

Supplementary Tables and Figures

Comparative Genomics Reveals Shared Mutational Landscape in Canine Hemangiosarcoma and Human Angiosarcoma

Table S1 - Canine cohort metadata

Case ID	Tissue preservation	Location	Nonsynonymous and splice site/region mutations	Sex	Age
HSA_1	fixed	liver	17	F	10
HSA_2	frozen	spleen	22	M	9
HSA_3	fixed	heart	36	F	11
HSA_4	frozen	spleen	26	F	10
HSA_5	fixed	liver	31	M	11
HSA_6	frozen	spleen	22	M	10
HSA_7	fixed	liver	18	M	6
HSA_8	fixed	heart	31	F	5
HSA_9	frozen	spleen	18	F	11
HSA_10	fixed	heart	10	F	12
HSA_11	frozen	spleen	26	M	7
HSA_12	fixed	heart	22	M	10
HSA_13	fixed	spleen	14	F	8
HSA_14	fixed	spleen	11	F	11
HSA_15	fixed	heart	25	F	15
HSA_16	frozen	spleen	38	M	10
HSA_17	frozen	heart	34	F	8
HSA_18	frozen	spleen	13	M	9
HSA_19	frozen	spleen	17	M	3
HSA_20	frozen	heart	22	M	9
HSA_21	fixed	heart	65	F	8
HSA_22	fixed	heart	35	M	12
HSA_23	frozen	spleen	5	F	11
HSA_24	fixed	liver	37	F	10
HSA_25	fixed	liver	27	M	12
HSA_26	frozen	spleen	3	F	14
HSA_27	frozen	spleen	43	F	9
HSA_28	frozen	heart	46	M	9
HSA_29	frozen	spleen	27	M	13
HSA_30	fixed	spleen	3	M	NA
HSA_31	fixed	spleen	44	M	NA
HSA_32	fixed	spleen	22	F	NA
HSA_33	fixed	spleen	7	M	NA
HSA_34	fixed	spleen	13	M	NA

HSA_35	fixed	heart	48	F	11
HSA_36	fixed	heart	16	F	9
HSA_37	fixed	heart	152	F	15
HSA_38	fixed	spleen	13	M	NA
HSA_39	fixed	heart	33	F	NA
HSA_40	fixed	heart	16	F	NA
HSA_41	frozen	heart	30	M	NA
HSA_42	fixed	liver	24	M	NA
HSA_43	fixed	spleen	46	F	NA
HSA_44	frozen	spleen	14	F	4
HSA_45	fixed	liver	23	F	5
HSA_46	fixed	liver	42	F	13
HSA_47	fixed	unknown	1	F	11

Table S2 - Canine library preparation, amplification, and complexity

Case ID	Tumor/ Normal	Sequencing depth	Input DNA	Overamplified	Tissue preservatio n	Nonsynonymous and splice site/region mutations	Library size
HSA_1	Normal	49	1000	Yes	EDTA		134561459
HSA_1	Tumor	53	1000	Yes	fixed	17	38155922
HSA_2	Normal	71	1000	Yes	EDTA		226048914
HSA_2	Tumor	91	1000	Yes	frozen	22	136254048
HSA_3	Normal	73	1000	Yes	EDTA		134978503
HSA_3	Tumor	26	1000	Yes	fixed	36	20412528
HSA_4	Normal	61	1000	Yes	EDTA		231846809
HSA_4	Tumor	99	1000	Yes	frozen	26	103917348
HSA_5	Normal	51	1000	Yes	EDTA		370312244
HSA_5	Tumor	41	1000	Yes	fixed	31	32017163
HSA_6	Normal	63	1000	Yes	EDTA		225490375
HSA_6	Tumor	84	1000	Yes	frozen	22	130755435
HSA_7	Normal	53	1000	Yes	EDTA		269484482
HSA_7	Tumor	89	1000	Yes	fixed	18	73256644
HSA_8	Normal	80	1000	Yes	EDTA		268801501
HSA_8	Tumor	75	1000	Yes	fixed	31	81740488
HSA_9	Normal	62	1000	Yes	EDTA		281443846
HSA_9	Tumor	101	1000	Yes	frozen	18	210031996
HSA_10	Normal	83	1000	No	EDTA		355514908
HSA_10	Tumor	78	1000	No	fixed	10	69807014
HSA_11	Normal	68	NA	No	EDTA		277032267
HSA_11	Tumor	126	1000	No	frozen	26	324015250

HSA_12	Normal	62	1000	Yes	EDTA		221713689
HSA_12	Tumor	55	1000	Yes	fixed	22	49450048
HSA_13	Normal	43	1000	Yes	EDTA		203071580
HSA_13	Tumor	91	1000	Yes	fixed	14	144056227
HSA_14	Normal	58	1000	Yes	EDTA		177387584
HSA_14	Tumor	61	1000	Yes	fixed	11	65437960
HSA_15	Normal	75	1000	Yes	EDTA		127216800
HSA_15	Tumor	56	1000	Yes	fixed	25	40991888
HSA_16	Normal	73	1000	Yes	EDTA		141452611
HSA_16	Tumor	56	1000	Yes	frozen	38	41118918
HSA_17	Normal	62	1000	No	EDTA		223257784
HSA_17	Tumor	114	NA	No	frozen	34	147787071
HSA_18	Normal	53	1000	Yes	EDTA		171084585
HSA_18	Tumor	78	1000	Yes	frozen	13	97513922
HSA_19	Normal	69	1000	Yes	EDTA		129594138
HSA_19	Tumor	75	1000	Yes	frozen	17	91271441
HSA_20	Normal	67	1000	Yes	EDTA		110209804
HSA_20	Tumor	91	1000	Yes	frozen	22	161197314
HSA_21	Normal	64	1000	No	EDTA		293332856
HSA_21	Tumor	144	309*	No	fixed	65	161501907
HSA_22	Normal	62	1000	Yes	EDTA		123858089
HSA_22	Tumor	57	1000	Yes	fixed	35	42916453
HSA_23	Normal	54	1000	Yes	EDTA		214634405
HSA_23	Tumor	84	1000	Yes	frozen	5	163422686
HSA_24	Normal	51	1000	Yes	EDTA		130312170
HSA_24	Tumor	56	1000	Yes	fixed	37	40995053
HSA_25	Normal	62	1000	No	EDTA		232499575
HSA_25	Tumor	46	1000	Yes	fixed	27	34254483
HSA_26	Normal	74	1000	No	EDTA		159151355
HSA_26	Tumor	93	381*	No	frozen	3	128242059
HSA_27	Normal	74	1000	Yes	EDTA		100619527
HSA_27	Tumor	96	1000	Yes	frozen	43	135472727
HSA_28	Normal	90	1000	No	EDTA		229798708
HSA_28	Tumor	109	469*	No	frozen	46	196472240
HSA_29	Normal	52	1000	No	EDTA		280852929
HSA_29	Tumor	125	425*	No	frozen	27	316081507
HSA_30	Normal	69	1000	Yes	EDTA		131692351
HSA_30	Tumor	85	1000	Yes	fixed	3	100942519
HSA_31	Normal	50	1000	Yes	EDTA		118651337
HSA_31	Tumor	75	1000	Yes	fixed	44	48558498
HSA_32	Normal	59	1000	Yes	EDTA		137223693

HSA_32	Tumor	40	1000	Yes	fixed	22	25433630
HSA_33	Normal	65	1000	Yes	EDTA		116541031
HSA_33	Tumor	54	1000	Yes	fixed	7	63455690
HSA_34	Normal	60	1000	Yes	EDTA		89817007
HSA_34	Tumor	74	1000	Yes	fixed	13	44486076
HSA_35	Normal	51	1000	No	EDTA		210786142
HSA_35	Tumor	114	295*	No	fixed	48	163041517
HSA_36	Normal	27	1000	Yes	EDTA		58556571
HSA_36	Tumor	45	1000	Yes	fixed	16	56260934
HSA_37	Normal	54	1000	No	EDTA		98731048
HSA_37	Tumor	128	871*	No	fixed	152	127593218
HSA_38	Normal	67	1000	Yes	EDTA		87139774
HSA_38	Tumor	45	1000	Yes	fixed	13	31958634
HSA_39	Normal	95	NA	No	EDTA		171064700
HSA_39	Tumor	93	355*	No	fixed	33	88831176
HSA_40	Normal	54	1000	Yes	EDTA		65023743
HSA_40	Tumor	18	1000	Yes	fixed	16	16470714
HSA_41	Normal	59	1000	No	EDTA		173375722
HSA_41	Tumor	97	480*	No	frozen	30	119131774
HSA_42	Normal	98	1000	No	EDTA		190927431
HSA_42	Tumor	108	941*	No	fixed	24	120828418
HSA_43	Normal	51	1000	Yes	EDTA		90620114
HSA_43	Tumor	158	373*	No	fixed	46	206945827
HSA_44	Normal	60	1000	Yes	EDTA		50917493
HSA_44	Tumor	42	1000	Yes	frozen	14	32736117
HSA_45	Normal	88	1000	No	EDTA		288287484
HSA_45	Tumor	108	292*	No	fixed	23	108587264
HSA_46	Normal	33	1000	Yes	EDTA		27281614
HSA_46	Tumor	40	1000	Yes	fixed	42	27533702
HSA_47	Normal	57	1000	Yes	EDTA		48624834
HSA_47	Tumor	16	1000	Yes	fixed	1	14145086

Sequencing depth, DNA input amount, whether library was overamplified, tissue preservation, number of nonsynonymous, splice site, and splice region mutations, and estimated library size (unique molecules) per library.

* estimated input amount.

Table S3 - COSMIC Cancer Gene Census genes

Gene	# samples	Gene	# samples
TP53	28	JAK1	1
PIK3CA	14	KAT6B	1
PIK3R1	4	KDM5A	1
CHD4	3	KDR	1
CACNA1D	2	KEAP1	1
LRP1B	2	KMT2A	1
MECOM	2	KMT2D	1
NRAS	2	LEF1	1
PAX3	2	MAP3K13	1
PTEN	2	MITF	1
AFF4	1	MTOR	1
AR	1	MYH11	1
ARID1A	1	MYH9	1
ATR	1	NCOR1	1
ATRX	1	NFE2L2	1
BCL9	1	NRG1	1
BRAF	1	NTRK3	1
BRCA2	1	NUP214	1
CASP8	1	PIK3CB	1
CBFA2T3	1	PLCG1	1
CDK12	1	PTPRK	1
CLTC	1	RBM10	1
CLTCL1	1	RNF213	1
DICER1	1	RNF43	1
ERBB4	1	SFRP4	1
ERC1	1	SLC34A2	1
FGFR3	1	TERT	1
FLT3	1	TMPRSS2	1
HOOK3	1	ZFHX3	1
IL6ST	1		

Genes mutated at least once in canine exome data, annotated as having likely causal somatic mutations in the COSMIC Cancer Gene Census. Significantly mutated genes in hemangiosarcoma samples bolded.

Table S4 - Summary of canine RNA-seq data

RNA-seq ID	Exome ID	Breed	Tissue	GEO ID	BioSample ID	Previously published
DHSA-0901		Golden Retriever	Spleen		SAMN12659339	No
DHSA-1001		Golden Retriever	Spleen		SAMN12659340	No
DHSA-1002_LIV	HSA_22	Golden Retriever	Liver		SAMN12659341	No
DHSA-1101	HSA_17	Golden Retriever	Heart		SAMN12659342	No
DHSA-1102	HSA_18	Golden Retriever	Spleen		SAMN12659343	No
DHSA-1204		Golden Retriever	Spleen		SAMN12659348	No
DHSA-1301		Portugese Water Dog	Spleen		SAMN12659344	No
DHSA-1302	HSA_13	Golden Retriever	Spleen		SAMN12659345	No
DHSA-1304		Mix (Labrador Retriever)	Liver		SAMN12659346	No
DHSA-1306	HSA_35	Golden Retriever	Heart		SAMN12659347	No
DHSA-1407		Golden Retriever	Heart		SAMN12659349	No
DHSA-1408		Portugese Water Dog	Spleen		SAMN12659350	No
DHSA-1409		German Shepherd Dog	Spleen		SAMN12659351	No
DHSA-1415	HSA_36	Golden Retriever	Heart		SAMN12659352	No
DHSA-1416		Mix	Spleen		SAMN12659353	No
DHSA-1423		Mix (Labrador Retriever)	Spleen		SAMN12659354	No
DHSA-1426		Golden Retriever	Spleen		SAMN12659355	No
DHSA-1434		Parsons Russell Terrier	Spleen		SAMN12659356	No
DHSA-1503		Golden Retriever	Spleen		SAMN12659357	No
DHSA-1504		Golden Retriever	Spleen		SAMN12659358	No
DHSA-1512		German Shepherd Dog	Spleen		SAMN12659359	No
DHSA-1513		German Shepherd Dog	Spleen		SAMN12659360	No
DHSA-1519		American Staffordshire Terrier	Spleen		SAMN12659361	No
CHAD-B7		Mix (Border collie)	Heart	GSM2498352	SAMN06368910	Yes
CHAD-G3		Golden Retriever	Spleen	GSM2498353	SAMN06368909	Yes
CHAD-G4	HSA_6	Golden Retriever	Spleen	GSM2498354	SAMN06368908	Yes
CHAD-G6		Golden Retriever	Spleen	GSM2498355	SAMN06368907	Yes
CHAD-G8		Golden Retriever	Spleen	GSM2498356	SAMN06368906	Yes
CHAD-P9		Portugese Water Dog	Liver	GSM2498357	SAMN06368905	Yes
DHSA-0501		Bernese Mountain Dog	Heart	GSM2498358	SAMN06368904	Yes
DHSA-0502	HSA_4	Golden Retriever	Spleen	GSM2498359	SAMN06368903	Yes
DHSA-0601		Golden Retriever	Spleen	GSM2498360	SAMN06368845	Yes
DHSA-0602	HSA_7	Golden Retriever	Spleen	GSM2498361	SAMN06368901	Yes

DHSA-0603		Portugese Water Dog	Heart	GSM2498362	SAMN06368900	Yes
DHSA-0604		Keeshond	Spleen	GSM2498363	SAMN06368899	Yes
DHSA-0605		Golden Retriever	Spleen	GSM2498364	SAMN06368898	Yes
DHSA-0606		German Shepherd Dog	Spleen	GSM2498365	SAMN06368897	Yes
DHSA-0701		Bichon Frise	Cutaneous	GSM2498366	SAMN06368896	Yes
DHSA-0702		Bullmastiff	Spleen	GSM2498367	SAMN06368895	Yes
DHSA-0803		Golden Retriever	Heart	GSM2498368	SAMN06368894	Yes
DHSA-0804	HSA_11	Golden Retriever	Omentum	GSM2498369	SAMN06368893	Yes
DHSA-0805		Golden Retriever	Spleen	GSM2498370	SAMN06368892	Yes
DHSA-0903		Golden Retriever	Spleen	GSM2498371	SAMN06368891	Yes
DHSA-0904	HSA_20	Golden Retriever	Heart	GSM2498372	SAMN06368890	Yes
DHSA-0905	HSA_21	Golden Retriever	Heart	GSM2498373	SAMN06368889	Yes
DHSA-0906	HSA_19	Golden Retriever	Spleen	GSM2498374	SAMN06368888	Yes
DHSA-0907		Portugese Water Dog	Liver	GSM2498375	SAMN06368887	Yes
DHSA-0908		Boxer	Abdominal mass	GSM2498402	SAMN06368928	Yes
DHSA-0909	HSA_24	Golden Retriever	Spleen	GSM2498376	SAMN06368886	Yes
DHSA-0910		Keeshond	Liver	GSM2498377	SAMN06368880	Yes
DHSA-1002	HSA_22	Golden Retriever	Spleen	GSM2498378	SAMN06368879	Yes
DHSA-1006		German Shepherd Dog	Spleen	GSM2498379	SAMN06368878	Yes
DHSA-1007		Gordon Setter	Spleen	GSM2498380	SAMN06368885	Yes
DHSA-1008	HSA_1	Golden Retriever	Liver	GSM2498381	SAMN06368884	Yes
DHSA-1009		German Shepherd Dog	Spleen	GSM2498382	SAMN06368883	Yes
DHSA-1010	HSA_29	Golden Retriever	Spleen	GSM2498383	SAMN06368882	Yes
DHSA-1011		Boxer	Spleen	GSM2498384	SAMN06368881	Yes
DHSA-1013		Labrador Retriever	Spleen	GSM2498385	SAMN06368877	Yes
DHSA-1014		Golden Retriever	Spleen	GSM2498386	SAMN06368876	Yes
DHSA-1015		Mix (Wolf)	Liver	GSM2498387	SAMN06368850	Yes
DHSA-1016		Golden Retriever	Heart	GSM2498388	SAMN06368849	Yes
DHSA-1017		Briard	Spleen	GSM2498389	SAMN06368848	Yes
DHSA-1103	HSA_26	Golden Retriever	Spleen	GSM2498390	SAMN06368847	Yes
DHSA-1106	HSA_27	Golden Retriever	Spleen	GSM2498391	SAMN06368846	Yes
DHSA-1107		Golden Retriever	Heart	GSM2498392	SAMN06368932	Yes
DHSA-1108		Labrador Retriever	Heart	GSM2498393	SAMN06368931	Yes
DHSA-1109	HSA_28	Golden Retriever	Heart	GSM2498394	SAMN06368856	Yes

DHSA-1110		Golden Retriever	Liver	GSM2498395	SAMN06368855	Yes
DHSA-1111		Golden Retriever	Spleen	GSM2498396	SAMN06368854	Yes
DHSA-1112		Portugese Water Dog	Spleen	GSM2498397	SAMN06368853	Yes
DHSA-1113		Saluki	Heart	GSM2498398	SAMN06368852	Yes
DHSA-1114		Golden Retriever	Spleen	GSM2498399	SAMN06368851	Yes
DHSA-1202		Golden Retriever	Spleen	GSM2498400	SAMN06368930	Yes
DHSA-1203		Mix (Labrador Retriever, Husky)	Bladder	GSM2498401	SAMN06368929	Yes

Summary of canine RNA-seq data used in this analysis. The RNA-seq ID is the ID under which the data was published, with GEO and BioSample IDs linking to each sample file. If the same dog was included in the exome dataset, the exome ID is given. In cases where the same dog was included, but different tumor locations were sequenced in the WES and RNA-seq, the Exome ID is noted in red. Fifty-one of the 74 RNA-seq samples had been previously published (1,2).

Table S5 - RNA-seq validation

Case ID	Variant	Location	Mutation	Fixed/ Frozen	VAF	Histo	ESTIMATE	Validated	A:T:C:G:N:<>+:-.*
HSA_36	chr6:10232318:ARPC1A:A:C	same	Missense	fixed	0.16	0.00	0.69	Yes	283 0:0:36:0:0:1:0:0:0
HSA_17	chr6:10238294:ARPC1A:G:A	same	Nonsense	frozen	0.17	0.20	0.53	Yes	249 8:0:0:0:0:3:0:0:0
HSA_21	chr15:8982528:ORC1:A:C	same	Missense	fixed	0.05	0.70	0.64	No	9 0:0:0:0:0:0:0:0:0
HSA_35	chr15:8982528:ORC1:A:C	same	Missense	fixed	0.08	0.50	0.71	No	16 0:0:1:0:0:0:0:0:0
HSA_18	chr34:12651933:PIK3CA:G:A	same	Missense	frozen	0.06	NA	0.53	No	9 0:0:0:0:0:0:0:0:0
HSA_4	chr34:12675674:PIK3CA:A:T	same	Missense	frozen	0.25	0.05	0.72	No	67 0:0:0:11:0:0:0:0:0
HSA_27	chr34:12675674:PIK3CA:A:G	same	Missense	frozen	0.23	0.60	0.42	No	38 0:0:0:1:0:1:0:0:0
HSA_28	chr34:12675674:PIK3CA:A:T	same	Missense	frozen	0.19	0.80	0.55	Yes	24 0:3:0:0:0:0:0:0:0
HSA_29	chr34:12675674:PIK3CA:A:G	same	Missense	frozen	0.11	0.23	0.71	Yes	29 0:0:0:11:0:0:0:0:0
HSA_36	chr34:12651893:PIK3CA:G:A	same	Missense	fixed	0.15	0.00	0.69	Yes	35 10:0:0:0:0:0:0:0:0
HSA_21	chr2:53522035:PIK3R1:A:G	same	Missense	fixed	0.17	0.70	0.64	Yes	41 0:0:0:5:0:0:0:0:0
HSA_18	chr3:21093342:RASA1:G:A	same	Nonsense	frozen	0.11	NA	0.53	No	20 0:0:0:0:0:0:0:0:0
HSA_28	chr3:21108103:RASA1:A:T	same	Nonsense	frozen	0.13	0.80	0.55	Yes	29 0:3:0:0:0:0:0:0:0
HSA_4	chr5:32563923:TP53:C:T	same	Missense	frozen	0.32	0.05	0.72	No	49 0:0:0:0:0:0:0:0:0
HSA_19	chr5:32563056:TP53:G:A	same	Missense	frozen	0.18	0.60	0.61	Yes	66 14:0:0:0:0:0:0:0:0
HSA_20	chr5:32563698:TP53:A:T	same	Missense	frozen	0.26	0.35	0.37	No	40 0:0:0:0:0:0:0:0:0
HSA_21	chr5:32563404:TP53:C:T	same	Missense	fixed	0.27	0.70	0.64	Yes	125 0:40:0:1:0:0:0:0:0
HSA_17	chr5:32563712:TP53:C:T	same	Missense	frozen	0.47	0.20	0.53	Yes	92 0:14:0:0:0:0:0:0:0
HSA_21	chr5:32564616:TP53:A:G	same	Missense	fixed	0.19	0.70	0.64	Yes	95 0:0:0:35:0:0:0:0:0
HSA_29	chr5:32563959:TP53:CCATAG:C	same	Frame shift	frozen	0.09	0.23	0.71	No	25 20:10:10:10:0:1:0:10:0
HSA_1	chr5:32561417:TP53:CG:C	same	Frame shift	fixed	0.17	0.10	0.61	No	82 0:0:0:15:0:2:0:14:0
HSA_1	chr5:32563056:TP53:G:A	same	Missense	fixed	0.07	0.10	0.61	Yes	52 14:0:0:0:0:2:0:0:0
HSA_13	chr5:32563400:TP53:C:T	same	Missense	fixed	0.42	0.80	0.64	Yes	198 0:148:0:0:0:0:0:0:0
HSA_35	chr5:32563410:TP53:A:C	same	Missense	fixed	0.19	0.50	0.71	Yes	267 0:0:106:0:0:4:0:0:0
HSA_35	chr5:32563904:TP53:T:C	same	Missense	fixed	0.32	0.50	0.71	Yes	256 0:0:83:0:0:4:0:0:0
HSA_11	chr34:12675666:PIK3CA:T:G	different	Missense	frozen	0.11	0.80	0.74	Yes	27 0:0:0:13:0:0:0:0:0
HSA_22	chr5:32563049:TP53:C:A	different-1	Missense	fixed	0.1	0.05	0.53	No	194 2:0:0:0:0:0:0:0:0
HSA_22	chr5:32563400:TP53:C:T	different-1	Missense	fixed	0.32	0.05	0.53	No	146 0:0:0:0:0:0:0:0:0
HSA_22	chr5:32563049:TP53:C:A	different-2	Missense	fixed	0.1	0.25	0.76	No	19 0:0:0:0:0:0:0:0:0
HSA_22	chr5:32563400:TP53:C:T	different-2	Missense	fixed	0.32	0.25	0.76	No	24 0:1:0:0:0:0:0:0:0
HSA_24	chr5:32563401:TP53:C:T	different	Missense	fixed	0.27	0.65	0.63	Yes	129 0:33:0:0:0:0:0:0:0
HSA_24	chr5:32563916:TP53:C:T	different	Missense	fixed	0.21	0.65	0.63	Yes	105 0:27:0:1:0:0:0:0:0
HSA_11	chr5:32564027:TP53:G:A	different	Missense	frozen	0.42	0.80	0.74	Yes	147 116:0:0:0:0:2:0:0:0

Validation of mutations found in exome cohort in the same individuals in RNA-seq data. White background - RNA-seq from same tumor location, grey background - RNA-seq from different tumor location. Grey text - frame-shift deletion excluded from validation. Histo - tumor purity based on histologic examination. ESTIMATE - tumor purity estimate based on RNA-seq data from the program ESTIMATE.

Table S6 - RNA-sequencing survey

	Golden	PWD	GSD	Mix	Boxer	Lab	Keeshond	Other	Total
<i>n</i>	22	6	6	6	2	2	2	8	54
<i>TP53</i>	6	3	1	3	0	0	1	0	14
<i>PIK3CA</i>	2	2	2	2	1	0	2	0	11
<i>PIK3R1</i>	1	1	0	0	0	1	0	1	4

Survey of specific mutations identified in the exome sequencing in SMGs in RNA-seq data from canine hemangiosarcoma tumors in 22 golden retrievers and 32 dogs from other breeds.

Table S7 - Enrichment of protein domains in hemangiosarcoma and angiosarcoma

(See Excel spreadsheet)

Table S8 - Canine somatic copy number aberrations by oaCGH

Gene	% with gain	% with loss
<i>TP53</i>	6	7
<i>PIK3CA</i>	10	4
<i>PIK3R1</i>	2	3
<i>ORC1</i>	7	2
<i>RASA1</i>	4	2
<i>ARPC1A</i>	2	0
<i>ATP5H</i>	0	0
<i>PTEN</i>	4	4
<i>VEGFA</i>	19	3
<i>MYC</i>	9	0
<i>CDKN2A/B</i>	0	22
<i>KDR</i>	22	0
<i>KIT</i>	17	0

Somatic copy number aberrations in SMGs, as well as in selected genes reported to be recurrently altered in canine and human literature, in a cohort of 66 hemangiosarcomas analyzed by oaCGH. (Thomas, *et al.*, manuscript in preparation)(3).

Table S9 - comparison of top SCNAs in human Angiosarcoma Project data with canine oaCGH data

Gene	Human		Canine	
	CNA	Freq	Gain	Loss
<i>PHF1</i>	AMP	43	2.9	1.5
<i>HOXA3</i>	AMP	33	2.9	1.5
<i>HOXA9</i>	AMP	30	8.7	5.8
<i>CD70</i>	DEL	27	11.6	1.5
<i>DAXX</i>	AMP	27	4.4	1.5
<i>HOXA11</i>	AMP	27	7.3	5.8
<i>KDR</i>	AMP	27	21.7	0
<i>PPM1D</i>	AMP	27	2.9	1.5
<i>ZNF331</i>	DEL	27	1.5	0
<i>CD36</i>	AMP	23	4.4	1.5
<i>DDX5</i>	AMP	23	8.7	0
<i>HOXA13</i>	AMP	20	7.3	5.8
<i>AXIN1</i>	DEL	20	2.9	21.7
<i>H3F3B</i>	AMP	17	4.4	4.4
<i>JAK3</i>	DEL	17	8.7	5.8
<i>PDGFRB</i>	AMP	17	2.9	2.9
<i>PIK3C2B</i>	AMP	17	4.4	8.7
<i>PTK6</i>	DEL	17	8.7	17.4
<i>TYRO3</i>	AMP	17	0	8.7
<i>ARFRP1</i>	DEL	17	13	17.4
<i>NDRG1</i>	AMP	17	8.7	2.9
<i>WWTR1</i>	AMP	17	1.5	2.9
<i>RTEL1</i>	DEL	17	13	17.4

Percentage copy number gain or loss in oaCGH data from 69 golden retriever hemangiosarcomas compared with the most frequent SCNAs (affecting >15% of patients) in known cancer genes in 30 primary tumor samples from The Angiosarcoma Project. SCNAs affecting >15% of patients in the same direction in both species bolded. (Thomas, *et al.*, manuscript in preparation)(3).

Figure S1 - Canine exome sequencing workflow

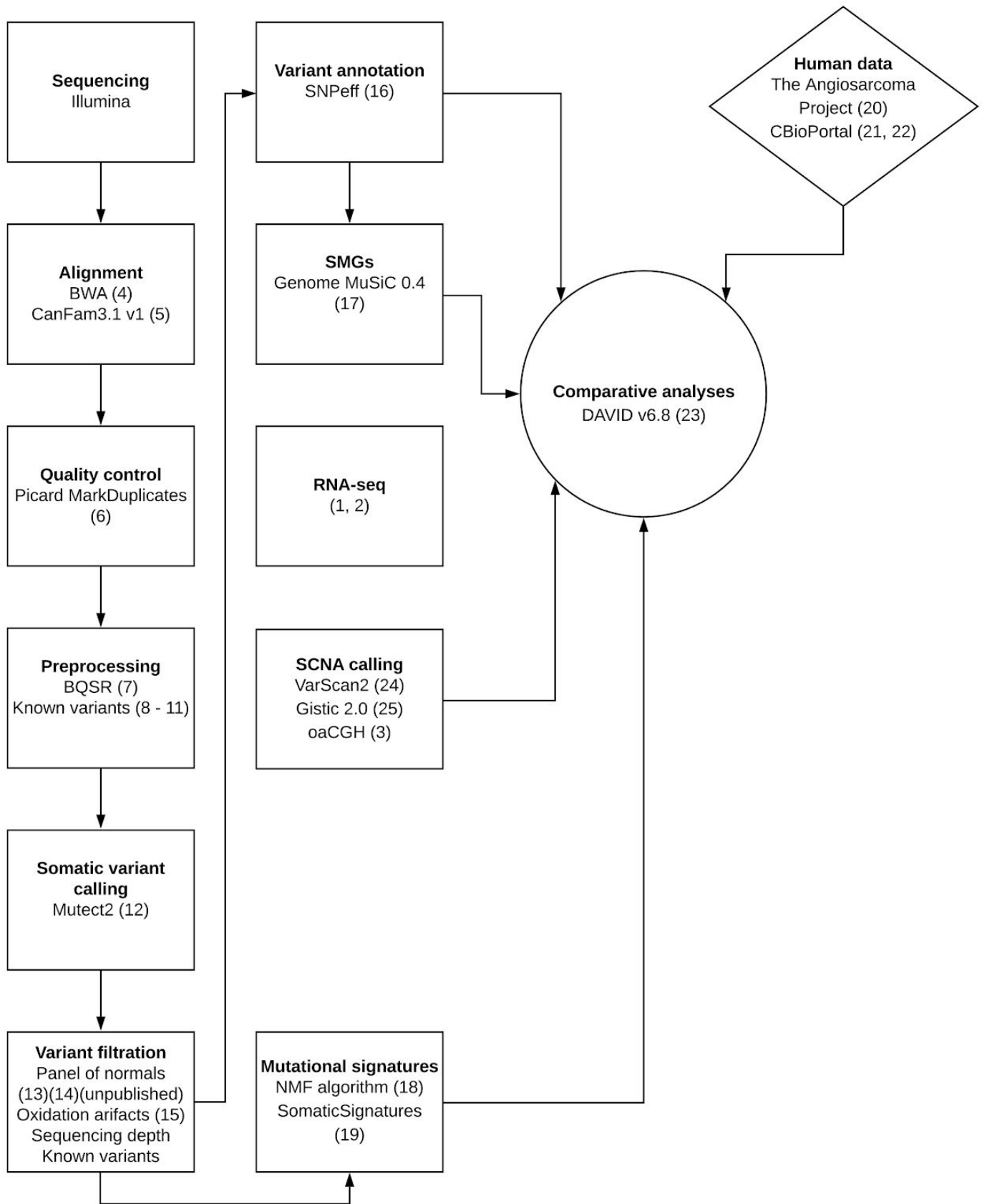


Figure S2 - Canine SMGs called in normal vs. overamplified libraries

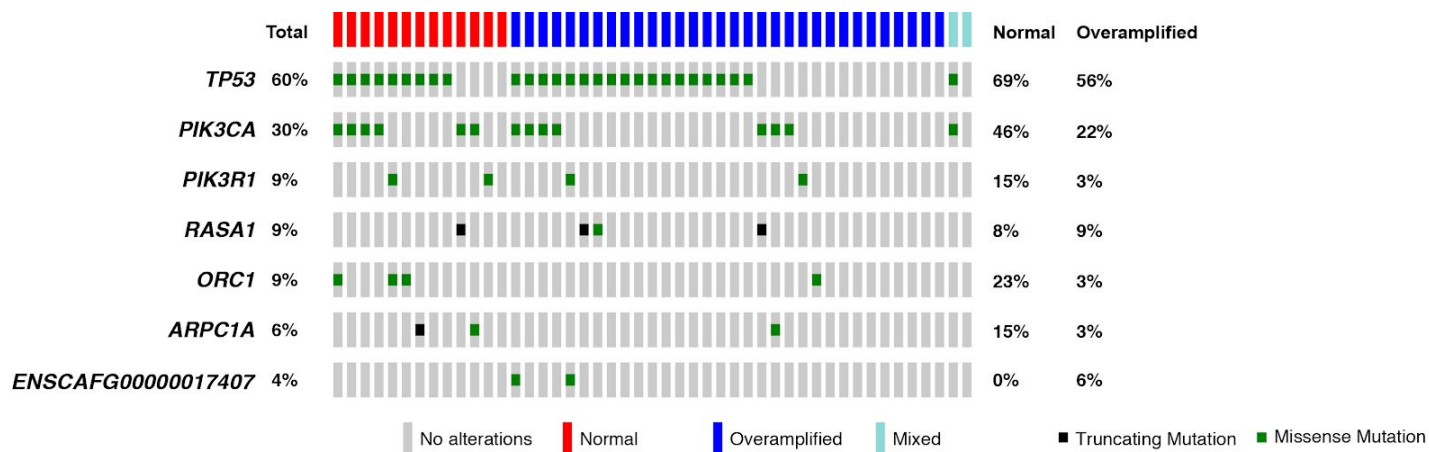
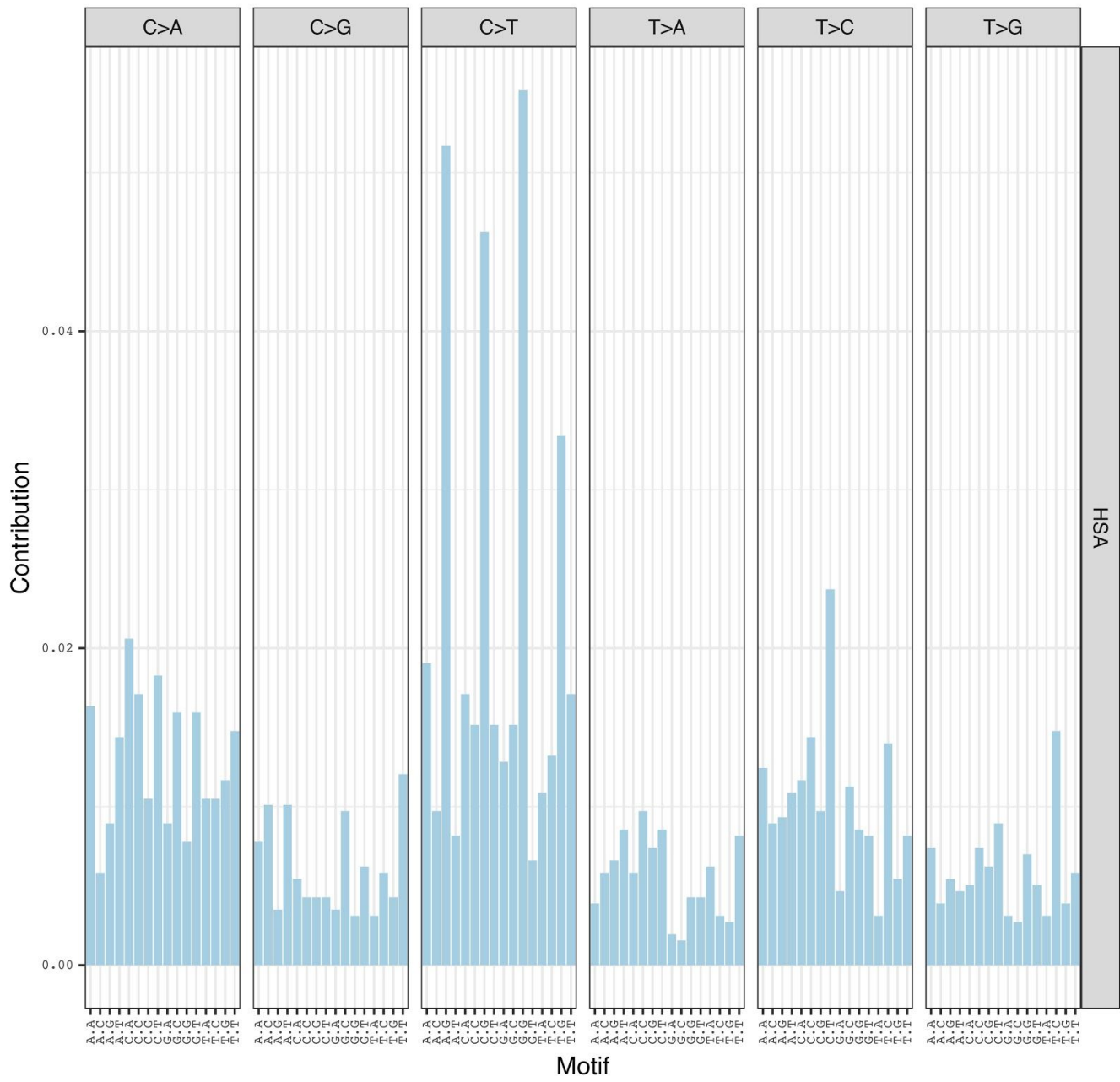
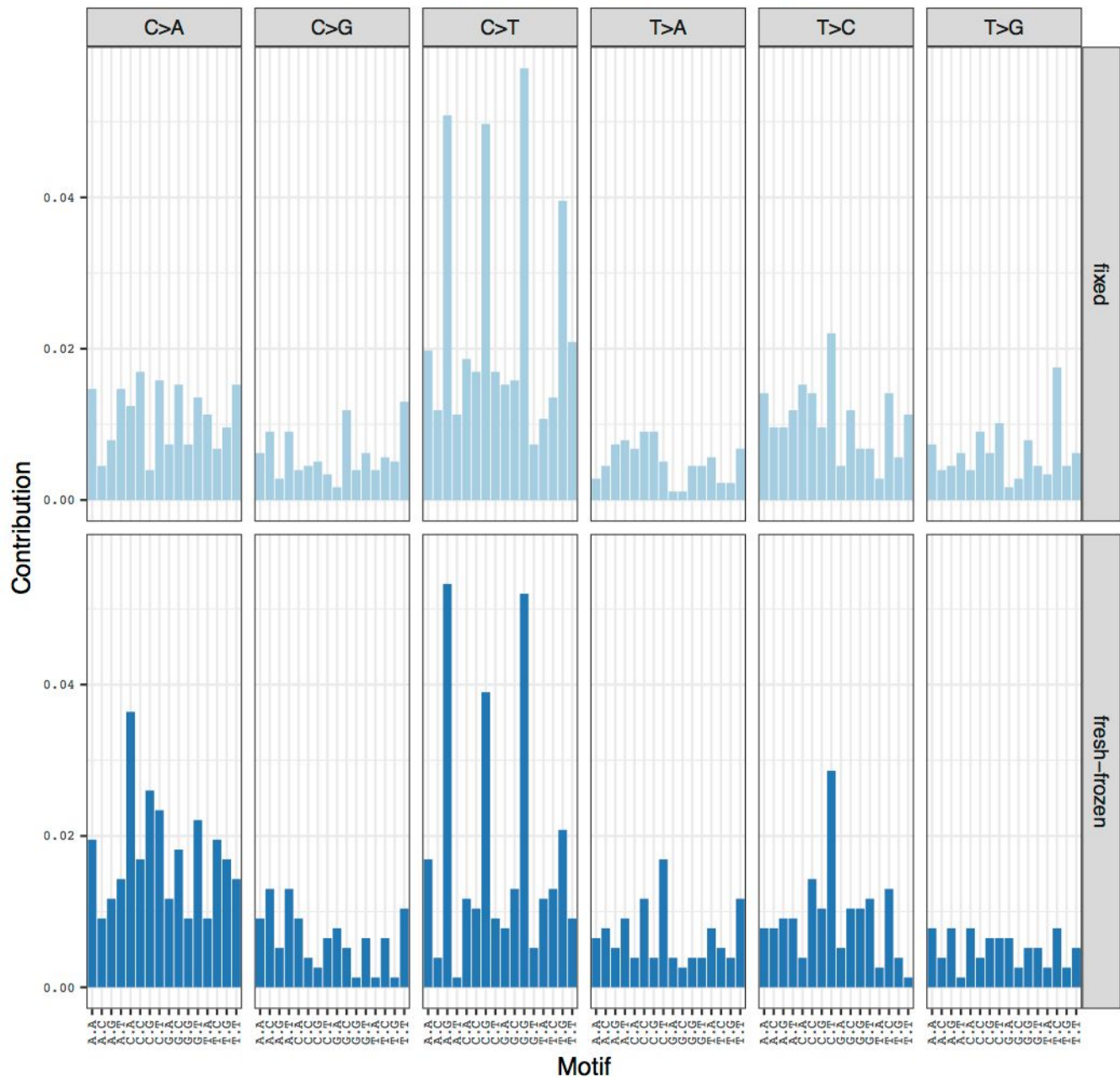


Figure S3 - Mutational landscape of entire canine cohort



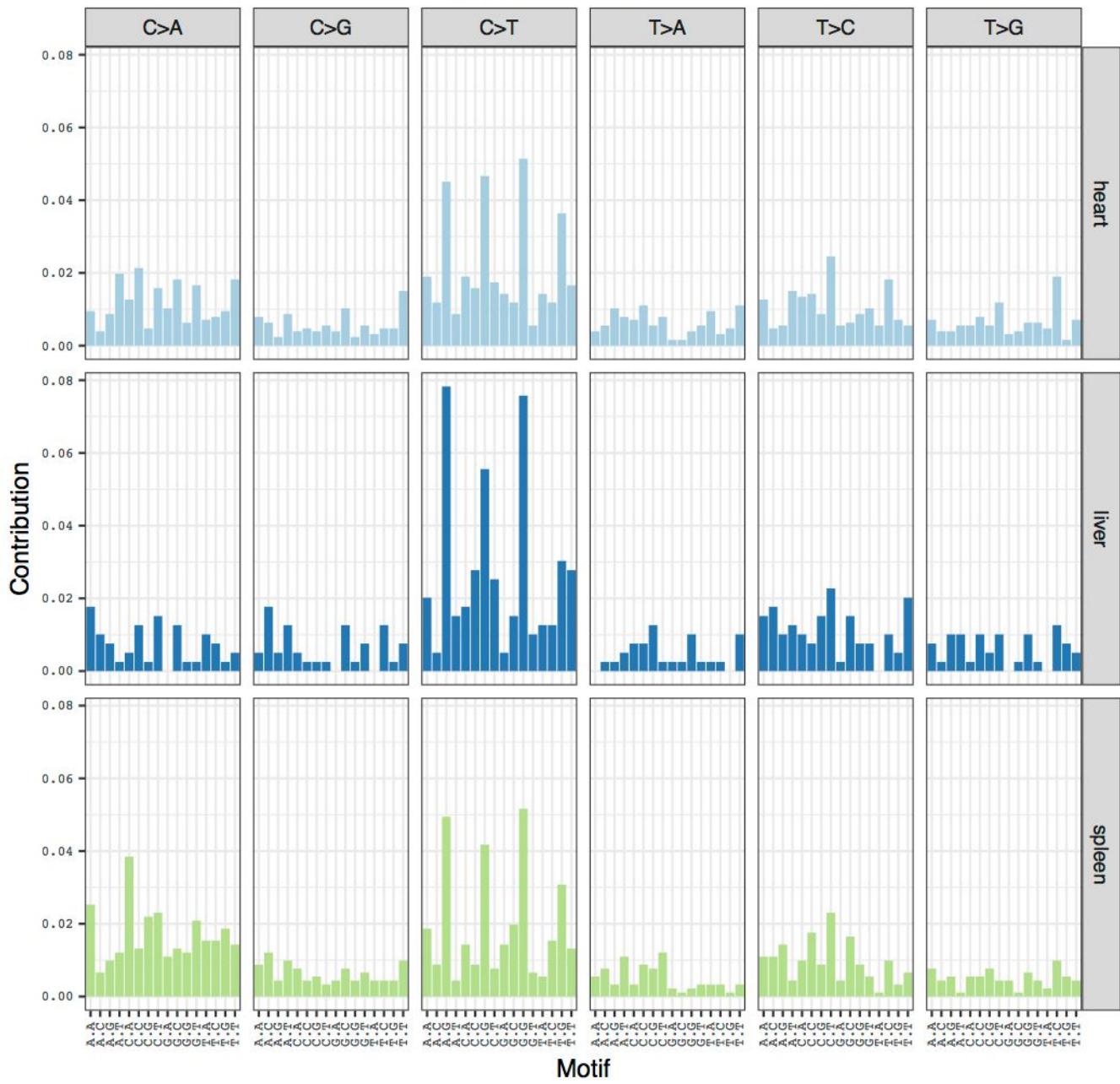
Mutational landscape of all canine hemangiosarcoma cases.

Figure S4 - Mutational landscape: FFPE vs Frozen



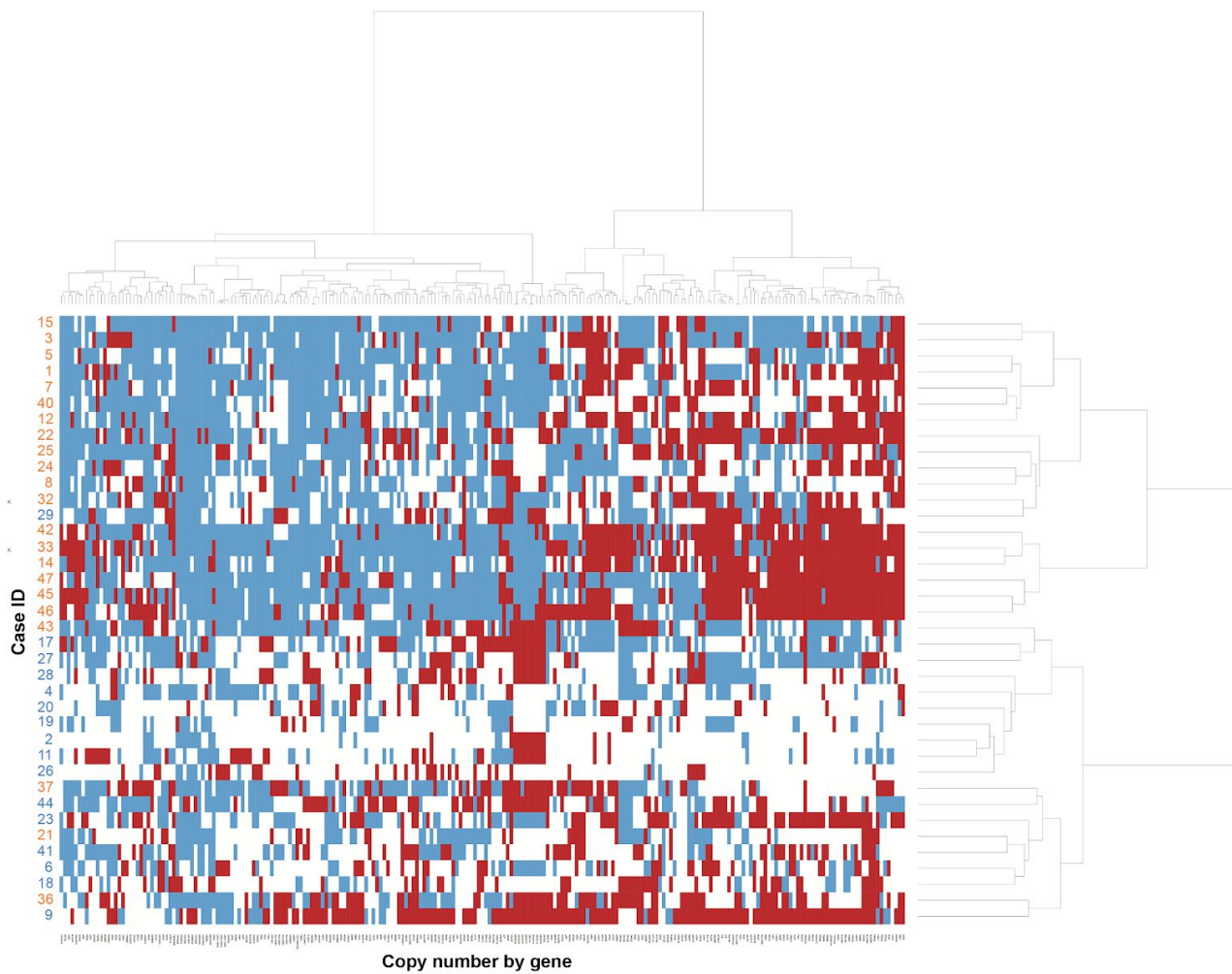
Mutational landscape of all canine cases, divided by tissue handling (fixed vs. frozen).

Figure S5 - Mutational landscape: Canine Tumor Location



Mutational landscape of all canine cases, divided by tumor location (heart, liver, spleen).

Figure S6 - FFPE vs Frozen exome SCNA data clustering



Unsupervised clustering of the VarScan2 copy number aberrations in the 38 canine hemangiosarcoma cases with fewer than 10,000 segments, showing clustering of amplifications (red) and deletions (red) per gene by sample. Case IDs show fixed (orange) or frozen (blue) tissue.

References

1. Gordon BH, Kim J-H, Sarver AL, Frantz AM, Breen M, Lindblad-Toh K, et al. Identification of three molecular and functional subtypes in canine hemangiosarcoma through gene expression profiling and progenitor cell characterization. *Am J Pathol.* 2014;184:985–95.
2. Borgatti A, Koopmeiners JS, Sarver AL, Winter AL, Stuebner K, Todhunter D, et al. Safe and Effective Sarcoma Therapy through Bispecific Targeting of EGFR and uPAR. *Mol Cancer Ther.* 2017;16:956–65.
3. Thomas R, Borst L, Rotroff D, Motsinger-Reif A, Lindblad-Toh K, Modiano JF, et al. Genomic profiling reveals extensive heterogeneity in somatic DNA copy number aberrations of canine hemangiosarcoma. *Chromosome Res.* 2014;22:305–19.
4. Li H, Durbin R. Fast and accurate short read alignment with Burrows-Wheeler transform. *Bioinformatics.* 2009;25:1754–60.
5. Hoepfner MP, Lundquist A, Pirun M, Meadows JRS, Zamani N, Johnson J, et al. An improved canine genome and a comprehensive catalogue of coding genes and non-coding transcripts. *PLoS One.* 2014;9:e91172.
6. Picard Tools - By Broad Institute [Internet]. [cited 2018 Mar 23]. Available from: <http://broadinstitute.github.io/picard>
7. Van der Auwera GA, Carneiro MO, Hartl C, Poplin R, Del Angel G, Levy-Moonshine A, et al. From FastQ data to high confidence variant calls: the Genome Analysis Toolkit best practices pipeline. *Curr Protoc Bioinformatics.* 2013;43:11.10.1–33.
8. Lindblad-Toh K, Wade CM, Mikkelsen TS, Karlsson EK, Jaffe DB, Kamal M, et al. Genome sequence, comparative analysis and haplotype structure of the domestic dog. *Nature.* 2005;438:803–19.
9. Vaysse A, Ratnakumar A, Derrien T, Axelsson E, Rosengren Pielberg G, Sigurdsson S, et al. Identification of genomic regions associated with phenotypic variation between dog breeds using selection mapping. *PLoS Genet.* 2011;7:e1002316.
10. Axelsson E, Ratnakumar A, Arendt M-L, Maqbool K, Webster MT, Perloski M, et al. The genomic signature of dog domestication reveals adaptation to a starch-rich diet. *Nature.* 2013;495:360–4.
11. Bai B, Zhao W-M, Tang B-X, Wang Y-Q, Wang L, Zhang Z, et al. DoGSD: the dog and wolf genome SNP database. *Nucleic Acids Res.* 2015;43:D777–83.
12. Cibulskis K, Lawrence MS, Carter SL, Sivachenko A, Jaffe D, Sougnez C, et al. Sensitive detection of somatic point mutations in impure and heterogeneous cancer samples. *Nat Biotechnol.* 2013;31:213–9.
13. Elvers I, Turner-Maier J, Swofford R, Koltochian M, Johnson J, Stewart C, et al. Exome sequencing of lymphomas from three dog breeds reveals somatic mutation patterns reflecting genetic background. *Genome Res.* 2015;25:1634–45.
14. Sakthikumar S, Elvers I, Kim J, Arendt ML, Thomas R, Turner-Maier J, et al. SETD2 Is Recurrently Mutated in Whole-Exome Sequenced Canine Osteosarcoma. *Cancer Res.* 2018;78:3421–31.
15. Costello M, Pugh TJ, Fennell TJ, Stewart C, Lichtenstein L, Meldrim JC, et al. Discovery and characterization of artifactual mutations in deep coverage targeted capture sequencing data due to oxidative DNA damage during sample preparation. *Nucleic Acids Res.* 2013;41:e67.
16. Cingolani P, Platts A, Wang LL, Coon M, Nguyen T, Wang L, et al. A program for annotating and predicting the effects of single nucleotide polymorphisms, SnpEff: SNPs in the genome of *Drosophila melanogaster* strain w1118; iso-2; iso-3. *Fly.* 2012;6:80–92.
17. Dees ND, Zhang Q, Kandoth C, Wendl MC, Schierding W, Koboldt DC, et al. MuSiC: identifying mutational significance in cancer genomes. *Genome Res.* 2012;22:1589–98.
18. Kim J, Mouw KW, Polak P, Braunstein LZ, Kamburov A, Kwiatkowski DJ, et al. Somatic ERCC2 mutations are associated with a distinct genomic signature in urothelial tumors. *Nat Genet.* 2016;48:600–6.
19. Gehring JS, Fischer B, Lawrence M, Huber W. SomaticSignatures: inferring mutational signatures from

single-nucleotide variants. *Bioinformatics*. 2015;31:3673–5.

20. Corrie Painter NW. The Angiosarcoma Project [Internet]. [cited 2018 Sep 24]. Available from: <https://ascproject.org/>
21. Cerami E, Gao J, Dogrusoz U, Gross BE, Sumer SO, Aksoy BA, et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. *Cancer Discov*. 2012;2:401–4.
22. Gao J, Aksoy BA, Dogrusoz U, Dresdner G, Gross B, Sumer SO, et al. Integrative analysis of complex cancer genomics and clinical profiles using the cBioPortal. *Sci Signal*. 2013;6:11.
23. Dennis G Jr, Sherman BT, Hosack DA, Yang J, Gao W, Lane HC, et al. DAVID: Database for Annotation, Visualization, and Integrated Discovery. *Genome Biol*. 2003;4:P3.
24. Koboldt DC, Zhang Q, Larson DE, Shen D, McLellan MD, Lin L, et al. VarScan 2: somatic mutation and copy number alteration discovery in cancer by exome sequencing. *Genome Res*. 2012;22:568–76.
25. Mermel CH, Schumacher SE, Hill B, Meyerson ML, Beroukhi R, Getz G. GISTIC2.0 facilitates sensitive and confident localization of the targets of focal somatic copy-number alteration in human cancers. *Genome Biol*. 2011;12:R41.