

A Bone Marrow Donor With Concomitant Deleterious Germline Variants In *MLH1* And *BRCA2*: What Risks Are Involved?

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Background

Multigene panel testing

- Cost and time-effective, may reveal double heterozygotes

Co-occurrence of cancer genetic syndromes

- Unclear if associated with a more severe or distinct phenotype
- Scarce reports of Lynch & HBOC syndromes

Donor-derived abnormalities

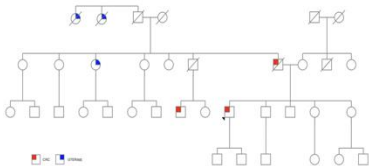
- The potential clinical significance for the recipient is still unknown

Objective

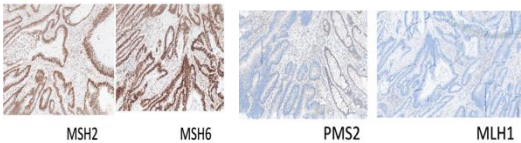
We describe a 53-year-old male with concurrent *MLH1* and *BRCA2* mutations, who was also a blood donor, discussing the implications for the recipients .

Case report

53y, male
Blood stem donor since 8 years ago



Invasive carcinoma of right colon, pT3 pN0 - stage II), with perineural invasion and loss of *MLH1* and *PMS2* expression



Gene / Transcript	Variant	Zygosity	Classification
<i>MLH1</i> (NM_000249.4)	c.1976G>T p.(Arg659Leu)	Heterozygous	Pathogenic
<i>BRCA2</i> (NM_000059.4)	c.8488-1G>A p.(?)	Heterozygous	Pathogenic

Discussion & Coments

Previous patients with *MLH1* & *BRCA2* mutations

<i>MLH1</i> (NM_000249.4)	<i>BRCA2</i> (NM_000059.4)	Clinical presentation	Referência
c.1381A>T, (p.Lys461*)	c.1310_1313del, (p.Lys437Ilefs*22)	Breast and vulvar squamous cell carcinoma, acute myelogenous leukemia	1
c.171_1718delGT	c.3492dupT	1 patient with colorectal cancer, 1 with colorectal & ovarian cancer	2

Implications for bone marrow recipients

- Genetic mutations in genes related to hematological malignancies, can lead to donor-derived malignancies post-transplantation in the recipients³
- Four levels of disclosure of abnormalities for the donors⁴
- The World Marrow Donor Association states that predonation testing of all unrelated stem cell donors is not recommended⁵

Selected references

¹Sorscher et al 2020; doi.org/10.1007/s 10549-020-05569-7. ²Ferrer-Avargues et al. 2021; doi:10.1002/cac2.12134. ³Williams et al. 2024; doi: 10.1016/j.jtct.2023.10.018. ⁴Candeliere et al. doi:10.1016/j.jtct.2022.03.029. ⁵Pryce et al. 2024;doi: 10.1016/j.jtct.2023.11.019.