OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH

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NAME: Lee, Jun Hee

eRA COMMONS USER NAME (credential, e.g., agency login): junheelee97

POSITION TITLE: Associate Professor

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

| INSTITUTION AND LOCATION | DEGREE  (if applicable) | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Republic of Korea | B.S. | 02/2000 | Biological Sciences |
| KAIST, Daejeon, Republic of Korea | M.S. | 02/2002 | Biological Sciences |
| KAIST, Daejeon, Republic of Korea | Ph.D. | 02/2006 | Biological Sciences |
| KAIST, Daejeon, Republic of Korea | Postdoc | 06/2007 | Biological Sciences |
| University of California, San Diego (UCSD), California, United States of America | Postdoc | 07/2011 | Pharmacology |

**A. Personal Statement**

My lab studies the relationship between stress, aging and metabolism, currently focusing on the following projects: (1) Stress-inducible Sestrins and their role in age- and obesity-associated metabolic pathologies, (2) Biochemical mechanisms underlying physiological functions of Sestrins, (3) Pathogenetic mechanisms of how autophagy is abrogated in human diseases including non-alcoholic fatty liver disease (NAFLD) and movement disorders, (4) Stress-induced protein inclusions and RNA granules and (5) Single cell-level understanding of stress-induced transcriptome changes.

**B. Positions and Honors**

POSITIONS and EMPLOYMENT

2000-2006 Graduate Student, Department of Biological Sciences, KAIST

2006-2007 Post-doctoral Researcher, as a mandatory military service, KAIST

2007-2011 Post-doctoral Fellow, Department of Pharmacology, School of Medicine, UCSD

2009-2011 Visiting Researcher, Sanford-Burnham Institute, La Jolla, USA

2011-2017 Assistant Professor, Department of Molecular and Integrative Physiology (MIP)  
University of Michigan (UM) Medical School

2011-2017 Research Assistant Professor, Institute of Gerontology, UM Medical School

2017-current Associate Professor with Tenure, Department of Molecular and Integrative Physiology  
University of Michigan (UM) Medical School

2017-current Research Associate Professor, Institute of Gerontology, UM Medical School

HONORS

1997 Excellence Scholarship for 1st class new students, awarded by KAIST

1997-1999 Academic Excellence Scholarship, awarded by KAIST

2000 Summa Cum Laude, awarded by KAIST

2000-2005 National Scholarship, awarded by MOST

2002-2018 Notable Korean Scientists, named 16 times by Biological Research Information Center (BRIC)

2006 Valedictorian, nominated by KAIST

2007-2008 Next Generation Fellowship, awarded by Korea Research Foundation (KRF)

2007 Ten Outstanding Scientists, named by Ministry of Science and Technology (MOST) and Korean Science and Engineering Foundation (KOSEF)

2008-2011 Human Frontier Science Program Long-term Fellow, awarded by International Human Frontier Science Program Organization (HFSPO)

2010 Postdoctoral Travel Award, awarded by Society for Developmental Biology

2011 University of Michigan Biological Scholar, awarded by UM Biological Science Scholars Program

2012-2013 Research Career Development Core Award, awarded by the Claude Pepper Older Americans Independence Center at the University of Michigan

2012-2016 Ellison New Scholar in Aging, awarded by the Ellison Medical Foundation (EMF)

2012-2015 Liver Scholar, awarded by the American Association for the Study of Liver Diseases (AASLD) and the American Liver Foundation (ALF)

2013-2015 Basic Science Award, awarded by the American Diabetes Association (ADA)

2017-2019 Glenn Award for Research in Biological Mechanisms of Aging, awarded by the Glenn Foundation for Medical Research.

**C. Contribution to Science**

Total 47 peer-reviewed publications, among which 31 are either first- or senior-author papers:

<http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/42149901/?sort=date&direction=descending>

1. Role of Sestrin against age- and obesity-associated diseases. Through Drosophila and mouse model systems, we have shown that Sestrin-family proteins are important for attenuating development of age- and obesity-associated pathologies.

a. Lee, J. H., Budanov, A. V., Park, E. J., Birse, R., Kim, T. E., Perkins, G. A., Ocorr, K., Ellisman, M. H., Bodmer, R., Bier, E.\*\*, Karin, M.\*\* (2010) Sestrin as a feedback inhibitor of TOR that prevents age-related pathologies. ***Science*** 327, 1213-1218. PMID: 20203043, PMCID: PMC2866632. [Cover Story] [\*\*, co-corresponding authors]

b. Lee, J. H., Bodmer, R., Bier, E., and Karin, M. (2010) Sestrins at the crossroad between stress and aging. ***Aging***, 2, 369-374. PMID: 20606249, PMCID: PMC2919257

c. Lee, J. H.\*,\*\*, Budanov, A. V.\*, Talukdar, S., Park, E. J., Park, H. L., Park, H. W., Bandyopadhyay, G., Li, N., Aghajan, M., Jang, I., Wolfe, A. M., Perkins, G. A., Ellisman, M. H., Bier, E., Scadeng, M., Foretz, M., Viollet, B., Olefsky, J., Karin, M.\*\* (2012) Maintenance of metabolic homeostasis by Sestrin 2 and Sestrin3. ***Cell Metab.*** 16, 311-321. PMID: 22958918, PMCID: PMC3687365. [\* Co-first authors, \*\* Co-corresponding authors]

d. Lee, J. H.\*, Budanov, A. V.\*, and Karin, M. (2013) Sestrins orchestrate cellular metabolism to attenuate aging. ***Cell Metab.***, 18, 792-801. PMID: 24055102, PMCID: PMC3858445. [\*, co-first authors]

2. Homeostatic roles of Sestrin in tissue metabolism and tumor suppression. Subsequent studies revealed critical physiological functions of Sestrins in adipose tissue, liver and colon in regulating metabolism and suppressing tumorigenesis.

a. Ro, S. H., Nam, M., Jang, I., Park, H. W., Park, H., Semple, I. A., Kim, M., Kim, J. S., Park, H., Einatd, P., Damarid, G., Golikovd, M., Feinstein, E., and Lee, J. H. (2014) Sestrin2 inhibits uncoupling protein 1 expression through suppressing reactive oxygen species. ***Proc. Natl. Acad. Sci. U S A***111, 7849-7854. PMID: 24825887, PMCID: PMC4040599.

b. Park, H. W., Park, H., Ro, S. H., Jang, I., Semple, I. A., Kim, D. N., Kim, M., Nam, M., Zhang, D., Yin, L., Lee, J. H. (2014) Hepatoprotective role of Sestrin2 against chronic ER stress. ***Nat. Commun.***5, 4233. PMID: 24947615, PMCID: PMC4074707.

c. Ro, S. H., Semple, I. A., Ho, A., Park, H. W., Lee, J. H. (2015) Sestrin2, a regulator of thermogenesis and mitohormesis in brown adipose tissue. ***Front. Endocrinol.***, 6, 114. PMID: 26257706, PMCID: PMC4513567.

d. Ro, S. H.\*, Xue, X.\*, Ramakrishnan, S. K., Cho, C. S., Namkoong, S., Jang, I., Semple, I. A., Ho, A., Park, H. W., Shah, Y. M.\*\*, Lee, J. H.\*\*(2016) Tumor suppressive role of Sestrin2 during colitis and colon carcinogenesis. ***Elife***, 5:e12204. PMID: 26913956, PMCID: PMC4805551.  
[\* Co-first authors, \*\* Co-corresponding authors]

3. Molecular mechanisms underlying the physiological functions of Sestrins. We further deciphered the molecular mechanisms underlying the metabolism-controlling functions of Sestrins through biochemical and structural studies.

a. Ro, S. H., Semple, I. A., Park, H., Park, H, Park, H. W., Kim, M., Kim, J. S., and Lee, J. H. (2014) Sestrin2 promotes Unc-51-like kinase 1 (ULK1)-mediated phosphorylation of p62/sequestosome-1. ***FEBS J.*** 281, 3816-3827. PMID: 25040165, PMCID: PMC4156532.

b. Kim, J. S.\*, Ro, S. H.\*, Kim, M., Park, H. W., Semple, I. A., Park, H., Cho, U. S., Wang, W., Guan, K. L., Karin M., and Lee, J. H. (2015) Sestrin2 inhibits mTORC1 through modulation of GATOR complexes. ***Sci. Rep.***, 5, 9502. PMID: 25819761, PMCID: PMC4377584. [\* Co-first authors]

c. Kim, H.\*, An, S.\*, Ro, S. H.\*, Telxeira, F. P., Park, G. J., Kim, C., Cho, C. S., Kim, J. S., Jakob, U., Lee, J. H.\*\*, Cho U. S.\*\* (2015) Janus-faced Sestrin2 controls ROS and mTOR signaling through two separate functional domains. ***Nat. Commun.***, 6, 10025. PMID: 26612684, PMCID: PMC4674687.  
[\* Co-first authors, \*\* Co-corresponding authors]

d. Ho, A., Cho, C. S., Namkoong, S., Cho, U. S., Lee, J. H. (2016) Biochemical Basis of Sestrin Physiological activities. ***Trends Biochem. Sci.***, 41, 621-632. PMID: 27174209, PMCID: PMC4930368.

4. Role of autophagy in preventing neurodegeneration and mobility disorder. Through genetic screening, we identified several autophagy regulators in Drosophila, and showed their roles in neuromuscular homeostasis. Genetic mutations in some of these autophagy-regulating genes were found to provoke familial neurodegenerative diseases in human patients.

a. Kim, M.\*, Park, H. L.\*, Park, H. W.\*, Ro, S. H., Nam, S., Reed, J. M., Guan, J. L., Lee, J. H. (2013) Drosophila Fip200 is an essential regulator of autophagy that attenuates both growth and aging. ***Autophagy*** 9, 1201-1213. PMID: 23819996, PMCID: PMC3748192. [\* Co-first authors]

b. Kim, M.\*\*, Semple, I., Kim, B., Kiers, A., Nam, S., Park, H. W., Park, H., Ro, S. H., Kim, J. S., Juhász, G., Lee, J. H.\*\* (2015) Drosophila Gyf/GRB10 interacting GYF protein is an autophagy regulator that controls neuron and muscle homeostasis. ***Autophagy*** 11, 1358-1372. PMID: 26086452, PMCID: PMC4590642. [\*\* Co-corresponding authors]

c. Kim, M.\*, Sandford, E.\*, Gatica, D., Qiu, Y., Liu, X., Zheng, Y., Schulman, B. A., Xu, J., Semple, I., Ro, S. H., Kim, B., Mavioglu, R. N., Tolun, A., Jipa, A., Takats, S., Karpati, M., Li, J. Z., Yapici, Z., Juhasz, G., Lee, J. H.\*\*, Klionsky, D. J.\*\*, Burmeister, M.\*\* (2016) Mutation in ATG5 reduces autophagy and leads to ataxia with developmental delay. ***eLife***, 5:e12245. PMID: 26812546, PMCID: PMC4786408. [\*, Co-first authors; \*\*, co-corresponding authors]

d. Kim, M.\*\*, Ho, A., Lee, J. H.\*\* (2017) Autophagy and Human Neurodegenerative Diseases-A Fly's Perspective. ***Int J Mol Sci.*** 18:e1596. PMID: 28737703, PMCID: PMC5536083. [\*\* Co-corresponding authors]

5. Stress-induced accumulation of protein inclusions and RNA granules. We investigated the mechanisms of how different stresses associated with obesity can impair autophagic flux and promote aggregation of proteins and RNA.

a. Park, H. W., Park, H., Semple, I. A., Jang, I., Ro, S. H., Kim, M., Cazares, V. A., Stuenkel, E. L., Kim, J. J., Kim, J. S., and Lee, J. H. (2014) Pharmacological correction of obesity-induced autophagy arrest using calcium channel blockers. ***Nat. Commun.***, 5, 4834. PMID: 25189398, PMCID: PMC4157315.

b. Park, H. W., and Lee, J. H. (2014) Calcium channel blockers as potential therapeutics for obesity-associated autophagy defects and fatty liver pathologies. ***Autophagy***, 10, 2385-2386.

c. Cho, C. S.\*, Park, H. W.\*, Ho, A., Semple, I. A., Jang, I., Park, H., Reilly, S., Saltiel, A. R., Lee, J. H. (2018) Lipotoxicity induces hepatic protein inclusions through TBK1-mediated p62/SQSTM1 phosphorylation. ***Hepatology***,68, 1331-1346*.* PMID: 29251796.[\*, co-first authors]

d. Namkoong, S., Ho, A., Woo, Y. M., Kwak, H. J.\*\*, Lee, J. H.\*\* (2018) Systematic Characterization of Stress-Induced RNA Granulation. ***Mol. Cell***, 70, 175-187. PMID: 29576526.  
[Cover Story] [\*\*, co-corresponding authors]

6. Genetic Dissection of Signal Transduction Pathways in Drosophila. During my graduate training, I focused on dissection of different signaling pathways, including Ras-MAPK and LKB1-AMPK pathways. This led to identification of novel regulatory mechanisms for the corresponding signaling pathways. These findings together constituted my M.S. thesis and Ph.D. thesis.

a. Lee, J. H.\*, Cho, K. S.\*, Lee, J., Kim, D., Lee, S. B., Yoo, J., Cha, G. H. and Chung, J. (2002). *Drosophila* PDZ-GEF, a guanine nucleotide exchange factor for Rap1 GTPase, reveals a novel upstream regulatory mechanism in the mitogen-activated protein kinase signaling pathway. ***Mol. Cell Biol.***22, 7658-7666. PMID: 12370312, PMCID: PMC135652. [\* Co-first authors]

b. Kim, M., Lee, J. H., Koh, H., Lee, S. Y., Jang, C., Chung C. J., Sung, J. H., Blenis, J., and Chung, J. (2006)\*. Inhibition of ERK-MAP kinase signaling by RSK during *Drosophila* development. ***EMBO J*.** 25: 3056-3067. PMID: 16763554, PMCID: PMC1500987.

c. Lee, J. H., Koh, H., Kim, M., Park, J., Lee, S. Y., Lee, S. and Chung, J. (2006) JNK pathway mediates apoptotic cell death induced by tumor suppressor LKB1 in *Drosophila*. ***Cell Death Differ.***13, 1110-1122. PMID: 16273080.

d. Lee, J. H.\*, Koh, H.\*, Kim, M.\*, Kim, Y., Lee, S. Y., Karess, R., Lee, S., Shong, M., Kim, J., Kim, J. and Chung, J. (2007) Energy-dependent regulation of cell structure by AMP-activated protein kinase. ***Nature*** 447, 1017-1020. PMID: 17486097. [\* Co-first authors]

**D. Research Support**

*A. Current Research Support*

1R01DK102850-01A1 (PI: Lee, Jun Hee) 04/01/2015-03/31/2020

NIH

Title: Mechanisms underlying Hepatoprotective Roles of Sestrin2

The goal of this support is to characterize the role of Sestrin2 against obesity-associated non-alcoholic fatty liver diseases (NAFLD) using mouse models.

1R01DK114131-01A1 (PI: Lee, Jun Hee) 09/01/2018-08/31/2021

NIH

Title: Protein inclusions in non-alcoholic steatohepatitis

The goal of this support is to clarify the mechanisms of how protein inclusions form during fatty liver and how they contribute to liver pathologies.

5R01DK111465-01 (PI: Cho, Uhn-Soo; co-I: Lee, Jun Hee) 09/01/2016-08/31/2021

NIH

Title: The molecular mechanisms of nutrient- and stress-dependent mTORC1 regulation mediated by human Sestrin2

The goal of this support is to determine how Sestrin2 mediates stress-dependent regulation of mTORC1 through combination of structural and molecular biological approaches.

Glenn Award for Research in Biological Mechanisms of Aging (PI: Lee, Jun Hee) 10/01/2017-9/30/2019

Glenn Foundation for Medical Research

Title: Role of Sestrin and autophagy signaling pathways in attenuation of aging and age-

associated pathologies

The major goal of this support is to supplement the financial resources that are already available to the PI’s lab in order to further the research the PI is doing associated with the biology of aging and the extension of the healthy human lifespan.

AASLD Pilot Research Award (PI: Lee, Jun Hee) 07/01/2018-06/30/2019

American Association for the Study of Liver Diseases

Title: Unraveling genetic, environmental and cell-to-cell variations in fatty liver transcriptome

The goal of this support is to establish single cell sequencing system for comprehensive analysis of hepatocyte transcriptome during fatty liver disease.

*B. Recently Completed Research Support*

New Scholar Award in Aging (PI: Lee, Jun Hee) 08/01/2012-07/31/2016

Ellison Medical Foundation (AG-NS-0932-12)

Title: Sestrins at the crossroads between nutrition, aging and metabolism

The major goal of this support is to generate and exploit mouse models for assessing the role of Sestrins in metabolic homeostasis in the context of aging and obesity.

1R21AG050903-01 (PI: Cho, Uhn-Soo & Lee, Jun Hee) 07/01/2015-6/30/2017

NIH

Title: Structure-based biochemical understanding of Sestrins in aging and metabolism

The goal of this support is to clarify the biochemical mechanism underlying Sestrin family protein’s aging- and metabolism-controlling activities.

1R21OD018265-01A1 (PI: Lee, Jun Hee) 04/01/2015-03/31/2018

NIH

Title: Identification of autophagy mediators through screening transgenic animal library

The goal of this support is to identify new autophagy mediators using Drosophila transgenic RNAi library.