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Mutant *p53* leads to enrichment of cancer stem cells that display ESC expression signature

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Mutation in the *p53* gene is a frequent alteration in human cancers which mostly leads to the acquiring of new oncogenic functions that promote tumorigenesis. In this study, we observed that bone marrow derived from mutant *p53* mice exhibit higher ability to form tumors compared to WT-MSCs. Cultivation of tumors obtained from mutant *p53* MSCs led to the selection of aggressive tumor-derived cell lines with an enhanced tumorigenic capacity as compared with their parental MSCs. The newly established tumor-derived cell lines were able to generate tumors following injection of as few as 100 cells, as well as displayed high expression of embryonic stem cell (ESC) signature. We were able to show that the enhanced tumor initiating capacity and the expression of ESC signature exhibited by the tumor-derived cell lines is mutant *p53* dependent. In order to confirm our findings in human settings, we utilized datasets from The Cancer Genome Atlas (TCGA). Expression levels of genes belonging to the ESC signature expressed by mutant *p53* derived tumor cell lines were examined in human tumors harboring *p53* missense mutation. In agreement with data obtained from mouse models, we identified 41 genes that were significantly and exclusively upregulated in human tumors harboring *p53* missense mutation. In conclusion, our results suggest that mutant *p53* oncogenic GOF in MSCs leads to the acquirement of CSC features, including enhanced expression of ESC signature. This ESC signature might assist to design a more specific cancer stem-cells targeted therapy for Li-Fraumeni patients and cancer at large.

Recent Publications:

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2. Wortzel, G. Koifman, V. Rotter, R. Seger, Z. Porat. (2017). High Throughput Analysis of Golgi Structure by Imaging Flow Cytometry. Sci Rep
3. Y. Shetzer, S. Kagan, G. Koifman, R. Sarig, I. Kogan-Sakin, M.Charni, T. Kaufman, M. Zapatka, A. Molchadsky, N. Rivlin, N. Dinowitz, S. Levin, G. Landan, I. Goldstein, N. Goldfinger, D. Pe'er, B. Radlwimmer, P. Lichter, V. Rotter and R. Aloni-Grinstein. (2014). The onset of p53 loss of heterozygosity is differentially induced in various stem cell types and may involve the loss of either allele. Cell death and differentiation
4. N. Rivlin, S. Katz, M. Doody, M. Sheffer, S. Horesh, A. Molchadsky, G. Koifman, Y. Shetzer, N. Goldfinger, V. Rotter and T. Geiger. (2014). Rescue of embryonic stem cells from cellular transformation by proteomic stabilization of mutant p53 and conversion into WT conformation. Proceedings of the National Academy of Sciences of the United States of America
5. N.Rivlin, G. Koifman and V. Rotter (2015). p53 orchestrates between normal differentiation and cancer. Seminars in cancer biology. Review

Biography

Gabriela Koifman did her BSc in Biotechnology and Environmental Sciences from Tel Hai academic college, MSc in Faculty of health science, Ben-Gurion University, Beer-Sheva, Israel and PhD in Molecular Cell Biology, Weizmann Institute of Science, Rehovot, Israel.

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