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Changes in Serum and Salivary Proteins in Canine Mammary Tumors

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Received: 27 March 2020; Accepted: 21 April 2020; Published: 24 April 2020

Simple Summary: The present study describes for the first time the differences in the serum and saliva proteomes between healthy bitches and bitches with mammary tumors using a high-throughput proteomic approach. More than 1000 proteins were identified and 35 in serum and 49 in saliva were significantly modulated. Additionally, their related pathways were discussed in order to improve understanding of the pathophysiology of the disease and one protein, serum albumin, was further validated. The results of the present study could be a source of potential biomarkers for canine mammary tumors in saliva and serum and increase the knowledge on the pathophysiology of the disease.

Abstract: The aim of this study was to evaluate changes in serum and saliva proteomes in canine mammary tumors (CMT) using a high-throughput quantitative proteomic analysis in order to potentially discover possible biomarkers of this disease. Proteomes of paired serum and saliva samples from healthy controls (HC group, $n = 5$) and bitches with CMT (CMT group, $n = 5$) were analysed using a Tandem Mass Tags-based approach. Twenty-five dogs were used to validate serum albumin as a candidate biomarker in an independent sample set. The proteomic analysis quantified 379 and 730 proteins in serum and saliva, respectively. Of those, 35 proteins in serum and 49 in saliva were differentially represented. The verification of albumin in serum was in concordance with the proteomic data, showing lower levels in CMT when compared to the HC group. Some of the modulated proteins found in the present study such as haptoglobin or S100A4 have been related to CMT or human breast cancer previously, while others such as kallikrein-1 and immunoglobulin gamma-heavy chains A and D are described here for the first time. Our results indicate that saliva and serum proteomes can reflect physiopathological changes that occur in CMT in dogs and can be a potential source of biomarkers of the disease.

Keywords: biomarker; cancer; canine mammary tumors; dog; proteomics; saliva; serum

1. Introduction

Mammary tumors are the most common cancer in intact female dogs, accounting for almost 50% of all tumors [1]. Approximately half of all canine mammary tumors (CMT) are diagnosed as malignant

by histological examination, leading to death due to distant metastases in many cases [2]. Several conditions such as hormonal imbalance, viruses, obesity, diet, genetic components, and oxidative stress contribute to CMT [1,3], although the pathogenesis has not been fully elucidated to date. It is known that many biological characteristics of mammary tumors are shared between humans and dogs such as histopathologic features, biological behaviour, metastatic pattern, antigenic phenotype and expression patterns of proliferating cell nuclear antigen, cytokeratins, and calponin [4]. Therefore, dogs have been proposed as an ideal model for the investigation of human breast cancer [5]. Furthermore, since humans and dogs share the same environment and are exposed to the same cancerogenic factors, spontaneously occurring malignancies in dogs have been considered as a valuable experimental model for investigation of human neoplasias [6].

Saliva is a non-invasive biological fluid that can reflect both systemic and local health-related conditions and possesses several benefits when used for sampling instead of invasive methods such as blood sampling. The advantages of using saliva include that it is a safer method for personnel and patients, it is easier to collect, and collecting saliva reduces sampling stress as it is pain-free [7]. In humans, proteomic analyses of saliva have proved to be a useful technique for discovering disease-related biomarkers in different pathologies including cancer [8]. In dogs, gel-free proteomics approaches such as Tandem Mass Tag (TMT) have been successfully used in serum and/or saliva in different infectious diseases such as pyometra [9], parvoviral enteritis [10] and leishmaniosis [11], as well as for metabolic diseases such as obesity [12].

Changes in serum and saliva proteomes in women with breast cancer have been described. In serum, higher levels of histone deacetylase proteins were detected in women with recurrent breast cancer in comparison to non-recurrent cases [13]. In saliva, Delmonico et al. [14] identified differences in alpha-2-macroglobulin, ceruplasmin, haptoglobin, hemopexin and vitamin D-binding, among others, in women with impalpable breast cancer in comparison to healthy women; and Giri et al. [15] identified 166 proteins with different expression in saliva of women with breast cancer in comparison to healthy controls [15]. In dogs, two studies were reported in which 2-DE gel proteomic analyses of canine mammary tumor tissues were performed. In one of the studies [16], of 21 proteins differentially modulated in healthy and diseased dogs, 19 were previously reported for human breast cancer. The second study [17] compared normal canine mammary gland tissue proteomes with tissues at different stages of malignant progression, identifying 48 proteins with significant changes. However, to the best of the authors' knowledge, there are no studies addressing changes in serum or saliva proteomes in dogs with mammary tumors.

The current study aims to explore for the first time changes in paired serum and saliva proteomes in bitches with mammary tumors compared to healthy ones by using TMT label-based gel-free proteomic approach. This study is expected to increase the knowledge on the pathogenesis of CMT and potentially discovering possible biomarkers for the detection of this disease.

2. Materials and Methods

2.1. Animals

A total of 10 client-owned bitches presenting at private veterinary clinics in Murcia, Spain, during January 2019 were involved in this study. A group of five bitches (3 mixed breeds, 1 Pinscher and 1 German shepherd; all spayed; aged 9.7 ± 3.6 years old) classified as healthy based on a complete physical examination, haematology and biochemistry were included as the control group (HC). Five bitches (4 mixed breeds and 1 Pinscher; all spayed; aged 12.0 ± 1.93 years old) diagnosed with mammary tumors (3 simple tubulopapillary carcinomas and 2 simple tubular carcinoma) were included as the mammary tumor (CMT) group. All dogs were submitted to general physical examination and general haematology and biochemistry were performed. Tumor staging was based on the 'Tumor, Node, Metastasis classification system' (TNM) [18], and all cases were diagnosed as grades 1 and 2 (tumor diameter ≤3 cm, and absence of regional lymph node or distant metastases). Dogs were excluded

if they were spayed less than one year ago, if there was possibility of concurrent diseases based on physical examination and laboratory analyses, or if gingivitis was detected. None of the serum and saliva samples showed haemolysis. All dogs with TNM were treated by surgical removal of the neoplasm and were alive and without relapse 6 months after the surgery.

All the procedures were approved by the ethics committees of the University of Murcia and the Ministry of Agriculture, Livestock, Fishing and Aquaculture of the Region of Murcia (A13170503).

2.2. Serum and Saliva Sampling

Surplus serum remainings after routine clinical biochemical analyses were stored at −80 °C until their use for the present study. Venipuncture of the jugular or cephalic vein was performed for blood collection. Whole blood was stored in tubes containing a coagulation activator and a gel separator and kept at room temperature (25 °C) until visible clot reaction. Samples were centrifuged (3500× *g*, 10 min) and the supernatants were stored at −80 °C until analysis.

Saliva samples were obtained as previously reported [19]. In brief, a small sponge was placed into the mouth and, when it was thoroughly moistened, it was then removed and placed into collection devices (Salivette saliva collection tube/V-Bottom, Sarstedt, Aktiengesellschaft & Co, Nümbrecht, Germany). After the samples were centrifuged (3000× *g*, 10 min, 4 °C), the supernatants were stored at −80 °C until analysis [20]. At least 0.2 mL of saliva was collected from each patient.

2.3. Proteomics Study of Saliva and Serum Samples and LC–MS/MS Analysis

A total of 35 µg of protein per sample was subjected to reduction, alkylation, digestion and labelling using 6-plex Tandem Mass Tag reagents, according to manufacturer instructions (Thermo Scientific) as described previously [10,11]. In brief, after protein determination using Bradford assay [21], 35 µg of sample and internal standards (consisting of a pool of 35 µg of each sample) were reduced for 1 h with 200 mM DTT (Sigma-Aldrich), alkylated for 30 min with 375 mM iodoacetamide (Sigma-Aldrich) and precipitated with ice-cold acetone (VWR, Llinars del Vallés, Barcelona, Spain). The next day, the samples were centrifuged, the acetone was decanted and the pellets were resuspended with 50 µL of 100 mM TEAB buffer and subsequently digested with trypsin (Promega, Madison, WI, USA) overnight at 37 °C (2.5 µg of trypsin per 100 µg of protein). The TMT labelling reagents were resuspended in LC–MS-grade anhydrous acetonitrile (Thermo Scientific, Waltham, MA, USA) and mixed with each sample for 1 h at room temperature. The reaction was quenched by adding 5% hydroxylamine (Thermo Scientific) for 15 min and the samples were combined at equal amounts. Then, 6 µg of each mixed sample set was placed in a well of a microplate, vacuum-dried and stored at −80 °C before further LC–MS/MS analysis. LC−MS/MS analysis was performed using the Dionex Ultimate 3000 RSLC nano-flow system (Dionex, Camberley, UK) and an Orbitrap Q Exactive Plus mass spectrometer (Thermo Fisher Scientific), as described elsewhere [22]. The SEQUEST algorithm, Proteome Discoverer (version 2.0., Thermo Fisher Scientific, Waltham, MA, USA), was used for peptide identification and relative quantification. A NCBI database search for *Canis Lupus* FASTA files was performed considering two missed trypsin cleavage sites, a precursor tolerance of 10 ppm and a fragment mass tolerance of 0.02 Da. The Percolator algorithm within the Proteome Discoverer workflow was used to determine the false discovery rate (FDR) for peptide identification, which was set at 1%.

2.4. Validation of Serum Biomarkers

For validation of serum biomarkers detected by proteomic analysis, serum samples from 25 bitches that were presented to the Department and Clinic of Animal Reproduction, University of Life Sciences, Lublin, Poland, were employed—healthy controls (n = 10; aged 7.5–11) and dogs with CMT stage 1–2 tumors (n = 15; aged 8–13).

Albumin in serum was selected for validation since it is commonly performed in routine biochemistry analysis in our laboratory and, therefore, that data were already available. Serum

albumin was determined using a commercially available kit (Albumin OSR 6102; Olympus Life and Material Science Europe GmbH, Irish branch, Ennis, Ireland), according to manufacturer instructions.

2.5. Statistical Analysis

All statistics were performed using R v3.2.2 [23]. First, proteins with fewer than two unique peptides and proteins with >90% missing data were removed from the analysis. Sample outliers were detected for each of the proteins using Dixon's test from R package *outliers* v0.14 [24]. If a sample outlier was significant ($p < 0.05$), it was removed from further analysis. As the majority of the analysed proteins did not follow normal distribution, as tested by the Shapiro–Wilk test, the Wilcoxon–Mann–Whitney test was performed in order to test for differences in protein abundance between groups. The fold change between the two groups was calculated as the mean protein abundance for the CMT group divided by the mean protein abundance for the HC group.

For the validation of serum biomarkers, the D'Agostino and Pearson omnibus normality test was employed to determine the distribution of data and, since data were not normally distributed, the non-parametric statistical Mann–Whitney U (two-way) test was used to compare between groups.

2.6. Bioinformatics Analysis

The proteins' GI accession numbers were converted into official gene symbols either using the DAVID conversion tool (https://david.ncifcrf.gov/conversion.jsp), UniProtKB ID mapping (https://www.uniprot.org/uploadlists/) or the SEQUEST search engine implemented into Proteome Discoverer [25]. Genes encoding the differentially abundant proteins in the CMT and HC groups were used to determine the GO terms overrepresented in CMT using the Protein Analysis Through Evolutionary Relationships (PANTHER) classification tool (http://www.pantherdb.org/).

Heatmaps were designed using R package *pheatmap* v1.0.12 [26].

3. Results

3.1. Proteomic Analysis in Serum

After the removal of proteins with fewer than 2 unique peptides, NMT <5% FDR, missing data and outliers, 379 serum proteins remained for statistical analysis (Table A1). The Wilcoxon–Mann–Whitney test revealed statistically significant different abundances in the HC and CMT groups for 35 proteins, corresponding to 16 unique genes after the removal of duplicates and isoforms, as summarized in Table 1 and Figure A1. The 35 proteins differentially expressed in serum in CMT and HC were used for subsequent bioinformatics analysis in terms of functional clusters, according to the PANTHER classification system (Table 2). The identified differentially modulated proteins in CMT and HC had three molecular functions: binding (40%), catalytic activity (30%) or molecular function regulators (30%). Three different biological processes were involved: 66% of proteins were involved in cellular process, 17% of proteins in biological adhesion and another 17% in localization. Regarding biological pathways, half of the proteins were involved in blood coagulation, while 25% were involved in the plasminogen activating cascade and in angiotensin II-stimulated signalling through G protein and beta-arrestin. Regarding protein class, 50% of proteins were enzyme modulators, followed by transfer/carrier proteins (17%), signalling molecules (17%), and receptors (16%).

Table 1. Proteins downregulated and upregulated in serum. In serum, 35 proteins were initially identified with statistically significant different abundances in CMT and HC. After the removing of duplicates and isoforms, there were 9 downregulated and 7 upregulated proteins.

GI Accession	Gene Symbol	Description	*p*-Value	Fold Change	Mean (SD) HC	Mean (SD) CMT
Proteins upregulated in CMT when compared to HC						
345791439	*SERPIND1*	Heparin cofactor 2	0.032	1.168	0.874 (0.061)	1.021 (0.092)
1239925760	*C5*	Complement component C5	0.016	1.194	0.875 (0.112)	1.045 (0.066)
1239899336	*C6*	Complement component C6	0.008	1.254	0.883 (0.109)	1.107 (0.068)
73967778	*FCN2*	Ficolin-2	0.048	1.443	0.873 (0.177)	1.260 (0.366)
258499	*HP*	Haptoglobin heavy chain	0.032	1.458	0.620 (0.151)	0.904 (0.182)
60734606	*IGHAC*	Immunoglobulin alpha heavy chain constant region	0.008	2.030	0.501 (0.077)	1.017 (0.223)
1304047	*FGA*	Fibrinogen A-alpha chain	0.016	5.683	0.394 (0.060)	2.239 (1.186)
Proteins downregulated in CMT when compared to HC						
16607715	*IL13RA2*	Interleukin-13 receptor subunit alpha-2	0.016	0.42	1.434 (0.686)	0.603 (0.102)
16607648	*IGHG*	Immunoglobulin gamma-heavy chain D	0.016	0.42	1.423 (0.672)	0.602 (0.099)
119637837	*SERPINF1*	Pigment epithelium-derived factor	0.008	0.78	1.178 (0.106)	0.915 (0.068)
1272414	*FN1*	Fibronectin	0.016	0.78	1.143 (0.041)	0.888 (0.103)
345777712	*AMBP*	Alpha-1-microglobulin/bikunin precursor	0.008	0.78	1.219 (0.100)	0.954 (0.051)
5821257	*AGT*	Angiotensinogen	0.016	0.81	1.094 (0.155)	0.886 (0.034)
3319897	*ALB*	Albumin	0.048	0.82	1.101 (0.059)	0.904 (0.193)
1239925762	*GSN*	Gelsolin	0.032	0.82	1.194 (0.141)	0.981 (0.074)
296089	*APOH*	Apolipoprotein H	0.032	0.90	1.009 (0.07)	0.911 (0.065)

Color represent relative abundance of the protein (red for downregulated, green for upregulated).

Table 2. Molecular function, biological process, pathways, and protein class as the number of genes and gene percentage of the differentially expressed proteins in the HC and CMT groups in serum and saliva based on the Protein Analysis Through Evolutionary Relationships (PANTHER) classification system.

Serum			Saliva		
	Gene	% Gene		Gene	% Gene
Molecular Function					
Binding (GO:0005488)	5	33.3	Binding (GO:0005488)	10	43.5
Catalytic activity (GO:0003824)	5	33.3	Catalytic activity (GO:0003824)	9	39.1
Molecular function regulator (GO:0098772)	4	26.7	Molecular function regulator (GO:0098772)	2	8.7
Molecular transducer activity (GO:0060089)	1	6.7	Structural molecule activity (GO:0005198)	2	8.7
Biological Process					
Biological regulation (GO:0065007)	4	28.6	Biological adhesion (GO:0022610)	2	4.2
Cellular process (GO:0009987)	4	28.6	Biological regulation (GO:0065007)	4	8.3
Localization (GO:0051179)	1	7.1	Cell population proliferation (GO:0008283)	1	2.1
Metabolic process (GO:0008152)	4	28.6	Cellular component organization or biogenesis (GO:0071840)	3	6.3
Response to stimulus (GO:0050896)	1	7.1	Cellular process (GO:0009987)	12	25
			Developmental process (GO:0032502)	2	4.2
			Growth (GO:0040007)	1	2.1
			Immune system process (GO:0002376)	2	4.2
			Localization (GO:0051179)	2	4.2
			Locomotion (GO:0040011)	1	2.1
			Metabolic process (GO:0008152)	9	18.8
			Multicellular organismal process (GO:0032501)	1	2.1
			Reproduction (GO:0000003)	1	2.1
			Reproductive process (GO:0022414)	1	2.1
			Response to stimulus (GO:0050896)	4	8.3
			Signaling (GO:0023052)	2	4.2
Pathways					
Angiotensin II-stimulated signaling through G proteins and beta-arrestin (P05911)	1	25	Adenine and hypoxanthine salvage pathway (P02723)	1	6.7
Blood coagulation (P00011)	1	25	B cell activation (P00010)	1	6.7
FAS signaling pathway (P00020)	1	25	CCKR signaling map (P06959)	1	6.7
Interleukin signaling pathway (P00036)	1	25	De novo purine biosynthesis (P02738)	1	6.7
			De novo pyrimidine deoxyribonucleotide biosynthesis (P02739)	1	6.7
			De novo pyrimidine ribonucleotides biosythesis (P02740)	1	6.7
			Glycolysis (P00024)	1	6.7
			Heterotrimeric G protein signaling pathway-Gi alpha and Gs alpha-mediated pathway (P00026)	1	6.7
			Heterotrimeric G protein signaling pathway-rod outer segment phototransduction (P00028)	1	6.7
			Integrin signalling pathway (P00034)	1	6.7
			Purine metabolism (P02769)	1	6.7
			Pyruvate metabolism (P02772)	1	6.7
			Salvage pyrimidine ribonucleotides (P02775)	1	6.7
			T cell activation (P00053)	1	6.7
			TCA cycle (P00051)	1	6.7
Protein Class					
Cytoskeletal protein (PC00085)	1	12.5	Calcium-binding protein (PC00060)	5	33.3
Intercellular signal molecule (PC00207)	1	12.5	Cytoskeletal protein (PC00085)	2	13.3
Protein-modifying enzyme (PC00260)	1	12.5	Extracellular matrix protein (PC00102)	1	6.7
Protein-binding activity modulator (PC00095)	4	12.550	Metabolite interconversion enzyme (PC00262)	5	33.3
Transfer/carrier protein (PC00219)	1	12.5	Protein-modifying enzyme (PC00260)	1	6.7
			Transmembrane signal receptor (PC00197)	1	6.7

Of the sixteen modulated proteins, seven were upregulated and nine were downregulated in CMT. Proteins with a fold increase greater than 2 were fibrinogen A-alpha chain (*FGA*) and IgA heavy chain constant region [*Canis lupus familiaris*]. The most downregulated proteins in CMT were interleukin-13 receptor subunit alpha-2 precursor [*Canis lupus familiaris*], immunoglobulin gamma-heavy chain A [*Canis lupus familiaris*], immunoglobulin gamma-heavy chain D [*Canis lupus familiaris*], and interleukin-13 receptor subunit alpha-2 precursor [*Canis lupus familiaris*].

3.2. Proteomic Analysis in Saliva

After the removal of proteins with fewer than two unique peptides, NMT <5% FDR, missing data and outliers, 730 proteins remained for statistical analysis (Table A2). The Wilcoxon–Mann–Whitney test identified 49 proteins (corresponding to 28 unique genes) with different abundances between the HC and CMT groups ($p < 0.05$), as summarized after the removal of duplicates and isoforms in Table 3 and Figure A2. Proteins differentially expressed in saliva between CMT and HC were used for subsequent bioinformatics analysis in terms of functional clusters, according to the PANTHER classification system, as shown in Table 2. The identified differentially modulated proteins in CMT and HC had five molecular functions: binding (37%), catalytic activity (28%), structural molecule activity (21%), molecular function regulators (7%), and molecular transducer activity (7%). Furthermore, proteins were involved in nine different biological processes—with 35%, 22%, and 13% of proteins involved with cellular process, metabolic process, and localization, respectively. Most proteins were involved in nucleic acid binding (50%), although there were also cytoskeletal proteins, isomerases and transfer/carrier proteins. Regarding biological pathways, the differentially modulated proteins were involved in *de novo* purine biosynthesis, de novo pyrimidine deoxyribonucleotide biosynthesis, *de novo* pyrimidine ribonucleotide biosynthesis, glycolysis (P00024), and salvage pyrimidine ribonucleotides (20% of proteins for each).

Of the 28 proteins, 27 were upregulated and 1 was downregulated. Protein S100-A6 (*S100A6*), major allergen Can f1 (*CANF1*), protein S100-A4 (*S100A4*), malate dehydrogenase (*MDH2*), and protein S100-A2 (*S100A2*) were the most upregulated proteins in MT, with >2 fold change. Kallikrein-1 (*KLK1*) was the only protein that was downregulated in the CMT group.

Finally, when proteomic results were compared between saliva and serum, the abundance of no protein changed statistically significantly in both serum and saliva.

3.3. Validation of Albumin

When the CMT and HC groups were compared, lower circulating concentrations of albumin were found in bitches with CMT (median (25–75th percentile), 2.9 (2.6–3.2) g/dL) in comparison to healthy controls (3.1 (3.1–3.4) g/dL) ($p = 0.0173$).

Table 3. Proteins downregulated and upregulated in saliva. In saliva, 49 proteins were initially identified with statistically significant different abundances in CMT and HC. After the removing of duplicates and isoforms, there were 27 upregulated and 1 downregulated proteins.

GI Accession	Gene Symbol	Description	*p*-Value	Fold Change	Mean (SD)	Mean (SD)
					HC	CMT
Proteins upregulated in CMT when compared to HC						
356582247	*NPC2*	NPC intracellular cholesterol transporter 2 precursor	0.032	1.282	0.738 (0.129)	0.946 (0.108)
1418259105	*PDIA3*	Protein disulfide-isomerase A3	0.032	1.324	0.753 (0.170)	0.997 (0.115)
558757359	*EZR*	Ezrin	0.032	1.331	0.713 (0.222)	0.949 (0.086)
1418304395	*CALM3*	Calmodulin 3	0.016	1.445	0.690 (0.230)	0.997 (0.121)
1418197013	*CALM2*	Calmodulin 2	0.032	1.48	0.791 (0.208)	1.171 (0.158)
1418206782	*MUC5B*	Mucin 5B	0.040	1.498	0.673 (0.179)	1.008 (0.145)
73948247	*LYPD3*	Ly6/PLAUR domain-containing protein 3	0.008	1.51	0.673 (0.097)	1.016 (0.090)
76363530	*TPI1*	Triosephosphate isomerase	0.008	1.512	0.746 (0.266)	1.128 (0.091)
73947736	*ACTN4*	Alpha actinin 4	0.032	1.521	0.728 (0.273)	1.107 (0.121)
1418202786	*PPIA*	Peptidyl-prolyl cis-trans isomerase A	0.032	1.524	0.862 (0.322)	1.314 (0.240)
73980076	*XDH*	Xanthine dehydrogenase/oxidase	0.016	1.526	0.671 (0.288)	1.024 (0.076)
57092971	*MDH1*	Malate dehydrogenase, cytoplasmic	0.016	1.575	0.703 (0.100)	1.107 (0.239)
545510196	*NME2*	Nucleoside diphosphate kinase B	0.008	1.649	0.641 (0.165)	1.057 (0.053)
356582340	*RPS27A*	Ubiquitin-40S ribosomal protein S27a	0.032	1.665	0.626 (0.292)	1.042 (0.222)
5441519	*UBA52*	Ubiquitin-ribosomal protein L40 fusion protein	0.032	1.665	0.626 (0.292)	1.042 (0.222)
1239902229	*UBB*	Polyubiquitin-B	0.032	1.665	0.626 (0.292)	1.042 (0.222)
73995130	*UBC*	Polyubiquitin-C	0.032	1.665	0.626 (0.292)	1.042 (0.222)
558695394	*ANXA1*	Annexin A1	0.016	1.687	0.591 (0.250)	0.997 (0.092)
1239889921	*UB*	Ubiquitin	0.032	1.704	0.618 (0.259)	1.053 (0.215)
1418293878	*CAP1*	Adenylyl cyclase-associated protein 1	0.016	1.735	0.618 (0.251)	1.072 (0.132)
1418294943	*PRDX1*	Peroxiredoxin 1	0.008	1.783	0.580 (0.247)	1.034 (0.110)
1418213540	*SPRR1A*	Cornifin A	0.016	1.853	0.543 (0.214)	1.006 (0.235)
1418313584	*S100A2*	Protein S100-A2	0.032	2.008	0.514 (0.249)	1.032 (0.303)
1239955263	*MDH2*	Malate dehydrogenase, mitochondrial	0.008	2.052	0.481 (0.179)	0.987 (0.229)
1391723726	*S100A4*	Protein S100-A4	0.032	2.177	0.468 (0.337)	1.019 (0.191)
3121745	*CANF1*	Major allergen Can f 1	0.016	2.315	0.496 (0.067)	1.148 (0.150)
1239912330	*S100A6*	Protein S100-A6	0.008	2.356	0.424 (0.273)	0.999 (0.071)
Proteins downregulated in CMT when compared to HC						
1418303522	*KLK1*	Kallikrein-1-like	0.016	0.556	1.652 (0.126)	0.919 (0.379)

Color represent relative abundance of the protein (red for downregulated, green for upregulated).

4. Discussion

In this report, serum and salivary proteomes showed changes in bitches with CMT when compared to healthy individuals. Some of the proteins that were modulated in the present study such as S100A4 or haptoglobin were also described in previous studies on canine mammary tumors [27] or human breast cancer [14,15,28,29], while other proteins including immunoglobulin gamma-heavy chains A and D or kallikrein-1 were described here for the first time as CMT-related proteins.

In serum, 35 of 379 proteins were differentially modulated in CMT. Fibrinogen A-alpha chain (*FGA*) was the most upregulated protein in serum in CMT. This protein is a degradation product of the alpha chain of fibrinogen [30] and its protective role against tumor growth and metastasis has been proposed previously [31]. Increases in fibrinogen degradation have been described in neoplasms and seem related to an increase in fibrin deposition in the tumor [32]. *FGA* has been proposed as a biomarker for HER2-positive breast cancer [33], although it can also appear increased in oral cancer [34] and in infectious diseases such as dirofilariosis or leishmaniosis [35].

The two most downregulated proteins in serum of bitches with CMT were interleukin-13 receptor subunit alpha-2 precursor and immunoglobulin gamma-heavy chains A and D. Interleukins are key immunoregulatory and anti-inflammatory cytokines in tumor cells, produced by different immune cells such as B, T, mast cells, dendritic or natural killer cells [36]. In dogs, the upregulation of interleukin-13 receptor subunit alpha-2 genes was observed in macrophages grown as a co-culture with canine mammary cancer cells [37]. In human breast cancer tissues, overexpression of interleukin-13 receptor subunit alpha-2 precursor has been suggested as an independent predictor of poorer outcome, playing important roles in cancer cell survival and progression, although it was dependent on the breast cancer subtype [38]. In the present study, dogs had cancers of low TNM grade and did not have relapses for at least 6 months, which could explain at least partially the observed low levels of this protein. Immunoglobulin gamma is the most abundant class of antibodies, predominant in the immune secondary response and participating in different important roles such as the activation of the complement cascade, or mediation of antibody-dependent cell cytotoxicity [39]. There is a lack of information on the possible relation between IgG and CMT and, therefore, further studies would be diserable in order to discern the possible reasons for the IgG downregulation observed in our study.

Additionally in serum, modulations of known acute-phase proteins (APP) in dogs with increases in haptoglobin and decreases in albumin were observed in the proteomic analysis of this study. While haptoglobin is considered a moderate APP in dogs that increases by approximately 2- to 5-fold, albumin is a negative APP that decreases during inflammation [40]. In agreement with our results, increases in serum haptoglobin concentrations were observed in dogs with mammary tumors when compared to healthy controls [41,42], as well as in dogs with hemolymphatic, mesenchymal, and epithelial tumors [40,43,44]. The downregulation of albumin in serum in CMT bitches was further verified previously by a commercially available kit using an automated analyser, showing a decrease in albumin in dogs with CMT in comparison to controls.

In saliva, three proteins of the S100A family, namely S100A2, S100A4, and S100A6, were among the most upregulated proteins in bitches with mammary tumors when compared to healthy controls. S100A proteins are a family of calcium-binding proteins with potential roles in different cancers including breast [45]. In breast cancer, the positive correlation between S100A4 expression and cancer progression has been described in several studies [28,46,47]. A controversial role in carcinogenesis has been described for S100A2, which has been proposed both as a tumor suppressor [48] and a tumor promotor [49]. Higher tissue expression of S100A2 was significantly correlated with worse overall survival in ovarian cancer patients [15], and S100A2 protein expression in saliva was observed to be higher in oral squamous cell carcinoma patients in comparison to other oral potentially malignant disorders. S100A6 expression has been associated with worse prognosis or the progression of several cancers including oncogynecology [50], colorectal [51], gastric [52], and renal [53]. In contrast, a recent study suggests a relation between S100A6 expression and better prognosis in breast cancer [54]. However, to the best of our knowledge, this is the first report in which the S100A family is described

in saliva of bitches with mammary tumors. Based on our results and previous studies in women, evaluation of the S100A family as possible biomarkers of prognosis and evolution of mammary tumors in dogs could be of interest in order to evaluate whether dogs with poorer prognosis can have higher values of these proteins.

Calmodulin-like proteins, namely CALM2 and CALM3, were also upregulated in saliva of bitches with mammary tumors. These proteins are described here as modulated in saliva in CMT for the first time. Previous studies in humans reported overexpression of calmodulins in serum of patients with breast cancer [55] and the use of calmodulin antagonists as a therapeutic strategy [56].

Kallikrein-1-like (KLK1) protein was the only downregulated protein in saliva of bitches with CMT. Both kallikrein genes and proteins might promote or inhibit cancer cell growth, angiogenesis, invasion and metastasis by different mechanisms [57]. Therefore, the role of KLK in cancer is still controversial, with several studies associating KLK with better or worse income. For example, the *in vitro* inhibition of KLK1 suppresses the invasiveness of breast cancer cells, and therefore it could be a defence mechanism [58]. On the other hand, KLK-mediated degradation of extracellular matrix proteins facilitates tumor cell invasion and metastasis [59], and higher serum levels of other kallikreins such as KLK5 [60], KLK10 [61], and KLK14 [62] have been found in women with breast cancer when compared to healthy ones. Hormonal regulation of KLK1 expression was suggested in human prostate and breast tissues [63] and its salivary secretion was proposed as modulated by age [64]. Nevertheless, to the best of the author's knowledge, this is the first report describing a downregulation of KLK1 in saliva in CMT, and the possible causes for its modulation should be further studied.

When serum and salivary proteomes were compared, approximately twice as many proteins were identified in saliva compared to serum (730 in saliva vs. 379 in serum). This is in agreement with previous studies reporting a higher number of proteins in saliva [65], and indicates that saliva can provide opportunities for the identification of new non-invasive biomarkers. This fact also suggests that a high number of proteins that appear in saliva are not transported from blood but may come from salivary glands, nasal and bronchial secretions, gingival crevicular fluid among others, and, thus, their origin should be investigated in future studies. In our study, none of the proteins were significantly differentially modulated in both serum and saliva at the same time, which reinforces the possible different origin of many proteins in serum and saliva.

The results of the present study suffer from some limitations. First, the included animals were client-owned bitches of different breeds, which may have influenced our results and increased variability since, for example, higher expression of p53 (which is generally associated with poorer overall survival) has been reported in large-breed dogs [66]. In addition, although these biomarkers were not studied in our reports, cancer-related biomarkers including estrogen receptor alpha (ERα), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) differ between the type and subtype of CMT and could have a potential influence in the results [67,68]. Finally, the sample size was relatively small, although it was greater than the minimum of three biological replicates recommended for proteomic studies [69]. Therefore, this study should be considered as a pilot study, and further research with larger populations are needed in order to confirm our findings and to evaluate the potential influence of variables such as age, breed, tumor type based on immunophenotype, and hormonal influence in addition to other possible confounding factors such as other types of neoplasms, different diseases or the presence of oral alterations such as gingivitis.

5. Conclusions

Dogs with CMT have changes in serum and saliva proteomes as compared to healthy dogs. Bioinformatic analyses in serum and saliva showed that most modulated proteins have binding or catalytic activity molecular functions. Proteins such as kallikrein-1 and immunoglobulin gamma-heavy chains A and D were related to CMT in this study for the first time, and could be considered as potential novel CMT biomarkers. In addition, some of the modulated proteins found in the present study such as haptoglobin or S100A4 have been related to CMT or human breast cancer previously,

which confirms the validity of our study design for CMT evaluation and the use of CMT as a model for breast cancer research. Overall, data presented in this report reflect the changes that occur in the proteome of serum and saliva in dogs with CMT and could be a potential source for the study of new biomarkers for this disease.

Author Contributions: Conceptualization, V.M., J.J.C., S.M.-S. and A.T.; formal analysis, L.F.-M. and A.H.; resources, R.D.; software, A.G.; supervision, V.M. and J.J.C.; validation, M.D.C.-A.; writing—original draft, L.F.-M. All authors have read and agreed to the published version of the manuscript.

Funding: L.F.-M. and M.D.C.-A. were granted with pre-doctoral contract 'FPU' of University of Murcia, Spain. A.T. has a post-doctoral fellowship "Ramón y Cajal" supported by the "Ministerio de Economía y Competitividad", Spain. This work was supported by a grant from the Program for Research Groups of Excellence of the Seneca Foundation, Murcia, Spain (grant 19894/GERM/15), European Commission ERA chair FP7 grant (VetMedZg #621394), and by the Seneca Foundation-Agency of Science and Technology of the Region of Murcia through the Subprogram of Support to the Scientific Leadership and the Transition to the Independent Investigation (20649/JLI/18).

Acknowledgments: The authors would like to thank the pet owners and their colleagues that kindly agreed to collaborate in this study.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

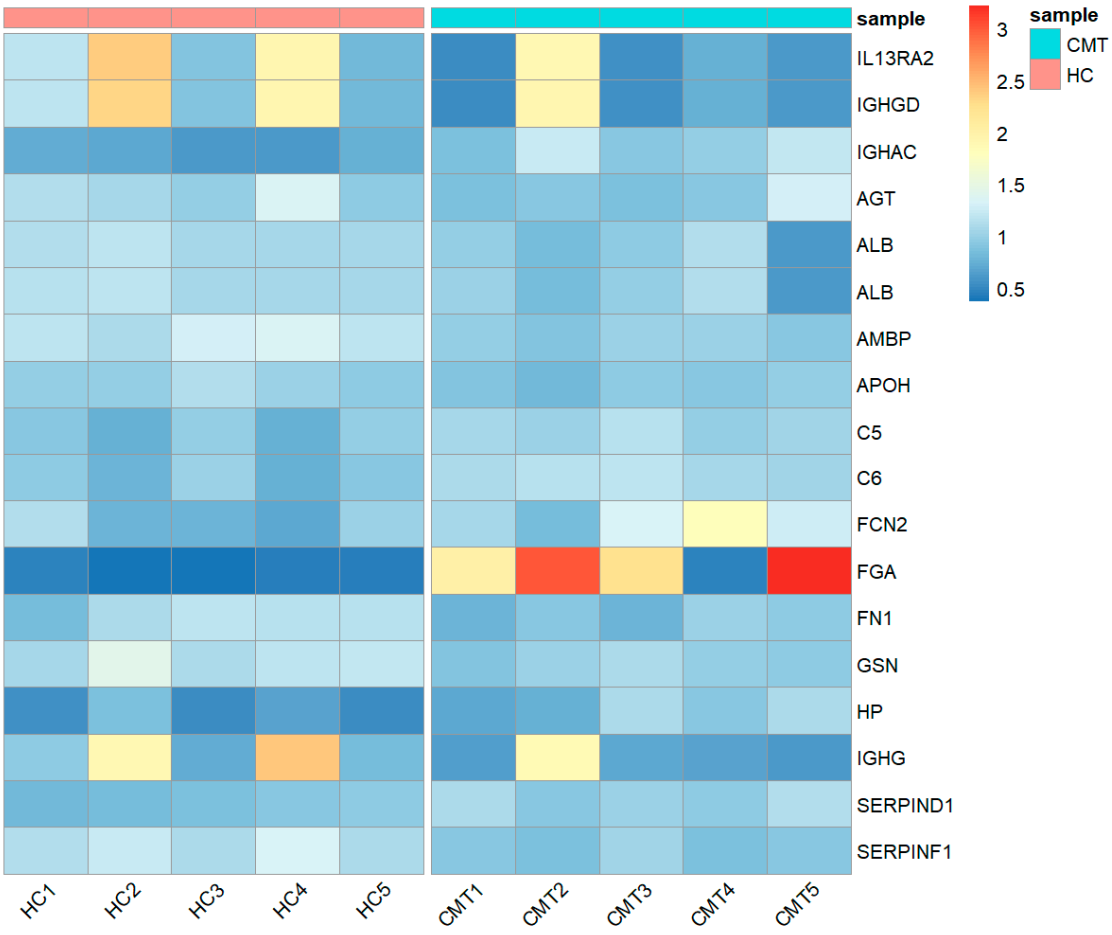

Figure A1. Heatmap showing the relative abundance (color) of serum proteins in healthy (HC) dogs and dogs with canine mammary tumors (CMT).

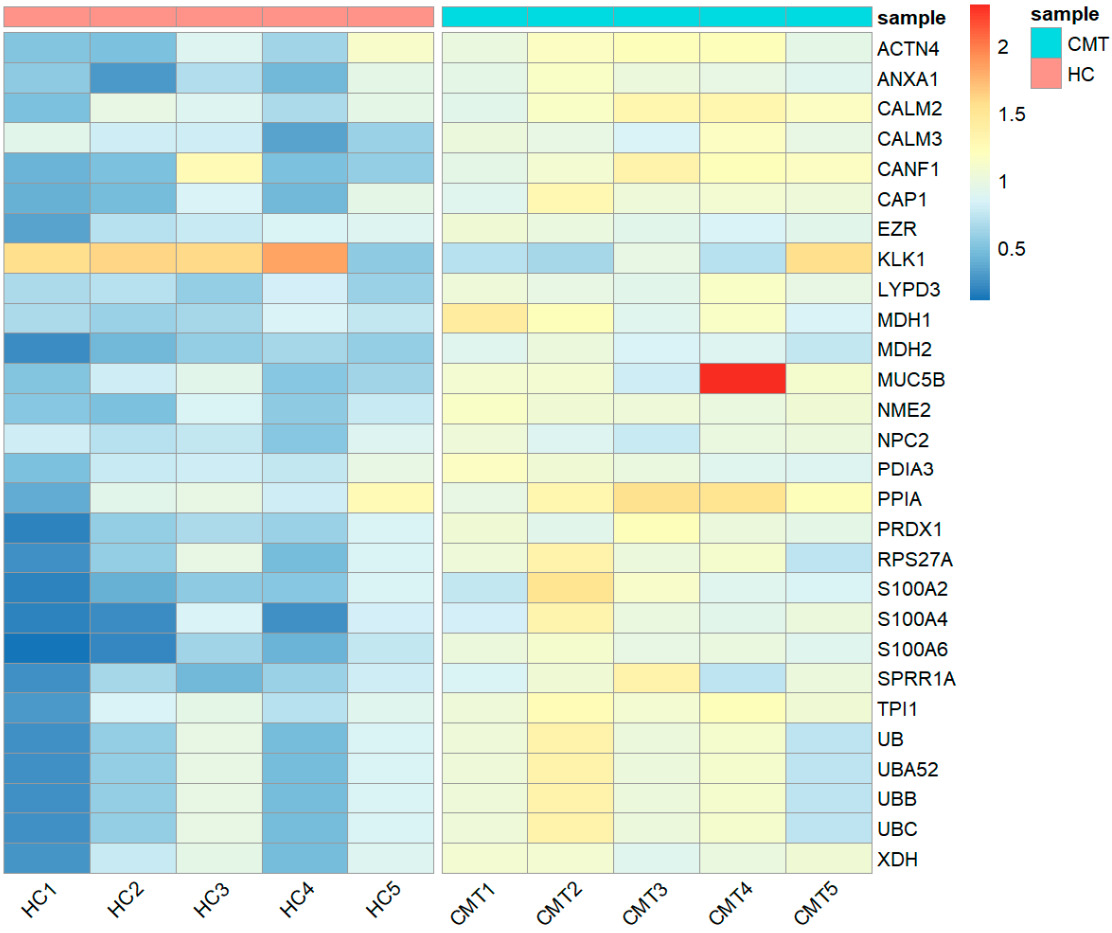

Figure A2. Heatmap showing the relative abundance (color) of salivary proteins in healthy (HC) dogs and dogs with canine mammary tumors (CMT).

Table A1. Serum proteins identified in dogs with canine mammary tumors (CMT) and healthy controls (HC).

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
C6	1418330227	7	complement component C6 [*Canis lupus dingo*]	0.326	0.008
C6	1239899336	7	complement component C6 [*Canis lupus familiaris*]	0.326	0.008
IGHAC	598107	9	IgA heavy chain constant region, partial [*Canis lupus familiaris*]	0.808	0.008
SERPINF1	119637837	5	pigment epithelium-derived factor [*Canis lupus familiaris*]	−0.364	0.008
SERPINF1	545510243	5	pigment epithelium-derived factor isoform X1 [*Canis lupus familiaris*]	−0.364	0.008
AMBP	1418322170	2	protein AMBP [*Canis lupus dingo*]	−0.354	0.008
AMBP	345777712	2	protein AMBP [*Canis lupus familiaris*]	−0.354	0.008
N/A	60734606	2	unnamed protein product, partial [*Canis lupus familiaris*]	1.021	0.008
N/A	60734607	5	unnamed protein product, partial [*Canis lupus familiaris*]	0.630	0.008
AGT	545494757	11	angiotensinogen [*Canis lupus familiaris*]	−0.190	0.016
AGT	5821257	3	angiotensinogen, partial [*Canis lupus familiaris*]	−0.304	0.016
C5	1418321303	31	complement C5 [*Canis lupus dingo*]	0.251	0.016
C5	1239925760	29	complement C5 [*Canis lupus familiaris*]	0.256	0.016
FGA	1304047	12	fibrinogen A-alpha chain, partial [*Canis lupus familiaris*]	2.507	0.016
FGA	1418336346	24	fibrinogen-alpha chain [*Canis lupus dingo*]	2.378	0.016
FGA	73978329	24	fibrinogen-alpha chain [*Canis lupus familiaris*]	2.378	0.016
FN1	1272414	11	fibronectin, partial [*Canis lupus familiaris*]	−0.364	0.016
GSN	1418322411	15	gelsolin isoform X1 [*Canis lupus dingo*]	−0.281	0.016
GSN	1418322413	15	gelsolin isoform X2 [*Canis lupus dingo*]	−0.281	0.016
GSN	1418322415	15	gelsolin isoform X3 [*Canis lupus dingo*]	−0.281	0.016
IGHGD	17066530	8	immunoglobulin gamma-heavy chain D [*Canis lupus familiaris*]	−1.073	0.016
N/A	16607648	6	unnamed protein product [*Canis lupus familiaris*]	−1.241	0.016
IL13RA2	16607715	6	interleukin-13 receptor subunit alpha-2 precursor [*Canis lupus familiaris*]	−1.250	0.016
N/A	16607724	8	unnamed protein product [*Canis lupus familiaris*]	−1.073	0.016
N/A	16607681	8	unnamed protein product, partial [*Canis lupus familiaris*]	−1.073	0.016
APOH	296089	13	apolipoprotein H; beta-2-glycoprotein I [*Canis lupus familiaris*]	−0.147	0.032
GSN	1239925762	14	gelsolin [*Canis lupus familiaris*]	−0.283	0.032
HP	258499	25	haptoglobin heavy chain, HpH chain [dogs, Peptide, 245 aa]	0.544	0.032
SERPIND1	345791439	11	heparin cofactor 2 [*Canis lupus familiaris*]	0.224	0.032
SERPIND1	1418264107	10	LOW QUALITY PROTEIN: heparin cofactor 2 [*Canis lupus dingo*]	0.224	0.032
N/A	16607678	3	unnamed protein product, partial [*Canis lupus familiaris*]	−1.184	0.032
ALB	3319897	2	albumin [*Canis lupus familiaris*]	−0.284	0.048
FCN2	73967778	4	ficolin-2 isoform X1 [*Canis lupus familiaris*]	0.529	0.048
FCN2	1239920689	4	ficolin-2 isoform X2 [*Canis lupus familiaris*]	0.529	0.048
ALB	1418328547	4	LOW QUALITY PROTEIN: serum albumin-like [*Canis lupus dingo*]	−0.276	0.048

Table A1. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
ALB	2147092	2	albumin—dog (fragment)	−0.338	0.056
FGB	1418336465	24	fibrinogen beta chain [*Canis lupus dingo*]	1.936	0.056
FN1	1272412	8	fibronectin, partial [*Canis lupus familiaris*]	−0.290	0.056
HP	73957095	30	haptoglobin-like [*Canis lupus familiaris*]	0.493	0.056
AOC3	57091057	2	membrane primary amine oxidase isoform X1 [*Canis lupus familiaris*]	0.342	0.056
AOC3	1418340066	2	membrane primary amine oxidase isoform X2 [*Canis lupus dingo*]	0.342	0.056
AOC3	1239918266	2	membrane primary amine oxidase isoform X3 [*Canis lupus familiaris*]	0.342	0.056
AOC3	1239918269	2	membrane primary amine oxidase isoform X4 [*Canis lupus familiaris*]	0.342	0.056
KLKB1	1418255638	7	plasma kallikrein isoform X1 [*Canis lupus dingo*]	−0.195	0.056
KLKB1	1239938505	6	plasma kallikrein isoform X2 [*Canis lupus familiaris*]	−0.195	0.056
HP	123511	30	Haptoglobin beta chain	0.493	0.056
RBP4	928175781	6	retinol-binding protein 4 [*Canis lupus familiaris*]	−0.397	0.056
F9	163948	3	factor IX [*Canis lupus familiaris*]	0.276	0.057
FGG	545524897	19	fibrinogen gamma chain isoform X1 [*Canis lupus familiaris*]	2.093	0.095
FGG	73977992	19	fibrinogen gamma chain isoform X2 [*Canis lupus familiaris*]	2.093	0.095
IGL-1	1239964876	2	immunoglobulin lambda-1 light chain isoform X32 [*Canis lupus familiaris*]	−0.364	0.095
IGL-1	1239964884	2	immunoglobulin lambda-1 light chain isoform X37 [*Canis lupus familiaris*]	−0.364	0.095
IGL-1	1239964904	2	immunoglobulin lambda-1 light chain isoform X48 [*Canis lupus familiaris*]	−0.364	0.095
IGL-1	1239964906	2	immunoglobulin lambda-1 light chain isoform X49 [*Canis lupus familiaris*]	−0.364	0.095
CPB2	1418275904	2	carboxypeptidase B2 [*Canis lupus dingo*]	0.672	0.100
C8A	1418311120	3	complement component C8 alpha chain isoform X1 [*Canis lupus dingo*]	−0.394	0.100
C8A	359319377	3	complement component C8 alpha chain isoform X1 [*Canis lupus familiaris*]	−0.394	0.100
C8A	1418311122	3	complement component C8 alpha chain isoform X2 [*Canis lupus dingo*]	−0.394	0.100
C8A	1239902894	3	complement component C8 alpha chain isoform X2 [*Canis lupus familiaris*]	−0.394	0.100
ACTC1	57108093	3	actin, alpha cardiac muscle 1 [*Canis lupus familiaris*]	0.128	0.111
ACTA1	1418509163	3	actin, alpha skeletal muscle [*Canis lupus dingo*]	0.128	0.111
ACTA1	545494777	3	actin, alpha skeletal muscle [*Canis lupus familiaris*]	0.128	0.111
ACTA2	1418341514	3	actin, aortic smooth muscle [*Canis lupus dingo*]	0.128	0.111
ACTB	924183513	4	actin, cytoplasmic 1 [*Canis lupus familiaris*]	0.128	0.111
ACTB	545500782	4	actin, cytoplasmic 1 isoform X1 [*Canis lupus familiaris*]	0.128	0.111
ACTB	1418248118	4	actin, cytoplasmic 2 [*Canis lupus dingo*]	0.128	0.111
ACTG1	924442847	4	actin, cytoplasmic 2 [*Canis lupus familiaris*]	0.128	0.111
ACTG2	1418210682	3	actin, gamma-enteric smooth muscle [*Canis lupus dingo*]	0.128	0.111
ACTB	5597005	3	beta-actin [*Canis lupus familiaris*]	0.128	0.111
C3	928164703	4	complement C3 [*Canis lupus familiaris*]	−0.374	0.111
LOC112676346	1418260262	2	uncharacterized protein LOC112676346 [*Canis lupus dingo*]	−0.698	0.111
F5	1418316947	2	coagulation factor V [*Canis lupus dingo*]	0.299	0.114
F5	545504920	2	coagulation factor V [*Canis lupus familiaris*]	0.299	0.114

Table A1. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
C1qB	1418507477	5	complement C1q subcomponent subunit B [*Canis lupus dingo*]	0.101	0.135
ADIPOQ	1418515478	3	adiponectin isoform X1 [*Canis lupus dingo*]	−0.302	0.151
ADIPOQ	1239977620	3	adiponectin isoform X2 [*Canis lupus familiaris*]	−0.302	0.151
ADIPOQ	54792748	3	adiponectin precursor [*Canis lupus familiaris*]	−0.302	0.151
ADIPOQ	15825495	3	adiponectin, partial [*Canis lupus familiaris*]	−0.302	0.151
ADIPOQ	204638075	3	adiponectin, partial [*Canis lupus*]	−0.302	0.151
APOA1	1418241889	5	apolipoprotein A-I [*Canis lupus dingo*]	−0.385	0.151
APOB	78499413	5	apolipoprotein B, partial [*Canis mesomelas*]	0.133	0.151
APOB	78499415	5	apolipoprotein B, partial [*Canis simensis*]	0.133	0.151
APOC2	1418304648	3	apolipoprotein C-II [*Canis lupus dingo*]	−0.395	0.151
APOC2	163903	3	apolipoprotein C-II precursor [*Canis lupus familiaris*]	−0.395	0.151
APOC3	163905	2	apolipoprotein C-III precursor [*Canis lupus familiaris*]	−0.429	0.151
APOC3	924859480	3	apolipoprotein C-III precursor [*Canis lupus familiaris*]	−0.396	0.151
C3	1418218430	8	complement C3 [*Canis lupus dingo*]	0.228	0.151
CFI	1418243013	10	complement factor I isoform X1 [*Canis lupus dingo*]	−0.093	0.151
CFI	1239976293	10	complement factor I isoform X1 [*Canis lupus familiaris*]	−0.093	0.151
CFI	1418243015	10	complement factor I isoform X2 [*Canis lupus dingo*]	−0.093	0.151
CFI	1239976295	10	complement factor I isoform X2 [*Canis lupus familiaris*]	−0.093	0.151
CFI	1418243017	10	complement factor I isoform X3 [*Canis lupus dingo*]	−0.093	0.151
CFI	545552242	10	complement factor I isoform X3 [*Canis lupus familiaris*]	−0.093	0.151
CFI	1418243019	9	complement factor I isoform X4 [*Canis lupus dingo*]	−0.090	0.151
CFI	928179004	9	complement factor I isoform X4 [*Canis lupus familiaris*]	−0.090	0.151
HPX	73988725	15	hemopexin [*Canis lupus familiaris*]	0.285	0.151
ITIH1	1418216242	21	inter-alpha-trypsin inhibitor heavy chain H1 [*Canis lupus dingo*]	−0.152	0.151
ITIH1	73985485	21	inter-alpha-trypsin inhibitor heavy chain H1 isoform X1 [*Canis lupus familiaris*]	−0.152	0.151
ITIH1	1239949881	20	inter-alpha-trypsin inhibitor heavy chain H1 isoform X2 [*Canis lupus familiaris*]	−0.155	0.151
ITIH3	1418216228	4	inter-alpha-trypsin inhibitor heavy chain H3 isoform X1 [*Canis lupus dingo*]	−0.372	0.151
ITIH3	1418216230	4	inter-alpha-trypsin inhibitor heavy chain H3 isoform X2 [*Canis lupus dingo*]	−0.372	0.151
KRT10	1418337563	6	keratin, type I cytoskeletal 10 isoform X1 [*Canis lupus dingo*]	−0.308	0.151
KRT10	928144438	6	keratin, type I cytoskeletal 10 isoform X1 [*Canis lupus familiaris*]	−0.308	0.151
KRT10	1418337565	6	keratin, type I cytoskeletal 10 isoform X2 [*Canis lupus dingo*]	−0.308	0.151
KRT10	928144440	6	keratin, type I cytoskeletal 10 isoform X2 [*Canis lupus familiaris*]	−0.308	0.151
KRT10	1418337567	6	keratin, type I cytoskeletal 10 isoform X3 [*Canis lupus dingo*]	−0.308	0.151
KRT10	928144442	6	keratin, type I cytoskeletal 10 isoform X3 [*Canis lupus familiaris*]	−0.308	0.151
ITIH3	928186331	4	LOW QUALITY PROTEIN: inter-alpha-trypsin inhibitor heavy chain H3 [*Canis lupus familiaris*]	−0.372	0.151
TF	928167632	3	serotransferrin [*Canis lupus familiaris*]	−0.104	0.151
LOC112676265	1418260227	2	uncharacterized protein LOC112676265 [*Canis lupus dingo*]	−0.505	0.151
HBB	227343817	14	chain B, crystal structure of dog (*Canis Familiaris*) hemoglobin	1.053	0.190

Table A1. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
HBA	194368499	2	chain C, hemoglobin subunit alpha	1.059	0.190
HBD	103484123	3	globin, partial [*Canis lupus familiaris*]	1.392	0.190
HBB	1418222274	13	hemoglobin subunit beta [*Canis lupus dingo*]	1.068	0.190
HBB	1418222276	8	hemoglobin subunit beta-like [*Canis lupus dingo*]	1.155	0.190
MGAM	1418324508	32	maltase-glucoamylase, intestinal isoform X1 [*Canis lupus dingo*]	0.233	0.190
MGAM	1239938912	32	maltase-glucoamylase, intestinal isoform X1 [*Canis lupus familiaris*]	0.233	0.190
MGAM	1418324514	32	maltase-glucoamylase, intestinal isoform X2 [*Canis lupus dingo*]	0.233	0.190
MGAM	928156540	32	maltase-glucoamylase, intestinal isoform X2 [*Canis lupus familiaris*]	0.233	0.190
HBA1	1101972892	9	TPA: globin A1 [*Canis lupus familiaris*]	1.152	0.190
TFRC	10946310	8	transferrin receptor [*Canis lupus familiaris*]	−0.296	0.190
TFRC	701217752	8	transferrin receptor protein 1 [*Canis lupus*]	−0.296	0.190
TFRC	387178037	8	transferrin receptor protein 1 [*Canis mesomelas*]	−0.296	0.190
MBL2	1418327084	2	mannose-binding protein C [*Canis lupus dingo*]	−0.640	0.200
MBL2	73953733	2	mannose-binding protein C [*Canis lupus familiaris*]	−0.640	0.200
APOB	78709133	8	apolipoprotein B, partial [*Canis adustus*]	0.375	0.206
APOB	78709135	8	apolipoprotein B, partial [*Canis aureus*]	0.375	0.206
APOB	78709137	7	apolipoprotein B, partial [*Canis latrans*]	0.375	0.206
APOB	78709143	8	apolipoprotein B, partial [*Canis simensis*]	0.375	0.206
A1BG	1418297237	13	alpha-1B-glycoprotein [*Canis lupus dingo*]	−0.165	0.222
A1BG	545487024	13	alpha-1B-glycoprotein [*Canis lupus familiaris*]	−0.165	0.222
APOB	78709141	6	apolipoprotein B, partial [*Canis mesomelas*]	0.435	0.222
CP	1418510222	26	ceruloplasmin isoform X1 [*Canis lupus dingo*]	0.141	0.222
CP	1418510226	26	ceruloplasmin isoform X2 [*Canis lupus dingo*]	0.141	0.222
CP	1418510228	26	ceruloplasmin isoform X3 [*Canis lupus dingo*]	0.141	0.222
CP	1418510230	26	ceruloplasmin isoform X4 [*Canis lupus dingo*]	0.141	0.222
FN1	1418343247	57	fibronectin isoform X1 [*Canis lupus dingo*]	−0.124	0.222
FN1	928182521	57	fibronectin isoform X1 [*Canis lupus familiaris*]	−0.124	0.222
FN1	1418343265	56	fibronectin isoform X10 [*Canis lupus dingo*]	−0.123	0.222
FN1	928182523	56	fibronectin isoform X10 [*Canis lupus familiaris*]	−0.123	0.222
FN1	1418343267	57	fibronectin isoform X11 [*Canis lupus dingo*]	−0.116	0.222
FN1	928182519	57	fibronectin isoform X11 [*Canis lupus familiaris*]	−0.116	0.222
FN1	1418343249	57	fibronectin isoform X2 [*Canis lupus dingo*]	−0.124	0.222
FN1	1239982239	57	fibronectin isoform X2 [*Canis lupus familiaris*]	−0.124	0.222
FN1	1418343251	57	fibronectin isoform X3 [*Canis lupus dingo*]	−0.124	0.222
FN1	1239982241	57	fibronectin isoform X3 [*Canis lupus familiaris*]	−0.124	0.222
FN1	1418343253	58	fibronectin isoform X4 [*Canis lupus dingo*]	−0.116	0.222
FN1	928182507	58	fibronectin isoform X4 [*Canis lupus familiaris*]	−0.116	0.222

Table A1. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
FN1	1418343255	58	fibronectin isoform X5 [*Canis lupus dingo*]	−0.116	0.222
FN1	928182509	58	fibronectin isoform X5 [*Canis lupus familiaris*]	−0.116	0.222
FN1	1418343257	56	fibronectin isoform X6 [*Canis lupus dingo*]	−0.123	0.222
FN1	1239982243	56	fibronectin isoform X6 [*Canis lupus familiaris*]	−0.123	0.222
FN1	1418343259	58	fibronectin isoform X7 [*Canis lupus dingo*]	−0.116	0.222
FN1	928182511	58	fibronectin isoform X7 [*Canis lupus familiaris*]	−0.116	0.222
FN1	1418343261	54	fibronectin isoform X8 [*Canis lupus dingo*]	−0.108	0.222
FN1	1239982245	54	fibronectin isoform X8 [*Canis lupus familiaris*]	−0.108	0.222
FN1	1418343263	58	fibronectin isoform X9 [*Canis lupus dingo*]	−0.116	0.222
FN1	928182513	58	fibronectin isoform X9 [*Canis lupus familiaris*]	−0.116	0.222
LOC611458	1418213976	58	pregnancy zone protein-like isoform X1 [*Canis lupus dingo*]	−0.209	0.222
LOC611458	545546412	57	pregnancy zone protein-like isoform X1 [*Canis lupus familiaris*]	−0.204	0.222
LOC611458	1418213978	59	pregnancy zone protein-like isoform X2 [*Canis lupus dingo*]	−0.205	0.222
LOC611458	545546414	58	pregnancy zone protein-like isoform X2 [*Canis lupus familiaris*]	−0.201	0.222
LOC611458	1418213980	51	pregnancy zone protein-like isoform X3 [*Canis lupus dingo*]	−0.177	0.222
LOC611458	1239967247	50	pregnancy zone protein-like isoform X3 [*Canis lupus familiaris*]	−0.172	0.222
CLEC3B	1418220357	5	tetranectin [*Canis lupus dingo*]	−0.175	0.222
CLEC3B	928162811	3	tetranectin [*Canis lupus familiaris*]	−0.197	0.222
F13B	545504208	4	coagulation factor XIII B chain [*Canis lupus familiaris*]	−0.209	0.229
F10	3328199	4	coagulation factor X, partial [*Canis lupus familiaris*]	0.093	0.257
F10	1418340495	4	coagulation factor X-like isoform X1 [*Canis lupus dingo*]	0.093	0.257
C8G	1418266608	2	complement component C8 gamma chain isoform X1 [*Canis lupus dingo*]	0.124	0.286
C8G	1239920398	2	complement component C8 gamma chain isoform X1 [*Canis lupus familiaris*]	0.124	0.286
GPX3	1418327853	7	glutathione peroxidase 3 [*Canis lupus dingo*]	−0.221	0.286
TFRC	1418200084	7	transferrin receptor protein 1 [*Canis lupus dingo*]	−0.280	0.286
ALB	6687188	4	albumin [*Canis lupus familiaris*]	−0.606	0.310
SERPINA3	73964432	12	alpha-1-antichymotrypsin [*Canis lupus familiaris*]	0.098	0.310
ALB	1104685307	4	chain A, serum albumin	−0.606	0.310
C2	1239928849	7	complement C2 isoform X1 [*Canis lupus familiaris*]	0.054	0.310
C2	1418290462	7	complement C2 isoform X2 [*Canis lupus dingo*]	0.054	0.310
C2	1239928853	7	complement C2 isoform X3 [*Canis lupus familiaris*]	0.054	0.310
C7	1418329743	15	complement component C7 isoform X3 [*Canis lupus dingo*]	0.061	0.310
GPLD1	545554529	13	phosphatidylinositol-glycan-specific phospholipase D isoform X1 [*Canis lupus familiaris*]	0.106	0.310
GPLD1	1418204633	13	phosphatidylinositol-glycan-specific phospholipase D isoform X2 [*Canis lupus dingo*]	0.106	0.310
APOD	928180090	4	apolipoprotein D [*Canis lupus familiaris*]	−0.075	0.341
CLU	163954	14	glycoprotein 80 [*Canis lupus familiaris*]	0.102	0.341
ITIH2	1418502140	18	inter-alpha-trypsin inhibitor heavy chain H2 [*Canis lupus dingo*]	−0.099	0.389

Table A1. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
ITIH2	73949158	18	inter-alpha-trypsin inhibitor heavy chain H2 [*Canis lupus familiaris*]	−0.099	0.389
LBP	345789637	6	lipopolysaccharide-binding protein [*Canis lupus familiaris*]	0.439	0.400
LBP	1418251736	5	LOW QUALITY PROTEIN: lipopolysaccharide-binding protein [*Canis lupus dingo*]	0.498	0.400
SERPINA3	1418345970	11	alpha-1-antichymotrypsin [*Canis lupus dingo*]	0.113	0.413
SAA1	227017	3	amyloid A protein	−2.012	0.413
IGJ; JCHAIN	1239965532	2	immunoglobulin iota chain-like [*Canis lupus familiaris*]	−0.095	0.413
SAA1	928166207	4	serum amyloid A protein [*Canis lupus familiaris*]	−1.497	0.413
SAA1	1418223200	4	serum amyloid A protein-like [*Canis lupus dingo*]	−1.497	0.413
SAA1	57102730	3	serum amyloid A protein-like [*Canis lupus familiaris*]	−2.012	0.413
SAA1	55741727	3	serum amyloid A1 precursor [*Canis lupus familiaris*]	−2.012	0.413
SERPINF2	1418267349	5	alpha-2-antiplasmin isoform X1 [*Canis lupus dingo*]	0.084	0.421
SERPINF2	73967363	5	alpha-2-antiplasmin isoform X1 [*Canis lupus familiaris*]	0.084	0.421
SERPINF2	1418267343	5	alpha-2-antiplasmin isoform X2 [*Canis lupus dingo*]	0.084	0.421
SERPINF2	545512145	5	alpha-2-antiplasmin isoform X2 [*Canis lupus familiaris*]	0.084	0.421
APOC1	1418304654	4	apolipoprotein C-I [*Canis lupus dingo*]	−0.211	0.421
C4BPB	1418315459	3	C4b-binding protein beta chain [*Canis lupus dingo*]	−0.082	0.421
C9	1418330062	6	complement component C9 [*Canis lupus dingo*]	0.103	0.421
C9	545496317	6	complement component C9 [*Canis lupus familiaris*]	0.103	0.421
FETUB	74003556	3	fetuin-B [*Canis lupus familiaris*]	0.626	0.421
HABP2	1418245880	3	hyaluronan-binding protein 2 [*Canis lupus dingo*]	−0.134	0.421
HABP2	545547980	3	hyaluronan-binding protein 2 [*Canis lupus familiaris*]	−0.134	0.421
ITIH1	545533419	17	inter-alpha-trypsin inhibitor heavy chain H1 isoform X3 [*Canis lupus familiaris*]	−0.122	0.421
GPLD1	928181234	11	phosphatidylinositol-glycan-specific phospholipase D isoform X3 [*Canis lupus familiaris*]	0.129	0.421
SERPINA5	1418346186	6	plasma serine protease inhibitor [*Canis lupus dingo*]	0.191	0.421
SERPINA5	545508405	6	plasma serine protease inhibitor [*Canis lupus familiaris*]	0.191	0.421
PLG	18139619	13	plasminogen, partial [*Canis lupus familiaris*]	−0.099	0.421
CFP	74007356	2	properdin [*Canis lupus familiaris*]	0.172	0.421
F2	359321961	19	prothrombin [*Canis lupus familiaris*]	0.055	0.421
APOE	3915605	11	Apolipoprotein E	0.210	0.421
SERPING1	1239944268	7	plasma protease C1 inhibitor [*Canis lupus familiaris*]	−0.098	0.516
AFM	1418328671	26	afamin [*Canis lupus dingo*]	−0.067	0.548
AFM	73975389	27	afamin [*Canis lupus familiaris*]	−0.068	0.548
A2M	1418213974	47	alpha-2-macroglobulin [*Canis lupus dingo*]	−0.034	0.548
A2M	345792424	47	alpha-2-macroglobulin [*Canis lupus familiaris*]	−0.034	0.548
APOB	78499407	5	apolipoprotein B, partial [*Canis aureus*]	0.033	0.548
APOB100	1418212773	74	apolipoprotein B-100 [*Canis lupus dingo*]	0.078	0.548
APOB100	545528321	74	apolipoprotein B-100 [*Canis lupus familiaris*]	0.078	0.548

Table A1. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
APOE	57036446	10	apolipoprotein E [*Canis lupus familiaris*]	0.211	0.548
F12	1418325925	3	coagulation factor XII isoform X1 [*Canis lupus dingo*]	−0.053	0.548
F12	73953994	3	coagulation factor XII isoform X1 [*Canis lupus familiaris*]	−0.053	0.548
F12	1418325927	3	coagulation factor XII isoform X2 [*Canis lupus dingo*]	−0.053	0.548
F12	545495643	3	coagulation factor XII isoform X2 [*Canis lupus familiaris*]	−0.053	0.548
F12	1418325929	3	coagulation factor XII isoform X3 [*Canis lupus dingo*]	−0.053	0.548
F12	1239898360	3	coagulation factor XII isoform X3 [*Canis lupus familiaris*]	−0.053	0.548
C7	1418329739	17	complement component C7 isoform X1 [*Canis lupus dingo*]	0.030	0.548
C7	73953824	17	complement component C7 isoform X1 [*Canis lupus familiaris*]	0.030	0.548
C7	1418329741	16	complement component C7 isoform X2 [*Canis lupus dingo*]	0.071	0.548
C7	1239899370	16	complement component C7 isoform X2 [*Canis lupus familiaris*]	0.071	0.548
FETUB	1418515534	3	fetuin-B [*Canis lupus dingo*]	0.146	0.548
HRG	1418515616	13	histidine-rich glycoprotein isoform X1 [*Canis lupus dingo*]	−0.303	0.548
HRG	545553762	12	histidine-rich glycoprotein isoform X1 [*Canis lupus familiaris*]	−0.304	0.548
IGJ; JCHAIN	345779666	5	immunoglobulin J chain [*Canis lupus familiaris*]	−0.081	0.548
IGL-1	1418263577	3	immunoglobulin lambda-1 light chain-like [*Canis lupus dingo*]	−0.285	0.548
QSOX1	928139154	3	LOW QUALITY PROTEIN: sulfhydryl oxidase 1, partial [*Canis lupus familiaris*]	0.061	0.548
SERPING1	1418207941	10	plasma protease C1 inhibitor [*Canis lupus dingo*]	−0.102	0.548
APOA2	597500968	5	Apolipoprotein A-II;	−0.138	0.548
QSOX1	1418315968	3	sulfhydryl oxidase 1 isoform X1 [*Canis lupus dingo*]	0.061	0.548
QSOX1	1418315970	3	sulfhydryl oxidase 1 isoform X2 [*Canis lupus dingo*]	0.061	0.548
QSOX1	1418315972	3	sulfhydryl oxidase 1 isoform X3 [*Canis lupus dingo*]	0.061	0.548
VTN	1418267888	5	vitronectin [*Canis lupus dingo*]	0.022	0.548
IGH-CH1	124390007	3	immunoglobulin heavy chain constant region CH1, partial [*Canis lupus familiaris*]	0.187	0.556
SAA1	1418223204	7	serum amyloid A protein [*Canis lupus dingo*]	−1.568	0.556
SAA1	545536980	7	serum amyloid A protein isoform X1 [*Canis lupus familiaris*]	−1.568	0.556
SAA1	164060	7	serum amyloid A protein, partial [*Canis lupus familiaris*]	−1.568	0.556
SAA1	164064	7	serum amyloid A protein, partial [*Canis lupus familiaris*]	−1.568	0.556
SAA1	164066	7	serum amyloid A protein, partial [*Canis lupus familiaris*]	−1.568	0.556
SAA1	164068	7	serum amyloid A protein, partial [*Canis lupus familiaris*]	−1.568	0.556
SAA1	1418223194	7	serum amyloid A protein-like [*Canis lupus dingo*]	−1.568	0.556
SAA1	545535766	7	serum amyloid A1 isoform X1 [*Canis lupus familiaris*]	−1.568	0.556
KRT1	1418221463	6	keratin, type II cytoskeletal 1 [*Canis lupus dingo*]	−0.250	0.629
KRT1	75062693	6	Keratin, type II cytoskeletal 1;	−0.250	0.629
PEPD	1418305616	2	xaa-Pro dipeptidase isoform X1 [*Canis lupus dingo*]	−0.179	0.629
PEPD	73948526	2	xaa-Pro dipeptidase isoform X1 [*Canis lupus familiaris*]	−0.179	0.629
PEPD	545489037	2	xaa-Pro dipeptidase isoform X2 [*Canis lupus familiaris*]	−0.179	0.629
APOB	62870505	2	apolipoprotein B, partial [*Canis lupus*]	0.277	0.667
APOB	256016957	2	apolipoprotein B, partial [*Canis lupus*]	0.277	0.667
APOB	269307499	2	apolipoprotein B, partial [*Canis lupus*]	0.277	0.667

Table A1. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
APOB100	925718015	2	apolipoprotein B-100, partial [Canis adustus]	0.277	0.667
APOB100	925718021	2	apolipoprotein B-100, partial [*Canis aureus*]	0.277	0.667
APOB100	925718027	2	apolipoprotein B-100, partial [*Canis aureus*]	0.277	0.667
APOB100	925718029	2	apolipoprotein B-100, partial [*Canis aureus*]	0.277	0.667
APOB100	925718033	2	apolipoprotein B-100, partial [*Canis latrans*]	0.277	0.667
APOB100	925718059	2	apolipoprotein B-100, partial [*Canis latrans*]	0.277	0.667
APOB100	925718053	2	apolipoprotein B-100, partial [*Canis lupus*]	0.277	0.667
APOB100	925718037	2	apolipoprotein B-100, partial [*Canis simensis*]	0.277	0.667
IGHE	1096665	2	Ig:SUBUNIT = epsilon	−1.005	0.667
THBS1	1418259722	4	thrombospondin-1 [*Canis lupus dingo*]	−0.341	0.667
THBS1	345794639	4	thrombospondin-1 [*Canis lupus familiaris*]	−0.341	0.667
LRG1	1418218016	7	leucine-rich alpha-2-glycoprotein [*Canis lupus dingo*]	0.005	0.683
SERPINF2	1418267345	4	alpha-2-antiplasmin isoform X3 [*Canis lupus dingo*]	0.046	0.690
SERPINF2	1239920122	4	alpha-2-antiplasmin isoform X3 [*Canis lupus familiaris*]	0.046	0.690
SERPINF2	1418267347	4	alpha-2-antiplasmin isoform X4 [*Canis lupus dingo*]	0.046	0.690
SERPINF2	1239920124	4	alpha-2-antiplasmin isoform X4 [*Canis lupus familiaris*]	0.046	0.690
C4BPA	1418315462	24	C4b-binding protein alpha chain [*Canis lupus dingo*]	0.079	0.690
CPN1	1418245069	3	carboxypeptidase N catalytic chain isoform X2 [*Canis lupus dingo*]	0.222	0.690
SERPINA6	545508387	3	corticosteroid-binding globulin [*Canis lupus familiaris*]	0.062	0.690
SERPINA6	1418346025	3	corticosteroid-binding globulin-like [*Canis lupus dingo*]	0.062	0.690
IGH	1340236572	2	immunoglobulin heavy chain variable region, partial [*Canis lupus familiaris*]	−0.176	0.690
IGJ; JCHAIN	19715661	2	immunoglobulin J chain, partial [*Canis lupus familiaris*]	−0.130	0.690
PLG	558695388	33	plasminogen precursor [*Canis lupus familiaris*]	−0.015	0.690
ACT	1418333042	2	actin, clone 302-like [*Canis lupus dingo*]	−0.005	0.700
ACTB	1222669	2	beta-actin, partial [*Canis lupus familiaris*]	−0.005	0.700
N/A	1418204343	2	C-C motif chemokine 14-like [*Canis lupus dingo*]	−0.109	0.700
N/A	1535087818	3	unnamed protein product [*Toxocara canis*]	−0.005	0.700
AZGP1	70909945	5	zinc alpha-2-glycoprotein 1, partial [*Canis lupus familiaris*]	−0.016	0.700
IGH-CH2	124390009	3	immunoglobulin heavy chain constant region CH2, partial [*Canis lupus familiaris*]	−0.019	0.722
ORM1	1418322788	8	alpha-1-acid glycoprotein 1-like [*Canis lupus dingo*]	0.258	0.730
C3	1418218853	5	complement C3-like [*Canis lupus dingo*]	−0.274	0.730
IGL-1	545544683	3	immunoglobulin lambda-1 light chain isoform X34 [*Canis lupus familiaris*]	−0.156	0.730
TF	1418510423	2	serotransferrin-like [*Canis lupus dingo*]	−0.219	0.730
C1r	1418256182	10	complement C1r subcomponent [*Canis lupus dingo*]	0.000	0.786
AHSG	1418515495	10	alpha-2-HS-glycoprotein [*Canis lupus dingo*]	−0.332	0.841
APOE4	283972739	5	apolipoprotein E4, partial [*Canis lupus familiaris*]	0.158	0.841
APOE4	283972741	5	apolipoprotein E4, partial [*Canis lupus familiaris*]	0.158	0.841
APOE4	283972753	5	apolipoprotein E4, partial [*Canis lupus familiaris*]	0.158	0.841
APOM	57094349	3	apolipoprotein M isoform X1 [*Canis lupus familiaris*]	−0.021	0.841
CD5L	590121823	15	apoptosis inhibitor of macrophage [*Canis lupus familiaris*]	−0.093	0.841

Table A1. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
CPN2	545553264	3	carboxypeptidase N subunit 2 [*Canis lupus familiaris*]	0.083	0.841
CD5L	1418317684	15	CD5 antigen-like [*Canis lupus dingo*]	−0.093	0.841
C1s	73997275	6	complement C1s subcomponent [*Canis lupus familiaris*]	−0.048	0.841
CFB	1418290466	27	complement factor B [*Canis lupus dingo*]	−0.039	0.841
CFB	345778397	27	complement factor B [*Canis lupus familiaris*]	−0.039	0.841
HRG	1418515618	9	histidine-rich glycoprotein isoform X2 [*Canis lupus dingo*]	−0.164	0.841
HRG	545553764	9	histidine-rich glycoprotein isoform X2 [*Canis lupus familiaris*]	−0.164	0.841
IGH-CH4	124390013	4	immunoglobulin heavy chain constant region CH4, partial [*Canis lupus familiaris*]	−0.280	0.841
IGH	208342048	3	immunoglobulin heavy chain variable region, partial [*Canis lupus familiaris*]	0.190	0.841
ITIH4	928186325	30	inter-alpha-trypsin inhibitor heavy chain H4 isoform X1 [*Canis lupus familiaris*]	0.002	0.841
ITIH4	1239883263	29	inter-alpha-trypsin inhibitor heavy chain H4 isoform X2 [*Canis lupus familiaris*]	0.002	0.841
ITIH4	928186327	30	inter-alpha-trypsin inhibitor heavy chain H4 isoform X3 [*Canis lupus familiaris*]	0.002	0.841
CPN2	1418198271	3	LOW QUALITY PROTEIN: carboxypeptidase N subunit 2-like [*Canis lupus dingo*]	0.083	0.841
MGAM2	1418324502	3	putative maltase-glucoamylase-like protein FLJ16351 [*Canis lupus dingo*]	−0.008	0.841
MGAM2	1239938902	3	putative maltase-glucoamylase-like protein FLJ16351 isoform X1 [*Canis lupus familiaris*]	−0.008	0.841
MGAM2	1239938904	3	putative maltase-glucoamylase-like protein FLJ16351 isoform X2 [*Canis lupus familiaris*]	−0.008	0.841
IGH	208342196	3	immunoglobulin heavy chain variable region, partial [*Canis lupus familiaris*]	0.122	0.857
SAA1	545536976	6	serum amyloid A protein-like [*Canis lupus familiaris*]	−1.160	0.886
CPN1	928175986	4	carboxypeptidase N catalytic chain isoform X1 [*Canis lupus familiaris*]	−0.001	0.905
CP	928167527	25	ceruloplasmin isoform X1 [*Canis lupus familiaris*]	0.060	0.905
CP	1239957836	25	ceruloplasmin isoform X2 [*Canis lupus familiaris*]	0.060	0.905
CP	73990367	25	ceruloplasmin isoform X3 [*Canis lupus familiaris*]	0.060	0.905
CP	1239957839	25	ceruloplasmin isoform X4 [*Canis lupus familiaris*]	0.060	0.905
C1qA	1418506879	2	complement C1q subcomponent subunit A [*Canis lupus dingo*]	0.063	0.905
IGL	164430486	2	immunoglobulin lambda light chain variable region, partial [*Canis lupus familiaris*]	0.079	0.905
IGL	164430516	2	immunoglobulin lambda light chain variable region, partial [*Canis lupus familiaris*]	0.079	0.905
ADIPOQ	1483452888	2	TPA: adiponectin C [*Canis lupus familiaris*]	0.063	0.905
VDB	1418328657	26	vitamin D-binding protein [*Canis lupus dingo*]	0.012	0.952
SERPINC1	359320010	23	antithrombin-III [*Canis lupus familiaris*]	0.044	1.000
APOA4	1418241891	25	apolipoprotein A-IV [*Canis lupus dingo*]	−0.057	1.000
APOA4	345799905	25	apolipoprotein A-IV [*Canis lupus familiaris*]	−0.057	1.000
CP	45826457	5	ceruloplasmin, partial [*Canis lupus familiaris*]	−0.042	1.000
F13A	1418205161	2	coagulation factor XIII A chain [*Canis lupus dingo*]	0.063	1.000
C4A	1239928570	60	complement C4-A [*Canis lupus familiaris*]	0.053	1.000
C4A	1418290456	62	complement C4-A-like [*Canis lupus dingo*]	0.036	1.000

Table A1. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
C8B	73956394	3	complement component C8 beta chain [*Canis lupus familiaris*]	0.003	1.000
HP	258498	4	haptoglobin light chain, HpL chain [dogs, Peptide, 83 aa]	0.127	1.000
HGFAC	1418333238	2	hepatocyte growth factor activator [*Canis lupus dingo*]	0.026	1.000
HGFAC	1239893961	2	hepatocyte growth factor activator isoform X1 [*Canis lupus familiaris*]	0.026	1.000
HGFAC	73532760	2	hepatocyte growth factor activator precursor [*Canis lupus familiaris*]	0.026	1.000
IGH-CH3	124390011	2	immunoglobulin heavy chain constant region CH3, partial [*Canis lupus familiaris*]	−0.077	1.000
IGL	164430480	2	immunoglobulin lambda light chain variable region, partial [*Canis lupus familiaris*]	0.019	1.000
IGM	146743249	3	immunoglobulin mu heavy chain variable region, partial [*Canis lupus familiaris*]	−0.219	1.000
LUM	1418336203	2	lumican [*Canis lupus dingo*]	−0.144	1.000
MFAP4	1418312041	2	microfibril-associated glycoprotein 4 [*Canis lupus dingo*]	−0.057	1.000
APOA4	704000372	21	Apolipoprotein A-IV	−0.054	1.000
PLG	130314	16	Plasminogen	0.013	1.000
PON1	73975797	13	serum paraoxonase/arylesterase 1 [*Canis lupus familiaris*]	−0.073	1.000
SHBG	1418312750	5	sex hormone-binding globulin isoform X1 [*Canis lupus dingo*]	−0.105	1.000
SHBG	1239901836	5	sex hormone-binding globulin isoform X2 [*Canis lupus familiaris*]	−0.105	1.000
TTR	1418314244	5	transthyretin [*Canis lupus dingo*]	−0.062	1.000
PROC	1418199974	16	vitamin K-dependent protein S [*Canis lupus dingo*]	0.024	1.000
PROC	1239976411	16	vitamin K-dependent protein S [*Canis lupus familiaris*]	0.024	1.000
VTN	62421376	2	vitronectin, partial [*Canis mesomelas*]	−0.013	1.000
AZGP1	560879429	8	zinc-alpha-2-glycoprotein precursor [*Canis lupus familiaris*]	0.158	1.000

Table A2. Salivary proteins identified in dogs with canine mammary tumors (CMT) and healthy controls (HC).

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
LYPD3	1418304786	4	ly6/PLAUR domain-containing protein 3 [*Canis lupus dingo*]	0.594	0.008
LYPD3	73948247	4	ly6/PLAUR domain-containing protein 3 [*Canis lupus familiaris*]	0.594	0.008
MDH2	1418307145	4	malate dehydrogenase, mitochondrial [*Canis lupus dingo*]	0.981	0.008
MDH2	1239955263	3	malate dehydrogenase, mitochondrial-like [*Canis lupus familiaris*]	1.037	0.008
MDH2	89574135	3	mitochondrial malate dehydrogenase 2, NAD, partial [*Canis lupus familiaris*]	0.831	0.008
NME2	545510196	3	nucleoside diphosphate kinase B isoform X1 [*Canis lupus familiaris*]	0.722	0.008
PRDX1	1418294943	4	peroxiredoxin-1 [*Canis lupus dingo*]	0.834	0.008
S100A6	1239912330	3	protein S100-A6 [*Canis lupus familiaris*]	1.236	0.008
TPI1	76363530	12	Triosephosphate isomerase	0.597	0.008
CAP1	1418293878	8	adenylyl cyclase-associated protein 1 isoform X1 [*Canis lupus dingo*]	0.795	0.016
CAP1	1418293884	8	adenylyl cyclase-associated protein 1 isoform X2 [*Canis lupus dingo*]	0.795	0.016
ANXA1	558695394	9	annexin A1 [*Canis lupus familiaris*]	0.754	0.016
CALM3	1418304395	2	calmodulin-3 isoform X2 [*Canis lupus dingo*]	0.531	0.016
CORO1A	1418213540	2	cornifin-A [*Canis lupus dingo*]	0.890	0.016
EZR	1418300273	7	ezrin isoform X2 [*Canis lupus dingo*]	0.437	0.016
KLK1	1418303522	3	kallikrein-1-like isoform X1 [*Canis lupus dingo*]	−0.846	0.016
KLK1	1418303524	3	kallikrein-1-like isoform X2 [*Canis lupus dingo*]	−0.846	0.016
CANF1	1418264299	13	major allergen Can f 1 [*Canis lupus dingo*]	1.211	0.016
MDH1	57092971	3	malate dehydrogenase, cytoplasmic [*Canis lupus familiaris*]	0.655	0.016
MDH2	1418335689	2	malate dehydrogenase, mitochondrial-like [*Canis lupus dingo*]	0.943	0.016
CANF1	3121745	13	Major allergen Can f 1	1.211	0.016
XDH	1418212080	7	xanthine dehydrogenase/oxidase isoform X1 [*Canis lupus dingo*]	0.610	0.016
XDH	73980076	7	xanthine dehydrogenase/oxidase isoform X1 [*Canis lupus familiaris*]	0.610	0.016
XDH	1418212082	7	xanthine dehydrogenase/oxidase isoform X2 [*Canis lupus dingo*]	0.610	0.016
XDH	545527502	7	xanthine dehydrogenase/oxidase isoform X2 [*Canis lupus familiaris*]	0.610	0.016
ACTN4	1418305407	13	alpha-actinin-4 isoform X1 [*Canis lupus dingo*]	0.619	0.032
ACTN4	1418305409	12	alpha-actinin-4 isoform X2 [*Canis lupus dingo*]	0.619	0.032
ACTN4	1418305411	13	alpha-actinin-4 isoform X3 [*Canis lupus dingo*]	0.619	0.032
ACTN4	73947736	12	alpha-actinin-4 isoform X4 [*Canis lupus familiaris*]	0.605	0.032
ACTN4	1418305415	11	alpha-actinin-4 isoform X5 [*Canis lupus dingo*]	0.603	0.032
CALM2	1418197013	2	calmodulin-2 [*Canis lupus dingo*]	0.566	0.032
NPC2	945179	3	CE1 [*Canis lupus familiaris*]	0.358	0.032
EZR	558757359	9	ezrin [*Canis lupus familiaris*]	0.413	0.032
NPC2	356582247	3	NPC intracellular cholesterol transporter 2 precursor [*Canis lupus familiaris*]	0.358	0.032
PPIA	1418202786	2	peptidyl-prolyl cis-trans isomerase A isoform X2 [*Canis lupus dingo*]	0.608	0.032
UBB	1418312167	3	polyubiquitin-B [*Canis lupus dingo*]	0.735	0.032
UBB	1239902229	3	polyubiquitin-B [*Canis lupus familiaris*]	0.735	0.032
UBC	1418260846	3	polyubiquitin-C [*Canis lupus dingo*]	0.735	0.032
UBC	73995130	3	polyubiquitin-C [*Canis lupus familiaris*]	0.735	0.032

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
PDIA3	1418259105	4	protein disulfide-isomerase A3 [*Canis lupus dingo*]	0.405	0.032
S100A2	1418313584	5	protein S100-A2 [*Canis lupus dingo*]	1.006	0.032
S100A4	1391723726	3	protein S100-A4 isoform 1 [*Canis lupus familiaris*]	1.123	0.032
S100A4	1473222592	3	protein S100-A4 isoform 2 [*Canis lupus familiaris*]	1.123	0.032
UBA52	1418311328	3	ubiquitin [*Canis lupus dingo*]	0.735	0.032
UBA52	5822852	3	ubiquitin, partial [*Canis lupus familiaris*]	0.735	0.032
UBA52	356582340	3	ubiquitin-40S ribosomal protein S27a [*Canis lupus familiaris*]	0.735	0.032
UBB	1239889921	2	ubiquitin-like [*Canis lupus familiaris*]	0.769	0.032
UBA52	5441519	3	ubiquitin-ribosomal protein L40 fusion protein [*Canis lupus familiaris*]	0.735	0.032
MUC5B	1418206782	2	LOW QUALITY PROTEIN: mucin-5B [*Canis lupus dingo*]	0.583	0.040
YWHAE	73967156	5	14-3-3 protein epsilon isoform X2 [*Canis lupus familiaris*]	0.684	0.056
ARPC2	1418341783	5	actin-related protein 2/3 complex subunit 2 [*Canis lupus dingo*]	0.763	0.056
ARPC4	928162268	4	actin-related protein 2/3 complex subunit 4 [*Canis lupus familiaris*]	1.028	0.056
ENO1	1418310054	15	alpha-enolase isoform X2 [*Canis lupus dingo*]	0.711	0.056
GLUL	158430851	2	chain A, glutamine synthetase	0.839	0.056
	1418503128	2	elongation factor 1-gamma [*Canis lupus dingo*]	0.399	0.056
	1418314796	2	elongation factor 1-gamma-like [*Canis lupus dingo*]	0.399	0.056
FLNA	74008809	6	filamin-A [*Canis lupus familiaris*]	0.850	0.056
FLNA	1418225135	6	filamin-A isoform X1 [*Canis lupus dingo*]	0.850	0.056
FLNA	1418225137	6	filamin-A isoform X2 [*Canis lupus dingo*]	0.850	0.056
ALDOA	1418280689	8	fructose-bisphosphate aldolase A [*Canis lupus dingo*]	0.672	0.056
GLUL	648216199	2	glutamine synthetase isoform 1 [*Canis lupus familiaris*]	0.839	0.056
GLUL	648216006	2	glutamine synthetase isoform 2 [*Canis lupus familiaris*]	0.839	0.056
HSP90AA1	1418344784	10	heat shock protein HSP 90-alpha [*Canis lupus dingo*]	0.625	0.056
HSP90AA1	928142969	8	heat shock protein HSP 90-alpha [*Canis lupus familiaris*]	0.625	0.056
PPIA	1239883019	3	peptidyl-prolyl cis-trans isomerase A [*Canis lupus familiaris*]	0.447	0.056
S100A11	928158750	2	protein S100-A11 [*Canis lupus familiaris*]	0.994	0.056
S100A11	1418213478	2	protein S100-A11, partial [*Canis lupus dingo*]	0.994	0.056
S100A12	1418313614	8	protein S100-A12-like [*Canis lupus dingo*]	1.044	0.056
S100A9	928140605	9	protein S100-A9 [*Canis lupus familiaris*]	1.322	0.056
S100A8	224969390	7	S100 calcium-binding protein A8 [*Canis lupus familiaris*]	1.215	0.056
SPINK5	1418507526	4	serine protease inhibitor Kazal-type 5 [*Canis lupus dingo*]	0.439	0.056
SPINK5	70794744	4	serine protease inhibitor Kazal-type 5 precursor [*Canis lupus familiaris*]	0.439	0.056
TKT	545533393	25	transketolase [*Canis lupus familiaris*]	0.608	0.056
TKT	1418216286	25	transketolase isoform X1 [*Canis lupus dingo*]	0.608	0.056
TKT	1418216288	25	transketolase isoform X2 [*Canis lupus dingo*]	0.608	0.056
CDH1	1418308718	3	cadherin-1 [*Canis lupus dingo*]	0.767	0.057
DPYD	1418288800	2	dihydropyrimidine dehydrogenase [NADP(+)] isoform X1 [*Canis lupus dingo*]	0.807	0.057
DPYD	1418288802	2	dihydropyrimidine dehydrogenase [NADP(+)] isoform X2 [*Canis lupus dingo*]	0.807	0.057

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
DPYD	1239908722	2	dihydropyrimidine dehydrogenase [NADP(+)] isoform X2 [*Canis lupus familiaris*]	0.807	0.057
N/A	1239891563	4	double-headed protease inhibitor, submandibular gland [*Canis lupus familiaris*]	0.236	0.057
VCL	305657831	3	metavinculin variant, partial [*Canis lupus familiaris*]	1.340	0.057
PNP	1418335936	3	purine nucleoside phosphorylase [*Canis lupus dingo*]	0.488	0.057
NPEPPS	1418337649	3	puromycin-sensitive aminopeptidase isoform X1 [*Canis lupus dingo*]	0.827	0.057
NPEPPS	545511022	3	puromycin-sensitive aminopeptidase isoform X1 [*Canis lupus familiaris*]	0.827	0.057
NPEPPS	1418337651	3	puromycin-sensitive aminopeptidase isoform X2 [*Canis lupus dingo*]	0.827	0.057
NPEPPS	1418337655	3	puromycin-sensitive aminopeptidase isoform X4 [*Canis lupus dingo*]	0.827	0.057
CDH1	550600200	3	Cadherin-1E-Cad/CTF1;	0.767	0.057
VCL	345798988	5	vinculin [*Canis lupus familiaris*]	1.280	0.057
VCL	1418326635	5	vinculin isoform X1 [*Canis lupus dingo*]	1.280	0.057
VCL	1418326637	5	vinculin isoform X2 [*Canis lupus dingo*]	1.280	0.057
CORO1A	345801939	5	coronin-1A [*Canis lupus familiaris*]	0.693	0.063
ARHGDIB	57106959	7	rho GDP-dissociation inhibitor 2 [*Canis lupus familiaris*]	0.511	0.063
VCP	1418320363	2	transitional endoplasmic reticulum ATPase [*Canis lupus dingo*]	0.450	0.063
VCP	1239927670	2	transitional endoplasmic reticulum ATPase isoform X2 [*Canis lupus familiaris*]	0.450	0.063
ACSS1	1418227068	2	acetyl-coenzyme A synthetase 2-like, mitochondrial [*Canis lupus dingo*]	0.774	0.086
ACSS1	359322579	2	acetyl-coenzyme A synthetase 2-like, mitochondrial [*Canis lupus familiaris*]	0.774	0.086
ACTR3	1418202110	4	actin-related protein 3 [*Canis lupus dingo*]	0.816	0.095
ACTR3	345784150	4	actin-related protein 3 [*Canis lupus familiaris*]	0.816	0.095
ENO1	1418310052	17	alpha-enolase isoform X1 [*Canis lupus dingo*]	0.626	0.095
ENO3	928134045	4	beta-enolase isoform X1 [*Canis lupus familiaris*]	0.845	0.095
ENO3	1418313159	4	beta-enolase isoform X2 [*Canis lupus dingo*]	0.845	0.095
CD177	1418304784	3	CD177 antigen [*Canis lupus dingo*]	0.732	0.095
GSTA4	1418292151	3	glutathione S-transferase A4-like [*Canis lupus dingo*]	0.750	0.095
GSTA4	1239929974	3	glutathione S-transferase A4-like [*Canis lupus familiaris*]	0.750	0.095
GSTM1	1418288349	11	glutathione S-transferase Mu 1 isoform X1 [*Canis lupus dingo*]	0.321	0.095
HSPA4	1239925350	5	heat shock 70 kDa protein 4 isoform X1 [*Canis lupus familiaris*]	0.538	0.095
HSPA4	545516431	5	heat shock 70 kDa protein 4 isoform X2 [*Canis lupus familiaris*]	0.538	0.095
HSPA4	1418322757	5	heat shock 70 kDa protein 4 isoform X3 [*Canis lupus dingo*]	0.538	0.095
HSPA8	545497049	8	heat shock cognate 71 kDa protein [*Canis lupus familiaris*]	0.629	0.095
HSPA4	62631867	5	heat shock protein Apg-2 [*Canis lupus familiaris*]	0.538	0.095
HISTH4	1418253529	3	histone H4-like [*Canis lupus dingo*]	0.857	0.095
LDHA	1418223224	10	L-lactate dehydrogenase A chain isoform X1 [*Canis lupus dingo*]	0.601	0.095
LDHA	545536994	10	L-lactate dehydrogenase A chain isoform X2 [*Canis lupus familiaris*]	0.601	0.095
ENO1	345800677	14	LOW QUALITY PROTEIN: alpha-enolase [*Canis lupus familiaris*]	0.676	0.095
ENO1	928125111	13	LOW QUALITY PROTEIN: alpha-enolase-like [*Canis lupus familiaris*]	0.627	0.095
CD177	1239888116	3	LOW QUALITY PROTEIN: CD177 antigen [*Canis lupus familiaris*]	0.732	0.095

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
LOC106558262	1239979503	3	LOW QUALITY PROTEIN: uncharacterized protein LOC106558262 [*Canis lupus familiaris*]	0.857	0.095
LOC112674420	1418253519	3	LOW QUALITY PROTEIN: uncharacterized protein LOC112674420 [*Canis lupus dingo*]	0.857	0.095
LOC488306	928180958	3	LOW QUALITY PROTEIN: uncharacterized protein LOC488306 [*Canis lupus familiaris*]	0.857	0.095
LCP1	1239955970	17	plastin-2 isoform X1 [*Canis lupus familiaris*]	0.573	0.095
LCP1	545537421	17	plastin-2 isoform X2 [*Canis lupus familiaris*]	0.573	0.095
PLS3	1239983604	12	plastin-3 [*Canis lupus familiaris*]	0.390	0.095
PLS3	1418318928	12	plastin-3 isoform X1 [*Canis lupus dingo*]	0.390	0.095
TF	928167632	2	serotransferrin [*Canis lupus familiaris*]	0.480	0.095
KLK1	264597	2	tissue kallikrein A beta-chain, CPK-A beta-chain {N-terminal} {EC 3.4.21.35} [dogs, pancreas, peptide partial, 38 aa]	−0.830	0.095
KLK1	264599	2	tissue kallikrein B beta-chain, CPK-B beta-chain {N-terminal} {EC 3.4.21.35} [dogs, pancreas, peptide partial, 39 aa]	−0.830	0.095
LOC100856160	928181068	3	uncharacterized protein LOC100856160 [*Canis lupus familiaris*]	0.857	0.095
LOC112674397	1418253487	3	uncharacterized protein LOC112674397 isoform X2 [*Canis lupus dingo*]	0.857	0.095
LOC112674463	1418253569	3	uncharacterized protein LOC112674463 [*Canis lupus dingo*]	0.857	0.095
AHCY	73991635	3	adenosylhomocysteinase [*Canis lupus familiaris*]	0.653	0.100
CALM1	1239893625	2	calmodulin, partial [*Canis lupus familiaris*]	0.718	0.100
APOA1	1418241889	15	apolipoprotein A-I [*Canis lupus dingo*]	0.813	0.111
PTMA	1418208278	2	prothymosin alpha [*Canis lupus dingo*]	1.138	0.111
PTMA	1418231166	2	prothymosin alpha [*Canis lupus dingo*]	1.138	0.111
PTMA	356582259	2	prothymosin alpha [*Canis lupus familiaris*]	1.138	0.111
ARPC2	1239981819	4	actin-related protein 2/3 complex subunit 2 [*Canis lupus familiaris*]	1.147	0.114
EEF2	1418240337	6	elongation factor 2 [*Canis lupus dingo*]	0.757	0.114
PSAP	545495176	8	prosaposin isoform X1 [*Canis lupus familiaris*]	0.188	0.143
PSAP	545495178	8	prosaposin isoform X2 [*Canis lupus familiaris*]	0.188	0.143
PSAP	73952852	8	prosaposin isoform X3 [*Canis lupus familiaris*]	0.188	0.143
PSAP	545495181	8	prosaposin isoform X4 [*Canis lupus familiaris*]	0.188	0.143
PSAP	545495183	8	prosaposin isoform X5 [*Canis lupus familiaris*]	0.188	0.143
PSAP	1418325065	8	prosaposin isoform X6 [*Canis lupus dingo*]	0.188	0.143
YWHAE	1418267412	4	14-3-3 protein epsilon isoform X1 [*Canis lupus dingo*]	0.741	0.151
YWHAE	1418267416	3	14-3-3 protein epsilon isoform X3 [*Canis lupus dingo*]	0.736	0.151
YWHAE	1418267418	3	14-3-3 protein epsilon isoform X4 [*Canis lupus dingo*]	0.736	0.151
YWHAQ	1418213116	3	14-3-3 protein theta [*Canis lupus dingo*]	0.531	0.151
ARPC3	1239964305	2	actin-related protein 2/3 complex subunit 3 isoform X1 [*Canis lupus familiaris*]	0.811	0.151
ARPC3	1418261548	2	actin-related protein 2/3 complex subunit 3 isoform X2 [*Canis lupus dingo*]	0.811	0.151
ARPC3	1418261550	2	actin-related protein 2/3 complex subunit 3 isoform X3 [*Canis lupus dingo*]	0.811	0.151
ANGPTL5	545514351	5	angiopoietin-related protein 5-like [*Canis lupus familiaris*]	−0.744	0.151

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
CSTM	1418503443	3	cystatin-M [*Canis lupus dingo*]	−0.757	0.151
DMBT1	928186547	3	deleted in malignant brain tumors 1 protein-like, partial [*Canis lupus familiaris*]	−0.479	0.151
FGG	545524897	6	fibrinogen gamma chain isoform X1 [*Canis lupus familiaris*]	0.613	0.151
FGG	73977992	6	fibrinogen gamma chain isoform X2 [*Canis lupus familiaris*]	0.613	0.151
HPX	73988725	7	hemopexin [*Canis lupus familiaris*]	0.612	0.151
HISTH4	50542205	2	histone H4, partial [*Canis lupus familiaris*]	0.794	0.151
CAPG	1418211040	6	macrophage-capping protein isoform X1 [*Canis lupus dingo*]	0.502	0.151
CAPG	545528000	6	macrophage-capping protein isoform X1 [*Canis lupus familiaris*]	0.502	0.151
MYH9	1418195836	21	myosin-9 [*Canis lupus dingo*]	0.566	0.151
MMP8	345799783	4	neutrophil collagenase [*Canis lupus familiaris*]	0.349	0.151
ELANE	1418220639	4	neutrophil elastase [*Canis lupus dingo*]	0.652	0.151
ELANE	50979246	4	neutrophil elastase precursor [*Canis lupus familiaris*]	0.652	0.151
PTGR1	1418321329	6	prostaglandin reductase 1 [*Canis lupus dingo*]	0.644	0.151
PTGR1	545517912	6	prostaglandin reductase 1 [*Canis lupus familiaris*]	0.644	0.151
MYH9	122135145	21	Myosin-9	0.566	0.151
ARHGDIA	73964747	3	rho GDP-dissociation inhibitor 1 [*Canis lupus familiaris*]	0.486	0.151
SERPINC1	359320010	2	antithrombin-III [*Canis lupus familiaris*]	0.800	0.190
GSTM1	1239908416	10	glutathione S-transferase Mu 1 isoform X2 [*Canis lupus familiaris*]	0.244	0.190
HP	258499	14	haptoglobin heavy chain, HpH chain [dogs, Peptide, 245 aa]	0.445	0.190
HP	73957095	16	haptoglobin-like [*Canis lupus familiaris*]	0.479	0.190
LEG1	1418301038	7	protein LEG1 homolog [*Canis lupus dingo*]	0.414	0.190
LEG1	1239885884	7	protein LEG1 homolog [*Canis lupus familiaris*]	0.414	0.190
APOA1	3915607	13	Apolipoprotein A-I	0.808	0.190
HP	123511	16	Haptoglobin	0.479	0.190
S100P	345798353	2	protein S100-P [*Canis lupus familiaris*]	0.598	0.198
KRT15	1418338550	4	keratin, type I cytoskeletal 15 [*Canis lupus dingo*]	0.430	0.200
SERPINB10	1418298925	2	serpin B10 [*Canis lupus dingo*]	0.035	0.200
SERPINB10	73945839	2	serpin B10 [*Canis lupus familiaris*]	0.035	0.200
YWHAZ	928151832	8	14-3-3 protein zeta/delta [*Canis lupus familiaris*]	0.445	0.222
YWHAZ	1418511015	7	14-3-3 protein zeta/delta-like [*Canis lupus dingo*]	0.494	0.222
ACTB	924183513	4	actin, cytoplasmic 1 [*Canis lupus familiaris*]	−0.283	0.222
ACTB	545500782	4	actin, cytoplasmic 1 isoform X1 [*Canis lupus familiaris*]	−0.283	0.222
ACTB	1418248118	4	actin, cytoplasmic 2 [*Canis lupus dingo*]	−0.283	0.222
ACTG1	924442847	4	actin, cytoplasmic 2 [*Canis lupus familiaris*]	−0.283	0.222
N/A	1418320657	10	allergen Fel d 4-like [*Canis lupus dingo*]	0.492	0.222
ACTN1	1418347612	5	alpha-actinin-1 isoform X1 [*Canis lupus dingo*]	0.411	0.222
ACTN1	1239915208	5	alpha-actinin-1 isoform X2 [*Canis lupus familiaris*]	0.411	0.222
ACTN1	1418347616	5	alpha-actinin-1 isoform X3 [*Canis lupus dingo*]	0.411	0.222
ACTN1	73963339	5	alpha-actinin-1 isoform X4 [*Canis lupus familiaris*]	0.411	0.222
ACTN1	73963357	5	alpha-actinin-1 isoform X5 [*Canis lupus familiaris*]	0.411	0.222

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
CP	1418510222	4	ceruloplasmin isoform X1 [*Canis lupus dingo*]	0.718	0.222
CP	928167527	3	ceruloplasmin isoform X1 [*Canis lupus familiaris*]	0.726	0.222
CP	1418510226	4	ceruloplasmin isoform X2 [*Canis lupus dingo*]	0.718	0.222
CP	1239957836	3	ceruloplasmin isoform X2 [*Canis lupus familiaris*]	0.726	0.222
CP	1418510228	4	ceruloplasmin isoform X3 [*Canis lupus dingo*]	0.718	0.222
CP	73990367	3	ceruloplasmin isoform X3 [*Canis lupus familiaris*]	0.726	0.222
CP	1418510230	4	ceruloplasmin isoform X4 [*Canis lupus dingo*]	0.718	0.222
CP	1239957839	3	ceruloplasmin isoform X4 [*Canis lupus familiaris*]	0.726	0.222
CANF2	296863542	7	chain A, crystal structure of dog lipocalin allergen Can f 2 and implications for cross-reactivity to the cat allergen Fel d 4	0.538	0.222
N/A	1374502923	10	chain D, lipocalin Can f 6 allergen	0.492	0.222
C3	1418218430	30	complement C3 [*Canis lupus dingo*]	0.561	0.222
C3	1239951704	28	complement C3 [*Canis lupus familiaris*]	0.547	0.222
FGA	1304047	2	fibrinogen A-alpha chain, partial [*Canis lupus familiaris*]	0.673	0.222
G6PD	1418225081	7	glucose-6-phosphate 1-dehydrogenase isoform X1 [*Canis lupus dingo*]	0.391	0.222
G6PD	1418225083	7	glucose-6-phosphate 1-dehydrogenase isoform X2 [*Canis lupus dingo*]	0.391	0.222
HSP90AB1	922059102	3	heat shock protein 90 kDa alpha class B member 1, partial [*Canis lupus familiaris*]	0.417	0.222
IGH-10	1494245227	5	immunoglobulin heavy chain IGH-10 [*Canis lupus familiaris*]	0.502	0.222
IGH-12	1494245231	5	immunoglobulin heavy chain IGH-12 [*Canis lupus familiaris*]	0.502	0.222
IGH-14	1494245235	5	immunoglobulin heavy chain IGH-14 [*Canis lupus familiaris*]	0.502	0.222
IGH-15	1494245237	5	immunoglobulin heavy chain IGH-15 [*Canis lupus familiaris*]	0.502	0.222
IGH-16	1494245239	5	immunoglobulin heavy chain IGH-16 [*Canis lupus familiaris*]	0.502	0.222
IGH-17	1494245241	5	immunoglobulin heavy chain IGH-17 [*Canis lupus familiaris*]	0.502	0.222
IGH-3	1494245213	5	immunoglobulin heavy chain IGH-3 [*Canis lupus familiaris*]	0.502	0.222
IGH-7	1494245221	5	immunoglobulin heavy chain IGH-7 [*Canis lupus familiaris*]	0.502	0.222
IGH-9	1494245225	5	immunoglobulin heavy chain IGH-9 [*Canis lupus familiaris*]	0.502	0.222
KLK1	1418303494	9	kallikrein-1 isoform X1 [*Canis lupus dingo*]	−0.633	0.222
KLK1	1418303496	9	kallikrein-1 isoform X2 [*Canis lupus dingo*]	−0.633	0.222
KLK1	55741639	8	kallikrein-1 precursor [*Canis lupus familiaris*]	−0.637	0.222
KRT13	1077167933	6	keratin, type I cytoskeletal 13 [*Canis lupus familiaris*]	0.758	0.222
SERPINB1	1418205376	11	leukocyte elastase inhibitor [*Canis lupus dingo*]	0.461	0.222
LDHA	1418345245	6	L-lactate dehydrogenase A chain-like [*Canis lupus dingo*]	0.429	0.222
LDHA	545507351	6	L-lactate dehydrogenase A chain-like [*Canis lupus familiaris*]	0.429	0.222
DMBT1	1418246878	11	LOW QUALITY PROTEIN: deleted in malignant brain tumors 1 protein [*Canis lupus dingo*]	−0.419	0.222
LDHA	1239958986	5	LOW QUALITY PROTEIN: L-lactate dehydrogenase A chain-like [*Canis lupus familiaris*]	0.647	0.222
CAPG	1418211046	4	macrophage-capping protein isoform X2 [*Canis lupus dingo*]	0.453	0.222
CAPG	928158112	4	macrophage-capping protein isoform X2 [*Canis lupus familiaris*]	0.453	0.222
CANF2	1418266307	7	minor allergen Can f 2 [*Canis lupus dingo*]	0.538	0.222
MPO	545511447	10	myeloperoxidase [*Canis lupus familiaris*]	0.546	0.222
MYH11	1418286550	5	myosin-11 isoform X1 [*Canis lupus dingo*]	0.470	0.222
MYH11	545502107	5	myosin-11 isoform X2 [*Canis lupus familiaris*]	0.470	0.222

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
MYH11	1418286554	5	myosin-11 isoform X3 [*Canis lupus dingo*]	0.470	0.222
MYH14	1418286556	5	myosin-11 isoform X4 [*Canis lupus dingo*]	0.470	0.222
OLFM4	1239956251	2	olfactomedin-4 [*Canis lupus familiaris*]	−0.529	0.222
CANF2	29292272	7	precursor Can f 2, partial [*Canis lupus familiaris*]	0.538	0.222
GDI2	1418501820	4	rab GDP dissociation inhibitor beta isoform X1 [*Canis lupus dingo*]	0.275	0.222
GDI2	1418501822	4	rab GDP dissociation inhibitor beta isoform X2 [*Canis lupus dingo*]	0.275	0.222
GDI2	1418501824	4	rab GDP dissociation inhibitor beta isoform X3 [*Canis lupus dingo*]	0.275	0.222
CANF2	3121746	7	Minor allergen Can f 2	0.538	0.222
SOD1	1418511817	6	superoxide dismutase [Cu-Zn] [*Canis lupus dingo*]	0.344	0.222
TXN	1418321566	4	thioredoxin [*Canis lupus dingo*]	0.346	0.222
TXN	1239928271	4	thioredoxin-like isoform X1 [*Canis lupus familiaris*]	0.346	0.222
TXN	1239928273	4	thioredoxin-like isoform X2 [*Canis lupus familiaris*]	0.346	0.222
N/A	16607663	5	unnamed protein product [*Canis lupus familiaris*]	0.502	0.222
N/A	16607675	4	unnamed protein product [*Canis lupus familiaris*]	0.502	0.222
N/A	16607718	5	unnamed protein product [*Canis lupus familiaris*]	0.502	0.222
ANXA2	1418258110	3	annexin A2 [*Canis lupus dingo*]	0.846	0.229
HSPA2	57090217	3	heat shock-related 70 kDa protein 2 [*Canis lupus familiaris*]	0.483	0.229
KRT2	1068388058	3	keratin, type II cytoskeletal 2 oral [*Canis lupus familiaris*]	0.841	0.229
KRT2	1239965760	3	keratin, type II cytoskeletal 2 oral isoform X1 [*Canis lupus familiaris*]	0.841	0.229
KRT2	1418221668	3	keratin, type II cytoskeletal 2 oral-like [*Canis lupus dingo*]	0.841	0.229
KRT76	15419605	3	masticatory epithelia keratin 2p [*Canis lupus familiaris*]	0.841	0.229
NQO2	1418205354	3	ribosyldihydronicotinamide dehydrogenase [quinone] [*Canis lupus dingo*]	0.502	0.229
NQO2	74003808	3	ribosyldihydronicotinamide dehydrogenase [quinone] [*Canis lupus familiaris*]	0.502	0.229
NQO1	1418308783	9	NAD(P)H dehydrogenase [quinone] 1 [*Canis lupus dingo*]	0.362	0.254
NQO1	545500084	10	NAD(P)H dehydrogenase [quinone] 1 [*Canis lupus familiaris*]	0.362	0.254
LYZ	9257149	2	chain A, X-ray crystal structure analysis of canine milk lysozyme (Apo-type)	−0.612	0.286
LYZ	13787135	2	chain B, lysozyme C	−0.612	0.286
LTF	84872712	8	lactoferrin, partial [*Canis lupus familiaris*]	−0.239	0.286
CES1	1418507047	7	liver carboxylesterase 1 [*Canis lupus dingo*]	0.183	0.286
LDHB	356461040	4	L-lactate dehydrogenase B chain [*Canis lupus familiaris*]	0.338	0.286
LDHB	1418299581	4	L-lactate dehydrogenase B chain-like [*Canis lupus dingo*]	0.338	0.286
LDHB	1418327082	3	L-lactate dehydrogenase B chain-like [*Canis lupus dingo*]	0.338	0.286
LDHB	1418514557	3	L-lactate dehydrogenase B chain-like [*Canis lupus dingo*]	0.338	0.286
LYZ	925114454	2	lysozyme C, milk isozyme-like precursor [*Canis lupus familiaris*]	−0.612	0.286
NME1	545510194	2	nucleoside diphosphate kinase A isoform X1 [*Canis lupus familiaris*]	0.560	0.286
N/A	124847	4	Double-headed protease inhibitor, submandibular gland	0.596	0.286
LYZ	8928188	2	Lysozyme C, milk isozyme;	−0.612	0.286
YWHAG	1418307161	4	14-3-3 protein gamma [*Canis lupus dingo*]	0.243	0.310
YWHAG	1239905645	4	14-3-3 protein gamma [*Canis lupus familiaris*]	0.243	0.310
HSPA5	345806081	5	78 kDa glucose-regulated protein [*Canis lupus familiaris*]	0.372	0.310
HSPA5	1418264760	5	endoplasmic reticulum chaperone BiP [*Canis lupus dingo*]	0.372	0.310
NCCRP1	73948372	3	F-box only protein 50 [*Canis lupus familiaris*]	0.342	0.310

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
FGA	1418336346	5	fibrinogen-alpha chain [*Canis lupus dingo*]	0.459	0.310
FGA	73978329	5	fibrinogen-alpha chain [*Canis lupus familiaris*]	0.459	0.310
H2AFZ	559767198	2	H2A histone family, member Z [*Canis lupus familiaris*]	0.417	0.310
HSP70	17298186	3	heat shock protein 70 [*Canis lupus familiaris*]	0.451	0.310
HIST1H2A	1239979771	2	histone H2A type 1 [*Canis lupus familiaris*]	0.417	0.310
HIST1H2AA	57110393	2	histone H2A type 1-A [*Canis lupus familiaris*]	0.417	0.310
HIST1H2AB	1418253446	2	histone H2A type 1-B/E [*Canis lupus dingo*]	0.417	0.310
HIST1H2AC	545554572	2	histone H2A type 1-C [*Canis lupus familiaris*]	0.417	0.310
HIST1H2AE	1418204456	2	histone H2A type 1-E [*Canis lupus dingo*]	0.417	0.310
HIST1H2AE	1239979741	2	histone H2A type 1-E [*Canis lupus familiaris*]	0.417	0.310
HIST1H2AE	1418253448	2	histone H2A type 1-E-like [*Canis lupus dingo*]	0.417	0.310
HIST1H2AE	1418253483	2	histone H2A type 1-E-like [*Canis lupus dingo*]	0.417	0.310
HIST1H2AE	74004170	2	histone H2A type 1-E-like [*Canis lupus familiaris*]	0.417	0.310
HIST1H2AH	928180938	2	histone H2A type 1-H [*Canis lupus familiaris*]	0.417	0.310
HIST1H2AH	1239979774	2	histone H2A type 1-H [*Canis lupus familiaris*]	0.417	0.310
HIST1H2AH	1418204540	2	histone H2A type 1-H-like [*Canis lupus dingo*]	0.417	0.310
HIST2H2AA	73981516	2	histone H2A type 2-A [*Canis lupus familiaris*]	0.417	0.310
HIST2H2AC	359321687	2	histone H2A type 2-C [*Canis lupus familiaris*]	0.417	0.310
HIST3H2A	545521932	2	histone H2A type 3 [*Canis lupus familiaris*]	0.417	0.310
HISTH2AJ	57106965	2	histone H2A.J [*Canis lupus familiaris*]	0.417	0.310
HISTH2AV	928186182	2	histone H2A.V isoform X1 [*Canis lupus familiaris*]	0.417	0.310
HISTH2AV	928186186	2	histone H2A.V isoform X3 [*Canis lupus familiaris*]	0.417	0.310
HISTH2AB	928180889	2	histone H2A-beta, sperm-like [*Canis lupus familiaris*]	0.417	0.310
HISTH2AX	545497152	2	histone H2AX [*Canis lupus familiaris*]	0.417	0.310
IGJ; JCHAIN	345779666	6	immunoglobulin J chain [*Canis lupus familiaris*]	−0.278	0.310
KRT4	1418221457	9	keratin, type II cytoskeletal 4 [*Canis lupus dingo*]	0.819	0.310
LPO	1418338512	22	lactoperoxidase [*Canis lupus dingo*]	−0.840	0.310
LPO	1239919186	20	lactoperoxidase [*Canis lupus familiaris*]	−0.810	0.310
ALB	1418328547	2	LOW QUALITY PROTEIN: serum albumin-like [*Canis lupus dingo*]	0.302	0.310
MYL12B	57089773	2	myosin regulatory light chain 12B [*Canis lupus familiaris*]	0.378	0.310
MYL9	1418314603	2	myosin regulatory light polypeptide 9 isoform X1 [*Canis lupus dingo*]	0.378	0.310
MYL9	345803346	2	myosin regulatory light polypeptide 9 isoform X2 [*Canis lupus familiaris*]	0.378	0.310
PGK1	74007807	4	phosphoglycerate kinase 1 [*Canis lupus familiaris*]	0.232	0.310
PIP	73978762	9	prolactin-inducible protein [*Canis lupus familiaris*]	−0.427	0.310
HSP70	56749085	3	Heat shock 70 kDa protein 1	0.451	0.310
SLPI	164499359	3	secretory leukocyte peptidase inhibitor, partial [*Canis lupus familiaris*]	−0.391	0.310
TALDO1	359321944	7	transaldolase [*Canis lupus familiaris*]	0.287	0.310
ZG16B	73959451	4	zymogen granule protein 16 homolog B [*Canis lupus familiaris*]	−1.886	0.310
ACTN2	1418509128	2	alpha-actinin-2 isoform X1 [*Canis lupus dingo*]	0.250	0.333
ACTN2	1418509130	2	alpha-actinin-2 isoform X2 [*Canis lupus dingo*]	0.250	0.333
ACTN3	1418503151	2	alpha-actinin-3 isoform X1 [*Canis lupus dingo*]	0.250	0.333
ACTN3	1418503153	2	alpha-actinin-3 isoform X2 [*Canis lupus dingo*]	0.250	0.333

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
ACTN3	1418503155	2	alpha-actinin-3 isoform X3 [*Canis lupus dingo*]	0.250	0.333
GSTO1	1418245560	3	glutathione S-transferase omega-1 [*Canis lupus dingo*]	0.417	0.333
UBA1	928183828	2	LOW QUALITY PROTEIN: ubiquitin-like modifier-activating enzyme 1 [*Canis lupus familiaris*]	0.521	0.333
ME1	545519773	2	NADP-dependent malic enzyme [*Canis lupus familiaris*]	0.802	0.333
ME1	1418348746	2	NADP-dependent malic enzyme isoform X1 [*Canis lupus dingo*]	0.802	0.333
ME1	1418348750	2	NADP-dependent malic enzyme isoform X3 [*Canis lupus dingo*]	0.802	0.333
UBA1	1418249227	2	ubiquitin-like modifier-activating enzyme 1 [*Canis lupus dingo*]	0.521	0.333
ARPC5	1418316200	2	actin-related protein 2/3 complex subunit 5 [*Canis lupus dingo*]	0.687	0.400
ADIRF	1239898218	2	adipogenesis regulatory factor [*Canis lupus familiaris*]	−0.128	0.400
CASP14	1239951047	2	LOW QUALITY PROTEIN: caspase-14 [*Canis lupus familiaris*]	0.558	0.400
MUC5B	1239945861	2	mucin-5B isoform X1 [*Canis lupus familiaris*]	0.500	0.400
UPP1	1418511026	3	uridine phosphorylase 1 [*Canis lupus dingo*]	0.851	0.400
UPP1	1239883228	3	uridine phosphorylase 1-like [*Canis lupus familiaris*]	0.851	0.400
PPIA	1418214537	2	ovostatin homolog 2-like [*Canis lupus dingo*]	0.035	0.413
YWHAS	1418505824	11	14-3-3 protein sigma [*Canis lupus dingo*]	0.311	0.421
ACT	1418333042	2	actin, clone 302-like [*Canis lupus dingo*]	−0.298	0.421
CA2	223556019	2	carbonic anhydrase 2 [*Canis lupus familiaris*]	0.096	0.421
CAMP	1418215404	6	cathelicidin antimicrobial peptide [*Canis lupus dingo*]	0.290	0.421
CAMP	50979214	6	cathelicidin antimicrobial peptide precursor [*Canis lupus familiaris*]	0.290	0.421
CRISP2	545519428	6	cysteine-rich secretory protein 2 isoform X1 [*Canis lupus familiaris*]	−0.357	0.421
CRISP2	1239929902	6	cysteine-rich secretory protein 2 isoform X2 [*Canis lupus familiaris*]	−0.357	0.421
FGB	1418336465	4	fibrinogen beta chain [*Canis lupus dingo*]	0.473	0.421
MMP9	2564101	7	gelatinase B [*Canis lupus familiaris*]	0.351	0.421
GDA	1418301814	4	guanine deaminase [*Canis lupus dingo*]	0.474	0.421
FCGBP	1418305257	2	IgGFc-binding protein isoform X1 [*Canis lupus dingo*]	−1.045	0.421
FCGBP	1418305259	2	IgGFc-binding protein isoform X2 [*Canis lupus dingo*]	−1.004	0.421
IGH-CH4	124390013	2	immunoglobulin heavy chain constant region CH4, partial [*Canis lupus familiaris*]	−0.255	0.421
IGHJ	1340239380	2	immunoglobulin heavy chain variable region, partial [*Canis lupus familiaris*]	−0.692	0.421
IGM	146743249	2	immunoglobulin mu heavy chain variable region, partial [*Canis lupus familiaris*]	−0.255	0.421
KRT1	1418221463	4	keratin, type II cytoskeletal 1 [*Canis lupus dingo*]	0.583	0.421
KRT5	1418221469	4	keratin, type II cytoskeletal 5 [*Canis lupus dingo*]	0.693	0.421
KRT5	1069415302	4	keratin, type II cytoskeletal 5 [*Canis lupus familiaris*]	0.693	0.421
LTF	339305353	2	lactotransferrin, partial [*Canis lupus familiaris*]	−0.424	0.421
GLO1	345778725	2	lactoylglutathione lyase [*Canis lupus familiaris*]	0.184	0.421
GPI	1418305580	15	LOW QUALITY PROTEIN: glucose-6-phosphate isomerase [*Canis lupus dingo*]	0.240	0.421
MMP9	1418252189	7	matrix metalloproteinase-9 [*Canis lupus dingo*]	0.351	0.421
MMP9	11034716	7	matrix metalloproteinase-9 [*Canis lupus familiaris*]	0.351	0.421
MMP9	50978992	6	matrix metalloproteinase-9 precursor [*Canis lupus familiaris*]	0.363	0.421
MYL6	345776590	3	myosin light polypeptide 6 isoform X1 [*Canis lupus familiaris*]	0.382	0.421
MYL6	1418269617	3	myosin light polypeptide 6 isoform X2 [*Canis lupus dingo*]	0.382	0.421

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
MYL6	1239922056	3	myosin light polypeptide 6 isoform X3 [*Canis lupus familiaris*]	0.382	0.421
SLPI	158936956	4	protease inhibitor [*Canis lupus familiaris*]	−0.439	0.421
KRT1	75062693	4	Keratin, type II cytoskeletal 1;	0.583	0.421
TPM3	1418313468	2	tropomyosin alpha-3 chain isoform X7 [*Canis lupus dingo*]	0.694	0.421
MUC19	1239968164	7	mucin-19 [*Canis lupus familiaris*]	0.020	0.486
SERPINA1	119637732	6	alpha-1 antitrypsin [*Canis lupus familiaris*]	−0.547	0.548
SERPINA1	1239913623	6	alpha-1-antitrypsin isoform X1 [*Canis lupus familiaris*]	−0.547	0.548
SERPINA1	1418345511	6	alpha-1-antitrypsin-like [*Canis lupus dingo*]	−0.547	0.548
A2M	1418213974	3	alpha-2-macroglobulin [*Canis lupus dingo*]	0.389	0.548
A2M	345792424	3	alpha-2-macroglobulin [*Canis lupus familiaris*]	0.389	0.548
ANGPTL5	1418194692	6	angiopoietin-related protein 5-like [*Canis lupus dingo*]	−0.465	0.548
LOC611632	1418510295	8	ceruloplasmin-like [*Canis lupus dingo*]	0.668	0.548
LOC611632	345788999	7	ceruloplasmin-like [*Canis lupus familiaris*]	0.668	0.548
CFL1	57099669	6	cofilin-1 [*Canis lupus familiaris*]	0.000	0.548
CFL2	1418315363	5	cofilin-1-like [*Canis lupus dingo*]	−0.005	0.548
SOD1	18150346	5	Cu/Zn superoxide dismutase [*Canis lupus familiaris*]	0.214	0.548
DMBT1	928175938	12	deleted in malignant brain tumors 1 protein isoform X1 [*Canis lupus familiaris*]	−0.364	0.548
DMBT1	928175949	12	deleted in malignant brain tumors 1 protein isoform X2 [*Canis lupus familiaris*]	−0.364	0.548
DMBT1	928175953	12	deleted in malignant brain tumors 1 protein isoform X3 [*Canis lupus familiaris*]	−0.364	0.548
FABP5	928174762	4	fatty acid-binding protein, epidermal [*Canis lupus familiaris*]	0.339	0.548
FETUB	1418515534	2	fetuin-B [*Canis lupus dingo*]	−0.083	0.548
FETUB	74003556	3	fetuin-B [*Canis lupus familiaris*]	−0.021	0.548
PYGL	562155348	13	glycogen phosphorylase, liver form [*Canis lupus familiaris*]	0.255	0.548
IGH-4	1494245215	6	immunoglobulin heavy chain IGH-4 [*Canis lupus familiaris*]	0.351	0.548
SERPINB1	1239979297	6	leukocyte elastase inhibitor [*Canis lupus familiaris*]	0.234	0.548
MSN	545558304	6	moesin isoform X1 [*Canis lupus familiaris*]	0.309	0.548
MSN	1418243364	6	moesin isoform X2 [*Canis lupus dingo*]	0.309	0.548
MSN	928185024	6	moesin isoform X3 [*Canis lupus familiaris*]	0.309	0.548
OPRPN	1418328391	8	opiorphin prepropeptide [*Canis lupus dingo*]	0.082	0.548
TGM3	1418250613	11	protein-glutamine gamma-glutamyltransferase E [*Canis lupus dingo*]	0.273	0.548
PKM	1239972768	7	pyruvate kinase PKM isoform X1 [*Canis lupus familiaris*]	−0.157	0.548
PKM	1418257040	6	pyruvate kinase PKM isoform X2 [*Canis lupus dingo*]	−0.168	0.548
PKM	1418257042	7	pyruvate kinase PKM isoform X3 [*Canis lupus dingo*]	−0.157	0.548
PKM	545550333	6	pyruvate kinase PKM isoform X3 [*Canis lupus familiaris*]	−0.168	0.548
PKM	1418257044	6	pyruvate kinase PKM isoform X4 [*Canis lupus dingo*]	−0.130	0.548
MMP9	4868451	3	type IV collagenase MMP-9, partial [*Canis lupus familiaris*]	0.344	0.548
N/A	16607721	6	unnamed protein product [*Canis lupus familiaris*]	0.351	0.548
HSP90AA1	734548054	2	heat shock protein HSP 90-alpha [*Toxocara canis*]	0.194	0.556
HYAL1	1239950142	7	hyaluronidase-1 isoform X3 [*Canis lupus familiaris*]	0.404	0.556
IGH-CH2	124390009	2	immunoglobulin heavy chain constant region CH2, partial [*Canis lupus familiaris*]	0.308	0.556
SCGB2A2	928186528	2	mammaglobin-A-like [*Canis lupus familiaris*]	1.489	0.556
PADI4	1418507405	2	protein-arginine deiminase type-4 [*Canis lupus dingo*]	0.388	0.556
N/A	1535091294	2	unnamed protein product [*Toxocara canis*]	0.194	0.556

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
MYH10	1418312500	4	myosin-10 isoform X2 [*Canis lupus dingo*]	0.405	0.571
MYH10	928134337	4	myosin-10 isoform X2 [*Canis lupus familiaris*]	0.405	0.571
MYH10	928134341	4	myosin-10 isoform X4 [*Canis lupus familiaris*]	0.405	0.571
MYH10	1418312506	4	myosin-10 isoform X5 [*Canis lupus dingo*]	0.405	0.571
MYH10	928134343	4	myosin-10 isoform X5 [*Canis lupus familiaris*]	0.405	0.571
MYH10	1418312512	4	myosin-10 isoform X6 [*Canis lupus dingo*]	0.405	0.571
C4A	1239928570	6	complement C4-A [*Canis lupus familiaris*]	0.202	0.629
C4A	1418290456	6	complement C4-A-like [*Canis lupus dingo*]	0.202	0.629
KNG1	1418515459	3	kininogen-1 isoform X1 [*Canis lupus dingo*]	0.070	0.629
KNG1	345796419	3	kininogen-1 isoform X1 [*Canis lupus familiaris*]	0.070	0.629
KNG1	1418515461	3	kininogen-1 isoform X2 [*Canis lupus dingo*]	0.070	0.629
KNG1	57109938	3	kininogen-1 isoform X2 [*Canis lupus familiaris*]	0.070	0.629
LDHA	1239955652	3	L-lactate dehydrogenase A chain-like isoform X1 [*Canis lupus familiaris*]	0.430	0.629
PGM1	928134704	2	phosphoglucomutase-1 isoform X1 [*Canis lupus familiaris*]	0.330	0.629
PGM1	73956158	2	phosphoglucomutase-1 isoform X2 [*Canis lupus familiaris*]	0.330	0.629
LOC611458	1418213980	5	pregnancy zone protein-like isoform X3 [*Canis lupus dingo*]	0.180	0.629
LOC611458	1239967247	5	pregnancy zone protein-like isoform X3 [*Canis lupus familiaris*]	0.180	0.629
TUBA1B	1418342112	2	tubulin alpha-1B chain isoform X1 [*Canis lupus dingo*]	0.544	0.629
TUBA1B	1418342114	2	tubulin alpha-1B chain isoform X2 [*Canis lupus dingo*]	0.544	0.629
TUBA8	1418342116	2	tubulin alpha-8 chain isoform X3 [*Canis lupus dingo*]	0.544	0.629
LOC112676265	1418260227	2	uncharacterized protein LOC112676265 [*Canis lupus dingo*]	−0.704	0.629
RPLP2	1418207290	2	60S acidic ribosomal protein P2 [*Canis lupus dingo*]	0.445	0.667
A2ML1	1418213935	6	alpha-2-macroglobulin-like protein 1 isoform X1 [*Canis lupus dingo*]	0.561	0.667
A2ML1	1239967618	6	alpha-2-macroglobulin-like protein 1 isoform X1 [*Canis lupus familiaris*]	0.561	0.667
A2ML1	1418213939	6	alpha-2-macroglobulin-like protein 1 isoform X2 [*Canis lupus dingo*]	0.561	0.667
A2ML1	1239967622	6	alpha-2-macroglobulin-like protein 1 isoform X2 [*Canis lupus familiaris*]	0.561	0.667
BPIFA1	73992235	2	BPI fold-containing family A member 1 [*Canis lupus familiaris*]	0.471	0.667
CAT	4115557	2	catalase [*Canis lupus familiaris*]	−0.006	0.667
CAT	12082093	2	catalase [*Canis lupus familiaris*]	−0.006	0.667
CAPZB	928128985	2	F-actin-capping protein subunit beta isoform X1 [*Canis lupus familiaris*]	1.088	0.667
CAPZB	928128987	3	F-actin-capping protein subunit beta isoform X2 [*Canis lupus familiaris*]	1.088	0.667
CAPZB	1418507824	2	F-actin-capping protein subunit beta isoform X3 [*Canis lupus dingo*]	1.088	0.667
CAPZB	1239893342	2	F-actin-capping protein subunit beta isoform X3 [*Canis lupus familiaris*]	1.088	0.667
CAPZB	545492085	3	F-actin-capping protein subunit beta isoform X4 [*Canis lupus familiaris*]	1.088	0.667
CAPZB	1239893345	2	F-actin-capping protein subunit beta isoform X5 [*Canis lupus familiaris*]	1.088	0.667
CAPZB	1239893349	2	F-actin-capping protein subunit beta isoform X7 [*Canis lupus familiaris*]	1.088	0.667
FOLR2	1418222123	2	folate receptor beta isoform X1 [*Canis lupus dingo*]	1.376	0.667
FOLR2	1239953679	2	folate receptor beta isoform X1 [*Canis lupus familiaris*]	1.376	0.667
FOLR2	1418222127	2	folate receptor beta isoform X2 [*Canis lupus dingo*]	1.376	0.667
FOLR2	928165121	2	folate receptor beta isoform X2 [*Canis lupus familiaris*]	1.376	0.667
HBE	1418222280	2	hemoglobin subunit epsilon [*Canis lupus dingo*]	−0.898	0.667

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
KRT14	1418338716	3	keratin, type I cytoskeletal 14 [*Canis lupus dingo*]	0.845	0.667
KRT24	1418339572	3	keratin, type I cytoskeletal 24 [*Canis lupus dingo*]	1.420	0.667
KRT24	345805399	3	keratin, type I cytoskeletal 24 [*Canis lupus familiaris*]	1.420	0.667
KRT78	73996461	2	keratin, type II cytoskeletal 78 [*Canis lupus familiaris*]	2.219	0.667
MGAM	1418324508	2	maltase-glucoamylase, intestinal isoform X1 [*Canis lupus dingo*]	0.923	0.667
MGAM	1239938912	2	maltase-glucoamylase, intestinal isoform X1 [*Canis lupus familiaris*]	0.923	0.667
MGAM	1418324514	2	maltase-glucoamylase, intestinal isoform X2 [*Canis lupus dingo*]	0.923	0.667
MGAM	928156540	2	maltase-glucoamylase, intestinal isoform X2 [*Canis lupus familiaris*]	0.923	0.667
MUC4	1418200086	3	mucin-4 [*Canis lupus dingo*]	0.994	0.667
MUC4	1239976879	3	mucin-4 [*Canis lupus familiaris*]	0.994	0.667
PLG	558695388	2	plasminogen precursor [*Canis lupus familiaris*]	0.726	0.667
PSMA1	1418204605	3	proteasome subunit alpha type-1 [*Canis lupus dingo*]	0.708	0.667
PSMA1	1418222965	3	proteasome subunit alpha type-1 [*Canis lupus dingo*]	0.708	0.667
PSMA1	1418258143	2	proteasome subunit alpha type-1-like [*Canis lupus dingo*]	1.060	0.667
PSMA3	1418345461	3	proteasome subunit alpha type-3 [*Canis lupus dingo*]	1.737	0.667
PSMA3	73963050	3	proteasome subunit alpha type-3 [*Canis lupus familiaris*]	1.737	0.667
PSMA4	1418514065	2	proteasome subunit alpha type-4 [*Canis lupus dingo*]	0.829	0.667
OXCT1	1418329836	2	succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial [*Canis lupus dingo*]	0.631	0.667
OXCT1	928131428	2	succinyl-CoA:3-ketoacid coenzyme A transferase 1, mitochondrial [*Canis lupus familiaris*]	0.631	0.667
WDR1	195546936	3	WD repeat-containing protein 1 [*Canis lupus familiaris*]	0.712	0.667
GSN	1239925762	7	gelsolin [*Canis lupus familiaris*]	−0.278	0.675
GSN	1418322411	7	gelsolin isoform X1 [*Canis lupus dingo*]	−0.278	0.675
GSN	1418322413	7	gelsolin isoform X2 [*Canis lupus dingo*]	−0.278	0.675
GSN	1418322415	7	gelsolin isoform X3 [*Canis lupus dingo*]	−0.278	0.675
YWHAB	1418252030	3	14-3-3 protein beta/alpha [*Canis lupus dingo*]	0.252	0.690
ACTB	5597005	2	beta-actin [*Canis lupus familiaris*]	−0.175	0.690
MPO	494395	3	chain C, myeloperoxidase	0.360	0.690
COTL1	1418309542	3	coactosin-like protein [*Canis lupus dingo*]	0.318	0.690
COTL1	359319594	3	coactosin-like protein, partial [*Canis lupus familiaris*]	0.318	0.690
FABP5	1418323952	3	fatty acid-binding protein 5 [*Canis lupus dingo*]	0.227	0.690
FABP5	1239986810	3	fatty acid-binding protein, epidermal [*Canis lupus familiaris*]	0.227	0.690
FABP5	1239971228	3	fatty acid-binding protein, epidermal isoform X1 [*Canis lupus familiaris*]	0.227	0.690
FABP5	1239971230	3	fatty acid-binding protein, epidermal isoform X2 [*Canis lupus familiaris*]	0.227	0.690
FABP5	1239971232	3	fatty acid-binding protein, epidermal isoform X3 [*Canis lupus familiaris*]	0.227	0.690
IGH-1	1494245209	7	immunoglobulin heavy chain IGH-1 [*Canis lupus familiaris*]	0.285	0.690
IGH-11	1494245229	7	immunoglobulin heavy chain IGH-11 [*Canis lupus familiaris*]	0.312	0.690
IGH-13	1494245233	7	immunoglobulin heavy chain IGH-13 [*Canis lupus familiaris*]	0.312	0.690
SCGB2A2	359321930	3	mammaglobin-A isoform X2 [*Canis lupus familiaris*]	0.143	0.690
SCGB2A1	1239883349	4	mammaglobin-B-like isoform X2 [*Canis lupus familiaris*]	0.143	0.690
PRDX6	1418316704	3	peroxiredoxin-6 [*Canis lupus dingo*]	0.289	0.690

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
PRDX6	1239911065	3	peroxiredoxin-6 [*Canis lupus familiaris*]	0.289	0.690
PFN1	1418313130	5	profilin-1 [*Canis lupus dingo*]	0.005	0.690
PFN1	1239901610	3	profilin-1 [*Canis lupus familiaris*]	0.061	0.690
VDB	1418328657	8	vitamin D-binding protein [*Canis lupus dingo*]	0.222	0.690
ORM1	1418322788	2	alpha-1-acid glycoprotein 1-like [*Canis lupus dingo*]	0.461	0.700
SLPI	1418249573	2	antileukoproteinase-like [*Canis lupus dingo*]	−0.016	0.700
EFHD2	1418506694	2	EF-hand domain-containing protein D2 [*Canis lupus dingo*]	0.355	0.700
EFHD2	928129121	2	EF-hand domain-containing protein D2 [*Canis lupus familiaris*]	0.355	0.700
GSTA2	1418292147	2	glutathione S-transferase A2 [*Canis lupus dingo*]	0.276	0.700
GSTA3	635545472	2	glutathione S-transferase alpha 3 [*Canis lupus familiaris*]	0.276	0.700
GSTA3	649656024	2	glutathione s-transferase alpha 3 [*Canis lupus familiaris*]	0.276	0.700
IGH	208342038	2	immunoglobulin heavy chain variable region, partial [*Canis lupus familiaris*]	0.059	0.700
KRT6A	545545386	6	keratin, type II cytoskeletal 6A isoform X1 [*Canis lupus familiaris*]	0.264	0.700
KRT6A	345791839	6	keratin, type II cytoskeletal 6A isoform X2 [*Canis lupus familiaris*]	0.264	0.700
KRT6A	1418221475	6	keratin, type II cytoskeletal 6A-like [*Canis lupus dingo*]	0.264	0.700
PLA2G7	1585652	2	platelet-activating factor acetylhydrolase	−0.337	0.700
PLA2G7	1418291961	2	platelet-activating factor acetylhydrolase isoform X1 [*Canis lupus dingo*]	−0.337	0.700
PLA2G7	545518207	2	platelet-activating factor acetylhydrolase isoform X1 [*Canis lupus familiaris*]	−0.337	0.700
PLA2G7	545518209	2	platelet-activating factor acetylhydrolase isoform X2 [*Canis lupus familiaris*]	−0.337	0.700
PLA2G7	1418291973	2	platelet-activating factor acetylhydrolase isoform X3 [*Canis lupus dingo*]	−0.337	0.700
AZGP1	70909945	4	zinc alpha-2-glycoprotein 1, partial [*Canis lupus familiaris*]	−0.295	0.700
AZGP1	560879429	4	zinc-alpha-2-glycoprotein precursor [*Canis lupus familiaris*]	−0.295	0.700
ACT4	734547721	2	actin-4 [*Toxocara canis*]	−0.101	0.730
ALB	6687188	2	albumin [*Canis lupus familiaris*]	−0.637	0.730
AHSG	1418515495	2	alpha-2-HS-glycoprotein [*Canis lupus dingo*]	−0.685	0.730
CALR	1418219369	6	calreticulin [*Canis lupus dingo*]	0.306	0.730
CALR	345787749	6	calreticulin [*Canis lupus familiaris*]	0.306	0.730
ALB	1104685307	2	chain A, serum albumin	−0.637	0.730
PPIA	8699209	4	cyclophilin A, partial [*Canis lupus familiaris*]	0.099	0.730
GSTM3	57088159	4	glutathione S-transferase Mu 3 isoform X2 [*Canis lupus familiaris*]	−0.020	0.730
IVL	1418213542	5	involucrin [*Canis lupus dingo*]	−0.226	0.730
IVL	545528998	5	involucrin [*Canis lupus familiaris*]	−0.226	0.730
LTF	339305351	2	lactotransferrin, partial [*Canis lupus familiaris*]	−0.021	0.730
LDHB	1418273448	3	L-lactate dehydrogenase B chain-like [*Canis lupus dingo*]	0.110	0.730
LDHB	1418319535	3	L-lactate dehydrogenase B chain-like [*Canis lupus dingo*]	0.110	0.730
PPIA	1418202784	4	peptidyl-prolyl cis-trans isomerase A isoform X1 [*Canis lupus dingo*]	0.099	0.730
IVL	124728	5	Involucrin	−0.226	0.730
TFF3	1418228196	2	trefoil factor 3 [*Canis lupus dingo*]	−0.095	0.730
TFF3	156875888	2	trefoil factor family peptide 3 [*Canis lupus familiaris*]	−0.095	0.730
TFF3	157061758	2	trefoil factor family peptide 3, partial [*Canis lupus*]	−0.095	0.730
TPM3	545504091	2	tropomyosin alpha-3 chain isoform X6 [*Canis lupus familiaris*]	0.444	0.730

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
A1BG	1418297237	3	alpha-1B-glycoprotein [*Canis lupus dingo*]	−0.109	0.841
A1BG	545487024	3	alpha-1B-glycoprotein [*Canis lupus familiaris*]	−0.109	0.841
BPIFB1	1418251074	13	BPI fold-containing family B member 1 [*Canis lupus dingo*]	−1.300	0.841
BPIFB1	545540364	15	BPI fold-containing family B member 1 isoform X1 [*Canis lupus familiaris*]	−1.327	0.841
BPIFB1	57104142	15	BPI fold-containing family B member 1 isoform X2 [*Canis lupus familiaris*]	−1.327	0.841
DSC2	3413469	6	desmocollin type 2, partial [*Canis lupus familiaris*]	−0.098	0.841
DSC2	1418314263	6	desmocollin-2 isoform X2 [*Canis lupus dingo*]	−0.098	0.841
DSC2	545506022	6	desmocollin-2 isoform X2 [*Canis lupus familiaris*]	−0.098	0.841
DSC2	1418314267	6	desmocollin-2 isoform X4 [*Canis lupus dingo*]	−0.098	0.841
DSC2	545506026	6	desmocollin-2 isoform X4 [*Canis lupus familiaris*]	−0.098	0.841
ENO2	1418256156	2	gamma-enolase [*Canis lupus dingo*]	0.256	0.841
GAPDH	6983847	2	glyceraldehyde-3-phosphate dehydrogenase [*Canis lupus familiaris*]	0.041	0.841
GAPDH	925115133	2	glyceraldehyde-3-phosphate dehydrogenase [*Canis lupus familiaris*]	0.041	0.841
GAPDH	1418292394	2	glyceraldehyde-3-phosphate dehydrogenase isoform X1 [*Canis lupus dingo*]	0.041	0.841
GAPDH	1418292396	2	glyceraldehyde-3-phosphate dehydrogenase isoform X2 [*Canis lupus dingo*]	0.041	0.841
GAPDH	1418260233	2	glyceraldehyde-3-phosphate dehydrogenase-like [*Canis lupus dingo*]	0.041	0.841
GAPDH	1239963916	2	glyceraldehyde-3-phosphate dehydrogenase-like [*Canis lupus familiaris*]	0.041	0.841
GAPDH	1418243839	2	glyceraldehyde-3-phosphate dehydrogenase-like isoform X1 [*Canis lupus dingo*]	0.041	0.841
GAPDH	1418243841	2	glyceraldehyde-3-phosphate dehydrogenase-like isoform X2 [*Canis lupus dingo*]	0.041	0.841
CLU	163954	8	glycoprotein 80 [*Canis lupus familiaris*]	0.132	0.841
IGHAC	598107	17	IgA heavy chain constant region, partial [*Canis lupus familiaris*]	−0.223	0.841
IGHJ	1340189905	2	immunoglobulin heavy chain variable region, partial [*Canis lupus familiaris*]	−0.803	0.841
IGL-1	1494245195	2	immunoglobulin light chain IGL-1, partial [*Canis lupus familiaris*]	0.157	0.841
IGL-3	1494245199	2	immunoglobulin light chain IGL-3, partial [*Canis lupus familiaris*]	0.157	0.841
IGL-7	1494245207	2	immunoglobulin light chain IGL-7, partial [*Canis lupus familiaris*]	0.157	0.841
LOC106559694	928153482	2	LOW QUALITY PROTEIN: glyceraldehyde-3-phosphate dehydrogenase-like [*Canis lupus familiaris*]	0.041	0.841
MUC7	1239933320	2	mucin-7 [*Canis lupus familiaris*]	−0.074	0.841
CANF2	29292274	5	precursor Can f 2, partial [*Canis lupus familiaris*]	0.318	0.841
PDIA3	73964749	7	protein disulfide-isomerase [*Canis lupus familiaris*]	0.037	0.841
SMR3A	1239933313	6	submaxillary gland androgen-regulated protein 3A isoform X1 [*Canis lupus familiaris*]	0.075	0.841
SMR3A	345779658	6	submaxillary gland androgen-regulated protein 3A isoform X2 [*Canis lupus familiaris*]	0.075	0.841
N/A	60734606	6	unnamed protein product, partial [*Canis lupus familiaris*]	−0.047	0.841
N/A	60734607	8	unnamed protein product, partial [*Canis lupus familiaris*]	−0.272	0.841
PYGL	7595920	2	glycogen phosphorylase, partial [*Canis lupus familiaris*]	0.071	0.857
LOC611458	1418213976	6	pregnancy zone protein-like isoform X1 [*Canis lupus dingo*]	0.161	0.857
LOC611458	545546412	6	pregnancy zone protein-like isoform X1 [*Canis lupus familiaris*]	0.161	0.857

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
LOC611458	1418213978	6	pregnancy zone protein-like isoform X2 [*Canis lupus dingo*]	0.161	0.857
LOC611458	545546414	6	pregnancy zone protein-like isoform X2 [*Canis lupus familiaris*]	0.161	0.857
GDI2	50978926	4	rab GDP dissociation inhibitor beta [*Canis lupus familiaris*]	−0.102	0.857
SERPINB5	1418298970	5	serpin B5 isoform X1 [*Canis lupus dingo*]	0.288	0.857
SERPINB5	345784333	5	serpin B5 isoform X1 [*Canis lupus familiaris*]	0.288	0.857
SERPINB5	1418298974	5	serpin B5 isoform X2 [*Canis lupus dingo*]	0.288	0.857
SERPINB5	1239884495	5	serpin B5 isoform X2 [*Canis lupus familiaris*]	0.288	0.857
TAGLN2	345797882	3	transgelin-2 [*Canis lupus familiaris*]	0.237	0.857
VIM	559098393	2	vimentin [*Canis lupus familiaris*]	0.136	0.857
HBB	1418222276	7	hemoglobin subunit beta-like [*Canis lupus dingo*]	0.121	0.886
0	1418192575	7	submaxillary mucin-like protein, partial [*Canis lupus dingo*]	−0.014	0.886
HBA1	1101972892	9	TPA: globin A1 [*Canis lupus familiaris*]	0.103	0.886
BPIFB2	1418249549	11	BPI fold-containing family B member 2 [*Canis lupus dingo*]	0.099	0.905
PGAM1	345792633	3	phosphoglycerate mutase 1 [*Canis lupus familiaris*]	−0.095	0.905
LTF	1418220429	33	lactotransferrin [*Canis lupus dingo*]	0.073	0.937
PGD	1418514978	10	6-phosphogluconate dehydrogenase, decarboxylating [*Canis lupus dingo*]	0.100	1.000
PYCARD	928137006	2	apoptosis-associated speck-like protein containing a CARD isoform X1 [*Canis lupus familiaris*]	−0.074	1.000
PYCARD	1418282931	2	apoptosis-associated speck-like protein containing a CARD isoform X2 [*Canis lupus dingo*]	−0.074	1.000
ACTB	1222669	2	beta-actin, partial [*Canis lupus familiaris*]	−0.040	1.000
BPIFA2	1418249553	16	BPI fold-containing family A member 2 [*Canis lupus dingo*]	−1.143	1.000
CAST	1418331380	2	calpastatin isoform X1 [*Canis lupus dingo*]	0.353	1.000
CAST	545492660	2	calpastatin isoform X1 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331398	2	calpastatin isoform X10 [*Canis lupus dingo*]	0.353	1.000
CAST	928129400	2	calpastatin isoform X10 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331400	2	calpastatin isoform X11 [*Canis lupus dingo*]	0.353	1.000
CAST	928129402	2	calpastatin isoform X11 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331402	2	calpastatin isoform X12 [*Canis lupus dingo*]	0.353	1.000
CAST	928129404	2	calpastatin isoform X12 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331404	2	calpastatin isoform X13 [*Canis lupus dingo*]	0.353	1.000
CAST	1239894403	2	calpastatin isoform X13 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331406	2	calpastatin isoform X14 [*Canis lupus dingo*]	0.353	1.000
CAST	928129406	2	calpastatin isoform X14 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331408	2	calpastatin isoform X15 [*Canis lupus dingo*]	0.353	1.000
CAST	928129408	2	calpastatin isoform X15 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331410	2	calpastatin isoform X16 [*Canis lupus dingo*]	0.353	1.000
CAST	928129410	2	calpastatin isoform X16 [*Canis lupus familiaris*]	0.353	1.000

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
CAST	1418331412	2	calpastatin isoform X17 [*Canis lupus dingo*]	0.353	1.000
CAST	928129416	2	calpastatin isoform X17 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331414	2	calpastatin isoform X18 [*Canis lupus dingo*]	0.353	1.000
CAST	928129412	2	calpastatin isoform X18 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331416	2	calpastatin isoform X19 [*Canis lupus dingo*]	0.353	1.000
CAST	928129414	2	calpastatin isoform X19 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331382	2	calpastatin isoform X2 [*Canis lupus dingo*]	0.353	1.000
CAST	928129389	2	calpastatin isoform X2 [*Canis lupus familiaris*]	0.353	1.000
CAST	1239894411	2	calpastatin isoform X20 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331384	2	calpastatin isoform X3 [*Canis lupus dingo*]	0.353	1.000
CAST	928129391	2	calpastatin isoform X3 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331386	2	calpastatin isoform X4 [*Canis lupus dingo*]	0.353	1.000
CAST	545492662	2	calpastatin isoform X4 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331388	2	calpastatin isoform X5 [*Canis lupus dingo*]	0.353	1.000
CAST	928129394	2	calpastatin isoform X5 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331390	2	calpastatin isoform X6 [*Canis lupus dingo*]	0.353	1.000
CAST	928129396	2	calpastatin isoform X6 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331392	2	calpastatin isoform X7 [*Canis lupus dingo*]	0.353	1.000
CAST	1239894395	2	calpastatin isoform X7 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331394	2	calpastatin isoform X8 [*Canis lupus dingo*]	0.353	1.000
CAST	1239894397	2	calpastatin isoform X8 [*Canis lupus familiaris*]	0.353	1.000
CAST	1418331396	2	calpastatin isoform X9 [*Canis lupus dingo*]	0.353	1.000
CAST	928129398	2	calpastatin isoform X9 [*Canis lupus familiaris*]	0.353	1.000
CTSG	928141642	2	cathepsin G [*Canis lupus familiaris*]	0.229	1.000
HSP90B1	39654740	2	chain A, endoplasmin	0.074	1.000
HSP90B1	71042092	2	chain A, endoplasmin	0.074	1.000
HSP90B1	116667120	2	chain A, endoplasmin	0.074	1.000
HSP90B1	1335512822	2	chain A, endoplasmin	0.074	1.000
HBB	227343817	15	chain B, crystal structure of dog (Canis Familiaris) hemoglobin	0.087	1.000
HSP90B1	159794957	5	chain B, endoplasmin	0.122	1.000
HSP90B1	159794959	5	chain B, endoplasmin	0.122	1.000
HSP90B1	1258500452	5	chain B, endoplasmin	0.122	1.000
HSP90B1	1379069777	2	chain B, endoplasmin	0.074	1.000
HSP90B1	159794950	3	chain G, endoplasmin	0.077	1.000
DSG1	1418314253	3	desmoglein-1 [*Canis lupus dingo*]	0.069	1.000
DSG1	545504019	3	desmoglein-1 isoform X1 [*Canis lupus familiaris*]	0.069	1.000
DSG1	4101628	3	desmoglein-1 precursor [*Canis lupus familiaris*]	0.069	1.000
HSP90B1	50979166	5	endoplasmin precursor [*Canis lupus familiaris*]	0.122	1.000
FN1	1418343247	4	fibronectin isoform X1 [*Canis lupus dingo*]	−0.029	1.000
FN1	928182521	4	fibronectin isoform X1 [*Canis lupus familiaris*]	−0.029	1.000
FN1	1418343265	4	fibronectin isoform X10 [*Canis lupus dingo*]	−0.029	1.000

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
FN1	928182523	4	fibronectin isoform X10 [*Canis lupus familiaris*]	−0.029	1.000
FN1	1418343267	5	fibronectin isoform X11 [*Canis lupus dingo*]	−0.029	1.000
FN1	928182519	5	fibronectin isoform X11 [*Canis lupus familiaris*]	−0.029	1.000
FN1	1418343249	4	fibronectin isoform X2 [*Canis lupus dingo*]	−0.029	1.000
FN1	1239982239	4	fibronectin isoform X2 [*Canis lupus familiaris*]	−0.029	1.000
FN1	1418343251	4	fibronectin isoform X3 [*Canis lupus dingo*]	−0.029	1.000
FN1	1239982241	4	fibronectin isoform X3 [*Canis lupus familiaris*]	−0.029	1.000
FN1	1418343253	5	fibronectin isoform X4 [*Canis lupus dingo*]	−0.029	1.000
FN1	928182507	5	fibronectin isoform X4 [*Canis lupus familiaris*]	−0.029	1.000
FN1	1418343255	5	fibronectin isoform X5 [*Canis lupus dingo*]	−0.029	1.000
FN1	928182509	5	fibronectin isoform X5 [*Canis lupus familiaris*]	−0.029	1.000
FN1	1418343257	4	fibronectin isoform X6 [*Canis lupus dingo*]	−0.029	1.000
FN1	1239982243	4	fibronectin isoform X6 [*Canis lupus familiaris*]	−0.029	1.000
FN1	1418343259	5	fibronectin isoform X7 [*Canis lupus dingo*]	−0.029	1.000
FN1	928182511	5	fibronectin isoform X7 [*Canis lupus familiaris*]	−0.029	1.000
FN1	1418343261	4	fibronectin isoform X8 [*Canis lupus dingo*]	−0.029	1.000
FN1	1239982245	4	fibronectin isoform X8 [*Canis lupus familiaris*]	−0.029	1.000
FN1	1418343263	5	fibronectin isoform X9 [*Canis lupus dingo*]	−0.029	1.000
FN1	928182513	5	fibronectin isoform X9 [*Canis lupus familiaris*]	−0.029	1.000
HBD	103484123	4	globin, partial [*Canis lupus familiaris*]	−0.602	1.000
GSTM3	1239908410	3	glutathione S-transferase Mu 3 isoform X1 [*Canis lupus familiaris*]	0.125	1.000
HSPB1	696633650	2	heat shock protein 27, partial [*Canis lupus familiaris*]	0.129	1.000
HSP90B1	672890024	5	heat shock protein 90 kDa beta member 1, partial [*Canis lupus familiaris*]	0.122	1.000
HSPB1	1418307159	3	heat shock protein beta-1 [*Canis lupus dingo*]	0.129	1.000
HSPB1	924442944	3	heat shock protein beta-1 [*Canis lupus familiaris*]	0.129	1.000
HSPB1	624685	3	heat shock protein [*Canis lupus familiaris*]	0.129	1.000
HBB	1418222274	13	hemoglobin subunit beta [*Canis lupus dingo*]	0.102	1.000
HYAL1	545533633	9	hyaluronidase-1 isoform X1 [*Canis lupus familiaris*]	−0.459	1.000
HYAL1	1418215838	9	hyaluronidase-1 isoform X2 [*Canis lupus dingo*]	−0.459	1.000
IGHAC	46392561	2	immunoglobulin alpha heavy chain constant regin variant A, partial [*Canis lupus familiaris*]	−0.732	1.000
IGJ; JCHAIN	19715661	2	immunoglobulin J chain, partial [*Canis lupus familiaris*]	0.052	1.000
KRT10	1418337563	6	keratin, type I cytoskeletal 10 isoform X1 [*Canis lupus dingo*]	−0.116	1.000
KRT10	928144438	6	keratin, type I cytoskeletal 10 isoform X1 [*Canis lupus familiaris*]	−0.116	1.000
KRT10	1418337565	6	keratin, type I cytoskeletal 10 isoform X2 [*Canis lupus dingo*]	−0.116	1.000
KRT10	928144440	6	keratin, type I cytoskeletal 10 isoform X2 [*Canis lupus familiaris*]	−0.116	1.000
KRT10	1418337567	6	keratin, type I cytoskeletal 10 isoform X3 [*Canis lupus dingo*]	−0.116	1.000
KRT10	928144442	6	keratin, type I cytoskeletal 10 isoform X3 [*Canis lupus familiaris*]	−0.116	1.000
LTF	559767226	35	lactotransferrin precursor [*Canis lupus familiaris*]	0.059	1.000
LTF	339305349	2	lactotransferrin, partial [*Canis lupus familiaris*]	0.070	1.000

Table A2. *Cont.*

Gene Name	Accession Number	No. Unique Peptides	Protein Description	Fold Change (log2)	*p*-Value
LRG1	1418218016	4	leucine-rich alpha-2-glycoprotein [*Canis lupus dingo*]	−0.066	1.000
LYZ	665505916	9	lysozyme C precursor [*Canis lupus familiaris*]	−0.934	1.000
MYH14	1418303612	2	myosin-14 isoform X1 [*Canis lupus dingo*]	0.544	1.000
MYH14	359318588	2	myosin-14 isoform X1 [*Canis lupus familiaris*]	0.544	1.000
MYH14	1418303616	2	myosin-14 isoform X2 [*Canis lupus dingo*]	0.544	1.000
MYH14	1239887368	2	myosin-14 isoform X2 [*Canis lupus familiaris*]	0.544	1.000
MYH14	1418303618	2	myosin-14 isoform X3 [*Canis lupus dingo*]	0.544	1.000
MYH14	1239887370	2	myosin-14 isoform X3 [*Canis lupus familiaris*]	0.544	1.000
MYH14	1418303620	2	myosin-14 isoform X4 [*Canis lupus dingo*]	0.544	1.000
MYH14	1239887372	2	myosin-14 isoform X4 [*Canis lupus familiaris*]	0.544	1.000
PEBP1	114326321	4	phosphatidylethanolamine-binding protein 1 [*Canis lupus familiaris*]	−0.063	1.000
PEBP4	1418230432	4	phosphatidylethanolamine-binding protein 4 isoform X1 [*Canis lupus dingo*]	0.265	1.000
PEBP4	345790561	3	phosphatidylethanolamine-binding protein 4 isoform X1 [*Canis lupus familiaris*]	0.265	1.000
PEBP4	1418230422	3	phosphatidylethanolamine-binding protein 4 isoform X2 [*Canis lupus dingo*]	0.278	1.000
PEBP4	1239961995	2	phosphatidylethanolamine-binding protein 4 isoform X2 [*Canis lupus familiaris*]	0.278	1.000
PEBP4	1418230424	2	phosphatidylethanolamine-binding protein 4 isoform X3 [*Canis lupus dingo*]	−0.267	1.000
PEBP4	1239961997	2	phosphatidylethanolamine-binding protein 4 isoform X3 [*Canis lupus familiaris*]	−0.267	1.000
PEBP4	1418230426	4	phosphatidylethanolamine-binding protein 4 isoform X4 [*Canis lupus dingo*]	0.265	1.000
PEBP4	1239961999	3	phosphatidylethanolamine-binding protein 4 isoform X4 [*Canis lupus familiaris*]	0.265	1.000
PEBP4	1418230428	4	phosphatidylethanolamine-binding protein 4 isoform X5 [*Canis lupus dingo*]	0.265	1.000
PEBP4	1239962001	3	phosphatidylethanolamine-binding protein 4 isoform X5 [*Canis lupus familiaris*]	0.265	1.000
PEBP4	1418230430	4	phosphatidylethanolamine-binding protein 4 isoform X6 [*Canis lupus dingo*]	0.265	1.000
PEBP4	345790559	3	phosphatidylethanolamine-binding protein 4 isoform X6 [*Canis lupus familiaris*]	0.265	1.000
N/A	1239884102	4	phospholipase A2 inhibitor and Ly6/PLAUR domain-containing protein, partial [*Canis lupus familiaris*]	−1.061	1.000
N/A	1418270515	2	poly(U)-specific endoribonuclease [*Canis lupus dingo*]	0.134	1.000
N/A	1239968362	2	poly(U)-specific endoribonuclease [*Canis lupus familiaris*]	0.134	1.000
N/A	1239931268	2	proteoglycan 4-like [*Canis lupus familiaris*]	0.054	1.000
IQGAP1	1418331169	3	ras GTPase-activating-like protein IQGAP1 [*Canis lupus dingo*]	0.226	1.000
LYZ	8928189	9	RecName: Full = Lysozyme C, spleen isozyme; AltName: Full = 1,4-beta-N-acetylmuramidase C	−0.934	1.000
SCGB1D1	1418504468	2	secretoglobin family 1D member 2-like [*Canis lupus dingo*]	1.105	1.000
SCGB1D1	545531237	2	secretoglobin family 1D member 2-like [*Canis lupus familiaris*]	1.105	1.000
SH3BGRL3	345794456	2	SH3 domain-binding glutamic acid-rich-like protein 3 [*Canis lupus familiaris*]	−0.011	1.000
SCGB1A1	922664320	2	uteroglobin, partial [*Canis lupus familiaris*]	−0.130	1.000
N/A	1239959951	2	vomeromodulin-like [*Canis lupus familiaris*]	0.098	1.000

References

1. Fonseca, C.S.; Daleck, C.R. Neoplasias mamárias em cadelas: Influência hormonal e efeitos da ovario-histerectomia como terapia adjuvante. *Ciênc. Rural* **2000**, *30*, 731–735. [CrossRef]
2. Benjamin, S.A.; Lee, A.C.; Saunders, W.J. Classification and behavior of canine mammary epithelial neoplasms based on life-span observations in Beagles. *Vet. Pathol.* **1999**, *36*, 423–436. [CrossRef] [PubMed]
3. da Silva, A.E.; Serakides, R.; Cassali, G.D. Carcinogênese hormonal e neoplasias hormônio-dependentes. *Ciênc. Rural* **2004**, *34*, 625–633. [CrossRef]
4. Zamani-Ahmadmahmudi, M.; Nassiri, S.M.; Rahbarghazi, R. Serological proteome analysis of dogs with breast cancer unveils common serum biomarkers with human counterparts. *Electrophoresis* **2014**, *35*, 901–910. [CrossRef] [PubMed]
5. MacEwen, E.G. Spontaneous tumors in dogs and cats: Models for the study of cancer biology and treatment. *Cancer Metastasis Rev.* **1990**, *9*, 125–136. [CrossRef]
6. Kycko, A.; Reichert, M. Proteomics in the search for biomarkers of animal cancer. *Curr. Protein Pept. Sci.* **2014**, *15*, 36–44. [CrossRef]
7. Cerón, J.J. Acute phase proteins, saliva and education in laboratory science: An update and some reflections. *BMC Vet. Res.* **2019**, *15*, 197. [CrossRef]
8. Sivadasan, P.; Gupta, M.K.; Sathe, G.J.; Balakrishnan, L.; Palit, P.; Gowda, H.; Suresh, A.; Kuriakose, M.A.; Sirdeshmukh, R. Human salivary proteome—A resource of potential biomarkers for oral cancer. *J. Proteom.* **2015**, *127*, 89–95. [CrossRef]
9. Franco-Martínez, L.; Horvatić, A.; Gelemanović, A.; Samardžija, M.; Mrljak, V.; Contreras-Aguilar, M.D.; Martínez-Subiela, S.; And, R.D.; Tvarijonaviciute, A. Changes in the salivary proteome associated with canine pyometra. *Front. Vet. Sci.* **2020**, in press.
10. Franco-Martínez, L.; Tvarijonaviciute, A.; Horvatić, A.; Guillemin, N.; Cerón, J.J.; Escribano, D.; Eckersall, D.; Kocatürk, M.; Yilmaz, Z.; Lamy, E.; et al. Changes in salivary analytes in canine parvovirus: A high-resolution quantitative proteomic study. *Comp. Immunol. Microbiol. Infect. Dis.* **2018**, *60*, 1–10. [CrossRef]
11. Martínez-Subiela, S.; Ceron, J.J.; Yilmaz, Z.; Martinez-Subiela, S.; Horvatic, A.; Escribano, D.; Pardo-Marin, L.; Kocaturk, M.; Mrljak, V.; Burchmore, R.; et al. Identification of novel biomarkers for treatment monitoring in canine leishmaniosis by high-resolution quantitative proteomic analysis. *Vet. Immunol. Immunopathol.* **2017**, *191*, 60–67. [CrossRef] [PubMed]
12. Tvarijonaviciute, A.; Barić-Rafaj, R.; Horvatic, A.; Muñoz-Prieto, A.; Guillemin, N.; Lamy, E.; Tumpa, A.; Ceron, J.J.; Martinez-Subiela, S.; Mrljak, V. Identification of changes in serum analytes and possible metabolic pathways associated with canine obesity-related metabolic dysfunction. *Vet. J.* **2019**, *244*, 51–59. [CrossRef] [PubMed]
13. Bera, A.; Russ, E.; Srinivasan, M.; Eidelman, O.; Eklund, M.; Hueman, M.; Pollard, H.B.; Hu, H.; Col, §.; Shriver, C.D.; et al. Proteomic Analysis of Inflammatory Biomarkers Associated With Breast Cancer Recurrence. *Mil. Med.* **2020**, *185*, 2020. [CrossRef] [PubMed]
14. Delmonico, L.; Bravo, M.; Silvestre, R.T.; Ornellas, M.H.F.; De Azevedo, C.M.; Alves, G. Proteomic profile of saliva and plasma from women with impalpable breast lesions. *Oncol. Lett.* **2016**, *12*, 2145. [CrossRef]
15. Giri, K.; Mehta, A.; Ambatipudi, K. In search of the altering salivary proteome in metastatic breast and ovarian cancers. *FASEB Bioadv.* **2019**, *1*, 191–207. [CrossRef]
16. Klopfleisch, R.; Klose, P.; Weise, C.; Bondzio, A.; Multhaup, G.; Einspanier, R.; Gruber, A.D. Proteome of metastatic canine mammary carcinomas: Similarities to and differences from human breast cancer. *J. Proteome Res.* **2010**, *9*, 6380–6391. [CrossRef] [PubMed]
17. Klose, P.; Weise, C.; Bondzio, A.; Multhaup, G.; Einspanier, R.; Gruber, A.D.; Klopfleisch, R. Is there a malignant progression associated with a linear change in protein expression levels from normal canine mammary gland to metastatic mammary tumors? *J. Proteome Res.* **2011**, *10*, 4405–4415. [CrossRef] [PubMed]
18. Owen, L. *TNM Classification of Tumours in Domestic Animals*; World Health Organization: Geneva, Switzerland, 1980.
19. Parra, M.; Tecles, F.; Martinez-Subiela, S.; Ceron, J. C-reactive protein measurement in canine saliva. *J. Vet. Diagnostic Investig.* **2005**, *17*, 139–144. [CrossRef] [PubMed]

20. Contreras-Aguilar, M.D.; Tecles, F.; Martínez-Subiela, S.; Escribano, D.; Bernal, L.J.; Cerón, J.J. Detection and measurement of alpha-amylase in canine saliva and changes after an experimentally induced sympathetic activation. *BMC Vet. Res.* **2017**, *13*, 266. [CrossRef]
21. Bradford, M.M. A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Anal. Biochem.* **1976**, *72*, 248–254. [CrossRef]
22. Horvatić, A.; Guillemin, N.; Kaab, H.; McKeegan, D.; O'Reilly, E.; Bain, M.; Kuleš, J.; Eckersall, P.D. Quantitative proteomics using tandem mass tags in relation to the acute phase protein response in chicken challenged with Escherichia coli lipopolysaccharide endotoxin. *J. Proteom.* **2019**, *192*, 64–77. [CrossRef] [PubMed]
23. R Core Team. *R: A Language and Environment for Statistical Computing*; R Foundation for Statistical Computing: Vienna, Austria, 2013.
24. Komsta, L. Package 'outliers'. *R Top. Doc.* 2015. Available online: https://cran.r-project.org/web/packages/outliers/ (accessed on 15 January 2020).
25. Doncheva, N.T.; Morris, J.H.; Gorodkin, J.; Jensen, L.J. Cytoscape StringApp: Network analysis and visualization of proteomics data. *J. Proteome Res.* **2019**, *18*, 623–632. [CrossRef] [PubMed]
26. Kolde, R. Pheatmap: Pretty Heatmaps in R Package. Version 61. 2012, pp. 1–7. Available online: https://cran.r-project.org/web/packages/pheatmap/ (accessed on 15 January 2020).
27. Kau, S.; Miller, I.; Tichy, A.; Gabriel, C. S100A4 (metastasin) positive mesenchymal canine mammary tumour spheroids reduce Tenascin C synthesis under DMSO exposure in vitro. *Vet. Comp. Oncol.* **2017**, *15*, 1428–1444. [CrossRef] [PubMed]
28. Platt-Higgins, A.M.; Renshaw, C.A.; West, C.R.; Winstanley, J.H.R.; De Silva Rudland, S.; Barraclough, R.; Rudland, P.S. Comparison of the metastasis-inducing protein S100A4 (p9ka) with other prognostic markers in human breast cancer. *Int. J. Cancer* **2000**, *89*, 198–208. [CrossRef]
29. Maděrka, M.; Pilka, R.; Neubert, D.; Hambálek, J. New serum tumor markers S100, TFF3 and AIF-1 and their possible use in oncogynecology. *Ceska Gynekol.* **2019**, *84*, 303–308.
30. Davie, E.W.; Fujikawa, K. Basic mechanisms in blood coagulation. *Annu. Rev. Biochem.* **1975**, *44*, 799–829. [CrossRef] [PubMed]
31. Wang, M.; Zhang, G.; Zhang, Y.; Cui, X.; Wang, S.; Gao, S.; Wang, Y.; Liu, Y.; Bae, J.H.; Yang, W.-H.; et al. Fibrinogen alpha chain knockout promotes tumor growth and metastasis through Integrin-AKT signaling pathway in lung cancer. *Mol. Cancer Res.* **2020**. [CrossRef]
32. Gerner, C.; Steinkellner, W.; Holzmann, K.; Gsur, A.; Grimm, R.; Ensinger, C.; Obrist, P.; Sauermann, G. Elevated plasma levels of crosslinked fibrinogen gamma-chain dimer indicate cancer-related fibrin deposition and fibrinolysis. *Thromb. Haemost.* **2001**, *85*, 494–501.
33. Shi, Q.; Harris, L.N.; Lu, X.; Li, X.; Hwang, J.; Gentleman, R.; Iglehart, J.D.; Miron, A. Declining plasma fibrinogen alpha fragment identifies HER2-positive breast cancer patients and reverts to normal levels after surgery. *J. Proteome Res.* **2006**, *5*, 2947–2955. [CrossRef]
34. Cheng, A.J.; Chen, L.C.; Chien, K.Y.; Chen, Y.J.; Chang, J.T.C.; Wang, H.M.; Liao, C.T.; Chen, I.H. Oral cancer plasma tumor marker identified with bead-based affinity-fractionated proteomic technology. *Clin. Chem.* **2005**, *51*, 2236–2244. [CrossRef] [PubMed]
35. Britti, D.; Gaspari, M.; Massimini, G.; Casalinuovo, F.; Morittu, V.M.; Cuda, G. Proteomic analysis in canine leishmaniasis. *Vet. Res. Commun.* **2010**, *34*, 91–96. [CrossRef] [PubMed]
36. Terabe, M.; Park, J.M.; Berzofsky, J.A. Role of IL-13 in regulation of anti-tumor immunity and tumor growth. *Cancer Immunol. Immunother.* **2004**, *53*, 79–85. [CrossRef] [PubMed]
37. Król, M.; Pawłowski, K.M.; Majchrzak, K.; Gajewska, M.; Majewska, A.; Motyl, T. Global gene expression profiles of canine macrophages and canine mammary cancer cells grown as a co-culture in vitro. *BMC Vet. Res.* **2012**, *8*, 16. [CrossRef] [PubMed]
38. Kwon, H.J.; Choi, J.E.; Bae, Y.K. Interleukin-13 receptor alpha 2 expression in tumor cells is associated with reduced disease-free survival in patients with luminal subtype invasive breast cancer. *Tumor Biol.* **2018**, *40*, 1–8. [CrossRef] [PubMed]
39. Gallastegui, C.; Bernardez, B.; Regueira, A.; Dávila, C.; Leboreiro, B. Inmunología. In *M. C. Gamundi Planas (Coordinadora), Farmacia Hospitalaria Tomo II*; Sociedad Española de Farmacia Hospitalaria: Madrid, Spain, 2002; pp. 1077–1106.

40. Cerón, J.J.; Eckersall, P.D.; Martínez-Subiela, S. Acute phase proteins in dogs and cats: Current knowledge and future perspectives. *Vet. Clin. Pathol.* **2005**, *34*, 85–99. [CrossRef]
41. Planellas, M.; Bassols, A.; Siracusa, C.; Saco, Y.; Giménez, M.; Pato, R.; Pastor, J. Evaluation of serum haptoglobin and C-reactive protein in dogs with mammary tumors. *Vet. Clin. Pathol.* **2009**, *38*, 348–352. [CrossRef]
42. Tecles, F.; Caldín, M.; Zanella, A.; Membiela, F.; Tvarijonaviciute, A.; Subiela, S.M.; Cerón, J.J. Serum acute phase protein concentrations in female dogs with mammary tumors. *J. Vet. Diagn. Investig.* **2009**, *21*, 214–219. [CrossRef] [PubMed]
43. Merlo, A.; Rezende, B.C.G.; Franchini, M.L.; Simões, D.M.N.; Lucas, S.R.R. Serum C-reactive protein concentrations in dogs with multicentric lymphoma undergoing chemotherapy. *J. Am. Vet. Med. Assoc.* **2007**, *230*, 522–526. [CrossRef]
44. Mischke, R.; Waterston, M.; Eckersall, P.D. Changes in C-reactive protein and haptoglobin in dogs with lymphatic neoplasia. *Vet. J.* **2007**, *174*, 188–192. [CrossRef]
45. Salama, I.; Malone, P.S.; Mihaimeed, F.; Jones, J.L. A review of the S100 proteins in cancer. *Eur. J. Surg. Oncol.* **2008**, *34*, 357–364. [CrossRef] [PubMed]
46. Rudland, P.S.; Platt-Higgins, A.; Renshaw, C.; West, C.R.; Winstanley, J.H.R.; Robertson, L.; Barraclough, R. Prognostic significance of the metastasis-inducing protein S100A4 (p9Ka) in human breast cancer. *Cancer Res.* **2000**, *60*, 1595–1603. [PubMed]
47. Pedersen, K.B.; Nesland, J.M.; Fodstad, O.; Maelandsmo, G.M. Expression of S100A4, E-cadherin, alpha- and beta-catenin in breast cancer biopsies. *Br. J. Cancer* **2002**, *87*, 1281–1286. [CrossRef] [PubMed]
48. Zha, C.; Jiang, X.H.; Peng, S.F. iTRAQ-Based Quantitative Proteomic Analysis on S100 Calcium Binding Protein A2 in Metastasis of Laryngeal Cancer. *PLoS ONE* **2015**, *10*, e0122322. [CrossRef] [PubMed]
49. Naz, S.; Bashir, M.; Ranganathan, P.; Bodapati, P.; Santosh, V.; Kondaiah, P. Protumorigenic actions of S100A2 involve regulation of PI3/Akt signaling and functional interaction with Smad3. *Carcinogenesis* **2014**, *35*, 14–23. [CrossRef] [PubMed]
50. Bai, Y.; Li, L.D.; Li, J.; Lu, X. Prognostic values of S100 family members in ovarian cancer patients. *BMC Cancer* **2018**, *18*, 1256. [CrossRef] [PubMed]
51. Komatsu, K.; Andoh, A.; Ishiguro, S.; Suzuki, N.; Hunai, H.; Kobune-Fujiwara, Y.; Kameyama, M.; Miyoshi, J.; Akedo, H.; Nakamura, H. Increased expression of S100A6 (calcyclin), a calcium-binding protein of the S100 family, in human colorectal adenocarcinomas. *Clin. Cancer Res.* **2000**, *6*, 172–177.
52. Wang, X.H.; Zhang, L.H.; Zhong, X.Y.; Xing, X.F.; Liu, Y.Q.; Niu, Z.J.; Peng, Y.; Du, H.; Zhang, G.G.; Hu, Y.; et al. S100A6 overexpression is associated with poor prognosis and is epigenetically up-regulated in gastric cancer. *Am. J. Pathol.* **2010**, *177*, 586–897. [CrossRef]
53. Lyu, X.; Li, H.; Ma, X.; Li, X.; Gao, Y.; Ni, D.; Shen, D.; Gu, L.; Wang, B.; Zhang, Y.; et al. High-Level S100A6 promotes metastasis and predicts the outcome of T1–T2 stage in clear cell renal cell carcinoma. *Cell Biochem. Biophys.* **2014**, *71*, 279–290. [CrossRef]
54. Zhang, S.; Wang, Z.; Liu, W.; Lei, R.; Shan, J.; Li, L.; Wang, X. Distinct prognostic values of S100 mRNA expression in breast cancer. *Sci. Rep.* **2017**, *7*, 39786. [CrossRef]
55. Hait, W.N.; Lazo, J.S. Calmodulin: A potential target for cancer chemotherapeutic agents. *J. Clin. Oncol.* **1986**, *4*, 994–1012. [CrossRef] [PubMed]
56. Fancy, R.M.; Kim, H.; Napier, T.; Buchsbaum, D.J.; Zinn, K.R.; Song, Y. Calmodulin antagonist enhances DR5-mediated apoptotic signaling in TRA-8 resistant triple negative breast cancer cells. *J. Cell. Biochem.* **2018**, *119*, 6216–6230. [CrossRef] [PubMed]
57. Borgoño, C.A.; Diamandis, E.P. The emerging roles of human tissue kallikreins in cancer. *Nat. Rev. Cancer* **2004**, *4*, 876–890. [CrossRef] [PubMed]
58. Wolf, W.C.; Evans, D.M.; Chao, L.; Chao, J. A synthetic tissue kallikrein inhibitor suppresses cancer cell invasiveness. *Am. J. Pathol.* **2001**, *159*, 1797–1805. [CrossRef]
59. Avgeris, M.; Mavridis, K.; Scorilas, A. Kallikrein-related peptidases in prostate, breast, and ovarian cancers: From pathobiology to clinical relevance. *Biol. Chem.* **2012**, *393*, 301–317. [CrossRef] [PubMed]
60. Yousef, G.M.; Polymeris, M.E.; Grass, L.; Soosaipillai, A.; Chan, P.C.; Scorilas, A.; Borgoño, C.; Harbeck, N.; Schmalfeldt, B.; Dorn, J.; et al. Human kallikrein 5: A potential novel serum biomarker for breast and ovarian cancer. *Cancer Res.* **2003**, *63*, 3958–3965.

61. Ewan King, L.; Li, X.; Cheikh Saad Bouh, K.; Pedneault, M.; Chu, C.W. Human kallikrein 10 ELISA development and validation in breast cancer sera. *Clin. Biochem.* **2007**, *40*, 1057–1062. [CrossRef]
62. Borgoño, C.A.; Grass, L.; Soosaipillai, A.; Yousef, G.M.; Petraki, C.D.; Howarth, D.H.C.; Fracchioli, S.; Katsaros, D.; Diamandis, E.P. Human Kallikrein 14: A new potential biomarker for ovarian and breast cancer. *Cancer Res.* **2003**, *63*, 9032–9041.
63. Koh, S.C.L.; Razvi, K.; Chan, Y.H.; Narasimhan, K.; Ilancheran, A.; Low, J.J.; Choolani, M.; Sahil, F.; Lutan, D.; Siddik, D.; et al. The association with age, human tissue kallikreins 6 and 10 and hemostatic markers for survival outcome from epithelial ovarian cancer. *Arch. Gynecol. Obstet.* **2011**, *284*, 183–190. [CrossRef]
64. Yousef, G.M.; Obiezu, C.V.; Luo, L.Y.; Black, M.H.; Diamandis, E.P. Prostase/KLK-L1 is a new member of the human kallikrein gene family, is expressed in prostate and breast tissues, and is hormonally regulated. *Cancer Res.* **1999**, *59*, 4252–4256.
65. Loo, J.A.; Yan, W.; Ramachandran, P.; Wong, D.T. Comparative human salivary and plasma proteomes. *J. Dent. Res.* **2010**, *89*, 1016–1023. [CrossRef] [PubMed]
66. Klopfleisch, R.; Gruber, A.D. Differential expression of cell cycle regulators p21, p27 and p53 in metastasizing canine mammary adenocarcinomas versus normal mammary glands. *Res. Vet. Sci.* **2009**, *87*, 91–96. [CrossRef] [PubMed]
67. Spoerri, M.; Guscetti, F.; Hartnack, S.; Boos, A.; Oei, C.; Balogh, O.; Nowaczyk, R.M.; Michel, E.; Reichler, I.M.; Kowalewski, M.P. Endocrine control of canine mammary neoplasms: Serum reproductive hormone levels and tissue expression of steroid hormone, prolactin and growth hormone receptors. *BMC Vet. Res.* **2015**, *11*, 235. [CrossRef] [PubMed]
68. Abadie, J.; Nguyen, F.; Loussouarn, D.; Peña, L.; Gama, A.; Rieder, N.; Belousov, A.; Bemelmans, I.; Jaillardon, L.; Ibisch, C.; et al. Canine invasive mammary carcinomas as models of human breast cancer. Part 2: Immunophenotypes and prognostic significance. *Breast Cancer Res. Treat.* **2018**, *167*, 459–468. [CrossRef] [PubMed]
69. Westermeier, R.; Naven, T.; Höpker, H.-R. Wiley InterScience (Online service). In *Proteomics in Practice: A Guide to Successful Experimental Design*; Wiley-VCH: Weinheim, Germany, 2008; ISBN 3527622306.