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MOLECULAR PHARMACOLOGY PROGRAM

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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.

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.](#)

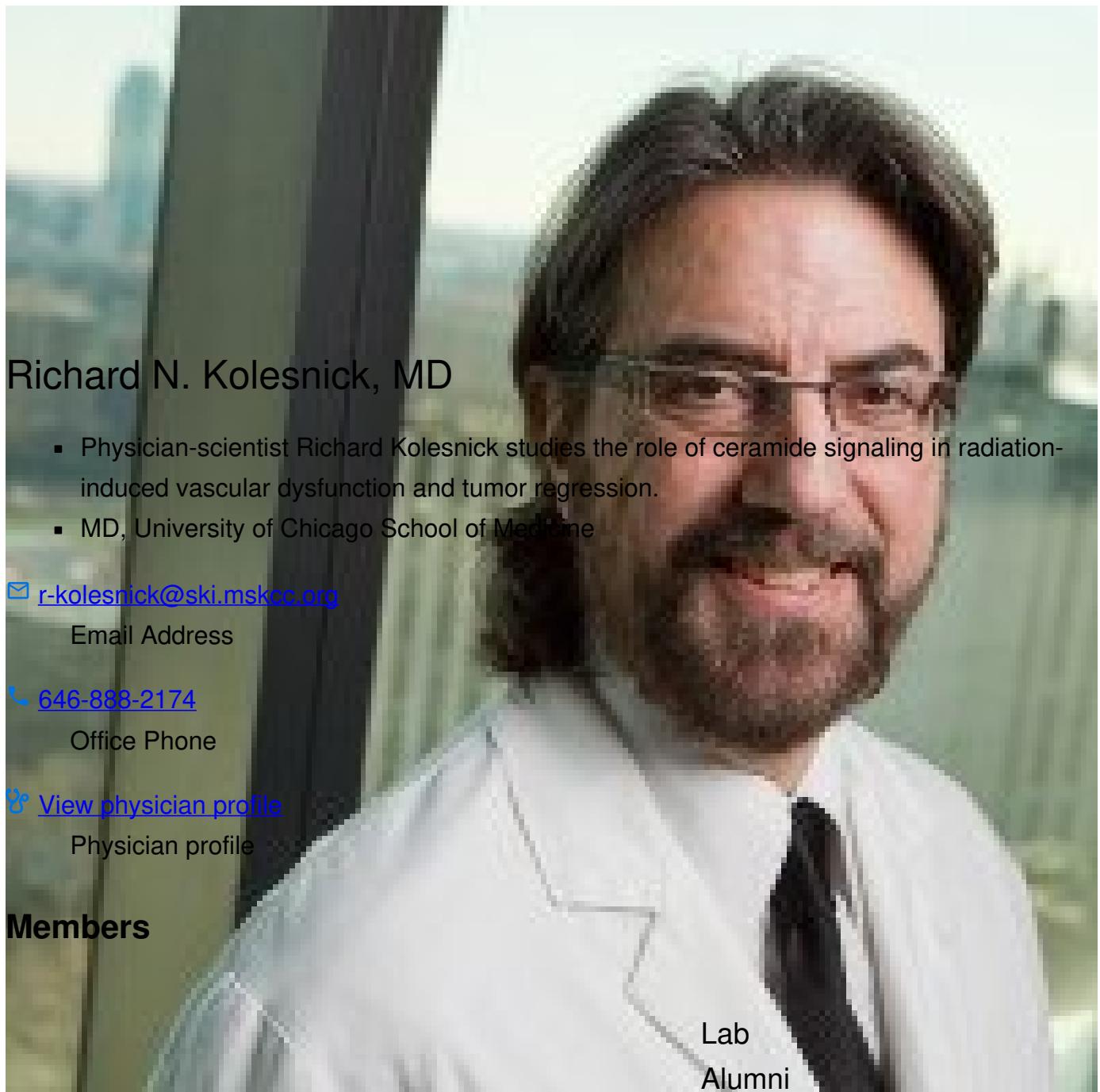
[Van Hell AJ, Haimovitz-Friedman A, Fuks Z, Tap WD, Kolesnick R. Gemcitabine kills proliferating endothelial cells exclusively via acid sphingomyelinase activation. Cell Signal. 2017; 34:86-91. doi: 10.1016/j.cellsig.2017.02.021.](#)

[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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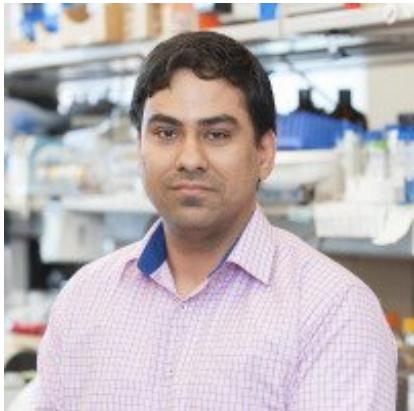
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Research Fellow



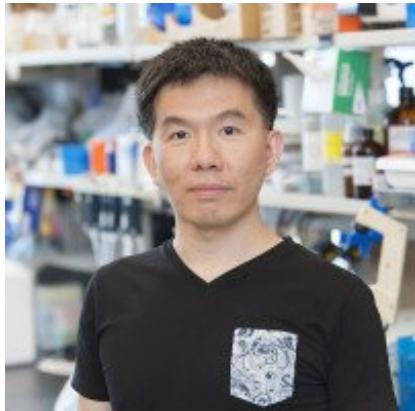
Skyla Duncan



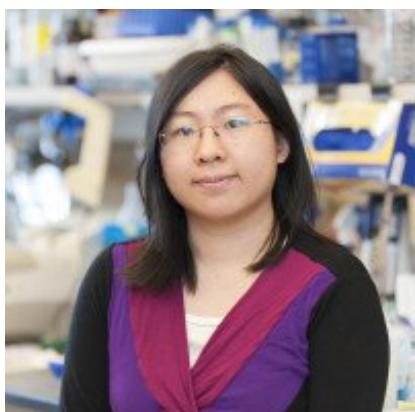
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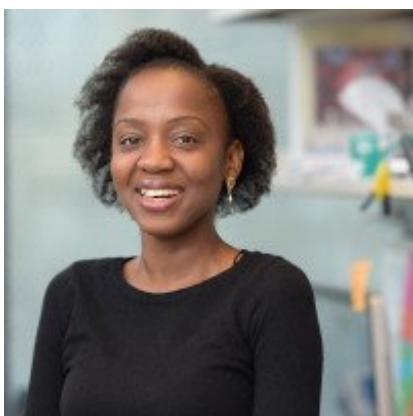
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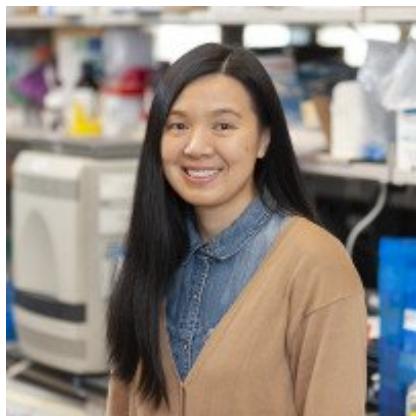
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public. Not all disclosed interests and relationships present conflicts of interest. MSK reviews all disclosed interests and relationships to assess whether a conflict of interest exists and whether formal COI management is needed.

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

- Ceramedix

Equity; Intellectual Property Rights

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