School of Life Sciences

Seminar Series

No. 2019-32

Thu., **12 December**, 4:00pm

Jukhyun Bio Auditorium(RM.121)

Korean

Interleukin-22 ameliorates neutrophil-driven nonalcoholic steatohepatitis

Speaker | Seonghwan Hwang

Affiliation | National Institutes of Health

Host | Prof. Steve K. Cho

광주과학기술원 생명과학부

Gwangju Institute of Science and Technology School of Life Sciences

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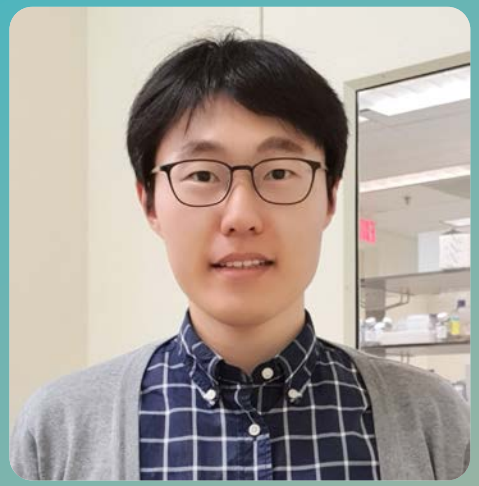

Seonghwan Hwang, Ph.D.

Education/Experience

2003.03-2007.02	B.S., Pharmacy, Seoul National University, Seoul, Korea
2007.03-2009.02	M.S., Pharmacology, Seoul National University, Seoul, Korea
2012.08-2017.05	Ph.D., Biomedical Sciences, Dept. of Molecular Genetics, University of Texas Southwestern Medical Center, Dallas, TX, USA (Advisor: Russell DeBose-Boyd, Ph.D.)
2009.01-2012.04	Research/Senior Scientist, Laboratory of Drug Evaluation, Yuhan Corporation, Yongin, Korea
2017.06-present	Postdoctoral fellow, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda, MD, USA (Supervisor: Bin Gao, M.D., Ph.D.)

Abstract

Nonalcoholic fatty liver disease (NAFLD) is a spectrum of disease that ranges from fatty liver to nonalcoholic steatohepatitis (NASH), cirrhosis, and hepatocellular carcinoma and is a leading cause of chronic liver disease worldwide. While fatty liver is mostly devoid of inflammation and is considered benign, 10-20% of patients with fatty livers progress to NASH, which is characterized by the presence of hepatocyte injury, inflammation, and fibrosis. A dominant feature observed in human NASH is a robust infiltration of neutrophils in the liver, which is not significantly observed in fatty livers in obese individuals or in high-fat diet (HFD)-fed mice. Hepatic expression of C-X-C motif chemokine ligand 1 (CXCL1), a key chemokine for neutrophil infiltration, is highly elevated in NASH patients but not in fatty livers in obese individuals or HFD-fed mice. Our recent work demonstrated that hepatic overexpression of Cxcl1 was sufficient to drive steatosis-to-NASH progression in HFD-fed mice through neutrophil-derived reactive oxygen species and activation of stress kinases. In this neutrophil-driven NASH model, interleukin (IL)-22 ameliorated liver injury through induction of metallothionein, one of the most potent antioxidant proteins. Moreover, metallothionein contributed to IL-22 inhibition of hepatic inflammation by attenuating the inclusion of inflammatory mitochondrial DNA in extracellular vesicles derived from damaged hepatocytes. With positive data from Phase I trial, IL-22 is a promising therapeutic agent for the treatment of NASH.