

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF MOLECULAR AND INTEGRATIVE PHYSIOLOGY
DEPARTMENT OF INTERNAL MEDICINE

Costas A. Lyssiotis, Ph.D., associate professor of molecular and integrative physiology, with tenure, Department of Molecular and Integrative Physiology, and associate professor of internal medicine, without tenure, Department of Internal Medicine, Medical School, is recommended for promotion to professor of molecular and integrative physiology, with tenure, Department of Molecular and Integrative Physiology, and professor of internal medicine, without tenure, Department of Internal Medicine, Medical School.

Academic Degrees:

Ph.D.	2010	The Scripps Research Institute, La Jolla, CA.
B.S.	2004	University of Michigan, Ann Arbor, MI.

Professional Record:

2021- present	Associate Professor (with tenure), Department of Molecular and Integrative Physiology, University of Michigan, Ann Arbor, MI
2021- present	Associate Professor (without tenure), Department of Internal Medicine, Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI
2015- 2021	Assistant Professor, Department of Molecular and Integrative Physiology, University of Michigan, Ann Arbor, MI
2015- 2021	Assistant Professor, Department of Internal Medicine, Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, MI

Summary of Evaluation:

Teaching: Dr. Lyssiotis has contributed greatly to teaching at the University of Michigan both in his laboratory and in the classroom. He co-teaches courses such as Responsible Conduct in Research (PIBS503), Tissue, Cellular, and Molecular Basis of Disease (PATH581), Advanced Concepts in Chemical Biology (BIOCHEM502), Cancer Biology (BIO554), and Nutrient Metabolism and Gut Physiology (PHYS514). His student teaching evaluations are exceptional and rank very good to excellent and highlight his talent for exciting and engaging his students. In 2021, Dr. Lyssiotis became the director of the Graduate Program in Cancer Biology which involves supervising programmatic requirements and course content, mentoring and meeting with the Ph.D. students, and oversight of the steering committee. Research learners include clinical fellows, post-doctoral fellows, graduate students, undergraduate students, visiting scholars, and high school students. He is the primary mentor on six federal grants including a National Institutes of Health (NIH) K08, an NIH F99, and an NIH F32. In the lab, he trains his mentees to be creative, fearless, and independent scientists.

Research: Dr. Lyssiotis is a world-renowned expert on cellular metabolism. His research has had significant impact on the field by identifying metabolic vulnerabilities for developing therapies

that target cancer-specific metabolism, or cause cancer to be more susceptible to current therapies. His laboratory has also developed metabolomics technologies and platforms that have made him internationally sought after as a collaborator to study metabolic pathways in many types of cancer. He has five granted patents, an additional three patents pending, and a pending disclosure. His funding is exceptional with more than 30 current grants, including as a multi-principal investigator on a NIH U01 grant studying fibroblast orchestration of the immune response in pancreatic cancer. He is the principal investigator on two NIH R01 grants and an NIH R37. He is a co-investigator on fourteen additional grants and has another fifteen grant applications pending. He has authored 160 peer reviewed manuscripts in high impact journals such as *Nature*, *Nature Communications*, and *Nature Cancer*, and was recognized by the Web of Science in 2020 and 2021 as a “Highly Cited Researcher” (top 1% across all sciences) with >16,000 citations in rank. His reputation is evidenced by two invited keynote speeches and 74 extramural invited presentations nationally and internationally including in France, Denmark, and Spain.

Recent and Significant Publications:

- Nwosu ZC, Ward MH, Sajjakulnukit P, Poudel P, Ragulan C, Kasperek S, Radyk M, Sutton D, Menjivar RE, Andren A, Apiz-Saab JJ, Tolstyka Z, Brown K, Lee H-J, Dzierozynski LN, He X, Hari PS, Ugras J, Nyamundanda G, Zhang L, Halbrook CJ, Carpenter ES, Shi J, Shriver LP, Patti GJ, Muir A, Pasca di Magliano M, Sadanandam A, Lyssiotis CA, “Uridine-derived ribose fuels glucose-restricted pancreatic cancer,” *Nature*, 2023 Jun;618(7963):151-158. PM37198494.
- Hong HS, Mbah NE, Shan M, Loesel K, Lin L, Sajjakulnukit P, Correa LO, Andren A, Lin J, Hayashi A, Magnuson B, Chen J, Li Z, Xie Y, Zhang L, Goldstein DR, Carty SA, Lei YL, Opipari AW, Argüello RJ, Kryczek I, Kamada N, Zou W, Franchi L, Lyssiotis CA, “OXPHOS Promotes Apoptotic Resistance and Cellular Persistence in TH17 cells in the periphery and tumor microenvironment,” *Sci Immunol*, 2022 Nov 25;7(77):eabm8182. PM36399539.
- Halbrook CJ, Thurston G, Boyer S, Anaraki C, Jimenez JA, McCarthy A, Steele NG, Kerk SA, Hong HS, Lin L, Law FV, Felton C, Scipioni L, Sajjakulnukit P, Andren A, Beutal AK, Singh R, Nelson BS, Van Den Bergh F, Krall AS, Mullen PJ, Zhang L, Batra S, Morgan JP, Stanger BZ, Christofk HR, Digman MA, Beard DA, Viale A, Zhang J, Crawford HC, Pasca di Magliano M, Jorgensen C, Lyssiotis CA, “Differential integrated stress response and asparagine production drive symbiosis and therapy resistance of pancreatic adenocarcinoma cells,” *Nat Cancer*, 2022 Nov;3(11):1386-1403. PM36411320.
- Kerk SA, Lin L, Myers A, Sutton D, Andren A, Sajjakulnukit P, Zhang L, Zhang Y, Jimenez JA, Nelson BS, Chen B, Robinson A, Thurston G, Kemp SB, Steele NG, Hoffman MT, Wen H-J, Long D, Ackenhusen SE, Ramos J, Gao X, Nwosu ZC, Galban S, Halbrook CJ, Lombard DB, Piwnica-Worms DR, Ying H, Pasca di Magliano M, Crawford HC, Shah YM, Lyssiotis CA, “Metabolic requirement for GOT2 in pancreatic cancer depends on environmental context,” *eLife*, 2022 Jul 11;11:e73245. PM35815941.
- Kim PK, Halbrook CJ, Kerk SA, Radyk M, Wisner S, Kremer DM, Sajjakulnukit P, Andren A, Hou SW, Trivedi A, Thursten G, Anand A, Yang L, Salamanca-Cardona L, Welling SD, Zhang L, Pratt MR, Keshari KR, Ying H, Lyssiotis CA, “Hyaluronic Acid Fuels Pancreatic Cancer Cell Growth,” *eLife*, 2021 Dec 24;10:e62645. PM34951587.

Service: Dr. Lyssiotis has an excellent service record. Internationally, he has served as an ad hoc reviewer on the Czech Science Foundation study section. He has organized a symposium for the New York Academy of Sciences six times and once for the American Association for Cancer Research Meeting where he was the educational session chair. Nationally, Dr. Lyssiotis is a permanent study section member of “Cancer Cell Biology” at the National Cancer Institute and is an ad hoc study section reviewer for several others including the Department of Defense. He is a scientific advisor for two therapeutic companies and on the advisory board for one pharma company. Dr. Lyssiotis serves as an associate editor of *Cancer & Metabolism* and serves on the editorial board of the *Journal of Biological Chemistry* and as a guest editor for a special issue of *Cancers, Metabolic Reprogramming and Vulnerabilities in Cancer*. He is an ad hoc reviewer for numerous scientific journals including *Nature*, *Cell Metabolism*, and *Cancer Cell*. Institutionally, Dr. Lyssiotis is an active member of many committees, including as lead and founder of the Cancer and Immune Metabolism Focus Group, founding member of the Mitochondrial Biology Interest Group, and co-directs the Pancreatic Disease Initiative at U-M.

External Reviewers:

Reviewer A: “Dr. Lyssiotis has prolifically authored or co-authored 133 peer-reviewed original research manuscripts and reviews with 69 published since 2021 as an Associate Professor, 15 as senior/corresponding author. His scholarly productivity has been supported by 4 extramural grants on which he is PI or MPI including 2 active R01s as well he lists 27 active grants to which it is presumed [sic] he provides collaborative assistance. This remarkable level of scholarly productivity not only reflects Dr. Lyssiotis’ own research interests but that he is internationally viewed as a key scientific contributor to enrich others’ science.”

Reviewer B: “In short, Dr. Lyssiotis is an active and leading member of the international cancer metabolism research community. He has published extensively in excellent journals over the course of his 19-year academic career-159 publications total and 131 papers published since joining the University of Michigan. He is active in peer review on national and international grant panels and scientific journals. He is consistently invited to present his work at top national and international conferences and symposia and has begun to take a leadership role in organizing these conferences for major research organizations...”

Reviewer C: “He has also played critical, influential roles in enhancing Michigan’s prestige in his service work that has national impact. For example, he is currently a member on the NIH NCI Cancer Cell Biology Study Section.”

Reviewer D: “Costas is clearly a star in his field and it seems he is just getting started. He has already made substantive contributions to our understanding of the biochemical underpinnings of pancreatic cancer that may catalyze the development of much needed new therapeutic options. Beyond this, Costas is great colleague and citizen of science. I am certain that he will continue to be a prized member of the UofM faculty...”

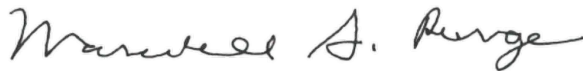
Reviewer E: “Dr. Lyssiotis also has a very impressive record of service. He has served as an ad hoc member of many grant review panels and is now a permanent member of the Cancer Cell Biology NIH study section. Beyond this, Dr. Lyssiotis has a strong record of service to the

university and the international research community through paper review, conference organization and many other activities.”

Reviewer F: “It is also noteworthy that Costas has trained numerous Ph.D. and Postdoctoral trainees and appears to be actively engaged in the overall education mission of the University of Michigan. Many of the grants listed are for his trainees, including highly competitive funding in the form [sic] of F99 NRSA grants [sic]. Of note, he’s been the Director of the Graduate Program in Cancer Biology since April 2022. Given the large number of trainees that have obtained Ph.D.s in his laboratory, this administrative role is highly appropriate.”

Summary of Recommendations:

Dr. Lyssiotis is a talented and world-renowned scientist, highly valued teacher, and dedicated institutional citizen. He has developed an internationally recognized research program focused on understanding the biochemical and metabolic pathways that enable pancreatic cancer tumor growth and immune evasion. His laboratory’s research has led to novel discoveries and has had a substantial impact on the field of pancreatic cancer research, and more broadly the entire cancer metabolism field. I am pleased to recommend Costas A. Lyssiotis, Ph.D. for promotion to professor of molecular and integrative physiology, with tenure, Department of Molecular and Integrative Physiology, and professor of internal medicine, without tenure, Department of Internal Medicine, Medical School.



Marschall S. Runge, M.D., Ph.D.
Executive Vice President for Medical Affairs
Dean, Medical School

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