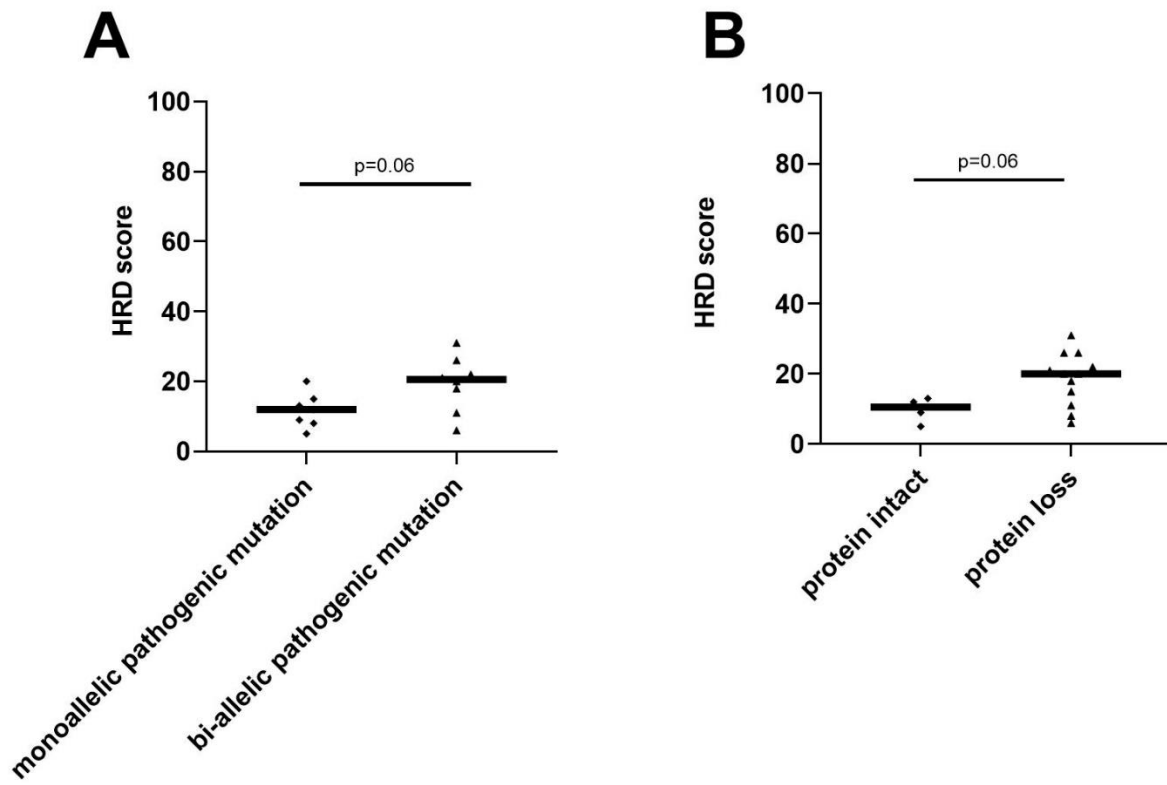


Supplementary Figure S1: HRD scores in JHU germline *BRCA2*-mutated cases by monoallelic vs bi-allelic mutation status.

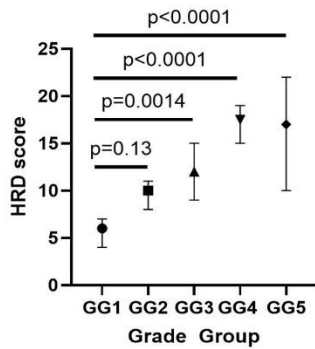


Supplementary Figure S2: (A) HRD scores in JHU germline *ATM*-mutated cases by monoallelic vs bi-allelic mutation status. (B) HRD scores in JHU germline *ATM*-mutated cases by protein status on immunohistochemistry.

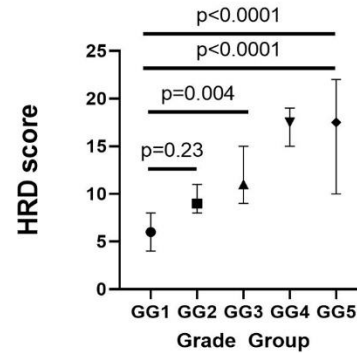
### Whole TCGA cohort

### TCGA without HR gene and TP53 mutant cases

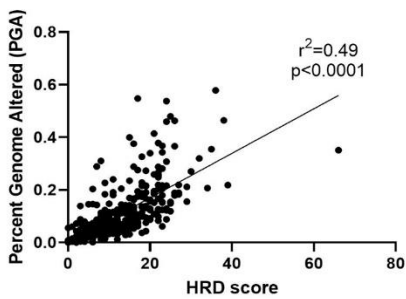
**A**



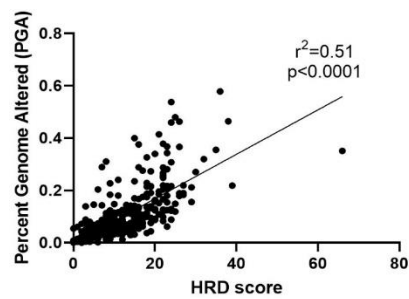
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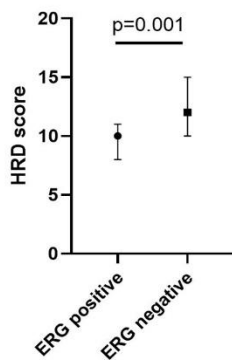
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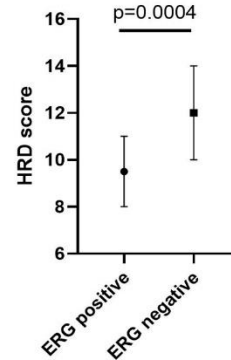
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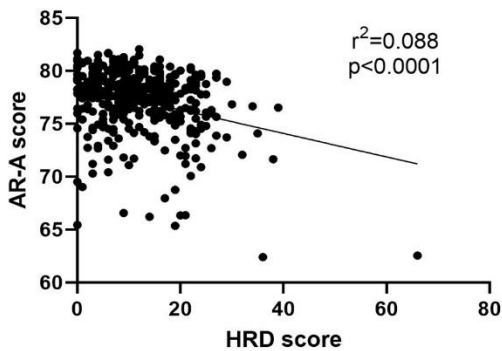
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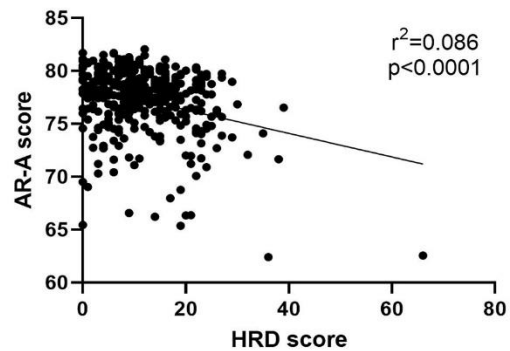
**F**



**G**

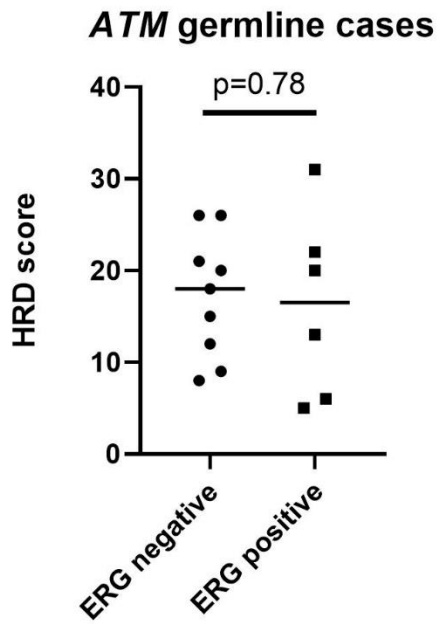
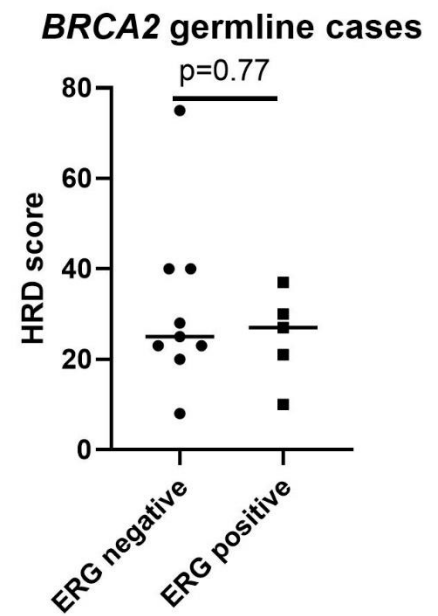


**H**



### Supplementary Figure S3: Association of HRD score with pathologic and molecular features.

(A,B) Association of HRD score with Gleason Grade Group in TCGA cohort; (C,D) Association of HRD score with percent genome altered in TCGA cohort; (E,F): Association of HRD score with *ERG* fusion status in TCGA cohort; (G,H) Association of HRD score with Androgen Receptor Activity (AR-A) score in TCGA cohort.

**A****B**

**Supplementary Figure S4: Association of ERG status with HRD score.** (A) Association of *ERG* status by immunohistochemistry with HRD score among JHU ATM germline mutated primary prostate tumors; (B) Association of *ERG* status by immunohistochemistry with HRD score among *BRCA2* germline mutated primary prostate cancers.

**Supp Table S1: Clinical-pathologic and molecular features of primary prostate tumors with germline *BRCA2* mutations**

ID	germline <i>BRCA2</i> mutation	Germline?	<i>BRCA2</i> mutation from tumor sequencing	LOH	Presumed biallelic?	age	Race	Gleason (Primary)	Gleason (Secondary)	Gleason (Sum)	Pathologic Stage	Myriad HRD
BRCA19	p.L2357Vfs*2	Germline inferred	p.L2357Vfs*2+Uncharacterized Large Rearrangement	Uncertain	Yes	56	W	5	4	9	T3bN0	failed
BRCA2	p.Y2215fs*13	Germline inferred	p.Y2215Sfs*13	No	No	63	W	5	4	9	T3bN0	27
BRCA9	p.S2670L	germline	p.S2670L	No	No	45	B	4	4	8	T2xN0	23
BRCA14	p.I2627F	germline	p.I2627F	No	No	62	W	4	3	7	T2N0	23
BRCA17	S1982R fs*22	germline	p.S1982Rfs*22	No	No	48	W	4	5	9	T3bN1	8
BRCA3	p.Y1710Vfs	germline	failed	failed	Uncertain	50	W	5	4	9	T3aN0	failed
BRCA12	p.S1982R fs*22	germline	not sent	not sent	Uncertain	61	W	4	5	9	T3aN0	not sent
BRCA1	p.V2263Efs*10	germline	p.V2263Efs*10	Yes	Yes	58	B	4	5	9	T3bN1	20
BRCA4	p.T1325fs*6	germline	p.A1327Cfs*4	Yes	Yes	66	W	3	3	6	T2N0	25
BRCA7	p.T1388Nfs*22	germline	p.N1049Pfs*4+p.L1390Wfs*20	Uncertain	Yes	71	W	ductal			T2N0	75
BRCA8	p.E3111*	germline	p.Q2501*+p.E3111*	Uncertain	Yes	50	W	5	4	9	T2xnN0	28
BRCA10	p.D3095E	germline	p.D3095E	Yes	Yes	52	W	4	5	9	T3bN1	21
BRCA11	p.A938P fs*21	germline	p.A938Pfs*21	Yes	Yes	58	W	4	5	9	T3bN0	40
BRCA13	p.I605Yfs*9	germline	p.I605Yfs*9	Yes	Yes	40	A	4	5	9	T3bN0	30
BRCA15	p.N319Kfs*8	germline	p.N319Kfs*8	Yes	Yes	68	A	5	4	9	T2N0	40
BRCA16	p.W1692M fs*3	germline	p.W1692Mfs*3	Yes	Yes	59	W	3	4	7	T3aN0	10
BRCA6	p.V1681Efs*7	germline inferred	p.V1681Efs*7	Yes	Yes	51	W	5	4	9	T3bN1	37

**Supp Table S2: Clinical-Pathologic and molecular features of primary prostate tumors with germline *ATM* mutation**

ID	<i>ATM</i> Mutation from germline sequencing	<i>ATM</i> mutation from tumor sequencing	Myriad-LOH	Presumed bi-allelic?	<i>ATM</i> IHC	Age	Race	Gleason (Primary)	Gleason (Secondary)	Gleason (Sum)	Pathologic Stage	Myriad HRD
ATM4	p.R2598*	p.R2598*	No	No	Intact	69	W	4	5	9	T3AN0MX	13
ATM9	p.R2546_S2548del	p.R2547_S2549del	No	No	Intact	49	W	4	5	9	T3AN0MX	5
ATM17	p.S274fs*	p.L275*	No	No	Intact	47	W	4	5	9	T2N0MX	12
ATM22	p.S160Afs*23	p.S160Afs*23	No	No	Intact	65	W	4	5	9	T3BN1MX	9
ATM11	p.K750K	p.K750K+p.A1272N (VUS)	No	No	Heterogeneous Loss	63	W	4	4	8	T2N0MX	8
ATM6	p.L2005fs*13	p.Q2007Rfs*11 + p.W3055C (VUS)	No	No	Loss	74	W	4	5	9	T3AN1MX	20
ATM13	p.S1905fs*25	p.S1905fs*25	No	No	Loss	44	W	4	3	7	T3BN0MX	15
ATM5	c.8988-1G>A	c.8988-1G>A	Yes	Yes	Heterogeneous Loss	53	W	4	5	9	T3AN0MX	20
ATM3	p.D2795fs*8	p.F2799Kfs*4	Yes	Yes	Loss	64	W	5	4	9	T2N0MX	6
ATM10	p.K750K	p.K750K	Yes	Yes	Loss	64	W	4	4	8	T2N0MX	31
ATM12	Duplication exon 48	Uncharacterized large rearrangement + p.I2356Vfs*2	Uncertain	Yes	Loss	55	W	4	5	9	T3BN0MX	18
ATM15	p.K2756*	p.K2756* + del exons 33-62	No	Yes	Loss	61	W	5	4	9	T3BN1MX	22
ATM20	p.L1107*	p.L1107*	Yes	Yes	Loss	60	W	4	3	7	T2N0MX	26
ATM16	p.N845fs*2	p.N845fs*2	Yes	Yes	Loss	69	W	5	4	9	T3AN0MX	21
ATM28	p.R447X* + del exons 1-32	p.R447* + del exons 1-32	No	Yes	Loss	65	W	4	5	9	T3BN1MX	11
ATM21	c.7629 +2 T>C	c.7629+2T>C	ND	Uncertain	Intact	60	W	3	4	7	T3AN0MX	failed
ATM1	p.T452fs*21	p.T452Nfs*21	Uncertain	Uncertain	Heterogeneous Loss	52	W	3	3	6	T2N0MX	failed
ATM18	p.K2756*	p.K2756*	Uncertain	Uncertain	Loss	54	W	4	3	7	T3AN0MX	failed
ATM8	p.G1458fs*15	p.G1458Qfs*15	Uncertain	Uncertain	Loss	75	W	4	5	9	T3AN0MX	26
ATM14	c.8786+1G>A	c.8786+1G>A	Uncertain	Uncertain	Loss	50	W	4	5	9	T3AN0MX	failed
ATM19	p.K2589*	p.K2589*	Uncertain	Uncertain	Loss	55	W	5	4	9	T3BN0MX	failed

**Supp Table S3: Clinical-pathologic and molecular features of primary prostate tumors with inferred somatic *ATM* mutation and protein loss**

ID	<i>ATM</i> mutation from tumor sequencing	Inferred germline or somatic	LOH	Presumed bi-allelic?	<i>ATM</i> IHC	Age	Race	Gleason (Primary)	Gleason (Secondary)	Gleason (Sum)	Pathologic Stage	Myriad HRD
ATM33	p.Q513*	indeterminate	Uncertain	Uncertain	Heterogeneous Loss	58	W	3	4	7	T2N0MX	11
ATM40	Complex Large Rearrangement+ p.V2766K (VUS)	somatic	No	No	Heterogeneous Loss	55	W	4	3	7	T3AN0MX	20
ATM37	p.Q2220Rfs*15	somatic	No	No	Heterogeneous Loss	59	W	4	4	8	T2N0MX	21
ATM38	c.185+1G>A	somatic	Yes	Yes	Heterogeneous Loss	56	W	4	4	8	T3BN0MX	11
ATM39	p.Q893*	somatic	Yes	Yes	Heterogeneous Loss	67	W	4	4	8	T3BN0MX	20
ATM32	Uncharacterized Large Rearrangement	somatic	Yes	Yes	Heterogeneous Loss	67	W	4	5	9	T3AN0MX	19
ATM23	p.Q1361*	somatic	Uncertain	Uncertain	Loss	57	W	4	5	9	T3BN0MX	25
ATM24	p.S743*	somatic	Uncertain	Uncertain	Loss	59	W	4	5	9	T3BN0MX	failed
ATM30	~28bp indel that takes out the exon 11/intron 11 splice boundary	somatic	yes	Yes	loss			5	4	9	T3AN0MX	20
ATM31	p.H2195Qfs*5	somatic	yes	Yes	loss			5	4	9	T3AN0MX	15
ATM25	p.L1722Rfs*25+ c.2124+1G>A	somatic	No	Yes	Loss	71	W	3	4	7	T3BN0MX	17

**Supp Table S4: Clinical-pathologic and molecular features of primary prostate tumors with germline *CHEK2* mutations**

ID	<i>CHEK2</i> mutation from germline sequencing	<i>CHEK2</i> mutation from tumor sequencing	Category	LOH	age	Race	Gleason (Primary)	Gleason (Secondary)	Gleason (Sum)	Pathologic Stage	Myriad HRD
CHEK4	p.T367Mfs*15	p.Thr367Metfs*15	Deleterious	0	60	W	5	4	9	T3AN0MX	9
CHEK8	p.T367Mfs*15	p.Thr367Metfs*15	Deleterious	0	62	W	4	5	9	T3BN0MX	FAILED
CHEK11	p.T367Mfs*15	p.Thr367Metfs*15	Deleterious	0	52	W	3	3	6	T2N0MX	9
CHEK16	p.T367Mfs*15	p.Thr367Metfs*15	Deleterious	0	66	W	4	4	8	T3BN0MX	11
CHEK18	p.R519X*	p.Arg519*	Deleterious	0	54	O	5	4	9	T3AN0MX	20
CHEK19	p.T367Mfs*15	p.Thr367Metfs*15	Deleterious	0	60	W	3	3	6	T2N0MX	4
CHEK7	c.1095 +1 G>T	c.1095+1G>T	Deleterious	0	49	W	4	5	9	T3BN0MX	7
CHEK10	p.T476M	No_deleterious variants detected	Suspected deleterious	0	59	W	4	5	9	T3AN0MX	23
CHEK2	p.S428F	p.Ser428Phe	Suspected deleterious	0	68	W	3	3	6	T2N0MX	4
CHEK3	p.R181C	p.Arg181Cys	Suspected deleterious	0	65	W	3	3	6	T2N0MX	FAILED
CHEK6	p.S428F	p.Ser428Phe	Suspected deleterious	0	63	W	4	4	8	T3AN0MX	13
CHEK12	p.S428F	p.Ser428Phe	Suspected deleterious	0	46	W	3	3	6	T2N0MX	1
CHEK13	p.S428F	p.Ser428Phe	Suspected deleterious	0	64	W	3	3	6	T2N0MX	24
CHEK14	p.S428F	p.Ser428Phe	Suspected deleterious	0	66	W	3	5	8	T3bN1MX	4
CHEK17	p.I157T	p.Ile157Thr	Suspected deleterious	0	58	W	4	4	8	T3AN0MX	5



**Supp Table S5: Clinical-pathologic characteristics of the 8 patients with *BRCA2*-altered prostate cancer with evaluable HRD scores and who underwent treatment with olaparib**

<b>Characteristic</b>	<b>Summary</b>
Age, yr Median	58 yr
Race White, % Non-white, %	63% 37%
Gleason sum 7-8 (grade group 3-4), % 9-10 (grade group 5), %	63% 37%
PSA at start of olaparib, ng/mL Median	19.4 ng/mL
Prior abiraterone Percentage	88%
Prior enzalutamide Percentage	75%
Prior taxane chemotherapy Percentage	63%
Number of prior systemic therapies Median	4
Presence of bone metastases Percentage	88%
Presence of visceral metastases Percentage	37%
Presence of pain Percentage	25%
ECOG performance status 0 1-2	50% 50%