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DNA Damage Response in Normal and Leukemia Hematopoietic Stem Cells

Position

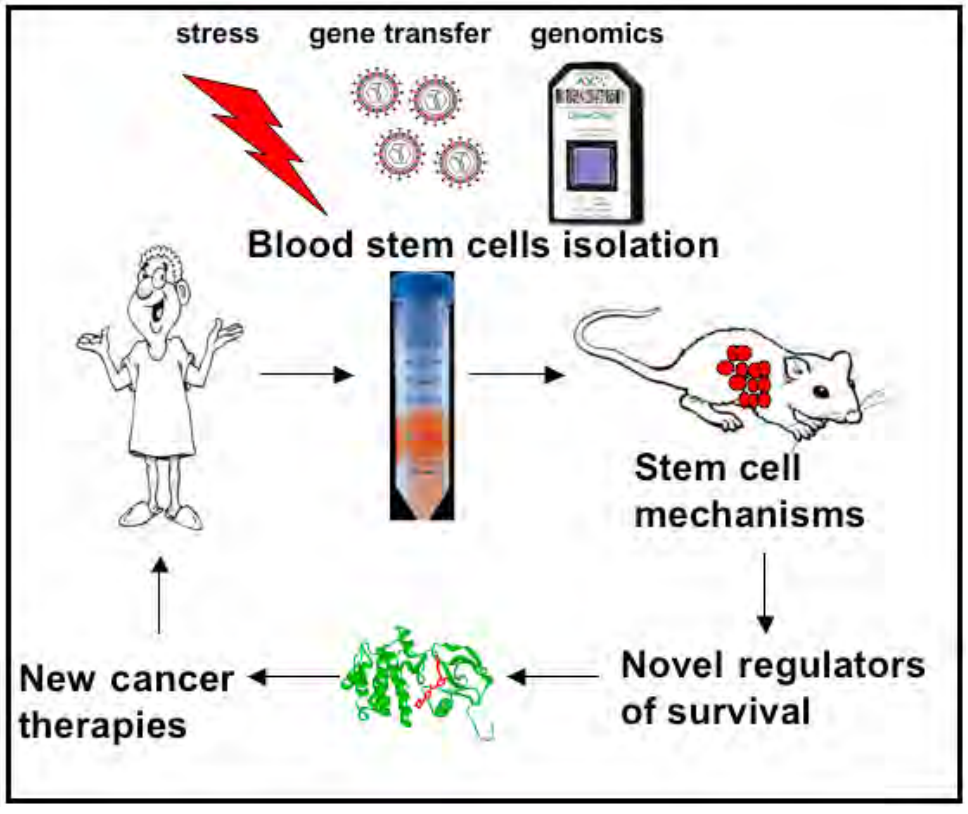
Senior Lecturer, Sackler Faculty of Medicine

Research

Accumulation of unrepaired DNA damage in hematopoietic stem cells (HSC) is associated with bone marrow failure and accelerated leukemogenesis. Our laboratory aims to understand how HSC cope with DNA damage to preserve normal blood regeneration and to limit the risk of leukemogenesis. In addition, we strive to discover how leukemia stem cells escape therapy and try to devise strategies to prevent this from happening. To address these questions we study DNA damage signaling and its outcomes in highly purified human normal and leukemia cell subsets. We employ flow cytometry, immunofluorescent and biochemical analyses, lentiviral gene transfer-mediated functional screens, expression/microRNA profiling, clonal *in vitro* assays and, most importantly, *in vivo* repopulation mouse assays of human normal HSC and leukemia-initiating cells.

Publications

Buganim, Y., I. Goldstein, D. Lipson, **M. Milyavsky,** S. Polak-Charcon, C. Mardoukh, H. Solomon, E. Kalo, S. Madar, R. Brosh, M. Perelman, R. Navon, N. Goldfinger, I. Barshack, Z. Yakhini, and V. Rotter. 2010. A novel translocation breakpoint within the BPTF gene is associated with a pre-malignant phenotype. *PLoS ONE*: 5: e9657.



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Chan G, Cheung LS, Yang W, **M. Milyavsky**, Sanders AD, Gu S, Hong WX, Liu AX, Wang X, Barbara M, Sharma T, Gavin J, Kutok JL, Iscove NN, Shannon KM, Dick JE, Neel BG, Braun BS. 2011. Essential role for Ptpn11 in survival of hematopoietic stem and progenitor cells. *Blood* 117:4253-61.

Louria-Hayon I., Ruston J.C.F., , Gish G, Jin J, Kofler M. M., Lambert J-P., Adissu H. A., **Milyavsky M**, Herrington R., Minden M. D., Dick J. E., Gingras A-C., Iscove N. N., and T. Pawson. 2013. The Lnk adaptor suppresses radiation resistance and radiation-induced B-cell malignancies by inhibiting IL-11 signaling. *Proc Natl Acad Sci USA* 110: 20599-604.

Review

Biechonski, S., and M. Milyavsky. 2013. Differences between human and rodent dna-damage response in hematopoietic stem cells: at the crossroads of self-renewal, aging and leukemogenesis. *Transl Cancer Res* 2:372-383.

Grants

2013-2015 FP7-PEOPLE-2012- Marie Curie Career Integration Grants (CIG)

2014-2015 ICRF Research Career Development Award

2014-2019 Israel Science Foundation (ISF) Grant: Elucidation of DNA damage response mechanisms in human normal and malignant hematopoietic stem cells.

2014-2016 Varda and Boaz Dotan Center for Hematological Malignancies: Chromatin Structures Governing Therapy Resistance In Myeloid Leukemia