

# Inherited DNA repair variants are associated with clonal hematopoiesis and cardiovascular risk in men with metastatic prostate cancer

## Authors

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Olisaemeka Ogbue,<sup>1\*</sup> Yael Kusne,<sup>2\*</sup> Osama Mosalem,<sup>3,4</sup> Kevin Thompson,<sup>5</sup> Alejandro Ferrer,<sup>1</sup> Krishna Kalari,<sup>5</sup> Winston Tan,<sup>6</sup> Leila A. Jones,<sup>5</sup> Brian A. Costello,<sup>7</sup> Daniel Childs,<sup>7</sup> Abhishek A. Mangaonkar,<sup>1</sup> Jenna A. Fernandez,<sup>1</sup> Christy Finke,<sup>1</sup> Terra L. Lasho,<sup>1</sup> Richard Weinshilboum,<sup>5</sup> Leiwei Wang<sup>1</sup> and Mrinal M. Patnaik<sup>1</sup>

<sup>1</sup>Division of Hematology, Mayo Clinic, Rochester, MN; <sup>2</sup>Division of Hematology, Mayo Clinic, Phoenix, AZ; <sup>3</sup>Department of Hematology, Mayo Clinic Florida, Jacksonville, FL; <sup>4</sup>Department of Medical Oncology, Saint Luke's Cancer Institute, Kansas City, MO; <sup>5</sup>Department of Health Sciences Research, Mayo Clinic, Rochester, MN; <sup>6</sup>Department of Oncology, Mayo Clinic Florida, Jacksonville, FL and <sup>7</sup>Department of Oncology, Mayo Clinic, Rochester, MN, USA

*\*OO and YK contributed equally as first authors.*

Correspondence:

M. M. PATNAIK - patnaik.mrinal@mayo.edu

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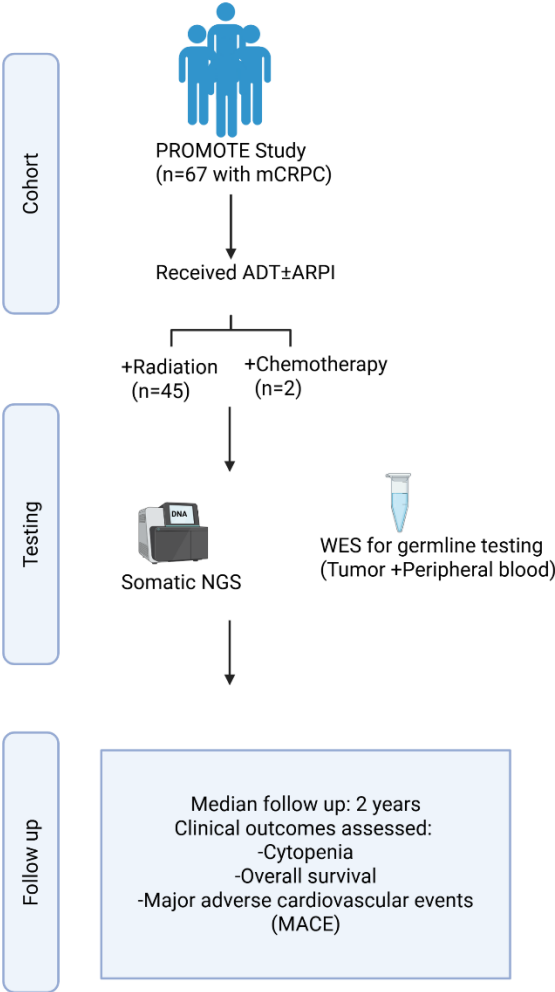
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# Inherited DNA Repair Variants are Associated with Clonal Hematopoiesis and Cardiovascular Risk in Men with Metastatic Prostate Cancer

## A. Supplementary figures

Figure S1



## B. Supplementary Tables

**Table S1- Somatic Clonal Hematopoiesis Variants**

Gene	Variant (cDNA)	Protein change	Variant Allele Frequency
ARID1A	c.2471_2472insG	S825Qfs*47	1.13%
ASXL1	c.1934dup	G646Wfs*12	1.85%
ASXL1	c.1934dup	G646Wfs*12	2.91%
ASXL1	c.2477del	G826Efs*12	3.72%
ASXL1	c.1934dup	G646Wfs*12	0.58%
ASXL1	c.2528_2529dup	T844*	0.72%
ASXL1	c.2898_2900del	G967del	44.20%
ASXL1	c.4196dup	L1399Ffs*25	0.55%
ASXL1	c.2618_2621dup	M875Sfs*6	0.80%
ASXL1	c.1934dup	G646Wfs*12	0.77%
ASXL1	c.1934dup	G646Wfs*12	23.20%
ATM	c.3285-1G>T	splice effect	1.59%
ATM	c.8494C>T	R2832C	1.72%
ATM	c.1470delT	T491Pfs*5	1.25%
ATM	c.2251-10T>G	c.2251-10T>G	37.90%
ATM	c.2965delA	T989Lfs*3	3.94%
ATM	c.8494C>T	R2832C	1.72%
ATM	c.8584+1G>T	splice effect	2.36%
BCL10	c.136del	I46Yfs*24	0.93%
BCL10	c.136del	I46Yfs*24	0.85%
BCL10	c.88G>T	E30*	1.87%
BCOR	c.1586del	N529Tfs*60	0.67%
BCORL1	c.732_736del	V245Sfs*25	1.96%
CDKN2A	c.199G>A	G67S	50.20%
CDKN2A	c.199G>A	G67S	50.20%
CHEK2	c.395del	R132Kfs*29	0.65%
CHEK2	c.591del	V198Ffs*7	1.45%
CHEK2	c.1169A>G	Y390C	1.83%
CREBBP	c.6882del	I2295Ffs*7	0.93%
CREBBP	c.4293_4297del	Y1433Gfs*2	0.90%
DNMT3A	c.1740del	W581Gfs*70	1.00%
DNMT3A	c.1474+1dup	splice effect	1.59%
DNMT3A	c.696dup	P233Afs*20	20.80%
DNMT3A	c.2711C>T	P904L	1.80%
DNMT3A	c.1240T>C	F414L	10.30%
DNMT3A	c.1238del	G413Afs*238	1.06%
DNMT3A	c.2147T>A	V716D	3.80%

DNMT3A	c.2255_2256insA	F752Lfs*5	3.13%
DNMT3A	c.1174dup	E392Gfs*3	1.77%
DNMT3A	c.1895del	K632Sfs*19	3.95%
DNMT3A	c.2054G>A	G685E	10.40%
DNMT3A	c.2043del	M682Cfs*23	0.79%
DNMT3A	c.805dup	A269Gfs*12	4.00%
DNMT3A	c.176del	P59Rfs*13	0.74%
DNMT3A	c.1903C>T	R635W	4.40%
DNMT3B	c.1329dup	V444Rfs*8	2.38%
ETV6	c.701dupC	L235Sfs*9	8.64%
HRAS	c.37G>T	G13C	1.57%
JAK1	c.1972G>A	V658I	16.00%
JARID2	c.2563del	E855Kfs*25	0.52%
KDM5C	c.3295C>A	L1099M	2.11%
KMT2D	c.11581_11582delGC	Q3861Tfs*150	1.30%
KMT2D	c.5047G>T	E1683*	1.75%
KMT2D	c.11581_11582delGC	Q3861Tfs*150	0.55%
MED12	c.6360G>C	Q2120H	8.33%
MED12	c.5815C>T	Q1939*	1.83%
MED12	c.631G>T	G211*	1.76%
NF1	c.4747G>T	E1583*	1.59%
NF1	c.5392del	Q1798Sfs*4	1.64%
NOTCH1	c.7244_7246del	P2415del	0.54%
NOTCH1	c.7244_7246del	P2415del	0.52%
NOTCH1	c.7244_7246del	P2415del	1.04%
NOTCH1	c.7244_7246del	P2415del	0.65%
NOTCH1	c.7244_7246del	P2415del	0.97%
NOTCH1	c.7244_7246del	P2415del	0.88%
PPM1D	c.1628delC	S543Lfs*4	0.84%
PPM1D	c.1601_1602delTT	F534*	1.08%
PPM1D	c.1538delT	L513*	1.32%
PPM1D	c.1636delC	L546*	2.76%
PPM1D	c.1714C>T	R572*	8.63%
PPM1D	c.1396_1399delATAC	I466Pfs*16	0.88%
PPM1D	c.1636dupC	L546Pfs*6	1.43%
PPM1D	c.1619delA	E540Gfs*7	2.14%
PPM1D	c.1717A>T	K573*	3.11%
PPM1D	c.1403C>G	S468*	1.63%
PPM1D	c.1615delG	E539Kfs*8	1.27%
PPM1D	c.1619delA	E540Gfs*7	1.30%
PTEN	c.1027-1G>T	splice effect	1.66%
SETD2	c.6358_6382del	F2120Pfs*76	0.76%

SRSF2	c.284C>A	P95H	1.67%
SRSF2	c.284C>A	P95H	9.56%
STAG2	c.1417-1G>T	splice effect	1.91%
SUZ12	c.532G>T	E178*	2.17%
TET2	c.4832delC	S1611Ffs*5	1.88%
TET2	c.5738G>A	G1913D	2.99%
TET2	c.4287dupT	G1430Wfs*48	1.83%
TET2	c.2318_2320dupGAT	S774*	2.13%
TET2	c.4633C>T	Q1545*	2.23%
TET2	c.3595-1G>T	splice effect	3.70%
TET2	c.4060dupA	R1354Kfs*47	0.59%
TET2	c.2716dupA	M906Nfs*18	0.92%
TET2	c.1965delA	K655Nfs*45	0.51%
TET2	c.4519C>T	Q1507*	2.58%
TET2	c.4990delC	Q1664Kfs*31	40.80%
TET2	c.3409+1G>A	splice effect	2.06%
TET2	c.3873G>A	W1291*	1.72%
TET2	c.1648C>T	R550*	1.76%
TET2	c.936_937delTA	T313Lfs*17	0.61%
TET2	c.5131delA	I1711Lfs*8	0.63%
TET2	c.685delA	T229Hfs*21	2.02%
TET3	c.3142G>T	E1048*	1.56%
TP53	c.818G>A	R273H	3.19%
TP53	c.646G>A	V216M	3.58%
U2AF1	c.101C>T	S34F	7.41%
U2AF1	c.470A>C	Q157P	1.57%
U2AF1	c.101C>T	S34F	2.42%
U2AF1	c.101C>T	S34F	3.05%
ZRSR2	c.399G>T	E133D	4.35%

**Table S2- Pathogenic and Likely Pathogenic Germline Variants**

<b>Chromosome</b>	<b>Coordinates</b>	<b>Ref&gt;Alt</b>	<b>AA change</b>	<b>Effect</b>	<b>Clinical significance</b>	<b>Gene</b>
17	7578403	C>A	C165F	Non-synonymous	Likely Pathogenic	<i>TP53</i>
17	7578478	G>C	P140R	Non-synonymous	Likely Pathogenic	<i>TP53</i>
11	108143541	TC>T	.	Frameshift	Pathogenic	<i>ATM</i>
11	108143539	T>TA	.	Frameshift	Pathogenic	<i>ATM</i>
11	108218004	A>G	.	Splice site	Pathogenic	<i>ATM</i>
11	108236062	CAG>C	.	Frameshift	Pathogenic	<i>ATM</i>
13	32900280	TAA>T	.	Frameshift	Pathogenic	<i>BRCA2</i>
13	32911442	G>GA	.	Frameshift	Pathogenic	<i>BRCA2</i>
13	32914935	C>CT	.	Frameshift	Pathogenic	<i>BRCA2</i>
13	32971044	ATACT>A	.	Frameshift	Pathogenic	<i>BRCA2</i>
17	7578212	G>A	R120*	Stop gained	Pathogenic	<i>TP53</i>
17	7579393	AG>A	.	Frameshift	Pathogenic	<i>TP53</i>
3	142226847	G>A	R1589*	Stop gained	Pathogenic	<i>ATR</i>

**Supplementary Figure Legend:**

**Figure S1:** Overview of Prostate Cancer Medically Optimized Genome Enhanced Therapy (PROMOTE) Study