Gina Lee, Ph.D.

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Research Area

- Cancer signaling and metabolism
- RNA biogenesis and chemical modification
- mTORC1-overactive TSC and LAM kidney tumors
- Dietary and genetic kidney diseases

Throughout my scientific career, I have been committed to revealing the interplay between oncogenic signaling, RNA biogenesis, and metabolic pathways in order to elucidate molecular mechanisms of tumorigenesis and identify effective treatments for human cancers **[1-5]**. In particular, my focus has been on mTORC1 (mechanistic target of rapamycin complex 1) signaling, which I studied extensively since my Ph.D. I have identified new downstream biological processes of mTORC1 using proteomic, transcriptomic, and metabolomic analysis of cancer cell lines, patient samples, and xenograft and genetic mouse tumor models. Especially, I found that mTORC1 plays a crucial role in the metabolic adaptation of cancer cells by enhancing RNA splicing and stability of key metabolic enzymes. These works came through as 6 first and 6 corresponding author papers, including those published in Cell (2017) **[1]** and Molecular Cell (2021, 2023) **[2,5]**, which highlighted RNA processing enzymes as a promising therapeutic target for the metabolic vulnerability of cancers. As a result of these studies, I have been invited to speak at prominent cancer meetings, including TSC (2015, 2023), Keystone (2017), AACR (2018), FASEB (2019), and CSHL (2019, 2021) conferences, and was honored with Breakout Prize (2019) for junior investigators.

In 2020, I launched my own lab at UC Irvine, where we continue to elucidate cancer metabolism and RNA signaling to provide new mechanistic insights and novel therapeutic interventions for human cancers. One of our current focuses is on cancer RNA epitranscriptome. Using molecular biology, biochemical, and mass spectrometry assays, we investigate the signaling and metabolic pathways that control RNA chemical modification, and the crosstalk between RNA modification and cellular metabolic processes. Our research has already yielded exciting results, including our recent discoveries of mTORC1-dependent m6A mRNA methylation regulation mechanisms and m6A-mediated chemotherapy resistance **[2-4]**. By continuing to uncover the new links between signal transduction, cellular metabolism, and RNA biogenesis and modification, I hope that our research will inspire innovative therapeutic avenues for treating human cancers.

Research projects and publications that I would like to highlight:

Department of Defense/CDMRP/TSCRP TS200022
04/2021-03/2024 (Role: PI)
Mechanistic understanding of m6A signaling and metabolism in TSC

Mary Kay Ash Foundation
07/2022-06/2024 (Role: PI)
Targeting eIF4A-ERα intersection for LAM treatment

NIH/NCI/K22 CA234399
09/2022-08/2025 (Role: PI)
Elucidating the regulation of RNA methylation by mTOR signaling in cancer

Trainee Fellowships

NIH/NIGMS/IMSD and MARC undergraduate research fellowship
05/2020-04/2023 (Recipient: Anica; Role: Mentor)

NIH/NIGMS/IMSD predoctoral fellowship
09/2021-08/2022 (Recipient: Ramirez; Role: Mentor)

NIH/NCI/T32 predoctoral fellowship
09/2022-08/2024 (Recipient: Ramirez; Role: Mentor)

#1. Lee G, Zheng Y, Cho S, Jang C, England C, Dempsey JM, Yu Y, Liu X, He L, Cavaliere PM, Chavez A, Zhang E, Isik M, Couvillon A, Dephoure NE, Blackwell TK, Yu JJ, Rabinowitz JD, Cantley LC, Blenis J. Post-transcriptional regulation of de novo lipogenesis by mTORC1-S6K1-SRPK2 signaling. **Cell** (2017) 171:1545-1558.

Commentary:
"SRPK2 acts downstream of mTORC1 to promote de novo lipogenesis" **Cancer Discovery** (2018).
"Intron splicing for lipid biosynthesis" **Science Signaling** (2018).

#2. Cho S*, Lee G*#, Pickering BF*, Jang C, Park J, He L, Mathur L, Kim S, Jung S, Tang H, Monette S, Rabinowitz JD, Perrimon N, Jaffrey SR#, Blenis J#. mTORC1 promotes cell growth via m6A-dependent mRNA degradation. **Molecular Cell** (2021) 81(10):2064-2075. #Corresponding author.

Commentary by Michael N. Hall (Lasker Award winner):
"More writing: mTORC1 promotes m6A mRNA methylation" **Molecular Cell** (2021).

#3. Mathur L, Jung S, Jang C#, Lee G#. Quantitative analysis of m6A RNA modification by LC-MS. **STAR Protocols** (2021) 2(3):100724.

#4. Kim J, Chun Y, Ramirez CB, Hoffner LA, Jung S, Jang K, Rubtsova VI, Jang C, Lee G#. MAPK13 stabilization via m6A modification limits anti-cancer efficacy of rapamycin. **Journal of Biological Chemistry** (2023) 299(9):105175.

#5. Cho S, Chun Y, He L, Ramirez CB, Ganesh KS, Jeong K, Song J, Cheong JG, Li Z, Choi J, Kim J, Koundouros N, Ding F, Dephoure N, Jang C, Blenis J#, Lee G#. FAM120A couples SREBP-dependent transcription and splicing of lipogenesis enzymes downstream of mTORC1. **Molecular Cell** (2023) 83(16):3010-3026.

Education and Positions

2020-	Assistant Professor, Department of Microbiology and Molecular Genetics, Chao Family Comprehensive Cancer Center, School of Medicine, UC Irvine
2012-2019	Postdoctoral Fellow, Harvard Medical School & Cornell University (Mentor: John Blenis)
2006-2011	PhD, KAIST (Korea Advanced Institute of Science and Technology) & Seoul National University (Mentor: Jongkyeong Chung)
2002-2005	BS, Dept. of Biological Science, KAIST

Grants

2022-2025	NIH/National Cancer Institute K22 Career Transition Award
2022-2024	Mary Kay Ash Foundation Women's Cancer Research Grant
2022	New Investigator Award, School of Medicine, UC Irvine
2022	Anti-Cancer Challenge Award, Chao Family Comprehensive Cancer Center, UC Irvine
2021-2024	Department of Defense/CDMRP/TSCRP Idea Development Award
2021	Cancer Systems Biology Research Award, Center for Complex Biological Systems, UC Irvine
2021	Finalist, Human Frontier Science Program
2014-2017	Postdoctoral Fellowship, Lymphangioleiomyomatosis (LAM) Foundation
2013-2015	Postdoctoral Fellowship, Tuberous Sclerosis Complex (TSC) Alliance
2012-2013	Postdoctoral Fellowship, National Research Foundation of Korea
2006-2010	Excellent Graduate Student Scholarship, Korea Government
2002-2005	Superior Academic Performance Scholarship, KAIST

Awards

2022	Excellence in Teaching Award, School of Medicine, UC Irvine
2019	Breakout Prize for Junior Investigators (awarded by Breakthrough Prize winners)
2018	Travel Award, Korean Society for Molecular and Cellular Biology
2011	Travel Award, Asia-Pacific Drosophila Research Conference, Taiwan
2010	Best Poster Award, FASEB Conference, AMPK: Central Regulatory System in Metabolism & Growth, Japan
2007	Chair Fund Recipient, Gordon Research Conference, Cancer Models & Mechanisms (Chair: William G. Kaelin), Switzerland
2006	Magna Cum Laude, KAIST

Professional Activities

2023	Organizing Committee and Session Chair, International TSC Conference, DC (supported by NIH R13NS134255)
2023	Invited Attendee, RNA Modification Workshop, National Academy of Sciences (NAS), DC
2023	Session Chair, Southern California Metabolism Meeting, CA
2021-	Scientific Advisory Board, RNA Metabolism Section, Cell Signaling Technology, MA
2021	Program Committee, Cell Growth Signaling Pathways, AACR Annual Conference
2019-	Member, RNA Society
2019-	Journal Reviewer (Nature, Nature Cancer, PNAS, Cell Reports, Nature Communications, Oncogene, Experimental and Molecular Medicine, Molecular Metabolism, JBC, FASEB)
2016-	Grant Review Panel (TSC Alliance (2016, 2021, 2023), DoD/CDMRP TSC Research Program (2021, 2023), Mary Kay Ash Cancer Foundation (2023), NIH/Cellular Signaling and Regulatory Systems Study Section (2023))
2016-2019	Co-leader, Monthly Tri-Institute Cancer Metabolism Meeting (Memorial Sloan Kettering Cancer Center, Rockefeller University, Weill Cornell Medicine), NY
2012-2014	Conference Organizing Committee, New England Bioscience Society, MA
2012-	Member, American Association for the Advancement of Science (AAAS)
2009-	Member, American Association for Cancer Research (AACR)

Publications (#Corresponding author; *Equal contribution; Lee lab trainees)

27. Kim J, Chun Y, Ramirez CB, Hoffner LA, Jung S, Jang K, Rubtsova VI, Jang C, Lee G#. MAPK13 stabilization via m6A modification limits anti-cancer efficacy of rapamycin. **Journal of Biological Chemistry** (2023) 299(9):105175.

Preprint:
Kim J, Chun Y, Ramirez CB, Hoffner LA, Jung S, Jang K, Rubtsova VI, Jang C, Lee G#. MAPK13 stabilization via m6A modification limits anti-cancer efficacy of rapamycin. **bioRxiv** (2022).

26. Cho S, Chun Y, He L, Ramirez CB, Ganesh KS, Jeong K, Song J, Cheong JG, Li Z, Choi J, Kim J, Koundouros N, Ding F, Dephoure N, Jang C, Blenis J#, Lee G#. FAM120A couples SREBP-dependent

transcription and splicing of lipogenesis enzymes downstream of mTORC1. **Molecular Cell** (2023) 83(16):3010-3026.

25. Yaron TM et al. Host protein kinases required for SARS-CoV-2 nucleocapsid phosphorylation and viral replication. **Science Signaling** (2022) 15(757):eabm0808.

Preprint:
Yaron TM et al. The FDA-approved drug Alectinib compromises SARS-CoV-2 nucleocapsid phosphorylation and inhibits viral infection in vitro. **bioRxiv** (2020).

24. Jang K, Heras CR, Lee G#. m^{6}A in the signal transduction network. **Mol Cells** (2021) 45(7):435-443.

23. Mathur L*, Jung S*, Jang C#, Lee G#. Quantitative analysis of m^{6}A RNA modification by LC-MS. **STAR Protocols** (2021) 2(3):100724.

22. Cho S*, Lee G*#, Pickering BF*, Jang C, Park J, He L, Mathur L, Kim S, Jung S, Tang H, Monette S, Rabinowitz JD, Perrimon N, Jaffrey SR#, Blenis J#. mTORC1 promotes cell growth via m^{6}A-dependent mRNA degradation. **Molecular Cell** (2021) 81(10):2064-2075.

Commentary by Michael N. Hall (Lasker Award winner):
"More writing: mTORC1 promotes m^{6}A mRNA methylation" **Molecular Cell** (2021).

21. Tang HW, Weng JH, Lee WX, Hu Y, Gu L, Cho S, Lee G, Binari R, Li C, Cheng ME, Kim AR, Xu J, Shen Z, Xu C, Asara JM, Blenis J, Perrimon N. mTORC1-chaperonin CCT signaling regulates m^{6}A RNA methylation to suppress autophagy. **PNAS** (2021) 118:e2021945118.

20. Kim J, Lee G#. Metabolic control of m^{6}A RNA modification. **Metabolites** (2021) 11:80.

19. Jang C#, Wada S, Yang S, Gosis B, Zeng X, Zhang Z, Shen Y, Lee G, Arany Z#, Rabinowitz JD#. The small intestine shields the liver from fructose-induced steatosis. **Nature Metabolism** (2020) 2:586-593.

18. Park JH, Lee G, Blenis J. Structural insights into the activation of mTORC1 on the lysosomal surface. **Trends in Biochemical Sciences** (2020) 45:367-369.

17. Krishnamoorthy GP, Davidson N, Leach SD, Lowe SW, Zhao Z, Lee G, Landa I, Nagarajah J, Saqcena M, Singh K, Wendel HG, Dogan S, Tamarapu PP, Blenis J, Ghossein RA, Knauf JA, Rätsch G, Fagin JA. EIF1AX and RAS mutations cooperate to drive thyroid tumorigenesis through ATF4 and c-MYC. **Cancer Discovery** (2019) doi: 10.1158/2159-8290.CD-18-0606.

16. Zheng Y, Lin TY, Lee G, Paddock MN, Momb J, Cheng Z, Li Q, Fei DL, Stein BD, Ramsamooj S, Zhang G, Blenis J, Cantley LC. Mitochondrial one-carbon pathway supports cytosolic folate integrity in cancer cells. **Cell** (2018) 175:1546-1560.

15. He L, Gomes AP*, Wang X*, Yoon SO*, Lee G, Nagiec M, Cho S, Chavez A, Islam T, Yu Y, Asara JM, Couvillon A, Kim BY, Blenis J. mTORC1 promotes metabolic reprogramming by suppression of Foxk1 phosphorylation. **Molecular Cell** (2018) 70:949-960. *co-second author

14. Jang C, Hui S, Lu W, Cowan AJ, Morscher RJ, Lee G, Liu W, Tesz GJ, Birnbaum MJ, Rabinowitz JD. The small intestine converts dietary fructose into glucose and organic acids. **Cell Metabolism** (2018) 27:351-361.

13. Lee G, Zheng Y, Cho S, Jang C, England C, Dempsey JM, Yu Y, Liu X, He L, Cavaliere PM, Chavez A, Zhang E, Isik M, Couvillon A, Dephoure NE, Blackwell TK, Yu JJ, Rabinowitz JD, Cantley LC, Blenis J. Post-transcriptional regulation of de novo lipogenesis by mTORC1-S6K1-SRPK2 signaling. **Cell** (2017) 171:1545-1558.

Commentary:
"SRPK2 acts downstream of mTORC1 to promote de novo lipogenesis" **Cancer Discovery** (2018).
"Intron splicing for lipid biosynthesis" **Science Signaling** (2018).

12. Wada S, Neinast M, Jang C, Ibrahim YH, Lee G, Babu A, Li J, Hoshino A, Rowe GC, Rhee J, Martina JA, Puertollano R, Blenis J, Morley M, Baur JA, Seale P, Arany Z. The tumor suppressor FLCN mediates an alternate mTOR pathway to regulate browning of adipose tissue. **Genes Dev.** (2016) 30:2551-2564.

11. Lai SS, Zhao DD, Cao P, Lu K, Luo OY, Chen WB, Liu J, Jiang EZ, Yu ZH, Lee G, Li J, Yu DC, Xu XJ, Zhu MS, Gao X, Li CJ, Xue B. PP2Acα positively regulates mice liver regeneration termination through AKT/GSK3β/Cyclin D1 pathway. **J. Hepatology** (2016) 64:352-360.

10. Csibi A*, Lee G*, Yoon SO, Tong H, Ilter D, Elia I, Fendt SM, Roberts TM, Blenis J. The mTORC1/S6K1 pathway regulates glutamine metabolism through the eIF4B dependent control of c-Myc translation. **Current Biology** (2014) 24:2274-2280.

9. Lee G, Blenis J. Akt-ivation of RNA Splicing. **Molecular Cell** (2014) 53:519-520.

8. Kim H, Lee JM*, Lee G*, Bhin J*, Oh SK, Kim K, Pyo KE, Lee JS, Yim HY, Kim KI, Hwang D, Chung J, Baek SH. DNA damage-induced RORα is crucial for p53 stabilization and increased apoptosis. **Molecular Cell** (2011) 44:797-810.

7. Lee G, Liang C, Park G, Jang C, Jung JU#, Chung J#. UVRAG is required for organ rotation by regulating Notch endocytosis in Drosophila. **Developmental Biology** (2011) 356:588-597.

6. Sun D*, Lee G*, Lee JH*, Kim H, Rhee H, Park S, Kim K, Kim Y, Kim BY, Hong J, Park C, Choy HE, Kim JH, Jeon YH, Chung J. A metazoan ortholog of SpoT hydrolyzes ppGpp and functions in starvation responses. **Nat. Struct. Mol. Biol.** (2010) 17:1188-1194.

5. Park J, Lee G, Chung J. The PINK1-Parkin pathway is involved in the regulation of mitochondrial remodeling process. **Biochem. Biophys. Res. Commun.** (2009) 378:518-523.

4. Hyun S*, Lee JH*, Jin H*, Nam JW, Namkoong B, Lee G, Chung J, Kim VN. Conserved MicroRNA miR-8/miR-200 and its target USH/FOG2 control growth by regulating PI3K. **Cell** (2009) 139:1096-1108.

3. Jang C, Lee G, Chung J. LKB1 induces apical trafficking of Silnoon, a monocarboxylate transporter, in Drosophila melanogaster. **J. Cell Biol.** (2008) 183:11-17.

2. Lee SB, Kim S, Lee J, Park J, Lee G, Kim Y, Kim JM, Chung J. ATG1, an autophagy regulator, inhibits cell growth by negatively regulating S6 kinase. **EMBO Report** (2007) 8:360-365.

1. Lee G, Chung J. Discrete functions of rictor and raptor in cell growth regulation in Drosophila. **Biochem. Biophys. Res. Commun.** (2007) 357:1154-1159.

Invited Talks and Seminars

2023	Chao Family Comprehensive Cancer Center Annual Retreat, CA
2023	International TSC Research Conference, DC
2022	Southern California Annual RNA Symposium, CA
2022	International Congress on Lipid & Atherosclerosis, Korea
2022	School of Medicine Dean's Research Council, UC Irvine, CA
2022	UC Irvine, Dept. of Microbiology & Molecular Genetics, CA
2022	Graduate School of Medical Science, KAIST, Korea
2022	Center for Complex Biological Systems Conference, UC Irvine, CA
2021	Starr Cancer Consortium, Annual Symposium, Cold Spring Harbor Laboratory, NY
2021	UCLA Metabolism Interest Group Meeting, CA

2020	UC Irvine, Dept. of Developmental & Cell Biology, CA
2020	Yonsei University, Dept. of Biotechnology, Korea
2020	UCSD & UCI RNA Club Meeting, CA
2020	Cancer Research Institute Annual Symposium, UC Irvine, CA
2019	New England Bioscience Society, MA
2019	FASEB: Protein Kinase and Phosphorylation, CA
2019	Starr Cancer Consortium, Annual Symposium, Cold Spring Harbor Laboratory, NY
2019	Moffitt Cancer Center, FL
2019	U Mass Medical School, RNA Therapeutics Institute, MA
2019	Albert Einstein College of Medicine, Dept. of Molecular Pharmacology, NY
2019	UC Irvine, Dept. of Molecular Biology and Biochemistry, CA
2019	Massachusetts General Hospital Cancer Center, Harvard Medical School, MA
2019	Cold Spring Harbor Laboratory, NY
2019	Salk Institute, CA
2018	International Conference of Korean Society for Molecular Cellular Biology, Korea
2018	Yale University Korean Biologist Meeting, CT
2018	New York Korean Biologists, Annual Symposium, NY
2018	Cornell University, Dept. of Chemistry and Chemical Biology, NY
2018	AACR: Targeting PI3K/mTOR Signaling, MA
2017	Keystone Symposia: PI3K Pathway in Cancer, NM
2016	Tri-state Cancer Metabolism Meeting, Princeton University, NJ
2015	International TSC Research Conference, UK

Teaching and Campus Service

2023	Faculty Search Committee, Microbiology & Molecular Genetics (UC Irvine)
2022-	Instructor, RNA Modification Module, MMG206 Gene Expression Class (UCI PhD Program)
2022	Guest Lecturer, RNA Modification, UCI NIH-T32 IDCR Cancer Biology Training Program
2021-	T32 Postdoc Mentoring Committee (NIH/NCI, UCI Cancer Research Training Program)
2021-	UCI PhD Program Admission/Interview Committee (CMB Cellular & Molecular Biosciences, MCSB Mathematical Computational & Systems Biology, and MSTP MD-PhD Programs)
2021	Career Session, International TSC & LAM Research Conference, DC
2020	Career Session, Korean Life Scientists (KOLIS) Annual Conference, CA
2009	Guest Lecturer, Genetics and Development (3344.747), Seoul National University
2006-2009	Teaching Assistant (2009: Head Teaching Assistant), Genetics Experiment (BS315), KAIST

Mentorship and Trainees

2023-	Krytal Hyunh (Undergraduate Student, UC Irvine)
2022-	Yujin Chun (Postdoctoral Fellow, UC Irvine)
2022	Laurence Seabrook (PhD rotation student, UC Irvine)
2021-	Ki-Hong Jang (Postdoctoral Fellow, UC Irvine)

2021- Cuauhtemoc (Temoc) Ramirez (PhD student, UC Irvine)

*NIH/NCI-IDCR T32 Cancer Research Fellowship

*NSF-GRFP Honorable Mention

*NIH/NIGMS-IMSD Fellowship

2021- Chloe Heras (Undergraduate Student, UC Irvine)

*Rose Hills Foundation Fellowship

*UCI Undergraduate Research Opportunities Program (UROP) Fellowship

*UCI Biological Sciences Excellence in Research Award

2021-2023 Lauren Hoffner (Postbac Research Assistant, UC Irvine; Career – PhD at Scripps Institute)

2021- Joohwan Kim, PhD (Postdoctoral Fellow, UC Irvine)

*Finalist, Global Young Scientist Award, Korean Society for Stem Cell Research

*Vicky Whittemore Travel Award, International TSC Research Conference, DC

*Postdoctoral Scholar Travel Award, UCI School of Medicine

2020-2023 Alexis Anica (Undergraduate Student, UC Irvine; Career – PhD at Cornell University)

*AMGEN Research Scholarship

*NIH/NIGMS-IMSD Fellowship

*NIH/NIGMS-MARC Fellowship

2020-2021 Lavina Mathur, MS (Research Assist., UC Irvine; Career - Research Professional at Stanford)

2018-2023 Kripa Ganesh (PhD student, Cornell University; Career – Life Sciences Consultant)

2018-2019 Avantika Gupta (Exchange PhD student from ETH; Career – Postdoc at MSKCC)

2017 Vanessa Osman (PhD rotation student, Cornell University)

2016-2020 Sungyun Cho (PhD student, Cornell University; Career – Postdoc at Cornell Univ.)

*Kwanjeong Overseas Scholarship

2016-2017 Joana Nunes (Exchange PhD student from Univ. of Porto; Career – Postdoc at Leiden Univ.)

*Vincent du Vigneaud Awards of Excellence, Cornell University

2016-2020 Andre Chavez (Postbac Research Assistant, Cornell Univ.; Career – PhD at Stony Brook Univ.)

*Turner Fellowship, Stony Brook University

2015 Shira Yomtoubian (PhD rotation student, Cornell University; Career – Postdoc at Salk Institute)

2014-2016 Christina England (Postbac Research Assist., Cornell Univ.; Career – MS at Univ. Cambridge)