Table S1. List of nsSNPs predicted by various *in silico* methods in *RET* gene.

SNP	Variant	SIFT	PolyPhen 2	I Mutant 3 0	SNAP	Align GVGD			Ref
						GV	GD	Prediction	
VAR_009459	P20L	0 25	0 799	Decrease	N	353 86	0	Class C0	[1]
rs76764689	S32L	0 13	0 245	increase	N N	208 55	106 06	Class C0	[2]
VAR_009492	L40P	0 00	1 00	Decrease	N N	0	97 78	Class C65	[2][3]
rs145633958	L56M	0 23	0 558	Decrease	N	234 72	12 95	Class C0	
rs77596424	P64L	0 06	0 95	increase	N N	99 13	1 7	Class C0	[4]
VAR_018153	R67H	0 54	0 002	Decrease	N	28 82	0	Class C0	[5]
rs142641173	T75M	0 10	0 991	Increase	N N	123 92	20 52	Class C0	
VAR_009460	R77C	0 18	1 000	increase	N N	28 82	169 74	Class C45	[6]
rs141679950	I88V	0 08	0 006	Increase	N N	28 68	0	Class C0	
VAR_006297	G93S	0 07	1 000	Decrease	N N	0	55 27	Class C55	[1]
rs201244749	D102N	0 01	0 007	Decrease	N N	0	23 01	Class C15	
rs76397662	R114H	0 09	0 001	Decrease	N N	125 13	4 81	Class C0	[7][5][8]
rs138265837	R133H	0 12	0 965	Decrease	N	0	28 82	Class C25	
VAR_006298	C142S	0 39	0 225	Decrease	N N	0	111 67	Class C65	
VAR_035711	V145G	0 00	0 009	Decrease	N N	0	109 55	Class C65	[9][8]
rs150261092	N151S	0 42	0 504	Decrease	N N	0	46 24	Class C45	
VAR_067102	P155L	0 09	0 921	Decrease	N N	0	97 78	Class C65	[8]
rs149403911	R163N	0 04	0 759	Decrease	N N	42 81	45 75	Class C0	[10]
rs200547906	T170I	0 14	0 213	Increase	N N	116 8	69 06	Class C0	
VAR_009462	F174S	0 14	0 964	Decrease	N N	0	154 81	Class C65	[11]
VAR_067103	R175P	0 10	0 999	Increase	N N	0	102 71	Class C65	[8]
VAR_009463	R180P	0 14	0 983	Increase	N N	26	96 53	Class C35	[12]
rs144801580	G183D	0 07	1 000	Decrease	N N	0	93 77	Class C65	

VAR_009464	C197Y	0 21	1 000	Decrease	N N	0	193 72	Class C65	[11]
rs76736111	P198T	0 03	0 877	Increases	N N	102 71	21 98	Class C0	[13]
rs79661516	R231H	0 38	0 998	Decrease	N N	0	28 82	Class C25	
rs112448213	C243S	0 00	0 023	Decrease	N N	99 13	1 7	Class C0	
rs145970248	T244I	0 24	0 018	Decrease	N N	109 43	0	Class C0	
rs61843232	A247D	0 62	0 000	Decrease	N	123 92	61 5	Class C0	
VAR_006300	E251K	0 37	0 004	Decrease	N N	140 23	0	Class C0	
rs139790943	V262A	0 04	0 676	Decrease	N	0	65 28	Class C65	
rs143209223	G275V	0 11	0 215	Increase	N N	109 55	0	Class C0	
rs139213499	V276I	0 23	0 001	Decrease	N	153 13	0	Class C0	
rs35118262	T278N	0 25	0 001	Decrease	N N	57 75	38 84	Class C0	[13][8]
rs34682185	V292M	0 01	1 000	Increase	N	42 81	101 29	Class C25	[14][8]
VAR_067106	D300N	0 23	1 000	Decrease	N	0	23 01	Class C15	[8]
rs77702891	R313N	0 13	0 795	Increase	N	0	85 11	Class C65	
VAR_067107	S316I	0 30	0 736	Decrease	N	82 67	97 31	Class C15	[8]
rs80236571	R330Q	0 21	0 917	Decrease	N N	0	85 11	Class C65	[8]
rs144981275	N336L	0 27	0 036	Decrease	N	0	152 33	Class C65	
VAR_067108	S339L	0 69	0 001	Decrease	N	162 52	0	Class C0	[8]
rs200641186	V347A	0 17	0 862	Decrease	N	0	65 28	Class C65	
VAR_009466	N359K	0 98	0 045	Decrease	N	0	93 88	Class C65	[14]
VAR_067110	R360Q	0 17	0 106	Decrease	N N	42 81	0	Class C0	[8]
VAR_009467	R360W	0 00	0 100	Decrease	N N	121 34	20 52	Class C0	[6][9]
rs199529397	R368H	0 11	0 150	Decrease	N	229 7	0	Class C0	
rs142338976	L375Q	0 17	1 000	Decrease	N	99 13	1 7	Class C0	
VAR_044393	V376A	0 33	0 997	Decrease	N N	0	65 28	Class C65	[8]
rs142338976	L375Q	0 17	1 00	Decrease	N	0	112 44	Class C65	

rs139813765	F381C	0 00	1 00	Decrease	N	0	204 39	Class C65	
rs115272158	A386V	0 28	0 0211	Decrease	N	130 02	35 66	Class C0	
rs78098482	F393L	0 80	0 998	Increase	N N	0	21 82	Class C15	[4]
rs183729115	V397M	0 20	0 994	Decrease	N	30 92	0	Class C0	[8]
VAR_006304	P399L	0 01	0 300	Increase	N N	0	97 78	Class C65	[2]
rs140638866	S401C	0 05	0 970	Decrease	N	91 55	104 21	Class C15	
VAR_067112	V412M	0 07	0 992	Increase	N	0	20 52	Class C15	[8]
rs201030628	R417H	1 00	0 002	Decrease	N	28 82	0	Class C0	
VAR_067113	G423R	0 41	0 999	Decrease	N N	0	125 13	Class C65	[8]
rs202053997	C430T	0 39	0 991	Decrease	N N	0	148 93	Class C65	
VAR_018155	A432E	1 00	0 233	Increase	N N	106 71	0	Class C0	[5]
rs115423919	G446R	0 45	0 756	Increase	N N	55 27	95 76	Class C25	
rs151148041	L452I	0 21	0 038	Decrease	N	0	4 86	Class C0	
rs145966037	V455I	0 41	0 000	Decrease	N	96 19	0	Class C0	
rs200334340	V467L	0 06	0 997	Decrease	N	0	30 92	Class C25	
rs138624658	R475Q	0 43	0 134	Decrease	N N	0	42 81	Class C35	
rs60881724	D489N	0 18	0 003	Decrease	N	152 22	0	Class C0	
rs9282834	D489N	0 18	0 003	Decrease	N	152 22	0	Class C0	[5][13]
rs201745826	A510V	0 19	0 0075	Decrease	N	26 87	63 12	Class C25	
rs199572076	L501V	1 00	0 001	Increase	N	30 92	0	Class C0	
rs201553718	E511K	0 39	0 181	Decrease	N	0	56 87	Class C55	
rs149238501	A513G	0 37	0 292	Decrease	N	70 56	39 93	Class C0	
rs75873440	G533C	0 00	1 000	Decrease	N N	0	158 23	Class C65	
rs148406803	T538R	0 53	0 756	Decrease	N	57 75	67 34	Class C15	
rs200047805	N554S	0 18	0 994	Decrease	N N	0	46 24	Class C45	
rs201972250	S561R	0 01	0 756	Increase	N N	46 24	83 23	Class C25	

rs147219360	D567N	0 03	1 000	Decrease	N	0	23 01	Class C15	
rs140464432	G568S	0 53	0 456	Decrease	N	0	55 27	Class C55	
rs144455821	N579L	0 45	0 342	Decrease	N	68 35	98 69	Class C15	
VAR_035712	G593E	0 06	1 000	Decrease	N N	0	97 85	Class C65	[9]
VAR_067116	E595Q	0 44	0 999	Decrease	N	0	29 27	Class C25	[8]
VAR_008966	R600Q	0 17	0 012	Decrease	N N	130 2	0	Class C0	[15]
rs199921511	Y606H	0 54	0 001	Decrease	N	101 54	0	Class C0	
rs77939446	C609T	0 03	1 000	Decrease	N N	0	148 93	Class C65	
rs77558292	C609R	0 00	1 000	Decrease	N N	0	179 53	Class C65	
rs80069458	C611T	0 00	1 00	Decrease	N N	0	148 93	Class C65	
rs79781594	C618S	0 12	0 960	Decrease	N N	204 39	64 25	Class C0	
rs76262710	C618R	0 00	0 560	Decrease	N N	204 39	80 92	Class C0	
rs79890926	C620T	0 00	0 698	Decrease	N N	0	148 93	Class C65	
rs77503355	C620S	0 01	0 765	Decrease	N N	0	111 67	Class C65	
rs77316810	C620R	0 02	0 006	Decrease	N N	0	179 53	Class C65	
VAR_006318	C620F	0 00	0 996	Decrease	N	0	204 39	Class C65	[16]
VAR_009476	Q626K	0 54	0 002	Decrease	N	0	53 23	Class C45	[17]
rs121913308	D631G	0 57	0 989	Decrease	N N	0	93 77	Class C65	
rs267607009	E632D	0 66	0 001	Decrease	N	44 6	0	Class C0	
rs267607010	L633V	0 53	0 004	Decrease	N	0	30 92	Class C25	
rs77709286	C634T	0 41	1 00	Decrease	N N	0	148 93	Class C65	
rs75996173	C634S	0 03	1 00	Increase	N N	0	111 67	Class C65	
rs75076352	C634R	0 00	1 00	Decrease	N				[18][19] [20][21]
VAR_012743	A639G	0 37	0 903	Decrease	N	58 02	29 17	Class C0	[22]
rs78935588	A640G	0 78	0 005	Decrease	N	0	60	Class C55	[23]
VAR_012744	A641G	0 29	0 216	Decrease	N	0	60	Class C55	[22]

rs77711105	V648I	0 69	0 014	Decrease	N	28 68	0	Class C0	
rs148935214	S649L	0 66	1 000	Decrease	N	0	144 08	Class C65	
rs146646971	K666N	0 06	0 999	Decrease	N N	0	93 88	Class C65	
rs3026759	N763L	0 01	0 997	Increase	N N	0	152 33	Class C65	
VAR_012744	P679L	0 80	0 998	Decrease	N	0	97 78	Class C65	[8]
rs184498773	A680T	0 11	0 403	Decrease	N N	0	58 02	Class C55	
rs141347316	P684S	0 23	0 973	Decrease	N	0	73 35	Class C65	
VAR_006331	S690P	0 25	0 002	Decrease	N	99 13	1 7	Class C0	
rs17857772	G691S	0 47	0 062	Increase	N	55 27	0	Class C0	
rs193922700	R694W	0 04	1 000	Decrease	N N	0	101 29	Class C65	
rs141185224	R694Q	0 56	0 511	Increase	N N	0	42 81	Class C35	
rs137855422	V706M	0 21	0 957	Decrease	N N	0	20 52	Class C15	
rs3026760	K710Q	0 13	0 999	Decrease	N N	0	53 23	Class C45	
rs147216744	K728Q	0 44	0 999	Decrease	N N	0	53 23	Class C45	
rs34288963	R749T	0 69	0 003	Decrease	N N	26	66 45	Class C25	
rs181856591	T754M	0 00	1 000	Decrease	N	0	81 04	Class C65	
VAR_009481	E762Q	0 04	1 000	Decrease	N	0	29 27	Class C25	[2]
rs199882293	N763I	0 00	0 996	Increase	N N	0	148 91	Class C65	
rs75075748	S765P	0 05	1 000	Decrease	N N	0	73 35	Class C65	[24]
rs78014899	E768D	0 16	0 987	Decrease	N	0	44 6	Class C35	[25][26] [27]
rs142793711	L769F	0 44	0 998	Decrease	N N	0	21 82	Class C15	
rs75686697	V778I	0 01	0 001	Decrease	N	30 92	0	Class C0	[10]
rs149148794	L790T	0 00	1 000	Increase	N	0	92 35	Class C65	
rs75030001	L790F	0 00	1 000	Increase	N N	0	21 82	Class C15	[28]
rs77724903	Y791F	0 02	0 563	Decrease	N N	0	21 61	Class C15	[12][28] [21]
rs79658334	**V804M**	**0 00**	**1 000**	**Decrease**	**N N**	**0**	**179 53**	**Class C65**	**[29][30]**

rs142318626	R817C	0 03	1 000	Increases	N N	241 31	80 92	Class C0	
rs142779213	G823Q	0 17	1 000	Decrease	N N	206 04	86 56	Class C0	
rs138847998	G823R	0 15	1 000	Decrease	N N	206 04	124 98	Class C15	
rs34617196	Y826S	0 23	0 654	Decrease	N N	247 85	48 55	Class C0	[13]
rs113005278	S829G	0 55	0 003	Decrease	N	217 79	0	Class C0	
rs200127630	G830R	0 25	0 005	Increase	N	242 52	0	Class C0	
rs147433153	N834T	0 33	0 005	Increase	N N	46 24	43 96	Class C0	
rs149891333	P841R	0 25	1 000	Increase	N N	99 13	1 7	Class C0	
rs55947360	R844L	0 06	1 000	Decrease	N N	0	43	Class C35	[30][13]
rs201101792	M848K	0 29	0 996	Increase	N N	99 13	1 7	Class C0	
rs141459368	E867D	0 40	0 996	Decrease	N N	0	44 6	Class C35	
rs145170911	V871I	0 29	0 993	Decrease	N N	0	28 68	Class C25	
VAR_006338	R873Q	0 00	1 000	Decrease	N	0	101 88	Class C65	
rs201487882	G885R	0 00	1 000	Decrease	N N	0	125 13	Class C65	
rs146838520	R886T	0 11	1 000	Decrease	N N	0	70 97	Class C65	
rs75234356	S891A	0 23	0 969	Decrease	N N	40 92	0	Class C0	[31]
VAR_044396	**G894S**	**0 00**	**1 000**	**Decrease**	**N N**	**0**	**55 27**	**Class C55**	**[10]**
rs76087194	**R897Q**	**0 00**	**1 000**	**Decrease**	**N N**	**0**	**99 13**	**Class C65**	[2][24]
rs267607011	S904C	0 05	1 000	Decrease	N N	32	0	Class C0	
rs200627072	V906M	0 09	1 000	Decrease	N N	0	20 52	Class C15	
VAR_067121	**K907T**	**0 00**	**1 000**	**Decrease**	**N N**	**0**	**77 74**	**Class C65**	[8]
rs78347871	R912L	0 00	1 000	Decrease	N N	0	101 88	Class C65	
rs74799832	**M918T**	**0 00**	**1 000**	**Decrease**	**N N**	0	81 04	Class C65	**[32][33]**
VAR_012745	**S922F**	**0 00**	**1 000**	**Decrease**	**N N**	**0**	**154 81**	**Class C65**	[22]
VAR_009487	**S922Y**	**0 00**	**1 000**	**Decrease**	**N N**	0	143 11	Class C65	**[35]**
VAR_067122	F961L	0 34	1 000	Decrease	N N	0	21 82	Class C15	[8]

rs76534745	R972G	0 01	0 572	Decrease	N N	26	120 17	Class C45	
VAR_006347	**P973L**	**0 00**	**1 000**	**Decrease**	**N N**	**0**	**97 78**	**Class C65**	[2]
VAR_006348	M980T	0 01	0 999	Decrease	N N	44	0	Class C0	
rs52803107	R982C	0 07	1 00	Decrease	N N	139 99	107 47	Class C15	
rs199718928	L994N	0 35	1 00	Decrease	N N	0	97 78	Class C65	
rs138912894	P1023L	0 18	1 00	Decrease	N N	0	23 01	Class C15	
rs200989078	D1031N	0 10	1 00	Decrease	N N	0	58 02	Class C55	
rs201740483	T1038A	0 18	1 00	Decrease	N N	99 13	1 7	Class C0	
rs200021472	T1038I	0 01	1 00	Increase	N N	0	97 78	Class C65	
rs79853121	P1039L	0 08	1 00	Decrease	N N	208 63	94 04	Class C0	[36]
VAR_044397	**P1049L**	**0 00**	**1 00**	**Decrease**	**N N**	**0**	**81 04**	**Class C65**	[10]
rs200956659	R1050Q	0 10	1 00	Decrease	N N	353 86	0	Class C0	
VAR_067123	L1052V	0 51	1 00	Decrease	N N	353 86	0	Class C0	[8]
VAR_009490	Y1062C	0 06	1 00	Decrease	N	353 86	0	Class C0	[8]
rs138010639	T1062H	0 10	Error	Decrease		353 86	0	Class C0	
VAR_009491	M1064T	0 28	0 998	Decrease	N N	353 86	0	Class C0	[8]
VAR_044398	P1067S	0 48	1 00	Decrease	N N	353 86	0	Class C0	[10]
VAR_041767	F1112Y		0 920	increase	N N	-	-	-	[13]

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Figure S1. Comparison of change in the surrounding amino acid residues of WT and mutant RET protein complex with vandetanib.

Change in the local environment of RET protein brought about by various mutations in **A)** Wild type **B)** V804M **C)** M918T **D)** S922Y. Color scheme – Vandetanib: Cyan, surrounding amino acids: Red

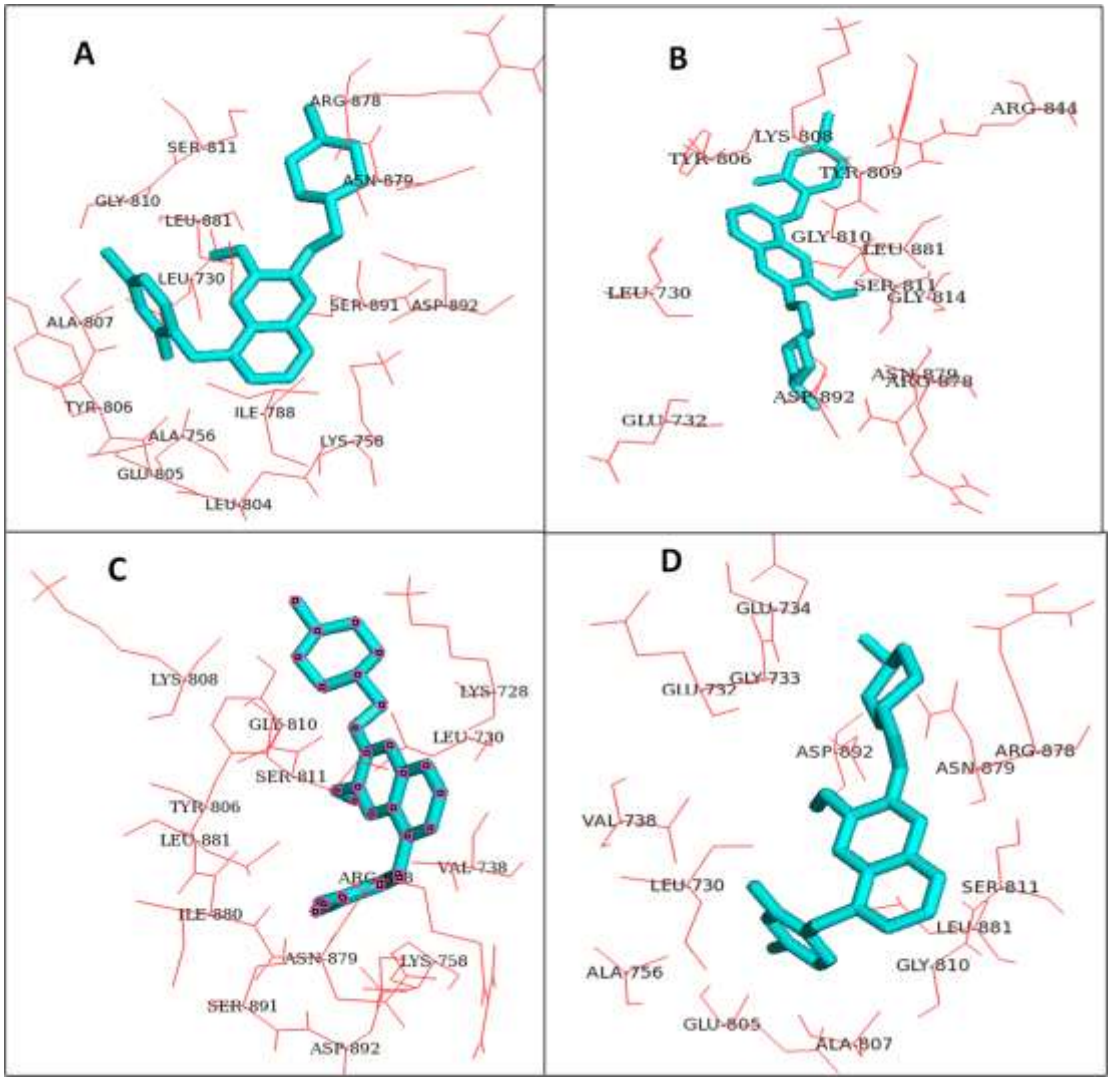

Figure S2. Overall RMSD curve of Wild type and mutant RET at 20 ns.

Two independent simulations (Black and Red) of each protein model. Time evolution of backbone RMSDs are shown as a function of time for **A)** Wild type **B)** V804M **C)** M918T **D)** S922Y.