Supplementary Information for:

Hypothesis Driven Single Nucleotide Polymorphism Search (HyDn-SNP-S)

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Table 1: Statistical results from applying HyDn SNPS to four cancer phenotypes

Breast cancer				Prostate cancer				Lung cancer				Melanoma cancer			
Genotypic genetic model															
SNP	**Gene**	**p.value**	**Location**	**SNP**	**Gene**	**p.value**	**Location**	**SNP**	**Gene**	**p.value**	**Location**	**SNP**	**Gene**	**p.value**	**Location**
rs1292504	POLD3	0.006	5' UTR	rs10898995	POLD3	0.045	5' UTR	rs675450	POLD3	0.002	5' UTR	rs2908280	POLD2	0.021	intron
rs524051	POLN	0.047	intron	rs2351000	POLG	0.024	intron	rs1787091	POLD3	0.024	5' UTR	rs1945132	POLD3	0.022	3' UTR
rs3218651	POLQ	0.023	H1201R	rs3218651	POLQ	0.018	H1201R	rs645541	POLD3	0.019	5' UTR	rs1638566	POLD4	0.003	intron
								rs676537	POLD3	0.016	5' UTR	rs2514258	POLD4	0.005	intron
								rs10793091	POLD3	0.013	5' UTR	rs7951732	POLD4	0.013	intron
								rs10793092	POLD3	0.007	5' UTR	rs1790735	POLD4	0.002	intron
								rs1433972	POLD3	0.031	5' UTR	rs41549716	POLG	0.02	Y831C
								rs7113533	POLD3	0.031	5' UTR	rs3135056	POLN	0.039	intron
								rs7943085	POLD3	0.016	intron	rs1745335	POLN	0.029	intron
								rs10793095	POLD3	0.002	3' UTR	rs487848	POLQ	0.006	A581V
								rs3176175	POLG	0.013	intron	rs532411	POLQ	0.005	A2304V
								rs758130	POLG	0	intron	rs3218634	POLQ	0.004	L2538V/L2538F
								rs6793252	POLQ	0.019	intron	rs702019	POLQ	0.045	intron
Recessive genetic model															
SNP	**Gene**	**p.value**	**Location**	**SNP**	**Gene**	**p.value**	**Location**	**SNP**	**Gene**	**p.value**	**Location**	**SNP**	**Gene**	**p.value**	**Location**
rs7113533	POLD3	0.05	5' UTR	rs10898995	POLD3	0.022	5' UTR	rs675450	POLD3	0.008	5' UTR	rs2908280	POLD2	0.007	intron
rs7932922	POLD3	0.038	3' UTR	rs1292504	POLD3	0.03	5' UTR	rs663016	POLD3	0.041	5' UTR	rs2887046	POLD3	0.028	no data
rs9328764	POLN	0.023	R425C	rs1638566	POLD4	0.033	intron	rs674306	POLD3	0.041	5' UTR	rs1945132	POLD3	0.022	no data
rs6830513	POLN	0.021	T378T	rs8305	POLI	0.044	A731T	rs10793091	POLD3	0.007	5' UTR	rs1638566	POLD4	0.017	intron
rs10011549	POLN	0.036	G336S	rs3218651	POLQ	0.02	H1201R	rs1433972	POLD3	0.008	5' UTR	rs2514258	POLD4	0.023	intron
rs10018786	POLN	0.033	M310L					rs7943085	POLD3	0.019	intron	rs7951732	POLD4	0.013	intron
rs3117813	POLN	0.041	intron					rs10793095	POLD3	0.004	3' UTR	rs1790735	POLD4	0.025	intron
rs3117816	POLN	0.035	intron					rs6592579	POLD3	0.041	3' UTR	rs41549716	POLG	0.02	Y831C

rs3117819	POLN	0.042	intron					rs10219168	POLD3	0.041	3' UTR	rs6941583	POLH	0.041	M647L
rs524051	POLN	0.015	intron					rs3176175	POLG	0.013	intron	rs6899628	POLH	0.039	3-UTR
rs1745335	POLN	0.049	intron					rs758130	POLG	0.008	intron	rs3734690	POLH	0.028	T478T
rs529966	POLN	0.042	intron					rs6793252	POLQ	0.019	intron	rs4640970	POLM	0.045	intron
rs618262	POLN	0.034	intron									rs3135056	POLN	0.025	intron
rs7659386	POLN	0.029	intron									rs6800901	POLQ	0.018	intron
rs3218651	POLQ	0.006	H1201R									rs5744990	POLE	0.036	L1903L

Additive genetic model

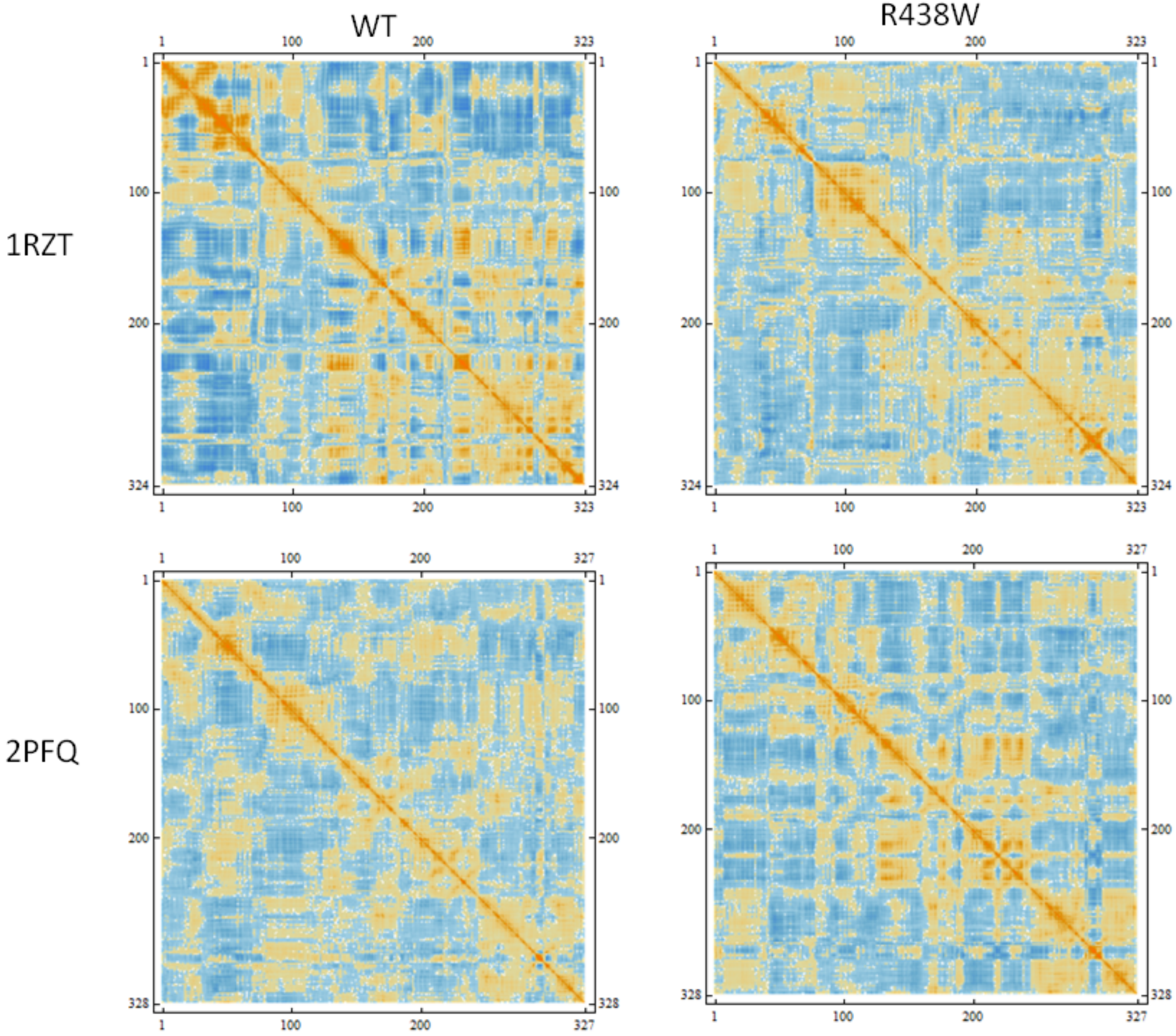
SNP	**Gene**	**p.value**	**Location**	**SNP**	**Gene**	**p.value**	**Location**	**SNP**	**Gene**	**p.value**	**Location**	**SNP**	**Gene**	**p.value**	**Location**
rs7113533	POLD3	0.023	5' UTR	rs2075070	POLD2	0.037	intron	rs10793091	POLD3	0.028	5' UTR	rs1945132	POLD3	0.022	intron
rs9328764	POLN	0.018	R425C	rs10898995	POLD3	0.014	5' UTR	rs10793092	POLD3	0.007	5' UTR	rs7951732	POLD4	0.013	intron
rs6830513	POLN	0.016	T378T	rs1292504	POLD3	0.035	5' UTR	rs1433972	POLD3	0.008	5' UTR	rs41549716	POLG	0.02	Y831C
rs10011549	POLN	0.027	G336S	rs1638566	POLD4	0.044	intron	rs7943085	POLD3	0.004	intron	rs6941583	POLH	0.045	M647L
rs10018786	POLN	0.026	M310L	rs2351000	POLG	0.033	intron	rs6592581	POLD3	0.024	3' UTR	rs6899628	POLH	0.043	3-UTR
rs3117813	POLN	0.041	intron					rs3176175	POLG	0.013	intron	rs3734690	POLH	0.031	T478T
rs1923775	POLN	0.019	intron					rs6793252	POLQ	0.019	intron	rs3135056	POLN	0.046	intron
rs524051	POLN	0.025	intron					rs574316	POLN	0.041	intron	rs6800901	POLQ	0.037	intron
rs1745335	POLN	0.038	intron									rs702019	POLQ	0.018	intron
rs529966	POLN	0.032	intron									rs5744990	POLE	0.031	L1903L
rs618262	POLN	0.027	intron												
rs7659386	POLN	0.022	intron												
rs6599418	POLN	0.046	intron												
rs3218651	POLQ	0.007	H1201R												
rs3730463	POLL	0.047	T221P												

Dominant genetic model

SNP	**Gene**	**p.value**		**SNP**	**Gene**	**p.value**		**SNP**	**Gene**	**p.value**		**SNP**	**Gene**	**p.value**	
rs1292504	POLD3	0.002	5' UTR	rs1673041	POLD1	0.029	intron	rs675450	POLD3	0.019	5' UTR	rs1638566	POLD4	0.049	intron
rs3730814	POLI	0.037	intron	rs2075070	POLD2	0.042	intron	rs1787091	POLD3	0.019	5' UTR	rs2514258	POLD4	0.049	intron
rs1923775	POLN	0.049	intron	rs3824999	POLD3	0.018	intron	rs645541	POLD3	0.008	5' UTR	rs1790735	POLD4	0.012	5' UTR
rs3821367	POLQ	0.018	intron	rs2351000	POLG	0.014	intron	rs663555	POLD3	0.041	5' UTR	rs3218784	POLI	0.041	I261M
rs3911713	POLQ	0.047	intron	rs1427463	POLG2	0.018	A169T	rs676537	POLD3	0.019	5' UTR	rs9328764	POLN	0.03	R425C
				rs607877	POLI	0.032	intron	rs10793092	POLD3	0.002	5' UTR	rs6830513	POLN	0.03	T378T
								rs7113533	POLD3	0.041	5' UTR	rs10011549	POLN	0.03	G336S
								rs7943085	POLD3	0.041	intron	rs10018786	POLN	0.03	M310L

							rs10793095	POLD3	0.041	3' UTR	rs2022302	POLN	0.03	H441H
							rs758130	POLG	0	intron	rs1745335	POLN	0.009	intron
											rs487848	POLQ	0.008	A581V
											rs532411	POLQ	0.008	A2304V
											rs3218634	POLQ	0.008	L2538V/L2538
											rs702019	POLQ	0.035	intron

Figure S1: Correlation plots from the four Polymerase Lambda simulations, these original correlation plots were used to generate the difference plots shown in Figure 4.



Movie S1: An animation of a mathematical interpolation between the binary and ternary conformations is shown, Loop 1 is colored purple, and the site of mutation R438 is shown in red and labeled. Within the conformational space available to Loop 1 visualized by this interpolation, the mutation is between 12Å and 14Å away.