin-A Kang; Young-Eun Choi; Young Hyun Kim; Sang Eun Lee; Cheol Lee; Dong Hyun Jo; Heeyoung Seok; Byong Seung Cho; Sung Hee Baek; Hyo-Soo Kim (corresponding). KAI1(CD82) is a key molecule to control angiogenesis and switch angiogenic milieu to quiescent state. Journal of Hematology & Oncology 2021 [IF=17.34]

Cyclase-associated protein 1 (CAP1) binds to Resistin or PCSK9, standing at the nodal point of metabolic diseases

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<Resistin-Cap1 biology>

Resistin is an adipose-secreted cytokine first identified as a mediator of insulin resistance in obese mice. In human, however, peripheral blood mononuclear cells and macrophages are the primary source of resistin. We demonstrated that resistin is a causal factor to aggravate atherosclerosis by stimulating monocytes and inducing vascular inflammation **(J Am College Cardiology 2011)[IF=27.2]**.

We identified adenylyl cyclase-associated protein 1 (CAP1) as a novel functional receptor for human resistin and clarified its intracellular signaling pathway to modulate inflammatory action of monocytes **(Cell Metabolism 2014)[31.4]**. We found that human resistin directly binds to CAP1 in human monocytes to mediate up-regulation of intracellular cAMP concentration, PKA activity and NF-kB related transcription of inflammatory cytokines such as IL-6, TNFα.

Resistin impairs mitochondrial function, leading to obesity-induced metabolic diseases. We analyzed the mitochondrial function in skeletal muscle in two mice model. A high-fat diet in humanized resistin mice increased fragmented and shorter mitochondria in the skeletal muscle, whereas resistin-knockout mice had healthy normal mitochondria. Moreover, our newly developed biomimetic selective blocking peptide could repress human resistin-mediated mitochondrial dysfunction. **(Metabolism 2023 press)[IF=13.9]**

Human Resistin is an Effector of the Endocannabinoid System and Induces Inflammation and Insulin Resistance. In human atheromatous plaques, cannabinoid 1 receptor (CB1R)-positive macrophage was colocalized with the resistin expression. In addition, resistin was exclusively expressed in the sorted CB1R-positive cells from human PBMCs. In CB1R-positive cells, endocannabinoid ligands induced resistin expression via the p38-Sp1 pathway. The regulation of resistin via the CB1R could be a potential therapeutic strategy for cardiovascular diseases by improving obesity-related inflammation and insulin resistance. **(Research 2024 in press)[IF-11.0]**.

<PCSK9-CAP1 biology>

To further substantiate the role of CAP1 in metabolism in vivo, we made TALEN-mediated CAP1 knock-out mouse. CAP1 homogenous knock-out mouse was lethal. The viable heterozygous CAP1 knock-out mice had higher protein levels of LDLR in the liver and lower LDL-C levels in the plasma, than the control mice. Mechanistic analysis revealed that PCSK9-induced endocytosis and lysosomal degradation of LDLR were mediated by caveolin but not by clathrin, which were dependent on binding

between CAP1 and caveolin-1 (**European Heart J 2019)[IF=39.3]**.

Another interesting biology here was uncovered by the observation that PCSK9 induced inflammation even in monocytes from *Ldlr*$^{-/-}$ mice. Systemic administration of AAV-PCSK9 aggravated atherosclerosis of the carotid artery in *Ldlr*$^{-/-}$ mice. We identified the pivotal role of PCSK9 in inducing inflammation and atherosclerosis independently of LDLR. Interaction of PCSK9 and CAP1 followed by activation of the SYK/PKCδ pathway may be a promising therapeutic target for inflammation-mediated disease. (**Nature Communications 2024) [IF=16.6]**