MOLECULAR PHARMACOLOGY PROGRAM

The Richard Kolesnick Lab

Richard N. Kolesnick, MD

Our laboratory focuses on the role of sphingolipid signaling as a stress response. In this pathway, generation of the second messenger ceramide in response to diverse environmental and pharmacologic stresses (heat, ionizing radiation, ultraviolet light, chemotherapeutic agents, oxidative challenges, etc.) occurs either by degradation of sphingomyelin or by de novo synthesis. The quality and quantity of the ceramide response, in combination with other signals, determines whether adaptation or apoptosis ensues. This pathway is evolutionarily conserved and is obligate for the heat shock response in yeast.

View Lab Overview →

Research Projects

Radiation Response Genes in the Worm Caenorhabditis elegans

Role of Ceramide-rich Membrane Macrodomains in Response to Stress

Requirement for Kinase Suppressor of Ras (KSR) in Ras-mediated Tumorigenesis

Ionizing Radiation Targets Endothelium to Induce Normal and Neoplastic Tissue Damage

Featured News

MEDIA ADVISORY

Antibody Therapy Prevents Gastrointestinal Damage following Radiation Exposure in Mice

A new study offers the first evidence of a drug capable of preventing lethal damage to the gastrointestinal (GI) tract caused by exposure to high levels of ionizing radiation, such as those occurring during a nuclear incident.

Publications Highlights

Bodo S, Campagne C, Thin TH, Higginson DS, Vargas HA, Hua G, Fuller JD, Ackerstaff E, Russell J, Zhang Z, Klingler S, Cho H, Kaag MG, Mazaheri Y, Rimner A, Manova-Todorova K, Epel B, Zatcky J, Cleary CR, Rao SS, Yamada Y, Zelefsky MJ, Halpern HJ, Koutcher JA, Cordon-Cardo C, Greco C, Haimovitz-Friedman A, Sala E, Powell SN, Kolesnick R, Fuks Z. Single-dose radiotherapy disables tumor cell homologous recombination via ischemia/reperfusion injury. J Clin Invest. 2018; pii: 97631.

Martin ML, Zeng Z, Adileh M, Jacobo A, Li C, Vakiani E, Hua G, Zhang L, Haimovitz-Friedman A, Fuks Z, Kolesnick R*, Paty PB*. Logarithmic expansion of LGR5$^{\pm}$ cells in human colorectal cancer. Cell Signal. 2018; 42:97-105. doi: 10.1016/j.cellsig.2017.09.018. * Equal co-author.

Van Hell AJ, Haimovitz-Friedman A, Fuks Z, Tap WD, Kolesnick R. Gemcitabine kills proliferating endothelial cells exclusively via acid sphingomyelinase activation. Cell Signal. 2017; 34:86-91. doi: 10.1016/j.cellsig.2017.02.021.

Zhang L, Adileh M, Martin ML, Klingler S, White J, Ma X, Howe LR, Brown AM, Kolesnick R. Establishing estrogen-responsive mouse mammary organoids from single Lgr5+ cells. Cell Signal. 2017; 29:41-51. doi: 10.1016/j.cellsig.2016.08.001.

Hua G, Yan Pan CW, Zeng Z, Lee SG, Martin ML, Haimovitz-Friedman A, Fuks Z, Paty PB, Kolesnick R. Distinct levels of radioresistance in Lgr5+ colonic epithelial stem cells versus Lgr5+ small intestinal stem cells. Cancer Res 2017; 77:2124-2133. doi: 10.1158/0008-5472.CAN-15-2870.

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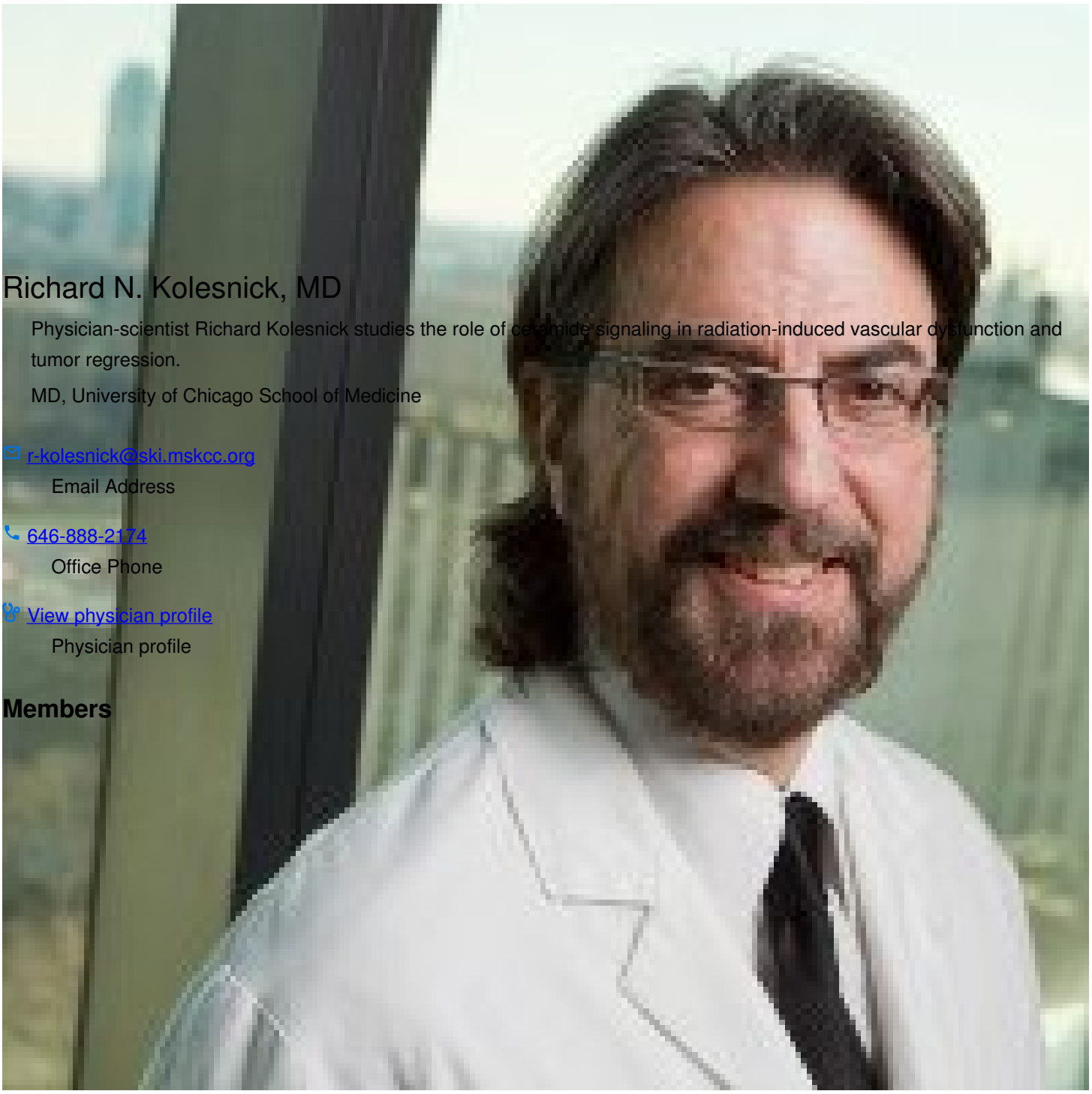
People



Richard N. Kolesnick, MD

Physician-scientist Richard Kolesnick studies the role of ceramide signaling in radiation-induced vascular dysfunction and tumor regression.

MD, University of Chicago School of Medicine

r-kolesnick@ski.mskcc.org
Email Address

646-888-2174
Office Phone

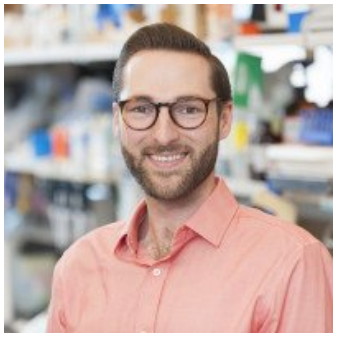
View physician profile
Physician profile

Members

Senior Research Technician

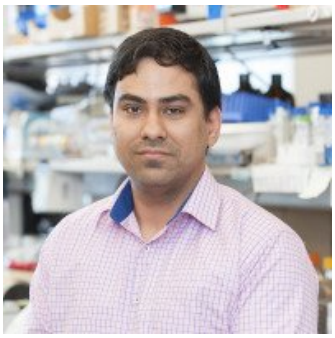
Zeinab Fereshteh

Research Fellow



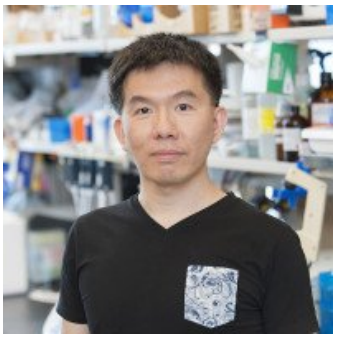
Charles Ferranti

Research Fellow



Aditya Ganju

Research Fellow

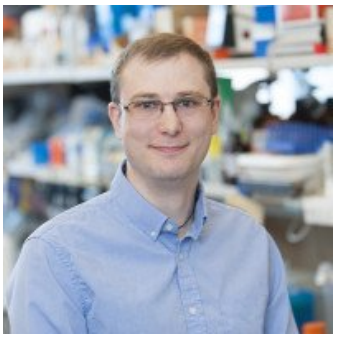


Kuo Shun Hsu

Research Fellow

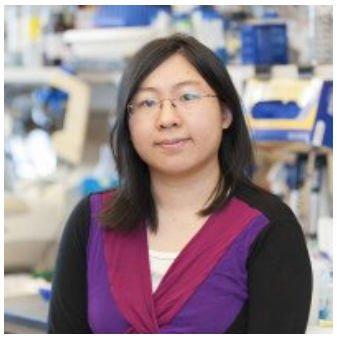
Hilda Polanco

SKI Administrative Assistant



Stefan Klingler

Research Fellow

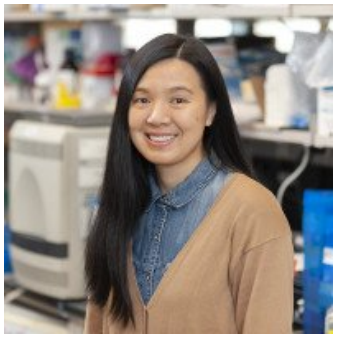


Christy Li

Graduate Student

Tambudzai Shamu

Laboratory Manager



Liyang Zhao

Research Fellow

Lab Alumni
+

Lab Affiliations
+

Get in Touch

r-kolesnick@ski.mskcc.org
Lab Head Email

646-888-2174
Office Phone

646-422-0281
Office Fax

646-888-2176
Lab Phone

Disclosures

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Doctors and faculty members often work with pharmaceutical, device, biotechnology, and life sciences companies, and other organizations outside of MSK, to find safe and effective cancer treatments, to improve patient care, and to educate the health care community.

MSK requires doctors and faculty members to report ("disclose") the relationships and financial interests they have with external entities. As a commitment to transparency with our community, we make that information available to the public.

Richard N. Kolesnick discloses the following relationships and financial interests:

Ceramedix

Equity; Intellectual Property Rights

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