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Abstract

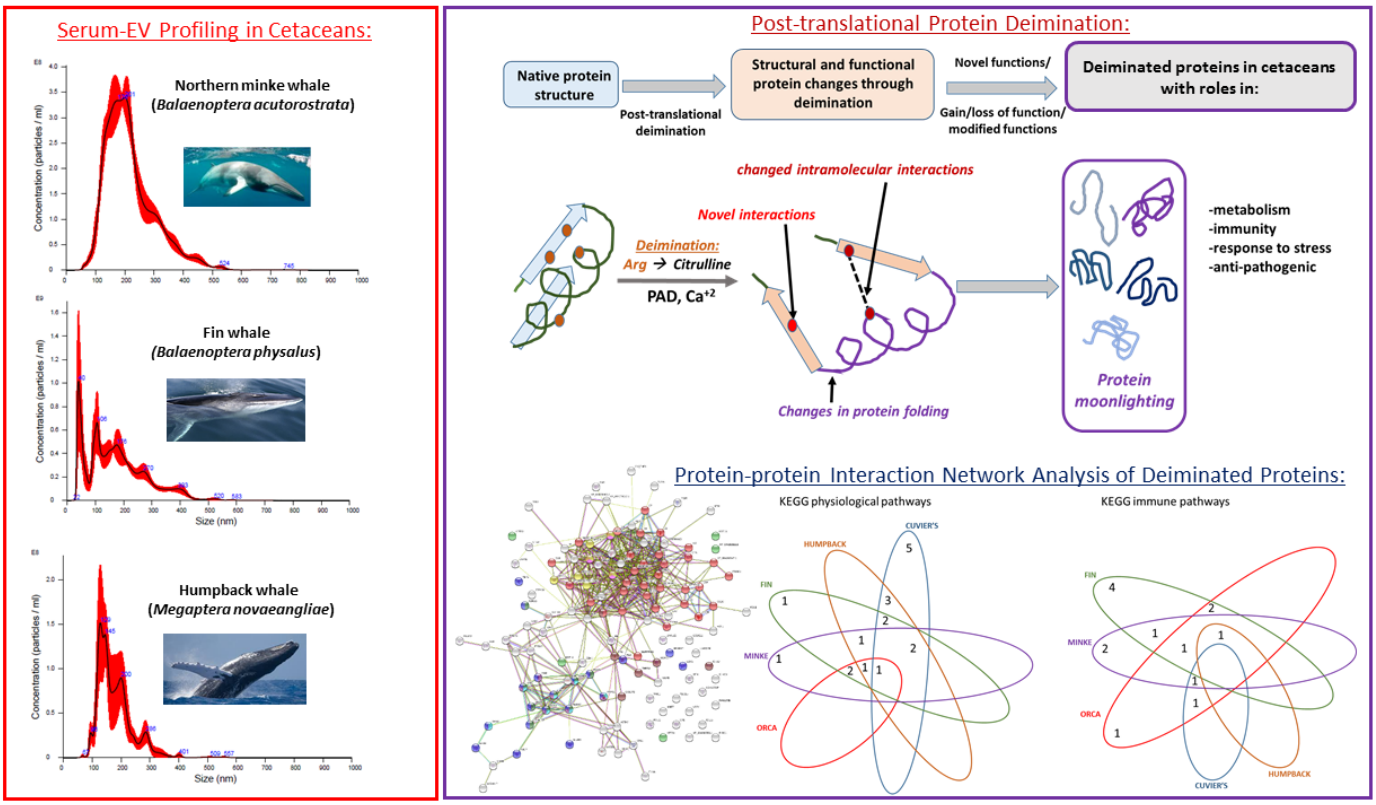
Peptidylarginine deiminases (PADs) are a family of phylogenetically conserved calcium-dependent enzymes which cause post-translational protein deimination. This can result in neo-epitope generation, affect gene regulation and allow for protein moonlighting via functional and structural changes in target proteins. Extracellular vesicles (EVs) carry cargo proteins and genetic material and are released from cells as part of cellular communication. EVs are found in most body fluids where they can be useful biomarkers for assessment of health status. Here, serum-derived EVs were profiled, and post-translationally deiminated proteins and EV-related microRNAs are described in 5 ceataceans: minke whale, fin whale, humpback whale, Cuvier's beaked whale and orca. EV-serum profiles were assessed by transmission electron microscopy and nanoparticle tracking analysis. EV profiles varied between the 5 species and were identified to contain deiminated proteins and selected key inflammatory and metabolic microRNAs. A range of proteins, critical for immune responses and metabolism were identified to be deiminated in cetacean sera, with some shared KEGG pathways of deiminated proteins relating to immunity and physiology, while some KEGG pathways were species-specific. This is the first study to characterise and profile EVs and to report deiminated proteins and putative effects of protein-protein interaction networks via such post-translationald deimination in cetaceans, revealing key immune and metabolic factors to undergo this post-translational modification. Deiminated proteins and EVs profiles may possibly be developed as new biomarkers for assessing health status of sea mammals.

Key words: Peptidylarginine deiminases (PADs); protein deimination; extracellular vesicles (EVs); microRNAs; cetaceans (*Balaenoptera acutorostrata; Balaenoptera physalus; Megaptera novaeangliae; Ziphius cavirostris; Orcinus orca*); immunity; metabolism.

Highlights

- Deiminated proteins were identified in whales and orca
- Key proteins of innate and adaptive immunity are deiminated in cetacean sera
- EV profiles were characterised in sera of 5 cetacean species
- Whale and orca serum-EVs are enriched in microRNAs compared to whole sera
- EV-cargo of immune related miR21, miR155 and metabolic miR210 expression varies between cetacean species
- Deiminated proteins and EV profiles are novel biomarkers in cetaceans

54 **GRAPHIC ABSTRACT**



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1. Introduction

Peptidylarginine deiminases (PADs) are phylogenetically conserved calcium-dependent enzymes which post-translationally convert arginine into citrulline in target proteins in an irreversible manner, causing functional and structural protein changes (Vossenaar, 2003; György et al., 2006; Wang and Wang, 2013; Bicker and Thompson, 2013). Protein deimination can affect gene regulation, cause generation of neoepitopes (Witalison et al., 2015; Lange et al., 2017) and may also allow for protein moonlighting, an evolutionary acquired phenomenon facilitating proteins to exhibit several physiologically relevant functions within one polypeptide chain (Henderson and Martin, 2014; Jeffrey, 2018). Regulation of proteins through such post-translational changes and protein moonlighting of post-translationally modified proteins in health and disease are of great interest, also with regard to effects on function of protein networks in evolutionary conserved and adapted pathways. PADs have been widely studied in a range of human pathologies, including cancer, autoimmune and neurodegenerative diseases (Wang and Wang, 2013; Witalison et al., 2015; Lange et al., 2017). Crucial roles for PADs have also been described in CNS regeneration and hypoxia (Lange et al., 2011; Lange et al., 2014; Fan et al., 2018; Yu et al., 2018). PADs are phylogenetically conserved and have been identified in diverse taxa from bacteria to mammals, with 5 tissue specific PAD isozymes in mammals, 3 in birds, 1 in bony fish and arginine deiminase homologues in parasites and bacteria (Vossenaar et al., 2003; Rebl et al., 2010; Lange et al., 2011; Magnadottir 2018a, Magnadottir et al., 2019a; Gavinho et al., 2019; Kosgodage et al., 2019). In whales some PADs have been reported as gene sequences, for example PADI2 (Gene ID: 102988183) and PADI3 (Gene ID: 102986659) in sperm whale (*Physeter catodon*) (see Supplementary Fig. 1 for phylogenetic analysis of known PADs in ceataceans). Hitherto, PAD-related studies or investigations into their deiminated protein products are though almost non-existent, besides recent studies on cetacean extracellular trap formation (ETosis), which is a phylogenetically conserved innate defence mechanism that can be mediated via PADs (Li et al., 2010; Villagra-Blanco et al., 2019; Imlau et al., 2020). Research on PADs in normal vertebrate physiology has furthermore been limited compared to studies on pathophysiology. Putative control of physiological and immunological processes via post-translational deimination of proteins remains therefore a relatively unexplored field and has been a focus of recent ongoing comparative studies in our laboratory in a range of taxa throughout phylogeny (Criscitiello et al., 2019 and 2020; Kosgodage et al., 2019; Pamenter et al., 2019; Magnadottir et al., 2018a,b and 2019a,b; Kosgodage et al., 2019; Magnadottir et al., 2020a,b; Lange et al., 2020; Phillips et al., 2020). This also includes the identification of regulatory effects of PADs on extracellular vesicle (EV) release as a phylogenetically conserved mechanism (Kholia et al., 2015; Gavinho et al., 2019; Kosgodage et al., 2019).

EVs participate in cellular communication via transfer of cargo proteins and genetic material, including microRNAs (Inal et al., 2013; Colombo et al., 2014; Lange et al., 2017; Kosgodage et al., 2018; Turchinovich et al., 2019; Vagner et al., 2019). EVs can be isolated from most body fluids and be used as biomarkers for assessment of health status (Hessvik and Llorente, 2018; Ramirez et al., 2018). While work on EVs has hitherto largely focussed on human pathologies, roles for EVs in normal physiology and immunity also play important roles. Furthermore, key roles for PADs have been established in cellular release of EVs and EV biogenesis (Kholia et al., 2015; Kosgodage et al., 2017; Kosgodage et al., 2018; Kosgodage et al., 2019). Comparative studies assessing EVs and EV cargo have highlighted important roles for EVs in response to infection (Iliev et al., 2018; Yang et al., 2019), in mucosal immunity (Magnadottir et al., 2019b) and in host-pathogen interactions (Gavinho et al., 2019). Importantly, EVs were also recently identified by our group as novel biomarkers in teleost fish in response to environmental sea temperature changes (Magnadottir et al., 2020a). In elasmobranches, EVs have been characterised in shark, where deiminated proteins were also identified as part of EV cargo (Criscitiello et al., 2019), and a recent studies have been carried out on EV profiling and protein deimination in peglagic seabirds (Phipllips et al., 2020) and pinnipeds (Magnadottir et al., 2020b).

Whales belong to cetaceans, which also include dolphins and porpoises, and have undergone extensive underwater adaptions, both anatomically and immunologically, to physiological stress linked to their marine environments (Beineke et al., 2010; Yim et al., 2013; Tsagkogeorga et al., 2015). Whales are thought to have diverged from terrestrial mammals about 50 million years ago, with toothed wales and baleen whales separated about 30 million years ago (McGowen et al., 2009; Meredith et al., 2011; Gatesy et al., 2013). Marine mammals are of considerable interest for comparative and evolutionary immunology due to their shared linage with terrestrial mammals (Beineke et al., 2010; Meredith et al., 2011; Villagra-Blanco et al., 2019). Research into their immune systems may also further current understanding for resistance to cancer, insulin resistance and adaptions to hypoxia, highly relevant to a number of human pathologies (Tsagkogeorga et al., 2015; Tian et al., 2016; Seluanov et al., 2018). While cetacens have been studied for a range of immunological factors (Beineke et al., 2010; Zhou et al., 2018; Gelain and Bonsembiante, 2019) and assessed for conserved immunological and physiological mechanisms, including at the genetic level (Yim et al., 2014; McGowen et al., 2014; Braun et al., 2015; Lopes-Marques et al., 2018; Zhou et al., 2018), less emphasis has been on proteomic studies. No studies have hitherto assessed aspects of putative regulation via post-translational modifications, such as deimination, which may affect protein-protein interaction networks and therefore be critical for physiological and immunological functions. Furthermore, comparative studies on EVs are scarce, including basic EV characterisation and identification, and have hitherto not been carried out in a cetacean species. While EVs are critical

124 factors in cellular communication and acknowledged biomarkers in a range of human
125 pathophysiologies, their potential for assessments of physiological status or the level of
126 environmental or immunological challenges in other taxa remains a vastly underexplored area. In
127 ongoing studies on deiminated protein pathways and EV profiling throughout phylogeny in our
128 laboratory, including in species with unusual metabolic and immunological adaptions, as well as in
129 human disease, we felt that a study on these parameters in ceataceans was warranted.

130 In order to identify putative PAD-mediated roles for regulation of physiological and immune pathways,
131 the current study assessed deiminated proteins and serum-derived EV profiles, including microRNA
132 (miR) markers, in five cetaceans. The species under study were northern minke whale (*Balaenoptera*
133 *acutorostrata*), fin whale (*Balaenoptera physalus*), humpback whale (*Megaptera novaeangliae*),
134 Cuvier's beaked whale (*Ziphius cavirostris*) and orca (*Orcinus orca*). The minke whale, fin whale and
135 humpback whale are mysticetes, while the orca is an odontocete and belongs to the family
136 Delphinidae. The Cuvier's beaked whale is most common beaked whale, an odontocete of the family
137 Ziphiidae, and the only member of the genus *Ziphius*, believed to represent the remant of an ancient
138 evolutinary lineage.

139 Whales are long-lived sea mammals and are, like other sea life, exposed to ongoing changes in sea
140 temperatures due to global warming as well as a range of environmental contaminants. This can
141 change sea animals' exposure to pathogens, some of which are adapted to certain temperatures, and
142 therefore result in opportunistic infections, including due to shift in habitat. Effects of virus-induced
143 immunosuppression, as well as increased bacterial and parasitic infections due to xenobiotic pollution,
144 affect a range of marine mammals globally (Kennedy 1998; Martinau et al., 1999; Jepson et al., 1999,
145 Wünschmann et al., 2001; Müller et al., 2004; Siebert et al., 2006; Siebert et al., 2009; Beineke et al.,
146 2010). Such increased disease susceptibility due to environmental factors, alongside effects of chronic
147 diseases and starvation, has received considerable attention although many aspects of aquatic
148 mammal's immune functions still remain to be fully understood (Beineke et al., 2010). A range of
149 critical knowledge gaps in cetacean host-pathogen interactions have furthermore recently been
150 highlighted, urging research in the field of cetacean immunology (Di Guardo et al., 2018). As
151 accumulative effects of pollution may impact long-living sea mammals, changes in inflammatory- and
152 other parameters in their biofluids, such as EVs and deiminated proteins, may be novel biomarkers
153 which could be used for assessment of environmental effects on their health status. Furthermore,
154 studying long-lived mammals that display cancer resistance, such as cetaceans, may be of translational
155 value for furthering current understanding of putative underlying pathophysiological mechanisms and
156 for longevity (Ma and Gladyshev, 2017; Seluanov et al., 2018).

Here we report for the first time deimination of key immune and metabolic proteins in whale and orca sera, characterise serum-derived EVs and assess EV-mediated export of key miRs involved in immune responses and metabolism. Our findings indicate both shared KEGG pathways for immunological and physiological functions in these cetaceans, as well as some differences in these parameters between the species under study. Furthermore, our findings verify that EVs are a better source for assessment of miR expression, compared to whole sera. This report is a first base-line study, indicating the potential for the development of a health-index biomarker test, based on deiminated proteins and EV profiling, as a novel tool to assess sea mammal health.

2. Materials and Methods

2.1 Sampling of whale and orca sera

Blood utilised in this study was collected from one individual animal of each of the following cetacean species: Northern minke whale (*Balaenoptera acutorostrata*), fin whale (*Balaenoptera physalus*), humpback whale (*Megaptera novaeangliae*), Cuvier's beaked whale (*Ziphius cavirostris*) and orca (*Orcinus orca*). Protocols for blood collection were ethically approved and conducted under licences of the Chief Veterinary Officer, the Icelandic Government's Ministry of Industries and Innovation (98020047; 13-23-04; 13-08-02). *Balenoptera acutorostrata* and *Balaenoptera physalus* were free ranging (South-Western Iceland) and samples collected post-mortem following euthanasia; *Megaptera novaeangliae* and *Ziphius cavirostris* were free ranging (South-Eastern Iceland) and blood samples were collected following stranding. *Orcinus orca* was captive (The Whale Sanctuary Project, Klettsvik Bay, Iceland) and blood was collected during routine health checks. Blood was collected live from the dorsal fin *vena caudalis* of the orca, but post-mortem from an intrathoracic vessel of the minke whale, fin whale, humpback whale and beaked whale, using vacutainers. After collection, the blood was processed by storing at room temperature for 2 h and thereafter overnight at 4 °C. Serum was collected after centrifugation at 2000 *g* for 20 min, aliquoted and frozen at -20 °C until further use. The animals were considered healthy upon sampling (further information available on these individuals on age, sex and reproductive status/maturity is provided in Supplementary Table 1).

2.2 Extracellular vesicle isolation and NTA analysis

For isolation of EVs, step-wise centrifugation and ultracentrifugation was used, based on previously established protocols (Kosgodage et al., 2018; Magnadottir et al., 2019b) and according to the recommendations of MISEV2018 (the minimal information for studies of extracellular vesicles 2018; Théry et al., 2018). Whale sera were diluted 1:4 in Dulbecco's PBS (DPBS which was ultrafiltered using

a 0.22 µm filter) by adding 250 µl serum to 750 µl DPBS per EV isolation. The diluted sera were centrifuged at 4,000 *g* for 30 min at 4 °C for removal of cells and cell debris and thereafter the supernatant was collected and centrifuged at 100,000 *g* for 1 h at 4 °C for EV enrichment. The resulting EV pellet was then resuspended and washed in 1 ml DPBS and ultracentrifuged again at 100,000 *g* for 1 h at 4 °C. The final EV-enriched pellet was then resuspended in 100 µl DPBS for nanoparticle tracking analysis (NTA), based on Brownian motion of particles in suspension (Soo et al., 2012). The EV samples were diluted 1/100 in DPBS and applied to the NanoSight NS300 system (Malvern, U.K.) using a syringe pump to ensure continuous flow of the sample. Videos were recorded for 5 x 90 sec, with approximately 30-60 particles per frame. The replicate histograms generated from the recordings were averaged for assessment of EV size distribution profiles.

2.3 Transmission Electron Microscopy

For electron microscopic imaging of EVs, these were isolated from whale and orca sera as described above. EV pellets were then fixed with 2.5 % glutaraldehyde in 100 mM sodium cacodylate buffer (pH 7.0) at 4 °C for 1 h and resuspended in 100 mM sodium cacodylate buffer (pH 7.0). The EVs were placed on to a grid containing a glow discharged carbon support film and stained with 2 % aqueous uranyl acetate (Sigma-Aldrich). Imaging was performed using a JEOL JEM 1400 transmission electron microscope (JEOL, Japan) operated at 80 kV at a magnification of 80,000 to 100,000. Digital images were recorded using an AMT XR60 CCD camera (Deben, UK).

2.4 Western blotting

Sera and serum-derived EV isolates (with each EV pellet isolated from 250 µl serum and reconstituted in 100 µl PBS after isolation and purification) were diluted 1:1 in 2x Laemmli sample buffer (containing 5 % beta-mercaptoethanl) and boiled for 5 min at 100 °C before separation on 4-20 % gradient TGX gels (BioRad U.K.). Following SDS-PAGE, transfer to nitrocellulose membranes was performed using semi-dry Western blotting at 15 V for 1 h. The membranes were blocked in 5 % bovine serum albumin (BSA, Sigma-Aldrich, U.K.) diluted in TBS-T (tris-buffered saline containing 0.1 % Tween-20) at room temperature (RT) for 1 h, followed by overnight incubation at 4 °C with the primary antibodies, which were diluted in TBS-T as follows: F95 (MABN328, Merck, U.K.) 1/1000; anti-PAD2 (ab50257, Abcam) 1/1000; anti-PAD3 (ab50246) 1/1000; anti-citH3-r2-r8-r17 (ab5103) 1/1000; CD63 (ab216130) 1/1000; Flotillin-1 (ab41927) 1/2000. After incubation with the primary antibodies, the membranes were washed in TBS-T for 3 x 10 min at room temperature (RT) and thereafter incubated in the corresponding secondary antibody (anti-rabbit IgG BioRad or anti-mouse IgM BioRad respectively, diluted 1/4000 in TBS-T) for 1 h, at RT. Membranes were then washed for 5 x 10 min in TBS-T, followed

by one wash for 10 min in TBS. Visualisation was performed using electrochemiluminescence (ECL, Amersham, U.K.) and the UVP BioDoc-ITTM System (Thermo Fisher Scientific, U.K.).

2.5 Immunoprecipitation and protein identification

For isolation of deiminated proteins from whale and orca sera, the F95 pan-deimination antibody (MABN328, Merck), which is developed against a deca-citrullinated peptide and specifically detects proteins modified by citrullination (Nicholas and Whitaker, 2002), was used in conjunction with the Catch and Release immunoprecipitation kit (Merck, U.K.). According to the manufacturer's instructions (Merck), 50 µl of serum was used per sample for F95 enrichment and immunoprecipitation was carried out overnight on a rotating platform at 4 °C. The F95 bound proteins were eluted using denaturing elution buffer (according to the manufacturer's instructions, Merck) and the F95 enriched eluates were thereafter analysed both by Western blotting and by liquid chromatography mass spectrometry (LC-MS/MS) for identification of deiminated protein targets (Cambridge Proteomics, U.K.). For LC-MS/MS, peak files were submitted to in-house Mascot (Matrix Science, Cambridge Proteomics) using the following databases for identification of species-specific protein matches: *Balaenoptera_acutorostrata*_20190523 (32,118 sequences; 20,395,764 residues); *Balaenoptera_physalus*_20190523 (333 sequences; 92,646 residues); *Megaptera_novaeangliae*_20190523 (259 sequences; 50,653 residues); *Ziphius_cavirostris*_20190523 (176 sequences; 49,360 residues) and *Orcinus_orca*_20190523 (333 sequences; 105,106 residues). Furthermore, the LC-MS/MS peak files from all five species under study were also submitted to a larger cetacean UniProt database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues; Cambridge Proteomics).

2.6 Protein interaction network analysis

STRING analysis (Search Tool for the Retrieval of Interacting Genes/Proteins; https://string-db.org/) was used for the identification of putative protein-protein interaction networks for the deiminated proteins identified in northern minke whale, fin whale, humpback whale, Cuvier's beaked whale and orca, respectively. Species selection in the STRING database was set to "cetacean" and protein-interaction network analysis was based on hits with "minke whale" for minke whale, but on hits with "orca" for fine whale, humpback whale, Cuvier's beaked whale and orca (note that protein-interaction network analsyis for minke whale using corresponding orca hits revealed a similar analysis as when using the minke whale STRING database, therefore the minke whale database was used for minke whale). Protein networks were built by using the function of "search multiple proteins" in STRING and applying basic settings and medium confidence, with colour lines between nodes indicating evidence-

based interactions for network edges as follows: known interactions (based on curated databases, experimentally determined), predicted interactions (based on gene neighbourhood, gene fusion, gene co-occurrence) or via text mining, co-expression or protein homology. Annotations for KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways identified were highlighted for physiological and immunological pathways identified by STRING (Fig. 4-8).

2.7. PAD sequence alignment and phylogenetic reconstruction

Pre-existing predicted PAD protein sequences for a number of cetaceans (Indo-Pacific humpback dolphin, *Sousa chinensis*; narwhal, *Monodon Monoceros*; sperm whale, *Physeter catodon*; common bottlenose dolphin, *Tursiops truncatus*; long-finned pilot whale, *Globicephala melas*; Pacific white-sided dolphin, *Lagenorhynchus obliquidens*; beluga *Delphinapterus leucas*; **narrow-ridged finless porpoise**, *Neophoncaena asiaeorientalis*; baiji, *Lipotes vexillifer*; minke whale, *Balaenoptera acutorostrata*; fin whale, *Balaenoptera physalus*; killer whale, *Orcinus orca*) were retrieved from NCBI searches (https://blast.ncbi.nlm.nih.gov/Blast.cgi?PAGE=Proteins) or by searching specific genome resources (*Balaena mysticetus*; http://www.bowhead-whale.org/). For the remaining cetacea species (Indo-Pacific bottlenose dolphin, *Tursiops aduncus;* North Pacific right whale, *Eubalaena japonica*; Sowerby's beaked whale, *Mesoplodon bidens*; Amazon River dolphin, *Inia geoffrensis*; Antarctic minke whale, *Balaenoptera bonaerensis*; Indus river dolphin, *Platanista minor*; harbour porpoise, *Phocoena phocoena*; vaquita, *Phocena sinus*; La Plata dolphin, *Potoporia blainvillei*; humpback whale, *Megaptera novaeangliae*), and the common hippopotamus, *Hippopotamus amphibius* (included as the closest living terrestrial relative of the cetacea), which had no pre-existing predicted PAD sequences, tBLASTn searches (https://blast.ncbi.nlm.nih.gov/Blast.cgi?PROGRAM=tblastn) searches using reference PAD protein sequences (*Orcinus orca*) were performed against available none annotated genome assemblies found NCBI. Where possible resultant scaffold matches were then used to predict PAD sequences using the FGENESH gene finder tool in Softberry (http://www.softberry.com). Resultant predicted PAD protein sequences were checked using BLASTp searches to ensure accuracy for the FGENESH protein prediction. Multiple sequence alignment was performed using ClustalW in Bioedit version 7 (Hall, 1999). Evolutionary analyses were conducted in MEGAX (Kumar et al., 2018). Phylogenetic relationships of the cetacean PAD proteins were inferred using the Neighbour-Joining method under the conditions of the Poisson correction distance model, with 1000 bootstrap replicates used to assess nodal support.

2.8 MicroRNA analysis in whale serum and EVs

Total whale and orca sera as well as the corresponding EV isolates, were assessed for relative changes in the expression of three key miRs related to inflammation (miR21), stress-response (miR155), hypoxia and metabolic activity (miR210), respectively. RNA was extracted from whole sera (50 µl of serum per isolation) and from EV preparations of the sera from each species (each EV pellet prepared from 250 µl serum per sample as before), using Trizol (Sigma, U.K.). The purity and concentration of the isolated RNA were measured using the NanoDrop Spectrophotometer at 260 nm and 280 nm absorbance. For cDNA production, the qScript microRNA cDNA Synthesis Kit (Quantabio, U.K.) was used according to the manufacturer's instructions. The cDNA was used to assess the expression of miR21, miR155 and miR210. U6-snRNA and has-let-7a-5p were used as reference RNAs for normalization of miR expression levels. The PerfeCTa SYBR Green SuperMix (Quantabio, U.K.) was used together with MystiCq microRNA qPCR primers for the miR21 (hsa-miR-21-5p), mir155 (hsa-miR-155-5p) and miR210 (hsa-miR-210-5p). All miR primers were obtained from Sigma (U.K.). Thermocycling conditions were used as follows: denaturation at 95 °C for 2 min, followed by 40 cycles of 95 °C for 2 sec, 60 °C for 15 sec, and extension at 72 °C for 15 sec. The 2ΔΔCT method (Livak and Schmittingen, 2001) was used for calculating relative miR expression levels and for normalisation. Each experiment was repeated three times.

2.8 Statistical Analysis

GraphPad Prism version 7 (GraphPad Software, San Diego, U.S.A.) was used to prepare graphs and NTA curves were generated using the NanoSight 3.0 software (Malvern Panalytical, UK). Significant differences were considered as $p \leq 0.05$, following one-way ANOVA.

3. Results

3.1 EV profile analysis of whale and orca sera

EVs from whale and orca sera were characterised by NTA for size profiling, by morphological analysis using transmission electron microscopy (TEM) and by Western blotting using EV-specific markers (Fig 1). NTA profiles of EVs revealed poly-dispersed EV populations which overall fell within a range of approximately 50 – 500 nm, albeit with some variation between the 5 cetaceans. For minke whale, main EV peaks were seen at 176 and 201 nm and a smaller peak at 524 nm (Fig. 1A); in fin whale main EV peaks were observed at 40, 108, 176, 270 and 393 nm; in humpback whale an EV profile between 67-401 nm, with main peaks at 129, 145, 200 and 286 nm was observed (Fig. 1C); Cuvier's beaked whale had a more monodispersed profile with one main EV peak at 146 nm within a 50-400 nm overall EV distribution (Fig. D); orca showed main EV peaks at 51 and 123 nm, with a smaller peak at 470 nm

(Fig. 1E). Western blotting confirmed that the EVs were positive for the EV-specific markers CD63 and Flot-1 (Fig. 1 A-E, see Western blot inserts for each species), which have been shown to be phylogenetically conserved from fish to mammals (Iliev et al., 2018; Criscitiello et al., 2019; Magnadottir et al., 2020a,b; Criscitiello et al., 2020). EVs were further characterised by morphology using TEM, confirming typical EV morphology and a poly-dispersed population (Fig. 1A-E, see inserted TEM images for each whale species). Overall yield of serum-derived EVs varied between the 5 species (Fig 2A), with 2.27 x 10^9 (+/- 4.21 x 10^8) EVs/ml for minke whale; 4.6 x 10^9 (+/- 2.14 x 10^8) EVs/ml for fin whale; 5.48 x 10^8 (+/- 4.85 x 10^7) EVs/ml for humpback whale; 7.52 x 10^9 (+/- 9.65 x 10^7) EVs/ml for Cuvier's beaked whale; and 8.84 x 10^9 (+/- 1.29 x 10^8) EVs/ml for orca (Fig. 2A). Some variation in modal size of EVs was also observed between the species (Fig. 2B).

3.2 PAD and deiminated proteins in whale and orca sera and serum-derived EVs

The presence of a PAD homologue was assessed in whale and orca sera by Western blotting via cross reaction with human PAD2 and PAD3 antibodies, showing expected 70-75 kDa size bands observed for PAD2 and PAD3, although more specifically for PAD2 (Fig. 3A), which is the phylogenetically most conserved PAD form. Deiminated histone H3 was detected in cetacean sera at the expected approximate 20 kDa size (Fig. 3B). Total deiminated proteins were detected in the whale and orca sera and in serum-derived EVs using the F95 pan-deimination antibody, with deimination positive bands detected in the range of 15-150 kDa (Fig. 3C-D), both in serum-derived EVs (Fig. 3C) and in whole sera (Fig. 3D).

3.3 LC-MS/MS analysis of deiminated proteins in whale and orca sera

Deiminated protein candidates were further identified in the sera of the wales and orca using F95 enrichment and LC-MS/MS analysis. Results for deiminated protein hits against species-specific databases for each species are listed below in Tables 1-5. It must be noted that differences in the number of peptide hits in this species-specific analysis is partly down to differences in the amount of annotated proteins available in the species-specific databases used for protein identification for the 5 species under study (see section 2.5). In Northern minke whale (*Balaenoptera acutorostrata*) over 90 deiminated protein candidates specific to minke whale were identified (Table 1); in fin whale (*Balaenoptera physalus*) 3 species specific proteins were identified to be deiminated (Table 2), but further hits were identified with other species (not shown); in humpback whale (*Megaptera novaeangliae*) 2 species-specific deiminated proteins (Table 3) and further hits (not shown) with other species were identified to be deiminated; in Cuvier's beaked whale (*Ziphius cavirostris*) 2 species specific (Table 4) and also further hits with other species (not shown) were identified as deiminated

protein candidates; in orca (*Orcinus orca*) 2 species specific hits (Table 5) and further hits with other species (not shown) were identified as deiminated protein candidates. Species-specific hits only, are listed in Tables 1-5. The protein hits identified by LC-MS/MS in all five cetacean species were furthermore assessed against a larger cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues), showing 137 cetacean hits for minke whale; 244 cetacean hits for fin whale, 155 cetacean hits for humpback whale, 88 cetacean hits for Cuvier's beaked whale and 106 cetacean hits for orca; these are represented in Supplementary Tables 2-6.

Table 1. Deiminated proteins identified by F95 enrichment in serum of Northern minke whale (*Balaenoptera acutorostrata*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Only peptide sequence hits scoring with *B. acutorostrata* are included. Peptide sequences and m/z values are listed. For protein hits identified against the full cetacean database see Supplementary Table 2.

Protein name	m/z	Peptide sequence	Score (p<0.05)[‡]	Total score
A0A452CHV5_BALAS	393.2478	*R.LLLNGVR.T*	34	3805
Apolipoprotein B-100	394.2573	*K.FIIPGLK.L*	34	
	401.2408	*K.LVEEALK.K*	35	
	401.2451	*K.LNVGGTIK.G*	48	
	408.7322	*K.VGVELSGR.A*	53	
	419.7792	*R.VQIPLLR.M*	46	
	420.7687	*K.ITQLLPR.E*	53	
	423.2292	*K.FLDSHVK.F*	23	
	427.2443	*K.ALDFFIK.S*	33	
	430.2469	*K.TLQELQK.L*	31	
	448.7325	*K.HINIDER.M*	44	
	463.7402	*R.AFYELQR.D*	36	
	465.2867	*K.LVEEALKK.S*	41	
	472.2370	*K.HVSEAICK.E*	43	
	474.2468	*R.TMEQLTPK.L*	27	
	475.2409	*K.SKDFPEAR.A*	34	
	477.2687	*R.ASTALVYTK.N*	79	
	480.7716	*K.ALSDLQSVK.T*	49	
	482.2586	*K.LEGTSSLTR.K*	61	
	486.2612	*R.SISTALDHK.I*	41	
	508.7799	*R.TWLQEALR.N*	48	
	509.3010	*K.LATALSLSNK.L*	53	
	523.3055	*K.IPSVQINFK.K*	47	
	524.2568	*K.LDVTTNNDR.K*	50	
	526.7632	*R.VPQTGMTFR.H*	28	
	527.7561	*K.LDNIYSSDK.F*	69	
	528.3140	*K.LQDLQLLGR.L*	79	
	530.7622	*K.VQGTEFSHR.L*	29	
	539.7800	*R.EVTIDAQFR.D*	29	
	569.7801	*K.QGFFPDSVNK.A*	39	
	570.2720	*K.EVYGFNPEGK.A*	43	
	576.2888	*K.LDFSSQADLR.S*	91	
	386.2034	*K.SNTVAGLHTEK.N*	23	
	583.8014	*K.NSLFFSAQPR.A*	51	
	586.8195	*K.VDGIWNLEVK.E*	38	
	394.5385	*K.LHVSEQNAQR.A*	37	

	592.7663	*K.NSEEFAAAMSK.Y*	56	
	594.7802	*K.ATGASYDYVNK.Y*	59	
	604.3036	*R.DLSGMDTILAR.I*	54	
	607.7716	*K.FSALDMTNNGK.L*	76	
	609.8400	*K.TLVEQGFTVPK.I*	36	
	611.3148	*R.VNQNIVYESR.F*	73	
	633.3312	*R.IYAIWEQNTK.N*	35	
	633.8564	*K.TEVIPPLVENR.Q*	61	
	643.3612	*K.AGQLEFIVPSPK.R*	67	
	644.3610	*K.NTLELSNGVLVK.V*	21	
	649.8460	*R.VPELDDEIQIK.A*	66	
	437.2271	*K.SKPTVSSSMELK.Y*	46	
	439.5771	*R.KGNVATEISIER.N*	62	
	659.2654	*R.DFSAEYEEDGR.Y*	46	
	664.3650	*K.SISLPSLDPVSGR.I*	37	
	671.8826	*R.ALSNEAVTSLLPK.L*	35	
	673.8498	*K.VNNQLTLDSNTK.Y*	66	
	680.8447	*R.ALTASTNNEGNLR.V*	77	
	465.5612	*K.YHQEYTGLDLR.D*	30	
	701.8931	*K.IAELSTSAQEIIK.S*	49	
	709.8564	*K.ALYWVDGQVPDR.V*	64	
	474.5720	*K.FQETLEDIRDR.V*	35	
	482.9245	*R.LGGLFLTSGEHTSK.A*	50	
	736.8526	*R.DPATGQLNGESNLR.F*	26	
	491.6045	*K.QVLLYPEKEEPK.H*	22	
	748.8682	*K.AASSFPVDLSDYPK.S*	31	
	779.4096	*R.ITENDLQIALDNAK.I*	36	
	793.8498	*R.VYQMDMQQEVQR.Y*	97	
	530.2961	*R.AYLHILGEELGFVK.L*	52	
	535.6262	*R.LFSGSNTLHLVSTTK.T*	46	
	810.4105	*R.GLQNSAEQVYQGAVR.Q*	66	
	873.9498	*R.DAVDQPQEFTLVASVK.Y*	26	
	591.6442	*K.ADAVVDLLSYHVQGSAK.T*	72	
	607.6126	*R.NDCTGNEDHTYLILR.V*	83	
	630.3152	*K.TEHESEVLFVGNTIEGK.S*	68	
	476.7531	*K.FLHSIFQEIEEDLKR.L*	49	
	645.3337	*R.EVLLQTFLDDTSPGDKR.L*	97	
	666.0055	*R.FELELKPTGEVEQYSAR.A*	78	
	674.3291	*K.SLYQELLAQEDHSGFQR.L*	66	
	685.6516	*R.SGVQMNTNFFHETGLEAR.V*	71	
	894.4321	*K.SQVQVHSGSLQNNIQLSNDQEEAR.L*	47	
A0A384B912_BALAS ***Alpha-2-macroglobulin isoform X2***	383.2107	*R.GEAFTLK.A*	27	2013
	403.7056	*K.GPTQEFK.K*	28	
	408.7685	*K.RTTVLVK.N*	35	
	442.2842	*R.DLKPAIVK.V*	41	
	443.7246	*K.YGAATFTR.T*	57	
	445.7268	*K.SLDEEAVK.E*	40	
	447.2201	*R.VTINMCR.K*	33	
	452.2178	*K.DMYSFLK.D*	32	
	460.7271	*K.DLSGFPER.L*	33	
	467.7532	*K.GPTQEFKK.R*	39	
	484.2370	*K.RQEFEMK.I*	37	
	507.7535	*R.YLNTGYQR.Q*	47	
	509.8003	*K.ATVLNYLPK.C*	43	
	510.7849	*R.GIPFFGQVR.L*	29	
	516.2911	*K.TQQLTAEIK.S*	43	
	530.7842	*R.IMQWQNLK.V*	39	

	552.7985	*R.SSGSLLNNAIK.G + Deamidated (NQ)*	74	
	558.8060	*R.QTVSWAVTPK.S*	80	
	387.2121	*K.AHTSFQISLR.V*	43	
	581.2902	*K.ICPQPQQYK.I*	21	
	587.7799	*K.MLETSDHVSR.T*	72	
	398.8926	*K.SFVHLEPLPR.E*	44	
	605.8249	*K.LPPNVVEESAR.A*	63	
	620.7793	*K.YEVENCLANK.V + Deamidated (NQ)*	67	
	629.8445	*R.LLSSPVVAEMGR.G*	96	
	429.2349	*K.VFTNSNIHKPK.I + Deamidated (NQ)*	46	
	651.8457	*K.VTASPQSLCALR.A*	73	
	669.8295	*R.NALFCLESAWK.S*	51	
	472.9477	*K.MVSGFIPLKPTVK.M*	50	
	716.8622	*K.IQEEGTEVELTGK.G*	90	
	726.7958	*K.EQETQCICGNGR.Q + Deamidated (NQ)*	72	
	497.6242	*M.VLVPSLLHTGTPEK.G*	58	
	507.9207	*R.SGTHVLPVHQGDMK.G + Oxidation (M)*	31	
	763.3966	*K.AAQVTIQSSGTFSTK.F*	88	
	548.9582	*R.TEVSNNHVLIYLDK.V*	60	
	555.6386	*R.VHLEASPAFLAVPGEK.E*	56	
	861.4429	*R.APSNEEVMFLTIQVK.G + Oxidation (M)*	53	
	594.0087	*K.DTVIKPLLVEPEGLEK.E*	53	
	914.9600	*K.QLTFPLSSEPFQGSYK.V*	48	
	943.4475	*K.FSQQLNSQGCFSQQVK.T*	54	
	631.0072	*K.GHFPLSVPVESDIAPVAR.L*	64	
	477.7818	*R.KDTVIKPLLVEPEGLEK.E*	36	
	969.9594	*K.EATFNSLLCPSGAEVSEK.L*	58	
	494.2693	*K.VGLNFSPAQSLPASHAHLK.V*	51	
	681.6161	*K.YSNPSNCFGGESHAVCEK.F*	71	
	683.0209	*K.AGALCLSSDTGLGLSPTASLR.A*	96	
	713.7236	*R.AQTVQAHYVLNGQVLQELK.E*	63	
	724.6433	*R.KYSNPSNCFGGESHAVCEK.F + Deamidated (NQ)*	75	
	549.7866	*R.GHELMHIIHISEPPTETVR.K*	72	
	801.7352	*R.QQNSQGGFSSTQDTVVALHALSK.Y*	67	
	812.0687	*K.KEEFPFALEVQTLPQTCDGPK.A*	60	
	622.3431	*K.NEESLVIVQTDKPIYKPGQTVK.F*	63	
	845.3623	*K.VYDYYETDEFAVAEYNAPCSK.D*	49	
	649.3291	*K.SLDEEAVKEDNSVHWTRPQKPK.A + Deamidated (NQ)*	31	
	775.3732	*R.VHLEASPAFLAVPGEKEQETQCICGNGR.Q + Deamidated (NQ)*	89	
	793.8655	*R.HYDGSYSTFGEQHGNNEGNTWLTAFVLK.S*	85	
	824.3633	*K.EDNEDCISHHNIYLNGIMYSPVSNTNEK.D + Deamidated (NQ)*	46	
	863.6284	*K.DHSPCYGYQWLSEEYEEAYHTANLVFSR.S*	28	
A0A383Z2B4_BALAS	385.7113	*K.ENIPAAR.Q*	38	**2339**
Complement C3	388.7367	*K.GVFVLNK.K*	39	
	400.7474	*R.VGLVAVDK.G*	52	
	402.2076	*K.VVPEGMR.V + Oxidation (M)*	34	
	417.2477	*R.LPYSVVR.N*	27	
	430.7455	*K.LLSTGVDR.Y*	41	
	437.7315	*R.DGTLELAR.S*	40	
	444.2327	*R.NEQVEIR.A*	47	
	451.7527	*K.IWDIVEK.A*	36	
	472.2767	*R.QEALELIK.K*	51	
	473.2628	*R.QPMTITVR.T*	54	
	476.2483	*K.FLNTATER.N*	37	
	479.7636	*K.LENDLLNK.F*	48	

	499.2950	*R.ISLAHSLTR.V*	63	
	539.2842	*R.DSCVGTLVVK.N*	42	
	546.8188	*K.NTLIIYLDK.V*	56	
	550.2806	*K.GYTQQLAYR.Q*	44	
	550.3271	*K.RQEALELIK.K*	39	
	551.2747	*R.VPITDGNGEAK.L + Deamidated (NQ)*	56	
	569.2968	*R.TLDPEHLGQK.G*	27	
	572.8036	*K.DFDTVPPVVR.W*	42	
	583.2883	*K.GSMILDICTR.Y*	62	
	587.3353	*R.IVWESASLLR.S*	67	
	587.8500	*R.HQQTLIIPPK.S*	32	
	597.7969	*R.YYTYLVMNK.G*	37	
	605.3170	*R.QPNSAYAAFLK.R*	36	
	409.8866	*K.KGYTQQLAYR.Q*	21	
	650.7977	*R.ACEPGVDYVYK.I*	30	
	673.3193	*K.FYYIDDPDGLK.V*	61	
	675.3480	*R.AQFILQGDACVK.A*	32	
	676.8200	*K.ENEDFTLTAQGK.G*	54	
	681.3184	*K.SGSDEVQVQQER.R*	88	
	685.8696	*K.TIYTPGSTVLYR.I*	57	
	687.3571	*R.EVVADSVWVDVR.D*	69	
	699.4239	*K.SSVPVPYVIVPLK.V*	33	
	473.9027	*K.VSHTLEDCLAFK.V*	42	
	526.5914	*K.AGDFLEDHYLELR.R*	58	
	829.8872	*K.AFLDCCEYIAQLR.L*	69	
	833.4464	*K.FVTVQADFGNVLVEK.V*	35	
	833.4814	*R.VLLNGVQPSQAAALVGK.S + Deamidated (NQ)*	22	
	852.9000	*K.AANLSDQVPDTESETK.I*	39	
	590.6614	*K.VHQYFNVGLIQPGAVK.V*	26	
	898.9664	*R.VELLYNPAFCSLATAK.K*	60	
	601.3332	*R.TGIPIVTSPYQIHFTK.T*	53	
	467.2613	*R.VELKPGETLNVNFHLR.T*	68	
	642.9693	*R.SEETKENEDFTLTAQGK.G*	36	
	704.3283	*K.AHYEDSPQQVFSAEFEVK.E*	51	
	715.0278	*K.ILLQGTPVAQMTEDAINGDR.L + Deamidated (NQ)*	89	
	1222.0769	*K.ADIGCTPGSGSDYAGVFTDAGLALK.T*	26	
	892.7664	*R.TMQALPYNTQDNSNNYLHLSVPR.V*	81	
A0A383ZXR0_BALAS ***Serum albumin***	395.2394	*K.IVTDLTK.V*	46	2314
	423.7320	*K.VTEEQLK.T*	22	
	433.7164	*K.ADFAEVSK.I*	49	
	445.2480	*K.LCAVASLR.E*	26	
	449.7443	*R.LCVLHEK.T*	28	
	457.2168	*K.DDNPDLPK.L*	34	
	457.2427	*K.YLYEIGR.R*	34	
	481.2510	*R.EQVLASSAR.Q + Deamidated (NQ)*	50	
	506.8237	*K.QIALVELVK.H*	50	
	509.2718	*K.SLHTLFGDK.L*	43	
	534.2449	*K.QNCELFEK.L*	61	
	536.2664	*K.SHCIAEVQK.D*	38	
	558.3192	*K.LVNEVTELAK.A*	57	
	569.7526	*K.CCTESLVNR.R*	58	
	570.8713	*K.KQIALVELVK.H*	72	
	576.2747	*K.ETCFALEGPK.L*	69	
	393.5316	*K.HKDDNPDLPK.L*	36	
	606.7807	*R.FNDLGEENFK.G*	77	
	646.3051	*K.ECCDKPLLEK.S*	25	
	657.3641	*R.HPEYSVSLLLR.I*	69	

	658.3209	*K.TVMGNFAAFVDK.C + Oxidation (M)*	79	
	678.2900	*K.GVFAECCQAADK.G*	56	
	699.3409	*K.YICENQATISAK.L*	66	
	705.7853	*K.ACVADESAANCDK.S*	84	
	717.7708	*R.ETYGEMADCCAK.Q*	74	
	490.6128	*R.RHPEYSVSLLLR.I*	63	
	753.9302	*K.LQPLVDEPQNLIK.Q*	38	
	756.4252	*K.VPQVSTPTLVEVSR.N*	83	
	756.8379	*K.DDPPACYATVFEK.L*	54	
	511.5983	*K.LKECCDKPLLEK.S*	62	
	768.4313	*K.LGEYLFQNALIVR.Y*	24	
	517.2570	*K.LKPDPDTLCSEFK.E*	55	
	547.3178	*K.KVPQVSTPTLVEVSR.N*	78	
	583.8923	*K.ECCHGDLLECADDR.A*	27	
	638.3090	*R.RPCFSALTVDETYEPK.A*	50	
	641.6367	*K.TFTFHADLCTLPENEK.Q*	43	
	980.4632	*K.DELPENLSPVAADFAEDK.E*	59	
	678.0515	*R.YTKKVPQVSTPTLVEVSR.N*	73	
	545.2658	*K.LKPDPDTLCSEFKENEQK.F*	42	
	735.0268	*R.HPYFYAPELLYYAHQYK.G*	35	
	562.7404	*K.ECCHGDLLECADDRADLAK.Y*	36	
	826.0563	*K.DELPENLSPVAADFAEDKEVCK.N*	55	
	753.8626	*K.SHCIAEVQKDELPENLSPVAADFAEDK.E*	61	
	706.5385	*K.SHCIAEVQKDELPENLSPVAADFAEDKEVCK.N*	76	
A0A384ALG4_BALAS	394.7163	*K.GSLLANGR.L + Deamidated (NQ)*	51	1968
Ceruloplasmin isoform X2	401.7099	*K.DPVCLAK.M*	20	
	458.7643	*R.KGSLLANGR.L + Deamidated (NQ)*	73	
	507.2159	*K.TYCSEPEK.V*	22	
	549.7883	*R.SYSIHAHGVK.T*	46	
	583.7699	*K.ANDEFIESNK.M*	76	
	587.7759	*K.MYYSAVDPTK.D*	45	
	595.2596	*R.EYTDGSFTNR.K*	49	
	403.5436	*R.IYHSHIDAPR.D*	43	
	629.8504	*K.HYLQVFNPIK.K*	48	
	637.3489	*R.SAPPPSASHVVPK.G*	28	
	664.8300	*K.GTFTYEWTVPK.E*	37	
	681.8541	*R.DTANLFPQTSLR.L*	59	
	456.2263	*K.AETGDTVYVHFK.N*	52	
	701.3909	*K.GTYPLSIEPIGVR.V*	75	
	746.3721	*K.ALYLQYTDETFK.T*	61	
	503.2819	*R.DIATGLIGPLIHCK.K*	60	
	756.3602	*R.QFTDSTFQVPGER.K*	57	
	506.9391	*R.RDTANLFPQTSLR.L*	43	
	785.8897	*K.TENPTVTPTAPGETR.T*	79	
	526.2732	*K.EVGPTYKDPVCLAK.M*	63	
	532.5693	*K.VDKDNEDFQESNR.M*	38	
	724.0344	*K.LISVDTEHSNIYLQNGPNR.I*	93	
	556.7984	*R.KPEEEHLGILGPQLHAGVGDK.V*	77	
	575.3015	*K.KLISVDTEHSNIYLQNGPNR.I*	37	
	777.3522	*R.SGAGIDDSPCIPWAYYSTVDR.V*	59	
	596.0428	*K.VRPGEQCMYILHANPEQGPGK.E*	69	
	796.7537	*R.GPEEEHLGILGPVISAEVGDTIR.V*	70	
	800.0380	*K.HYYIGIIETTWDYASDHGEK.K*	52	
	825.0328	*R.MFTTAPDQVDKENEDFQESNK.M*	50	
	648.2806	*K.TYCSEPEKVDKDNEDFQESNR.M*	94	
	866.0801	*K.AGLQAFFWVQDCQKPSSENDIR.G*	53	
	669.1016	*K.ERGPEEEHLGILGPVISAEVGDTIR.V*	69	

	744.3796	*K.ELHHLQELNLSNAFLDKEEFYIGSK.Y*	50	
	998.7731	*R.LFMQPDTEGTFDVECLTTDHYTGGMK.Q + Deamidated (NQ)*	37	
	669.3148	*K.VRPGEQCMYILHANPEQGPGKEDSNCVTR.I*	36	
A0A383Z5R5_BALAS	397.7057	*K.GTDFNLK.D*	23	1707
Serotransferrin	426.7085	*K.DSANGFLK.I + Deamidated (NQ)*	27	
	455.7112	*R.GSVDEFEK.C*	36	
	461.7534	*K.KGTDFNLK.D*	49	
	468.2747	*R.VPSHAVVAR.S*	59	
	475.2332	*K.LCQLCAGK.G*	45	
	500.2445	*K.TSYIDCIK.A*	26	
	503.7895	*K.YVTAVANLR.Q*	62	
	531.7373	*K.INHCEFDK.F*	24	
	542.2485	*R.YYGYSGAFR.C*	48	
	564.2920	*K.KTSYIDCIK.A*	38	
	575.8166	*K.THYYAVAVVK.K*	50	
	597.7642	*R.ECLPNNYER.Y*	47	
	426.9117	*K.THYYAVAVVKK.G*	48	
	431.1960	*R.WCTVSSHEASK.C*	39	
	656.2932	*K.FFSEGCAPGSPR.N*	81	
	678.3365	*K.VFDTGPFVSCVK.K*	69	
	696.8361	*R.EILDAQQDEFGK.H*	58	
	701.8334	*K.SSDPDLNWNNLK.D*	41	
	705.8417	*K.CLMDGVGDVAFVK.H*	79	
	723.3185	*K.ENTGGNNPEEWAK.T*	94	
	765.8958	*K.FTPESGYYAVAVVK.K*	42	
	550.2707	*K.GISEDFQLFSSPHGK.D*	44	
	878.3733	*K.IECESAESTEECIAK.I*	48	
	602.2895	*K.GEADAMSLDGGHIYIAGK.C*	40	
	956.9316	*K.TLQEDDFELLCTDGTR.K*	82	
	662.6082	*K.HGSDCSSSFCLFHSETK.D*	76	
	665.6106	*K.CACSNHEPYFGYSGAFK.C*	47	
	1028.0111	*K.CLAPLQNAITYESYLGNK.Y*	30	
	758.3589	*K.SVEEASDCFLAQGPNHAVVSR.E*	81	
	589.5130	*K.INHCEFDKFFSEGCAPGSPR.N*	51	
	601.0450	*R.KSVEEASDCFLAQGPNHAVVSR.E*	47	
	665.8179	*K.HTTVLENLPDEADKDEYELLCR.D*	77	
A0A384B6G0_BALAS	390.7158	*R.IASFSQK.C*	30	1145
Kininogen-1	423.2580	*K.AVDTALKK.Y*	40	
	436.7635	*K.ATVQVVAGK.K*	58	
	478.7635	*K.YSIVFTAR.E*	55	
	489.2745	*K.AYVDIQLR.I*	43	
	493.2605	*K.HSLILNCK.A + Deamidated (NQ)*	59	
	500.8110	*K.KATVQVVAGK.K*	86	
	530.7878	*K.RPPGFSPFR.S*	35	
	542.2828	*K.SGNQFVLYR.V*	78	
	542.8111	*K.KYSIVFTAR.E*	44	
	567.7400	*K.EGDCPVQSDK.T*	50	
	603.3133	*K.ADVYVVPWEK.K*	35	
	668.2909	*R.TDDPDTFYSFK.Y*	47	
	692.3344	*K.ENFLFLTPDCK.S*	72	
	698.3058	*K.SLSNGNIGECTDK.A + Deamidated (NQ)*	82	
	723.8487	*K.LNVENNGTFYFK.I + Deamidated (NQ)*	30	
	918.4359	*K.CDLYPVEDFVQPPTR.I*	36	
	967.5248	*K.IYPTVNCQSLGQISLLK.R*	64	
	688.0506	*K.KIYPTVNCQSLGQISLLK.R*	59	
	869.3638	*K.TWQDCDYGDSAQAATGECTATVAK.R*	64	

	725.8627 1190.0765	*R.ICAGCPRPIPVDSPELEEPLDHSIAK.L* *K.FSVATQTCQITPAEGPVVTAQYDCLGCLHPISTESPDLEPVLR.H*	38 39	
A0A383ZCJ5_BALAS ***Hemopexin***	416.7208 472.7288 495.7317 498.7498 503.7473 524.2593 551.3079 579.7387 669.3749 674.3301 727.3198 759.3982 547.2525 558.6348 932.4734 999.4752 814.8939 890.0217	*R.GPVDAAFR.H* *R.FWDFTTK.T* *K.LDPDVMER.C* *K.VNSLLGCPH.-* *K.VDAALCTEK.S* *K.VWEYPPEK.E* *R.QLWWLDLK.L* *R.DYFMPCPGR.G + Oxidation (M)* *K.LNVTEALPQPQK.V* *K.GDKVWEYPPEK.E* *R.SWQAVGNCSSAMR.W* *R.CSPDLVLSALLSDK.H* *K.HGATYAFSGSHYWR.L* *K.RCSPDLVLSALLSDK.H* *K.LGAQATWTELPWPHEK.V* *R.FNPVTGDMYPNYPLDVR.D* *K.EFGSPHGINLDTVDAAFTCPGSSLLHVMAGR.Q* *K.LLQEEFPGIPSPVDAAVECHHEECLHEGVLFFQGNHMR.F + Deamidated (NQ); Oxidation (M)*	58 46 55 73 52 40 28 43 66 31 97 82 68 58 79 95 74 52	1094
A0A383ZWG8_BALAS ***Keratin, type II cytoskeletal 5***	405.7086 414.2185 442.7271 453.7370 469.7508 473.2596 508.2349 513.7318 533.7618 541.8033 547.2675 567.2844 571.2634 576.7801 597.7913 619.7900 621.7853 640.3489 649.8187 436.8897 453.5542 476.2464 565.9468	*R.QSSVSFR.S* *R.FASFIDK.V* *R.TSFTSVSR.S* *R.FLEQQNK.V* *R.SLYNLGGSK.R* *R.GRLDSELR.N* *K.HEISEMNR.M* *K.DVDAAYMNK.V* *K.YEDEINKR.T* *R.FASFIDKVR.F* *K.AQYEEIANR.S* *R.KLLEGEECR.L* *K.DYQELMNTK.L* *K.NKYEDEINK.R* *K.YEELQQTAGR.H* *R.NMQDLVEDFK.N* *R.TEAESWYQTK.Y* *K.LSLDVEIATYR.K* *R.TTAENEFVMLK.K + Oxidation (M)* *K.NKYEDEINKR.T* *R.NTKHEISEMNR.M* *R.TTAENEFVMLKK.D + Oxidation (M)* *K.DVDAAYMNKVELEAK.V*	21 39 57 25 52 36 39 41 41 64 50 64 58 41 67 55 41 53 42 55 52 54 48	1092
A0A384ALK4_BALAS ***Fibronectin***	386.2217 397.2442 555.7750 569.2718 585.2289 611.2642 646.3669 441.9092 694.3301 477.9213 716.3938	*K.SEPLIGR.K* *R.ITGYVIK.Y* *R.STTPDITGYR.I* *R.FTNVGPDTMR.V* *R.YQCYCYGR.G* *R.TFYSCTTEGR.Q* *R.GATYNIIVEAIK.D* *K.LGVRPSQGGEAPR.E* *R.TFYQIGESWEK.F* *R.WSRPQAPITGYR.I* *R.VPGTSASATLTGLTR.G*	32 23 49 40 22 71 49 78 54 22 96	1016

	772.3859	*R.SYTITGLQPGTDYK.I*	32	
	515.2748	*K.EATIPGHLNSYTIK.G*	31	
	797.4046	*K.QYNVGPSATQYPLR.N*	60	
	542.5823	*K.LSCQCLGFGSGHFR.C*	71	
	622.6376	*R.HTTLQTTSAGSGSFTDVR.T*	78	
	691.9559	*R.GFNCESKPEPEETCFDK.Y*	39	
	727.7036	*K.NLHLETNPDTGVLTVSWER.S*	55	
	604.5263	*R.RPGAEPGHEGSTGHSYNQYSQR.Y*	47	
	830.7435	*R.TEIDKPSQMQVTDVQDNSISVR.W*	47	
	863.1167	*R.TKTETITGFQVDAIPANGQTPIQR.T + Deamidated (NQ)*	23	
A0A383YWT8_BALAS	433.2243	*K.SGEQVAFK.C*	65	929
Complement factor H-like	434.2106	*K.FSCIQGR.I*	40	
isoform X1	457.7689	*K.VENAIIQK.E*	38	
	486.2400	*K.HTICINGR.W + Deamidated (NQ)*	66	
	508.2472	*R.DVSCVNPPK.V*	30	
	511.2604	*R.EAFTMIGPR.S*	41	
	547.7775	*K.EYLQGETVR.V*	58	
	554.2986	*R.TLGSIVMVCK.D*	21	
	603.2486	*K.CTSGFEYGER.G*	83	
	624.2720	*K.LSYTCEDGFR.I*	64	
	663.2846	*K.SCDMPVFENAR.A*	49	
	722.9049	*K.QPTILNGYPLSLK.E + Deamidated (NQ)*	25	
	741.8846	*K.SCAPPPQLLSGEVK.E*	48	
	499.9125	*R.CSFKPCDFPVIK.H*	27	
	556.2786	*K.LSCSQPPQVDHGTIK.S*	53	
	610.3134	*K.WTQPPQCIATEELKK.C*	33	
	955.9242	*R.GDAVCTEFGWTPVPSCK.E*	21	
	688.0054	*K.EEAQIQSCPPPPQIPNTR.D*	33	
	758.3656	*R.LGQQFTYHCDQYFVTPLR.T*	64	
	976.7631	*K.DSYQHGEEVIYNCDEGFGIDGPASIR.C*	74	
A0A383Z8T4_BALAS	418.2499	*R.LALEVYK.L*	35	864
C4b-binding protein alpha	489.3052	*K.LISSFLGLK.S*	61	
chain isoform X7	556.2587	*K.QSIVFDCDK.G*	64	
	561.7481	*R.CTADGTWSPK.T*	27	
	585.7771	*K.CEPPPAISNGK.H + Deamidated (NQ)*	38	
	587.2454	*K.SGIDNSCTYR.Y + Deamidated (NQ)*	71	
	603.2824	*K.ADGPTTVTCQR.N*	65	
	426.8777	*R.YYCLSGYKPK.A*	23	
	434.2032	*R.KSGIDNSCTYR.Y*	41	
	668.2800	*R.YGDEVSYTCNK.K*	42	
	474.9221	*K.ALCLKPEIEHGR.L*	61	
	736.8660	*K.LMQCLPTPEEVR.L*	57	
	743.8723	*K.TISVWNPSPPTCK.K*	33	
	779.8806	*R.CGNPGELLNGQVTAK.T + Deamidated (NQ)*	57	
	866.9597	*K.LYVEIQQLELQNDK.A*	65	
	938.9174	*K.SGDAIYECDEGYTLVGK.N*	40	
	744.6987	*K.YGYQKPTEEEVYDIGTALR.Y*	46	
	580.0076	*K.TPECYPDCDSPPVIAHGHHK.L*	39	
P0DMA6|APOA1_BALAS	413.2325	*R.AHVETLR.Q*	26	856
Apolipoprotein A-I	430.2295	*K.VQELQDK.L*	35	
	450.2508	*R.EQLGPVTR.E*	56	
	492.2794	*K.VAPLGEELR.E*	63	
	506.7929	*K.AKPALEDLR.Q*	59	
	530.2787	*K.LTPLAEEMR.D*	66	
	540.7534	*R.EFWDNLEK.E*	40	
	558.3066	*R.QKVQELQDK.L*	47	

	385.5595	*K.VREQLGPVTR.E*	39	
	608.8429	*K.VSILAAIDEASK.K*	74	
	612.3716	*R.QGLLPVLENLK.V*	54	
	416.2120	*K.EGGGSLVQYHAK.A + Deamidated (NQ)*	25	
	632.8199	*K.WQEELQIYR.Q*	48	
	633.8221	*K.VQPYLDEFQK.K*	26	
	464.9137	*K.KWQEELQIYR.Q*	40	
	714.8544	*R.DYVTQFEASALGK.Q*	79	
	490.2732	*R.VKDFATVYVDAIK.D*	48	
	599.2880	*R.EFWDNLEKETESLR.Q*	31	
A0A384BF87_BALAS ***Haptoglobin***	393.2293	*K.DIAPTLR.L*	36	722
	419.2086	*K.DYVEVGR.V*	27	
	429.7501	*K.QLVEIEK.V*	39	
	437.2558	*R.IIGGSLDAK.G*	68	
	460.7349	*K.GSFPWQAK.M*	27	
	490.7511	*R.VGYVSGWGR.N*	68	
	492.7956	*K.AKDIAPTLR.L*	42	
	573.7747	*K.HYEGSTVPEK.K*	33	
	587.8271	*K.VSSILDWVQK.T*	57	
	425.5507	*K.HYEGSTVPEKK.T*	40	
	667.3484	*R.NANFIFTEHLK.Y*	42	
	674.3165	*K.SCATAEYGVYVK.V*	53	
	843.9261	*K.VPTDETVMPICLPSK.D*	29	
	604.3366	*K.VLLHPDYSEVDIGLIK.L*	58	
	648.6652	*R.EKVPTDETVMPICLPSK.D*	34	
	718.7053	*K.SPVGVQPILNEHTFCAGLSK.Y*	69	
A0A383ZI56_BALAS ***Inter-alpha-trypsin inhibitor heavy chain H4 isoform X2***	420.7505	*K.ILGDLGPR.D*	46	584
	430.2478	*K.GSELVVAGK.L*	34	
	474.2815	*K.NVIFVIDK.S*	26	
	500.2831	*K.LALDNGGLAR.R*	46	
	571.3327	*K.AGLLLLSSPDR.V*	63	
	633.3223	*R.ITGGSSADPVFSK.R*	88	
	668.3364	*K.AAAQEQYSAAVAR.G*	26	
	452.5808	*K.LRDQNPDVLSAK.V*	48	
	695.8338	*R.VAEQEEAFQSPR.Y*	87	
	563.9771	*R.KTEQFQVSVSVAPAAK.V*	72	
	973.4864	*K.SPEQQQDTVLDGNFIVR.Y*	48	
A0A383ZCZ3_BALAS ***Hemoglobin subunit beta***	463.7501	*M.VHLTAEEK.S*	31	705
	473.7715	*K.SAVTALWAK.V*	58	
	518.7888	*K.VLASFSDGLK.H*	32	
	563.7844	*K.LHVDPENFR.L*	20	
	575.3408	*K.VVAGVANALAHK.Y*	73	
	637.8652	*R.LLVVYPWTQR.F*	55	
	640.4269	*R.LLGNVLVIVLAR.H*	76	
	664.8438	*K.VNVEEVGGEALGR.L*	88	
	712.8574	*K.EFTPELQAAYQK.V*	67	
	739.8492	*K.GTFATLSELHCDK.L*	87	
	882.9093	*R.FFEAFGDLSTADAVMK.N*	118	
A0A383ZRJ1_BALAS ***Keratin, type I cytoskeletal 14***	404.2033	*R.LAADDFR.T*	55	512
	405.2238	*R.LASYLDK.V*	46	
	515.3005	*R.VLDELTLAR.A*	54	
	532.8088	*R.LASYLDKVR.A*	53	
	553.7667	*K.VTMQNLNDR.L + Oxidation (M)*	92	
	572.7508	*K.DAEDWFFSK.T*	37	
	575.2972	*R.DVTSSSRQIR.T + Deamidated (R)*	28	
	629.7778	*K.NHEEEMNALR.G + Oxidation (M)*	42	

	701.3325	*R.GQVGGDVNVEMDAAPGVDLSR.I + Oxidation (M)*	81	
	538.7844	*K.VTMQNLNDRLASYLDKVR.A + Oxidation (M)*	26	
A0A383ZST7_BALAS	432.7446	*R.VFQTLEK.N*	40	**493**
Complement C5 isoform	447.7866	*R.LPLDLVPK.T*	34	
X1	456.2365	*R.IVACASYK.L*	38	
	474.2325	*K.WLSEEQR.Y*	41	
	549.3197	*K.LQGTLPIEAR.E*	65	
	555.7875	*R.VTFDSETAIK.E*	38	
	591.2880	*R.ESYAGTTLDPK.G*	31	
	668.8057	*K.TTCVNADLEEGK.Q*	62	
	674.3805	*K.IIAITEENAFVK.Y*	55	
	676.3415	*R.VDQQLTDYEIK.D*	47	
	513.5767	*K.TSTSEEICSFHLK.I*	22	
	814.4074	*R.GEQIQLSGTVYNYR.T*	23	
A0A384BAA9_BALAS	429.7251	*K.GNAAELQR.S*	33	**491**
Apolipoprotein A-IV	493.2884	*K.LAPLTESVR.G*	40	
	544.2851	*K.IDQNVEELK.A*	42	
	558.2883	*K.IDQNVEELR.R*	82	
	638.8320	*R.SLAPYAQDVQGK.L*	40	
	437.9069	*K.LVPFATELHER.L*	55	
	692.8688	*R.TQVNAQAQQLQR.Q*	74	
	613.9874	*K.LGPLAGDVEDHLSFLEK.D*	58	
	653.9971	*R.SLAKLSSHLDQQVETFR.H + Deamidated (NQ)*	68	
A0A383Z9Z9_BALAS	542.8118	*R.WGPETLLLR.L*	46	456
Alpha-mannosidase	558.8038	*R.ETTLAANQLR.A*	33	
	568.2965	*K.LATAQGQQYR.T*	79	
	597.8640	*K.EVLAPQVVLAR.G*	53	
	623.8615	*R.VLVIQNEYIR.A*	68	
	482.2321	*R.LEHQFAVGEDSGR.N*	29	
	910.9919	*R.IYITDGNVQLTVLTDR.S*	81	
	620.6356	*R.SQGGSSLSDGSLELMVHR.R*	67	
A0A383ZV20_BALAS	440.7245	*K.INDYVEK.G*	33	431
Alpha-1-antitrypsin	444.7557	*K.AVLTIDEK.G*	45	
	504.7717	*K.KINDYVEK.G*	48	
	548.7980	*K.LSISGTYDLK.T*	69	
	440.5420	*R.DFHVDEETTVK.V*	51	
	533.2636	*K.NLYHSEAFSINFR.D*	63	
	553.9299	*K.WEKPFEAEHTTER.D*	42	
	461.9787	*K.VFSNGADLSGITEEVPLK.L*	58	
	938.9814	*K.VFSNGADLSGITEEVPLK.L + Deamidated (NQ)*	23	
A0A383ZWF6_BALAS	414.2185	*R.FASFIDK.V*	39	388
Keratin, type II	453.7370	*R.FLEQQNK.V*	25	
cytoskeletal 6A-like	541.8033	*R.FASFIDKVR.F*	64	
isoform X2	567.2844	*R.KLLEGEECR.L*	64	
	570.2737	*K.DYQELMNVK.L*	41	
	590.3036	*K.YEELQLTAGR.H*	56	
	602.3222	*K.WTLLQEQGTK.T*	47	
	640.3489	*K.LSLDVEIATYR.K*	53	
A0A383ZRG8_BALAS	404.2033	*R.LAADDFR.L*	55	369
Keratin, type I	561.7931	*R.LEQEIATYR.S*	68	
cytoskeletal 15	601.8044	*R.QSVEADINGLR.R + Deamidated (NQ)*	81	
	651.3330	*R.ALEEANADLEVK.I*	78	
	453.5722	*R.QSVEADINGLRR.V + Deamidated (NQ)*	47	
	460.5807	*K.TRLEQEIATYR.S*	43	

A0A384A3E4_BALAS	380.2158	*M.VLSPTDK.S*	47	365
Hemoglobin subunit alpha	395.7083	*R.VDPANFK.L*	23	
isoform X1	559.7540	*R.MFMNFPSTK.T + Oxidation (M)*	43	
	626.8616	*K.FLASVSTVLTSK.Y*	86	
	539.5939	*K.IGNHSAEYGAEALER.M*	59	
	466.2274	*K.TYFPHFDLGHDSAQVK.G*	31	
	593.7971	*K.AVGHMDNLLDALSDLSDLHAHK.L*	57	
A0A384AZC9_BALAS	454.2658	*K.YINKEIK.N*	21	338
Clusterin	455.2451	*R.GSLFFNPK.S*	46	
	485.7313	*K.FMETVAEK.A*	42	
	523.7895	*K.SLLGSLEEAK.K*	46	
	616.8101	*K.TLIEQTNEER.K*	71	
	719.8353	*R.ASNIMDELFQDR.F*	80	
	666.6522	*R.KFQDTQYYSPFSSFPR.G*	32	
A0A452CBF7_BALAS	416.7299	*K.VTQLTDR.W*	47	334
Desmoplakin isoform X1	431.7552	*R.GLVGIEFK.E*	33	
	454.2658	*R.YIELLTR.S*	45	
	459.7684	*R.LPVDIAYK.R*	36	
	471.7719	*R.QVQNLVNK.S*	38	
	565.3095	*K.IEVLEEELR.L*	57	
	587.8157	*R.LLQLQEQMR.A + Oxidation (M)*	42	
	610.7909	*R.ETQSQLETER.S*	40	
A0A384B1Q0_BALAS	407.2576	*K.ILEPTLK.S*	41	328
Vitamin D-binding protein	469.7449	*R.DLSSFIEK.G*	35	
	489.7603	*K.ELPEYTVK.I*	24	
	588.7716	*R.ICSQYSAYGK.E*	70	
	433.5865	*R.KTHIPEVFLSK.I*	24	
	678.8436	*K.VLDQYTFDLSR.K*	64	
	614.9946	*R.GKLPDATETELEELVAK.R*	36	
	903.0740	*K.HQPQEFPTYVEPTNDEICEAFR.K*	35	
A0A384A7N6_BALAS	428.7480	*K.AGAVNPTVK.F*	52	323
Dipeptidyl peptidase 4	552.2830	*R.VLEDNSALDK.M*	79	
	604.7866	*K.MLQDVQMPSK.K + 2 Oxidation (M)*	41	
	755.8278	*K.WEYYDSVYTER.Y*	59	
	607.6143	*R.YMGLPTPEDNLDHYR.N*	34	
	858.4322	*R.AENFKQVEYLLIHGTADDNVHFQQSAQISK.A*	59	
A0A383ZRE5_BALAS	405.2238	*R.LASYLDK.V*	46	306
Keratin, type I	515.3005	*R.VLDELTLAR.A*	54	
cytoskeletal 17 isoform X1	531.7534	*K.ATMQNLNDR.L*	54	
	561.7931	*R.LEQEIATYR.R*	68	
	629.7778	*K.NHEEEMNALR.G + Oxidation (M)*	43	
	460.5807	*K.TRLEQEIATYR.R*	42	
A0A383ZRY6_BALAS	406.7840	*R.LVQLLVK.A*	26	275
Junction plakoglobin	412.8674	*R.ISEDKNPDYR.K*	55	
	618.8478	*R.VSVELTNSLFK.H*	36	
	684.8066	*R.TMQNTSDLDTAR.C + Oxidation (M)*	96	
	714.4056	*R.ALMGSPQLVAAVVR.T + Oxidation (M)*	36	
A0A452CBL8_BALAS	527.3082	*R.YLTVAAIFR.G*	66	272
Tubulin beta-2A chain	546.2818	*R.LHFFMPGFAPLTSR.G + Oxidation (M)*	76	
isoform X2	653.6653	*K.GHYTEGAELVDSVLDVVR.K*	94	
	776.3582	*K.FWEVISDEHGIDPTGSYHGDSDLQLER.I*	35	
A0A384AFQ0_BALAS	406.7473	*R.LPVIENK.V*	28	262
Plasminogen	425.2395	*R.DVVLFEK.R*	21	
	510.7323	*R.TPENFPCR.N*	26	
	549.2380	*R.NLEENYCR.N*	31	
	561.7552	*R.WEFCDIPR.C*	30	

	432.5549	*K.HNIFTPEANPR.A*	29	
	491.5804	*R.GTVAVTVSGHTCQR.W*	46	
	784.0802	*K.VVLGAHQETAVEDSVQEIQVAK.L*	51	
A0A383ZM34_BALAS	566.3240	*R.VGVIDLSPFGK.F*	106	257
Dimethylglycine	614.7959	*K.WTTTQYTEAK.A*	67	
dehydrogenase,	575.2853	*R.ISYTGELGWELYHR.R*	57	
mitochondrial isoform X1	779.4244	*K.KADIINIVNGPITYSPDILPMVGPHQGVR.N*	27	
A0A383ZRY3_BALAS	404.2033	*R.LAADDFR.T*	55	252
Keratin, type I	521.3062	*R.IVLQIDNAR.L*	37	
cytoskeletal 19	553.7667	*K.VTMQNLNDR.L + Oxidation (M)*	92	
	561.7931	*R.LEQEIATYR.N*	68	
A0A383YQI3_BALAS	467.7716	*K.AIYEAVLR.S*	34	192
Xaa-Pro dipeptidase	484.2400	*R.EASFEGISK.F*	59	
	557.3424	*K.VPLALFALNR.R*	27	
	489.2755	*R.LADRIHLEELTR.I*	31	
	493.9339	*R.VFKTDMELEVLR.Y*	41	
A0A384B2P9_BALAS	401.2265	*R.DLLDIGR.N*	41	191
Complement factor B	481.7398	*R.LPQSTTCR.Q*	52	
	497.2843	*K.ALFVSELSK.D*	39	
	501.2668	*K.DVSEVVTPR.F*	29	
	696.8091	*R.LEDSVTYYCSR.G*	31	
A0A384B2W1_BALAS	448.2590	*R.GQIVSVHR.E*	21	181
Complement C4	454.7454	*R.SGFLSIER.L*	42	
	585.3170	*K.LQDAPSGQVVR.G*	41	
	769.3969	*K.VENSISSANTFLGAK.V*	28	
	778.4198	*K.ILSLAQEQVGGSPEK.L*	50	
A0A383Z8T4_BALAS	868.8886	*K.LSCTSSGWSPAAPQCK.A*	87	176
C4b-binding protein alpha	938.9143	*K.SGDAIYECDEGYTLVGK.N*	88	
chain isoform X7				
A0A384B7A3_BALAS	463.7584	*K.QPPAWSIK.D*	23	160
selenoprotein P	528.7536	*K.DDFLIYDR.C*	39	
	549.7421	*K.TLEDEGFCK.N*	49	
	623.0826	*R.LVYHLGLPYSFLTSSHVEDAIK.T*	50	
A0A383ZWH5_BALAS	404.2033	*R.LAADDFR.V*	55	155
Keratin, type I	521.3062	*R.IVLQIDNAR.L*	37	
cytoskeletal 18	533.2643	*R.AQYDELAQK.N*	25	
	553.8142	*R.LASYLERVR.S*	38	
A0A452C4G6_BALAS	490.2336	*R.ATNYNPGSR.S*	47	154
lysozyme C	492.2796	*R.VVQDPQGIK.A*	21	
	700.8442	*R.STDYGIFQINSR.Y*	86	
A0A383ZW41_BALAS	543.3140	*K.EIIDLVLDR.I*	57	153
Tubulin alpha chain	470.9295	*R.QLFHPEQLITGK.E*	23	
	573.6323	*R.NLDIERPTYTNLNR.L*	36	
	777.3443	*R.AFVHWYVGEGMEEGEFSEAR.E*	37	
A0A452C7H9_BALAS	438.7630	*R.IFLQDIK.K*	41	144
Ferritin heavy chain-like	449.2144	*K.YFLHQSHEER.E*	31	
	515.9064	*R.QNYHQDSEAAINR.Q*	72	
A0A384AF15_BALAS	488.7278	*K.AGFAGDDAPR.A*	64	141
Actin, cytoplasmic 2	566.7672	*R.GYSFTTTAER.E*	55	
	652.0265	*R.VAPEEHPVLLTEAPLNPK.A*	22	
A0A383YRP6_BALAS	420.2108	*K.FDTISEK.T*	45	136
Antithrombin-III	456.2691	*R.LPGIVAEGR.N*	59	
	764.3883	*K.AFLEVNEEGSEAAASTVIGIAGR.S*	32	
A0A383ZRJ1_BALAS	404.2033	*R.LAADDFR.T*	36	135
Keratin, type I	405.2238	*R.LASYLDK.V*	23	
cytoskeletal 14	1043.4943	*R.GQVGGDVNVEMDAAPGVDLSR.I*	78	

A0A384AFN8_BALAS ***Superoxide dismutase***	845.1037 698.3638	*K.LTAVSVGVQGSGWGWLGFNKEQGR.L* *K.EKLTAVSVGVQGSGWGWLGFNKEQGR.L*	80 50	130
A0A452CDN2_BALAS ***Keratin, type I cytoskeletal 12***	405.2238 532.8088 561.7629	*R.LASYLDK.V* *R.LASYLDKVR.A* *K.MTMKNLNDR.L*	46 53 21	120
A0A383Z527_BALAS ***Triosephosphate isomerase***	489.5794 801.9481 434.7322	*K.TATPQQAQEVHEK.L* *K.VVLAYEPVWAIGTGK.T* *K.TATPQQAQEVHEKLR.G*	42 30 46	118
A0A452C549_BALAS ***Immunoglobulin lambda-1 light chain***	830.9147	*K.YAASSYLALTASEWK.S*	117	117
A0A384AEC5_BALAS ***Beta-2-glycoprotein 1***	505.2635 477.5748 872.9594	*R.ATVIYEGEK.V* *R.TCPKPDELPFAR.V* *K.LPVCAPTTCPPPPIPK.F*	40 37 34	111
A0A384AU56_BALAS ***Arginase***	474.7794 557.2958	*K.DIVYIGLR.D* *R.GGVEEGPTVLR.K*	33 76	109
A0A384B6M8_BALAS ***Fetuin-B***	500.3157 595.2817	*K.LVVLPFPSK.E* *K.SVSVTCDFFK.S*	73 35	108
A0A383ZV15_BALAS ***Heat shock protein HSP 90-alpha***	408.2605 757.3957	*R.ALLFVPR.R* *R.GVVDSEDLPLNISR.E*	41 67	108
A0A384B2D0_BALAS ***Heat shock protein HSP 90-beta***	415.2681 757.3957	*R.ALLFIPR.R* *R.GVVDSEDLPLNISR.E*	36 67	102
A0A384AGF6_BALAS ***Fructose-bisphosphate aldolase***	401.2451 566.7927 745.8580	*R.ALQASALK.A* *R.ALANSLACQGK.Y* *R.LQSIGTENTEENR.R*	33 35 32	101
A0A383ZNS6_BALAS ***Fibrinogen beta chain***	490.7239 891.4093	*R.QDGSVDFGR.K* *K.DNENVINEYSSQLEK.H*	30 69	99
A0A383YX88_BALAS ***Inter-alpha-trypsin inhibitor heavy chain H2***	465.7194 494.9440 791.9318	*K.HADPDFTK.K* *K.AHVTFKPTVAQQR.K* *K.IQPSGGTNINEALLR.A*	25 26 42	93
A0A384A960_BALAS ***Alpha-2-antiplasmin***	574.7888 648.8311 761.7364	*R.NPNPGAQPEPK.E* *K.LGNQEPGGQTAPK.K* *R.GISDQSLVVSSVQHQSTLELR.E*	27 34 30	90
A0A384BAB1_BALAS ***Apolipoprotein C-III***	865.9330	*K.DALTSVQESQVAQQAR.G*	87	87
A0A452C549_BALAS ***Immunoglobulin lambda-1 light chain***	830.9166	*K.YAASSYLALTASEWK.S*	89	89
A0A383ZWG2_BALAS ***Keratin, type II cuticular Hb6***	453.7370 611.8196 632.3506	*R.FLEQQNK.L* *R.ATAENEFVTLK.K* *K.LGLDIEIATYR.R*	25 32 25	82
A0A384BC72_BALAS ***Unconventional myosin-Vb isoform X4***	396.2076 429.7501 444.2327	*R.IIGANMR.T + Deamidated (NQ); Oxidation (M)* *K.LQVQLEK.K + Deamidated (NQ)* *K.NELNELR.K*	31 22 30	82
A0A384A9E5_BALAS ***Vitronectin***	645.2896 675.3448	*R.GLYCYELDEK.A* *K.GIPDNVDAALALPAHSYSGR.E*	31 50	80
A0A383ZQR0_BALAS ***Histone H3.1-like***	416.2502 495.2926	*K.STELLIR.K* *K.VFLENVIR.D*	28 50	77
A0A384BAE9_BALAS ***Phosphotriesterase-related protein***	565.8066	*R.VLQEAGADISK.T*	76	76
A0A452CPB6_BALAS ***Complement component C9***	516.2723 699.3558	*K.VVEESELAR.T* *R.AIADYINEFSVR.K*	50 25	76

A0A452CB89_BALAS ***Unconventional myosin-XV***	422.2686 523.3142	*K.IILLQSR.A + Deamidated (NQ)* *K.TEATKLILR.Y + Deamidated (R)*	46 30	75
A0A383ZIC9_BALAS ***L-lactate dehydrogenase***	624.8040	*R.VIGSGCNLDSAR.F*	74	74
A0A384A978_BALAS ***14-3-3 protein epsilon isoform X1***	628.7988	*R.YLAEFATGNDR.K*	68	68
A0A384A061_BALAS ***Cathepsin G-like***	451.9123 849.7634	*R.RTDTLHDVQIR.V* *R.AIPHPGYNPQNNENDIMLLQLR.S*	28 39	66
A0A383ZVX9_BALAS ***Protein kinase C-binding protein NELL2***	572.2315	*R.LDQCYCER.T*	64	64
A0A384AG73_BALAS ***Histone H2A***	425.7666 458.2725	*R.HLQLAIR.N* *K.KMRIIPR.H + 2 Deamidated (R)*	31 31	62
A0A384BA01_BALAS ***Heparin cofactor 2 isoform X1***	449.2447 544.7905	*K.FALDLYR.A* *K.QVPVLDDFR.A*	40 22	62
A0A384B0X4_BALAS ***Glutathione synthetase***	436.7455	*K.ILSNNPSK.G*	60	60
A0A452CCD2_BALAS ***Alpha-1B-glycoprotein***	567.3012	*R.FPLGAVTGDTR.G*	60	60
A0A383YT12_BALAS ***Annexin***	622.8151	*R.TNQELQEINR.V*		
A0A383ZP87_BALAS ***Charged multivesicular body protein 5***	466.7456 572.8304	*K.KMREGPAK.N + Oxidation (M)* *K.ISRLDAELVK.Y + Deamidated (R)*	21 36	57
A0A383Z9P7_BALAS ***Polymeric immunoglobulin receptor***	486.2736 758.7378	*K.IVEGEPSLK.V* *K.SNADLQVLKPETELIYGDLR.G*	32 24	56
A0A383Z8Q9_BALAS ***Heterogeneous nuclear ribonucleoproteins A2/B1 isoform X1***	594.8271	*K.IDTIEIITDR.Q*	56	56
A0A452CGT3_BALAS ***Periplakin***	473.2628 487.2586	*R.QSLQLEAR.R + Deamidated (NQ)* *R.GELQQLQR.R + 2 Deamidated (NQ)*	21 37	
A0A383ZLI1_BALAS ***Microtubule-associated protein 1B***	528.3140 626.8099	*R.AIGNIELGIR.S* *K.ETKNAANTSTSK.S + Deamidated (NQ)*	25 30	54
A0A383ZSV7_BALAS ***Tenascin isoform X1***	568.2903	*K.APTTQVESFR.V*	51	51
A0A383YYI6_BALAS ***Serine/threonine-protein phosphatase***	466.2614 473.2596	*K.QTIETAIR.G* *R.AAARAESLR.A + Deamidated (R)*	21 29	50
A0A384B0M0_BALAS ***E3 ubiquitin-protein ligase SH3RF1***	452.2299	*K.EDELELR.K*	47	47
A0A384A314_BALAS ***Hydroxyacylglutathione hydrolase, mitochondrial isoform X1***	435.7740	*K.ALLEVLGR.L*	46	46
A0A383ZYA9_BALAS ***F-box only protein 50***	410.2362	*R.TVIAQHHVAPR.T*	46	46
A0A383YRQ8_BALAS ***Histone H2B***	408.7324	*R.EIQTAVR.L*	45	45
A0A383ZNS6_BALAS	474.7266	*R.ECEEIIR.N*	45	45

Fibrinogen beta chain				
A0A384ATV8_BALAS ***Glycerol-3-phosphate dehydrogenase [NAD(+)]***	436.2840	*K.GALGISLIK.G*	44	44
A0A383Z1U4_BALAS ***Complement C3-like isoform X1***	652.8309	*R.VFVSNPDGSPASK.V*	43	43
A0A383ZQ81_BALAS ***Trypsin-like***	588.3214	*R.TLNNDIMLIK.L + Deamidated (NQ)*	43	43
A0A383YW83_BALAS ***Desmoglein-1***	513.7371	*R.TMNNFLDR.E + Oxidation (M)*	43	43
A0A383ZIZ4_BALAS ***Rootletin***	453.7302 487.2586	*R.TLSEEATR.L* *K.GQLQQELR.R + 2 Deamidated (NQ)*	21 22	43
A0A383ZUP7_BALAS ***Protein S100***	494.7593	*K.LLQTECPK.F*	42	42
A0A383ZJG1_BALAS ***Basement membrane-specific heparan sulfate proteoglycan core protein***	549.7988	*R.IGAPTNLEQR.A*	42	42
A0A384AJC0_BALAS ***protrudin isoform X1***	610.8038	*R.IGAPTNLEQR.A*	42	42
A0A452C841_BALAS ***Ankyrin repeat domain-containing protein 24***	539.5939	*R.ARQAQSRAQEALER.A + Deamidated (NQ); 2 Deamidated (R)*	42	42
A0A452C9S2_BALAS ***DnaJ homolog subfamily C member 14-like***	492.2611 398.8752	*R.RKEYIMK.R + Oxidation (M)* *R.SPGRHQLGGKR.S + Deamidated (NQ); Deamidated (R)*	22 22	40
A0A383ZSX3_BALAS ***Protein AMBP***	483.7103	*K.ECLQTCR.T*	39	39
A0A383YSS2_BALAS ***Thioredoxin reductase 1***	624.3392	*R.QFVPIKVEQIEAGTPGR.L + 2 Deamidated (NQ)*	39	39
A0A452CBX0_BALAS ***Myosin-1-like***	468.2629	*K.CASLKKTK.Q*	38	38
A0A383YQ74_BALAS ***60S ribosomal protein L30***	879.4589	*R.VCTLAIIDPGDSDIIR.S*	36	36
A0A383ZYL4_BALAS ***Carbonic anhydrase 2***	527.9437	*K.YAAELHLVHWNTK.Y*		
A0A383ZZQ3_BALAS ***N6-adenosine-methyltransferase catalytic subunit***	508.7721	*K.QLDSLRER.L*	36	36
A0A384ANP8|A0A384ANP8_BALAS ***HERV-H LTR-associating protein 1***	460.5570	*K.QKCLENICKSV.- + Deamidated (NQ)*	35	35
A0A384A168|A0A384A168_BALAS ***Catalase***	487.7490	*K.NLSVEDAAR.L*	35	35
A0A384AEC5_BALAS ***Beta-2-glycoprotein 1***	759.6873	*K.TSYAPGEEIVYTCQPGYVSR.G*	34	34
A0A384A9V8|A0A384A9V8_BALAS ***SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily A***	424.7348	*K.KNVFNPK.R + 2 Deamidated (NQ)*	34	34

containing DEAD/H box 1 isoform X2				
A0A384BAV9_BALAS ***Collagen alpha-1(IV) chain isoform X1***	642.3357	*K.ILYHGYSLLYVQGNER.A*	34	34
A0A452CIN7_BALAS ***Pleckstrin homology domain-containing family G member 3***	483.2744	*K.SKVYQLAR.Q + Deamidated (NQ)*	34	34
A0A383YWG2_BALAS ***Kinesin-like protein KIF21A***	483.2744	*R.ASQQINALR.S + 2 Deamidated (NQ)*	33	33
A0A384ACX2_BALAS ***Charged multivesicular body protein 4c***	514.8088	*K.RAALQALKR.K + Deamidated (NQ); Deamidated (R)*	33	33

[ǂ]Ions score is -10*Log(P), where P is the probability that the observed match is a random event. Individual ions scores > 32 indicated identity or extensive homology ($p < 0.05$). Protein scores were derived from ions scores as a non-probabilistic basis for ranking protein hits. Cut-off was set at Ions score 20.

Table 2. Deiminated proteins identified by F95 enrichment in serum of fin whale (*Balaenoptera physalus*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Only peptide sequence hits scoring with *B. physalus* are included. Peptide sequences and m/z values are listed. For protein hits against the full cetacean database see Supplementary Table 3.

Protein name	m/z	Peptide sequence	Score (p<0.05)[ǂ]	Total score
Q0QES7_BALPH ***Glyceraldehyde-3-phosphate dehydrogenase***	406.2101 435.2576 685.3741 778.9081 539.2985 910.4540	*K.LTGMAFR.V* *K.VIPELNGK.L* *R.GAAQNIIPASTGAAK.A* *R.VPTPNVSVVDLTCR.L* *K.AITIFQERDPANIK.W* *K.IVSNASCTTNCLAPLAK.V*	40 42 77 97 33 92	381
O02673_BALPH ***Gamma fibrinogen***	486.5787	*R.SDGPAKPNGIDSATK.I*	46	46
Q0QEQ3_BALPH ***Isocitrate dehydrogenase 1***	690.3438	*K.VEISYTPSDGSPK.T*	22	22

[ǂ]Ions score is -10*Log(P), where P is the probability that the observed match is a random event. Individual ions scores > 15 indicated identity or extensive homology ($p < 0.05$). Protein scores were derived from ions scores as a non-probabilistic basis for ranking protein hits. Cut-off was set at Ions score 20.

Table 3. Deiminated proteins identified by F95 enrichment in serum of humpback whale (*Megaptera novaeangliae*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Only peptide sequence hits scoring with *M. novaeangliae* are included. Peptide sequences and m/z values are listed. For protein hits against the full cetacean database see Supplementary Table 4.

Protein name	m/z	Peptide sequence	Score (p<0.05)[ǂ]	Total score
A1E0X3_MEGNO ***Beta-actin***	488.7276 652.0251	*K.AGFAGDDAPR.A* *R.VAPEEHPVLLTEAPLNPK.A*	51 27	78
R9S009_MEGNO ***Myoglobin***	479.0133	*K.YLEFISDAIIHVLHSR.H*	47	47

[ǂ]Ions score is -10*Log(P), where P is the probability that the observed match is a random event. Individual ions scores > 13 indicated identity or extensive homology ($p < 0.05$). Protein scores were derived from ions scores as a non-probabilistic basis for ranking protein hits. Cut-off was set at Ions score 20.

Table 4. Deiminated proteins identified by F95 enrichment in serum of Cuvier's beaked whale (*Ziphius cavirostris*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Only peptide sequence hits scoring with *Z. cavirostris* are included. Peptide sequences and m/z values are listed. For protein hits against the full cetacean database see Supplementary Table 5.

Protein name	m/z	Peptide sequence	Score (p<0.05)[ǂ]	Total score
MYG_ZIPCA ***Myoglobin***	395.7186 455.7348 475.7403 434.2224 708.9197 773.8487 818.9368 464.2471 933.5031 638.3455 397.2168	*K.ASEDLKK.H* *K.GHPETLEK.F* *K.YKELGFHG.-* *K.GHPETLEKFDK.F* *K.HGHTVLTALGGILK.K* *R.HPSDFGADAQAAMTK.A* *K.VEADLSGHGQEILIR.L* *K.GHHEAELKPLAQSHATK.H* *M.GLSEAEWQLVLHVWAK.V* *K.YLEFISDAIIHVLHSR.H* *K.KGHHEAELKPLAQSHATK.H*	31 31 46 37 89 126 102 51 85 57 42	696
A8IY74_ZIPCA ***Recombination activating protein 1***	612.8331	*R.KGHQPSTQLTK.K*	23	23

[ǂ]Ions score is -10*Log(P), where P is the probability that the observed match is a random event. Individual ions scores > 14 indicated identity or extensive homology ($p < 0.05$). Protein scores were derived from ions scores as a non-probabilistic basis for ranking protein hits. Cut-off was set at Ions score 20.

Table 5. Deiminated proteins identified by F95 enrichment in serum of orca (*Orcinus orca*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Only peptide sequence hits scoring with *O. orca* are included. Peptide sequences and m/z values are listed. For protein hits against the full cetacean database see Supplementary Table 6.

Protein name	m/z	Peptide sequence	Score (p<0.05)[ǂ]	Total score
G8Z0F2_ORCOR ***Adiponectin***	533.7796	*R.SAFSVGLETR.V*	42	42
G8Z0E8_ORCOR ***Cytoplasmic beta-actin***	398.2398 895.9500	*K.IIAPPER.K* *K.SYELPDGQVITIGNER.F*	33 68	101

[ǂ]Ions score is -10*Log(P), where P is the probability that the observed match is a random event. Individual ions scores > 15 indicated identity or extensive homology ($p < 0.05$). Protein scores were derived from ions scores as a non-probabilistic basis for ranking protein hits. Cut-off was set at Ions score 20.

3.4 Protein interaction network analysis

STRING analysis (Search Tool for the Retrieval of Interacting Genes/Proteins; https://string-db.org/) was used for the identification of putative protein-protein interaction networks for the deiminated proteins identified in northern minke whale, fin whale, humpback whale, Cuvier's beaked whale and orca, respectively – based on identification of protein hits using the larger cetacean database following LC-MS/MS analysis. These networks were based on the STRING cetacean database for minke whale (constructed using minke whale hits), while hits with orca were used for constructing protein-interaction networks for fin whale, humpback whale, Cuvier's beaked whale and orca. As protein-interaction network analysis for minke whale, using the corresponding orca STRING database, revealed a similar analysis as when using the minke whale STRING database, the minke whale STRING

database was used for the analysis of protein-interaction networks in minke whale (Figure 4). The PPI enrichment *p*-value for all protein networks identified in the 5 ceataceans under study was $p < 1.0 \times 10^{-16}$, indicating that the deiminated protein hits have more interactions among themselves than what would be expected for a random set of proteins of similar size. Annotations for KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways identified for the deiminated protein hits, which relate to physiological and immunological pathways, are represented in Fig. 4-8, with some shared pathways common between all or some of the species, while other pathways identified were species-specific (see Venn Diagram in Fig. 9). Physiological KEGG pathways identified for deiminated proteins included the complement and coagulation cascades, renin-angiotensin system, oestrogen signalling pathway, cholesterol metabolism, vitamin digestion and absorption, glycolysis/gluconoegenesis, biosynthesis of amino acids, fat digestion and absorption, metabolic pathways, carbon metabolism, ECM-receptor interaction, nitrogen metabolism, pentose phosphate pathway, HIF-1 signalling, thyroid hormone synthesis and proximal tubule bicarbonate reclamation (Fig. 4A, 5A, 6A, 7A, 8A). KEGG pathways for immune defences/host-pathogen interactions included *Staphylococcus aureus* infection, systemic lupus erythematosus (SLE), amoebiasis, ferroptosis, phagosome, necroptosis, prion diseases, pertussis, metabolism of xenobiotics, cancer, prion diseases and tryptamosomiasis (Fig. 4B, 5B, 6B, 7B, 8B). Figures 4-8 highlight the different KEGG pathways for deiminated proteins identified in the cetaceans under study, while the Venn diagrams in Fig. 9 show the number of common and species-specific physiological (Fig. 9A) and immune related (Fig. 9B) pathways identified for the deiminated protein hits identified. Relevance of these KEGG pathways for physiology and immunity of the cetacean species under study are further discussed in the discussion.

3.5 Phylogenetic reconstruction of PAD sequences.

Five well supported and distinct clades representing each PAD were formed within the Neighbour-joining phylogeny (Supp. Fig. 1). The PAD1 clade appeared to resolve the best supported phylogenetic topology with the cetacean sequences falling into two subclades, one for the Odontoceti and one for the Misticety, with La Planta dolphin (*Pontoporia blainvillei*) as a paraphyletic group. The first PAD1 "Odontoceti" subclade was further split into two clades, one representing members of the Lipotidae and Iniideae, and the other further split into a Delphinidae clade and another clade comprising Montodontidae and Phocoenidae lineages. The second PAD1 "Misticety" subclade also formed two further clades, one representing members of the Ziphiidae and the other representing members of the Physeteridae, Balaenidae and Balaenopteridae.

The PAD2, PAD3, PAD4 and PAD6 clades do not show the same differentiation into such distinct groups as for PAD1 (Supp. Fig. 1). Interestingly, the PAD sequences for the common hippopotamus, *Hippopotamus amphibius*, were intermingled with the cetacean sequences within each of the

458 respective PAD clades, with the exception of the *H. amphibius* PAD3 which formed the expected
459 paraphyletic clade (Supp. Fig. 1).
460
461 **3.6 Analysis of inflammatory and metabolic microRNAs in whale sera and serum derived EVs**
462 The inflammatory and stress related miR21, miR155 and the metabolic and hypoxia related miR210
463 were assessed both in whole sera and in EVs isolated from sera of the 5 cetaceans. Species-specific
464 differences were observed in the relative expression all three miRs as shown in Fig. 10. Furthermore,
465 EVs were found to be a better source of miRs, compared to whole sera (Fig. 10). The highest relative
466 levels of miR21 were found in humpback whale EVs, followed by minke whale (Fig. 10A), while relative
467 miR155 expression was highest in minke whale EVs (Fig. 10B) and miR210 relative levels were highest
468 in orca, followed by humpback whale (Fig. 10C).
469
470 **4. Discussion**
471 This is the first study to characterise deiminated protein networks, extracellular vesicles (EVs) and
472 microRNA (miR) EV-cargo in cetacean sera. Deiminated proteins were identified and compared in the
473 5 different cetacean species under study: Northern minke whale (*Balaenoptera acutorostrata*), fin
474 whale (*Balaenoptera physalus*), humpback whale (*Megaptera novaeangliae*), Cuvier's beaked whale
475 (*Ziphius cavirostris*) and orca (*Orcinus orca*). The findings presented here unravel novel aspects of post-
476 translational deimination in key proteins of metabolism, innate and adaptive immunity in these sea
477 mammals.
478 PAD homologues were identified in whale sera by Western blotting via cross reaction with human
479 PAD2 and PAD3. PAD2 is the phylogenetically most conserved PAD form (Vossenaar et al., 2003;
480 Magnadottir et al., 2018a), and in cetacean sera PAD-positive bands were seen at an expected 70 - 75
481 kDa size, similar to as seen for other mammalian PADs.

482 Deiminated histone H3, a marker of neutrophil extracellular trap formation (NETosis), was detected
483 in the whale and orca sera. NETosis is partly driven by PADs (Li et al., 2010), is conserved throughout
484 phylogeny (Magnadottir et al., 2018a; Magnadottir et al., 2019a; Criscitiello et al., 2019), and is
485 important in innate immune defences against a range of pathogens including bacteria, viruses and
486 helminths (Brinkmann et al., 2004; Palić et al., 2007; Branzk et al., 2014; Schönrich and Raftery, 2016).
487 Indeed, NET/ETosis has recently been related to parasitic defence mechanisms in cetaceans (Villagra-
488 Blanco et al., 2019). NETosis has furthermore been associated with clearance of apoptotic cells and
489 tissue remodelling (Magnadottir et al., 2018a; Magnadottir et al., 2019a) as well as being associated
490 with chronic pathologies (Lee et al., 2017; O'Neil and Kaplan, 2019), neurodegenerative diseases
491 (Pietronigro et al., 2017) and cancer (Gonzalez-Aparicio and Alfaro, 2019). Histones undergo various

post-translational modifications that affect gene regulation and can also act in concert (Bird, 2007; Latham et al., 2007). In addition to acetylation, phosphorylation and ubiquitination, histones are indeed known to undergo deimination, including H2B (Sohn et al., 2015) and H3 as identified here in minke whale. Other histones known to undergo deimination are H2A (Hagiwara et al., 2005) and H4 (Chen et al., 2014; Kosgodage et al., 2018), both of which were also identified here as deimination targets based on the larger cetacean database search (Supplementary Tables 2-5).

Further deiminated proteins identified here in whale and orca sera by F95 enrichment and LC-MS/MS analysis included key immune, nuclear and metabolic proteins. Most species-specific protein hits were found for minke whale which, has to be noted, also had the largest searchable species-specific database and therefore the most annotations for identification of species-specific proteins. Furthermore, all protein hits from the LC-MS/MS analysis for deiminated proteins isolated from the individual cetaceans were also assessed against a larger common cetacean database (Supplementary Tables 2-6). The protein list for species-specific deiminated proteins identified in minke whale was submitted to STRING (Search Tool for the Retrieval of Interacting Genes/Proteins) analysis (https://string-db.org/) to predict putative protein-protein interaction networks. For deiminated proteins identified in minke whale serum, PPI enrichment value for 85 of the identified deiminated proteins was found to be $p < 1x10^{-16}$, which indicates that these proteins have more interactions among themselves than what would be expected for a random set of proteins of similar size, drawn from the genome. Such enrichment indicates that the proteins are at least partially biologically connected, as a group. KEGG pathways involved in immunity and metabolism are highlighted for the minke whale species-speficic derived STRING protein network analysis in Supplementary Fig 2.

In addition to the species-specific analysis of protein interaction networks, based on the species-specific UniProt databases for each of the cetaceans under study, a wider analysis of deiminated protein hits based on a larger cetacean UniProt database was used to create protein-protein interaction networks in STRING (Figures 4-8). These revealed both common/shared deiminated protein pathways related to physiology and immunity as well as highlighting some differences in deiminated KEGG pathways between the species under study (Fig. 9). KEGG pathways for the complement and coagulation cascades were identified in all 5 cetacean species, and form part of the acute phase response and first line of immune defences against invading pathogens as well as in the clearance of necrotic or apoptotic cells (Dodds and Law, 1998; Fishelson et al., 2001; Gelain and Bonsembiante, 2019). Pathways for glycolysis/gluconeogenesis were identified in minke, fin, humpback and Cuvier's beaked whale. Recent studies in dolphins have identified low activity of the glycolysis metabolic pathway (Suzuki et al., 2018) and changes in glycolysis pathways has been assessed in diving vertebrates (Hochachka et al., 1975). Post-translationally deiminated proteins in

glycolysis pathways have been recently identified in the naked mole-rat (*Heterocephelus glaber*) (Pamenter et al., 2019), where changes in glycolysis has for example been related to anoxia resistance (Park et al., 2017). How deimination of glycoloysis pathway related proteins play roles in hypoxia tolerance and cancer-resistance remains to be further investigated. Oestrogen signalling patways were identified as deiminated in minke whale, fin whale and humpback whale. Oestrogen has been studied in a range of cetaceans, including during pregnancy (Robeck et al., 2016) and as a marker for environmental pollution in orca at the mRNA expression level (Buckman et al., 2011), while post-translational modification and putative effects of deimination on oestrogen signalling remains to be investigated. KEGG pathways relating to cholesterol metabolism were identified in minke whale, fin whale, humpback whale and orca, while KEGG pathways for fat digestion and absorption were identified to be deiminated in minke whale, fin whale and orca. Cholesterol has been studied in whales in relation to lifespan (Borchman et al., 2017) and lipidomics are being developed as a diagnostic tool for metabolic and physiological state in whales, including cholesterol (Tang et al., 2018). Roles for post-translational modifications, including deimination, in cholesterol metabolism remain to be fully understood. KEGG pathways relating to vitamin digestion and absorption were identified to be deiminated in minke whale, finwhale and orca. Disruption of vitamin profiles has been identified in cetaceans in response to exposure to environmental pollutants (Desforges et al., 2013; Pedro et al., 2019), but to what extend deimination plays a role in vitamin processing is not known. KEGG pathways for biosynthesis of amino acids were identified to be deiminated in minke whale, fin whale, humpback whale and Cuvier's beaked whale. Such deimination may be of considerable interest as amino acid assessment for mammalian metabolism is being developed for health management of cetaceans (Suzuki et al, 2018) and for research into ageing and disease, including in cetacean samples (Fry and Carter, 2019). Pathways for carbon metabolism were identified in fin whale, humpback whale and Cuvier's beaked whale, while nitrogen metabolism pathways were identified in humpback whale and Cuvier's beaked whale. Both pathways have been untilised to assess environmental contamination in whales (Borrell et al., 2018; Pinzone et al., 2019). Pathways relating to HIF-1 signalling were identified in Cuvier's beaked whale and humpback whale, which correlates with these two cetaceans being the most deep diving of the species under study; for example gas and fat embolic syndrome is a pathologic condition of *Ziphiidae* and mirrors decompression sickness identified in human divers (Fernández et al., 2005; Di Guardo et al., 2019). Deiminated protein pathways related to HIF-1 signalling have also recently been identified in the naked mole-rat, which is known for unusual resistance to hypoxia (Pamenter et al., 2019), while studies on hypoxia in the CNS have revealed roles for PAD-mediated pathways (Lange et al., 2014; Fan et al., 2018; Yu et al., 2018).

559 Other deiminated KEGG physiological pathways identified to be species-specific were renin-
560 angoistensin system (minke whale), proximal tubule biocarbonate reclamation (Cuvier's beaked
561 whale), ECM-receptor interaction (fin whale), and in Cuvier's beaked whale KEGG pathways for thyroid
562 hormone synthesis, fructose, mannose and pyruvate metabolism, as well as mineral absorption were
563 identified to be deiminated. The renio-angiotensin system plays pivotal roles in maintaining blood
564 pressure and extracellular volume homeostasis (Yang and Xu, 2017). It is critical for osmoregulation in
565 cetaceans and has been studied in relation to adaptions due to their evolutionary transition from
566 terrestrial to hyperosmotic envornments (Oritz, 2001; Zu et al., 2013). Cetacean kidneys have several
567 evolutionary adaptions, including larger size and relatively large ratio of medulla to renal cortex, which
568 allows for production of highly concentrated urine (Zu et al., 2013). Furthermore, hormonal regulation
569 of salt and water balance is of great importance, while overall molecular mechanisms underlying these
570 specialised pathways still remain to be fully explored. Proximal tubule bicarbonate reclamation
571 pathways werehere identified to be deiminated in Cuvier's beaked whale, and these are critical for
572 kidney function in whales (Maluf and Gassman, 1998) and are primary target of kidney injury in human
573 and animal models (Chevalier, 2016). Therefore post-translationally mediated regulation of proteins
574 involved in these pathways, including deimination identified here, may be of some interest for
575 osmoregulation and specialised kidney function in ceatceans as well as for andvancing therapeutic
576 strategies in kidney disease (Chevalier, 2016). ECM-receptor interactinos play direct and indirect roles
577 in control of a range of cellular activities including adhesion, migration, differentiation, proliferation
578 and apoptosis and are widely studied in cancer, including at the transcriptome level (Bao et al., 2019).
579 KEGG pathways for both ECM-receptor interaction and focal adhesion have been identified to be
580 enriched in EVs of mesenchymal stem cells (Mardpour et al., 2019), and both pathways were here
581 found enriched in deiminated proteins in fin whale only. Roles for regulation of these pathways via
582 post-translational deimination have not been investigated. Thyroid hormones have been studied in a
583 range of whales and dolphins, including for evaluation of energetics and stress (Suzuki et al., 2018;
584 Hunt et al., 2019), as well as environmental pollution (Buckmann et al., 2011; Villanger et al., 2011;
585 Hunt et al., 2017; Simond et al., 2019). PADs have been related to thyroid cancer (Guo et al., 2017)
586 and deimination of histone H3 has been linked to autoimmune thyroid disease (Morshed et al., 2019),
587 while physiological effects of deimination on thyroid hormone synthesis remain to be investigated.
588 Fructose, mannose and pyruvate metabolism are associated with glycolytic pathways, which have
589 been found to be of low activity in ceataceans (Suzuki et al., 2018) and therefore regulatory
590 mechanisms via deimination may be of relevance for understanding of cancer and insulin resistance
591 pathways (Brown et al., 2016; Guzmán-Flores et al., 2018). In cetaceans, ATP-mediated control of
592 pyruvate is associated with aerobic-anaerobic transition during diving (Storey and Hochachka, 1974),

but to what extent post-translational modifications are involved in regulating proteins involved in these processes remains to be investigated.

Notably, KEGG pathways for host-pathogen interactions were enriched in all five cetacean species under study, with pathways relating to bacterial infection in all five species, amoebiasis in minke whale and fin whale and trypanosomiasis in Cuvier's beaked whale and orca. KEGG immune pathways for viral infection were identified in fin whale only, as well as cancer related pathways and metabolism of xenobiotics by cytochrome P450, a detoxification system in a range of marine mammals (Goksøyr et al., 1995) and a biomarker for environmental stress (Waugh et al., 2011; Bachman et al., 2015; Righetti et al., 2019). KEGG pathways relating to autoimmunity were identified in minke whale, fin whale and orca. Pathways relating to ferroptosis, a form of regulated cell death and implicated in multiple physiological and pathological processes (Xie et al., 2016; Shi et al., 2019), were furthermore identified in minke whale, Cuvier's beaked whale and orca, while pathways relating to phagosome and necroptosis, critical for necrotic and infectious diseases (Xia et al., 2020), were identified in minke whale. These findings highligth novel roles for protein deimination in infection, chronic diseases and host-pathogen interactions in ceataceans. While exact mechanistic pathways will need to be followed up and validated, the current findings of post-translational deimination in these KEGG pathways add to the acknowledged lack of information for host-pathogen interactions in ceataceans (Di Guardo et al., 2018). Transmission of marine morbilliviruses for example requires further research into host-specific factors (Jo et al., 2018; Di Guardo and Mazzariol, 2019; Ohishi et al., 2019) and research into immune mechanisms in relation to bacterial infections, including multidrug-resistant bacteria and opportunistic infection, are of pivotal importance (Reif et al., 2017; Mazzariol et al., 2018). In addition, specific roles for deiminated protein cargo exported in EVs will also need to be assessed as deiminated protein enrichment has been shown to differ in EVs compared to whole plasma and serum (Criscitiello et al., 2019 and 2020; Pameneter et al., 2019; Magnadottir et al., 2020a). Further to previously identified roles for PAD-mediated NETosis/ETosis in cetaceans in response to zoonotic diseases (Villagara-Blance et al., 2019; Imlau et al., 2020), also verified in the present study, newly recognized targets of deimination in cetaceans are identified here and highlight putative roles for regulation of immunological pathways via such post-translational deimination. Selected deiminated protein candidates, based on identification from the species-specific search for the individual cetaceans under study, which are involved in immune, nuclear and metabolic functions are discussed below in relation to roles in physiology and pathology:

Adiponectin was identified to be deiminated in orca only and is in human the most abundant secreted adipokine with pleiotropic roles in physiological and pathophysiological processes (Fiaschi, 2019). It

has received considerable interest in the field of metabolic and obesity research (Frankenberg et al., 2017; Spracklen et al., 2019), as well as in diabetes (Yamauchi et al., 2003), due to its key function in regulating glucose (Yamauchi et al., 2002; Kadowaki & Yamauchi, 2005; Almabouada et al., 2013). Adiponectin is furthermore linked to longevity (Chen et al., 2019), regenerative functions (Fiaschi et al., 2014), myopathies (Gamberi et al., 2019) and cancer (Parida et al., 2019). Adiponectin also plays roles in reproduction, embryo pre-implantation and embryonic development (Barbe et al., 2019). Due to the range of functions in relation to key pathophysiologies, there is a great interest in drug development to modulate adiponectin signalling (Fiaschi, 2019). Recent studies in rheumatoid arthritis made a correlation between inflammation, autoantibodies and adiponectin levels (Hughes-Austin et al., 2018; Liu et al., 2019). Post-translational deimination may be a hitherto unrecognized mechanism for adiponectin and of relevance for metabolic adaptions, as adiponectin was recently identified as a deimination candidate in naked mole-rat and llama (*Lama glama*), both which display unusual metabolism and adaption to extreme environments (Pamenter et al, 2019; Criscitiello et al., 2020). Deimination may allow for protein moonlighting functions via changes in protein folding and therefore interaction with other proteins. Adiponectin is a small 244 aa protein (NP_001171271.1) in humans and contains 2 unfolded regions and 7 arginine sites, while orca adiponectin (XP_004278522.1) has also 2 unfolded regions and 7 arginine sites, that could be subjected to PAD-mediated deimination and therefore modulate adiponectin folding and function, depending on which arginine is deiminated. STRING analysis for orca adiponectin and relevant KEGG pathways are shown in Supplementary Fig. 3 (Supplementary Fig. 3A and 3B). Given that orca will have some unique physiological characteristics, the identification of post-translational deimination of this key metabolic protein may be of great interest for comparative metabolic studies.

Albumin is a major acidic plasma protein in vertebrates and serves as a transport molecule for fatty acids, bilirubin, steroids, amino acids and copper, as well as having roles in maintaining the colloid osmotic pressure of blood (Peters, 1996; Metcalf et al., 2007). In aquatic animals, albumin has been identified as a putative health marker in response to environmental conditions in porpoises (Nabi et al., 2017) and for assessment of serum chemistry in wild beluga whales (*Delphinapterus leucas*) (Norman et al., 2012). In teleost fish, albumin levels were shown to be raised upon heavy metal exposure in water (Firat and Kargin, 2010). While albumin is known to be a glycoprotein in some species (Metcalf et al., 1998; Tao et al., 2019), roles for post-translational deimination remain to be further understood. Indeed, albumin was recently found to be deiminated in teleost fish (Magnadottir et al., 2019a).

Alpha-2-macroglobulin was found deiminated in minke whale serum. It forms part of the innate immune system and clears active proteases from tissue fluids (Armstrong and Quigley, 1999). Alpha-2-M is phylogenetically conserved from arthropods to mammals, is found at high levels in mammalian plasma and is closely related to other thioester containing proteins, complement proteins C3, C4 and C5 (Sottrup-Jensen et al., 1987; Davies and Sim, 1981). Alpha-2-M was recently found to be deiminated in shark (Criscitiello et al., 2019), camelid (Criscitiello et al., 2020), naked mole-rat and Antarctic seabirds (Phillips et al., 2020) and this may contribute to phylogenetically conserved and adapted functions in immune responses.

Alpha-1-microglobulin/bikunin precursor (AMBP protein) was here found deiminated in minke whale serum. It has been linked to oxidative stress and altered protein composition of subcutaneous adipose tissue in chronic disease (Gertow et al., 2017) but has not been identified as deiminated in any species before to our knowledge.

Antithrombin-III was here found to be deiminated in minke whale serum. It is a phylogenetically conserved hepatic glycoprotein and found in blood plasma (Jordan, 1983). Antithrombin forms part of the coagulation system and in whales, intestinal heparin has been found to bind with high affinity for antithrombin III (Uchiyama et al., 1990) and studied in coagulation (Oshima, 1990). Roles in disease are linked to thrombosis, pulmonary embolism (Amiral and Seghatchian, 2018) and angiogenesis in cancer (O'Reilly et al., 1999). Antithrombin-III furthermore has anti-inflammatory action and is linked to kidney diseases (Lu et al., 2017). Glycosylation has been found to affect the activity of antithrombin (McCoy al., 2003). Post-translational deimination has also been shown to affect its function by converting antithrombin to a form with a four-fold higher affinity for heparin pentasaccharide (Pike et al., 1997) and its deimination was recently identified also in seabirds (Phillips et al., 2020). Therefore post-translational modifications, including deimination, seem to play important roles in the functional diversity of antithrombin-III.

Apolipoproteins A-I, A-IV, B-100 and C-III were here identified as deiminated in minke whale serum. Apolipoprotein A-I is primarily involved in lipid metabolism where conformational plasticity and flexibility are of importance (Arciello et al., 2016). Apo A-I is also associated with regulation of mitochondrial function and bioenergetics (White et al., 2017). Furthermore, Apo A-I has been shown to have a regulatory role in the complement system by affecting membrane attach complex (MAC) assembly (Hamilton et al., 1993; Jenne et al., 1991; French et al., 1994). ApoB-100 is conserved between cetacean and other mammals (Amrine-Madsen et al., 2003), synthesised by the liver and

plays parts of innate immune responses (Peterson et al., 2008). ApoB-100 is furthermore associated with ER stress and insulin resistance (Su et al., 2009) as well as lipid metabolism disorders (Andersen et al., 2016). ApoA-IV is a lipid binding protein, primarily synthesized in the small intestine and involved in a range of physiological proteins including lipid absorption and metabolism, glucose homeostasis, platelet aggregation and thrombosis (Qu et al., 2019). Apo-CIII is a glycoprotein secreted by liver and small intestine and has roles in secretion of triglyceride-rich VLDL particles from hepatic cells under lipid rich conditions (Sundaram et al., 2010). Apo-CIII is also produced within pancreatic islets and linked to diabetes (Juntti-Berggren and Berggren, 2017). The roles for post-translational deimination in protein moonlighting of these apolipoproteins in whale physiology may be of considerable interest. Deimination of some apolipoproteins has previously been also identified for in other vertebrates, including camelids (Criscitiello et al., 2020), naked mole-rat (Pamenter et al., 2019) and teleost fish (Magnadottir et al., 2019a).

Beta-2-glycoprotein 1 (apolipoprotein H) was here identified as deiminated in minke whale. It is a 38 kDa multifunctional plasma protein which binds cardiolipin. It has roles in agglutination and has anti-coagulation activity in serum (Rikarni et al., 2015). Furthermore it is implicated in anti-phospholipid syndrome (Radic and Pattanaik, 2018; Yin et al, 2018). Its post-translational deimination has recently been identified also in naked mole-rat (Pamenter et al., 2019) and may be of some interest in relation to moonlighting functions in physiology, in addition to roles in autoimmunity.

Ceruloplasmin is a serum ferroxidase with antioxidative function and roles in iron homeostasis and carries over 90 % of the copper in plasma (Liu et al., 2011). In aquatic animals, ceruloplasmin has been shown to contribute to acute immune responses in teleost fish (Lü et al., 2013). It is also upregulated as an acute phase protein in response to growth hormone (Yada, 2007) and upon heavy metal exposure (Firat and Kargin, 2010), as well as being upregulated in response to bacterial challenge (Liu et al., 2011). Ceruloplasmin is furthermore related to bacterial resistance (Sahoo et al., 2013) and parasitic infection (Kovacevic et al., 2015; Henry et al., 2015). As fish have been shown to use iron deprivation as a nutritional immunity mechanism, by withholding iron from iron-requiring pathogens (Lange et al., 2001; Martínez et al., 2017), such uses in other aquatic animals, including whales, may be possible. Ceruloplasmin has been identified to be deiminated in teleost fish (Magnadottir et al., 2019a) as well as in the naked mole-rat (Pameneter et al., 2019) and it may be postulated that post-translational deimination may facilitate the diverse functions of ceruloplasmin.

Clusterin (apolipoprotein J) was identified here as deiminated in minke whale serum. It is a glycoprotein and a stress-activated ATP-independent molecular chaperone for protein folding and involved in clearance of cellular debris and apoptosis (Jones and Jomary, 2002; Wilson and Zoubeidi, 2017). Furthermore, clusterin is involved in a range of diseases related to oxidative stress, including inflammatory diseases, neurodegeneration, cancer and ageing (Yao et al., 2018; Foster et al., 2019). In seal brains, clusterin has been found to be four-fold higher expressed than in any other mammalian brain transcriptome. It has been postulated that elevation of this stress related gene may contribute to the hypoxia tolerance of diving mammals (Fabrizius et al., 2016). Roles for post-translational deimination in the function of clusterin in whale physiology may therefore be of interest.

A range of **complement components** was here identified as deiminated in minke whale serum. This included complement component C3, C5, C9, C1q, complement component C4-binding protein, complement factor B and factor H. The complement system forms part of the first line of immune defences against invading pathogens and also participates in the clearance of necrotic or apoptotic cells (Dodds and Law, 1998; Sunyer and Lambris, 1998; Fishelson et al., 2001; Carrol and Sim, 2011). The complements system is furthermore implicated in regeneration (Del-Rio-Tsonis et al., 1998; Haynes et al., 2013) and tissue remodelling (Lange et al., 2004a; 2004b; Lange et al., 2005; Lange et al., 2006; Lange et al., 2019). ***Complement component C3*** plays a central role in all pathways of complement activation and can also be directly activated by self- and non-self surfaces via the alternative pathway without a recognition molecule (Dodds and Law, 1998; Dodds, 2002). This is to our knowledge the first report of deiminated complement C3 in a mammalian species, while C3 was recently identified by our group in deiminated form in teleost fish (Magnadottir et al., 2019a and 2019b) as well as in elasmobranch shark (Criscitiello et al., 2019). Post-translational deimination of C3 may possibly influence its function including in the generation of the convertase, its cleavage ability, binding and deposition. ***Complement component C5*** plays important roles in inflammation and apoptosis. It is cleaved into C5a, which has pleiotropic biologic functions including as anaphylotoxin (Klos et al., 2009) while C5b forms the basis of the membrane attach complex (MAC) (Morgan et al., 2016). In cellular *in vitro* models, C5 has previously been reported to undergo deimination by *Porphyromonas gingivalis*, which evades complement-mediated killing by disabling anaphylatoxin C5a protein function via deimination of a critical C-terminal arginine (Bielecka et al., 2014). ***Complement component C9*** participates in the formation of the membrane attack complex, leading to lysis of the pathogen. C9 has previously been found to be deiminated in teleost fish (Magnadottir et al., 2019a). ***Complement C1q*** can activate the classical complement system by binding to the Fc region of immunoglobulins that are bound to antigen (Reid et al., 2002; Reid, 2018). Interestingly, an essential

role for arginine in C1q has been suggested for C1q-IgG interaction (Kojouharova et al., 2004). C1q also serves as a potent pattern recognition molecule which recognises self, non-self and altered self-signals (Nayak et al., 2012; Reid, 2018). ***Complement component C4-binding protein*** (C4BP) is a large glycoprotein, synthesised in the liver. It acts as an inhibitor of the classical and lectin pathways of the complement system and has multifaceted roles in immunity and homeostasis. C4BP is a cofactor for serine protease factor I, and besides C4-binding functions, it can also bind to C3b and accelerate decay of the C3 convertase. C4BP binds necrotic and apoptotic cells, as well as DNA, and therefore is involved in tissue clearance post injury (Ermert and Bloom, 2016). ***Complement factor B*** is a phylogenetically conserved activation protease of the complement system (Nonaka, 2014). ***Complement factor H*** is a major regulator of the alternative complement pathway and factor H family proteins are involved in modulating a range of cellular functions (Józsi et al., 2019). The deimination of the various complement components identified here may have diverse effects on complement activity and add to moonlighting functions of the complement system in homeostasis and immune defences. Recent comparative studies have indeed highlighted deimination of a range of complement proteins, and this is of considerable importance for understanding the diversity of complement function throughout phylogeny (Magnadottir et al., 2018a; Magnadottir et al., 2019a; Lange et al., 2019; Pameneter et al., 2019; Criscitiello et al., 2019 and 2020).

Charged multivesicular body protein 4c was identified as deiminated in minke whale serum. It is a core component of the endosomal sorting required for transport complex III (ESCRT-III) which is involved in multivesicular bodies (MVBs) formation and sorting of endosomal cargo proteins into MVBs and is furthermore involved in cell division (Carlton et al., 2012). It is also associated to cancer (Sadler et al., 2018) and to the regulation of viral replication (Li et al., 2013).

Desmoplakin was here identified to be deiminated in minke whale serum. Desmoplakin is a unique and critical component of desmosomal cell-cell junctions and involved in integrity of the cytoskeletal intermediate filament network (Bendrick et al., 2019). It has been shown to be required for epidermal integrity and embryo morphogenesis (Bharathan and Dickinson, 2019), as well as in the coordination of cell migration (Bendrick et al., 2019). Mutations in desmoplakin have been linked to multiple allergies, severe dermatitis and metabolic wasting (SAM) syndrome (Liang et al., 2019). It is also linked to Carvajal syndrome, involving altered skin and hair abnormalities, and heart diseases (Reichl et al., 2018; Yermakovich et al., 2018; Chen et al., 2019). Desmosomal proteins have been shown to have both tumour-promoting and tumour-suppressive functions, depending of cancer types and can regulate cell proliferation, differentiation, migration, apoptosis, and impact treatment sensitivity in

different types of cancers (Zhou et al., 2017). Desmoplakin was recently identified to be also deiminated in camelid serum EVs, but not whole plasma (Criscitiello et al., 2020). As the roles of desmosomal proteins in cancer and metastasis are not fully understood, the identification of deiminated desmoplakin in minke whale serum may be of some interest and add to understanding of pleiotropic functions throughout phylogeny via such post-translational modification.

Dimethylglycine dehydrogenase (DMGDH), mitochondrial isoform X1 was here identified as deiminated in minke whale serum. It is a mitochondrial matrix enzyme with roles in choline degradation, one-carbon metabolism and electron transfer to the respiratory chain (Augustin et al., 2016). DMGDH is a key metabolic enzyme, linked to diabetes, kidney disease (Zhu et al., 2018; Magnusson et al., 2015), carcinoma and metastasis (Liu et al., 2016).

Dipeptidylpeptidase 4 (DPP4, also known as CD26) was here identified to be deiminated in minke whale serum. DPP4 controls glucose homeostasis and has complex roles in inflammation and homeostasis, including in liver cytokine expression, while its activity in plasma has been shown to correlate with body weight and fat mass (Varin et al., 2019). Furthermore, roles for DDP4 in cancer have been found to relate to its post-translational processing of chemokines, thereby limiting lymphocyte migration to sites of inflammation and tumours (Barreira da Silva et al., 2015). DPP4 inhibitors have therefore been suggested as a strategy to enhance tumour immunotherapy (Barreira da Silva et al., 2015). Furthermore, serum DDP4 activity levels in primary HIV infection were found to be significantly decreased and to correlate with inflammation and HIV-induced intestinal damage (Ploquin et al., 2018). The identification of DPP4 as a deimination candidate has previously been verified in camelids (Criscitiello et al., 2020) and may be of some relevance as such post-translational modification can affect DPP4 structure and function, allowing for moonlighting functions in pathological and pathophysiological milieus throughout phylogeny.

Fetuin-B was identified as deiminated in minke whale. It is a member of the fetuin family and part of the cystatin superfamily of cysteine protease inhibitors (Lee et al., 2009). Fetuin-B is a hepatokine, secreted by hepatocytes and linked to the regulation of the insulin and hepatocyte growth factor receptors, to metabolism as well as metabolic dysfunction, including insulin resistance and chronic kidney disease (Meex and Watt, 2017; Lin et al., 2019). Fetuins have further functions in osteogenesis and bone resorption, response to systemic inflammation and infection (Qu et al., 2018; Li et al., 2017) as well as in fertilisation (Stöcker et al., 2014; Fang et al., 2019). The structure of mammalian plasma fetuin-B has been extensively studied and fetuin-B is described throughout phylogeny from

cartilaginous fishes to mammals (Cuppari et al., 2019). Post-translational deimination of fetuin-B has not been reported before.

Fibrinogen is a glycoprotein, synthesised in liver (Tennent et al., 2007) and forms part of the acute phase response as part of the coagulation cascade (Tiscia and Margaglione, 2018). Fibriongen is well described in cetaceans (Gatesy, 1997; Terasawa et al., 2008). In humans, impaired mechanism of fibrinogen formation and fibrin polymerization are implicated in various pathologies including coagulopathies and ischemic stroke (Weisel and Litvinov, 2013). Acquired fibrinogen disorders are also associated with cancer, liver disease or post-translational modifications (Besser and MacDonald, 2016). Fibrinogen is indeed a known deimination candidate and this post-translational modification contributes for example to its antigenicity in autoimmune diseases (Hida et al., 2004; Okumura et al., 2009; Muller and Radic, 2015; Blachère et al., 2017), and deimination has also bee identified in other taxa, including camelids (Criscitiello et al., 2020) and naked mole-rat (Pamenter et al., 2019). In aquatic animals, fibrinogen has been associated with teleost host defence against pathogens (Blanco-Abad et al., 2018), in acute phase and stress responses during temperature acclimation (Dietrich et al., 2018) and upon exposure to tetrodotoxin (Kiriake et al., 2016). Fibrinogen and gamma-fibrinogen were here found to be deiminated in minke whale and fin whale respectively.

Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was identified as deiminated in fin whale (*Balaenoptera physalus*). GAPDH has key metabolic functions in glycolysis but also has pleiotropic non-metabolic functions including in apoptosis, transcription activation and axonal transport (Tarze et al., 2007; Zala et al., 2013; Sirover 2018; Butera et al., 2019). GAPDH has been identified to have a range of moonlighting functions, including in iron metabolism (Boradia et al., 2014) and is associated to various pathologies (Sirover 2018). GAPDH has been shown to be regulated via post-translational modifications (Tristan et al., 2011; White and Garcin, 2017; Butera et al., 2019) and was recently identified as a deimination candidate in brain-cancer (Kosgodage et al., 2018), as well as in plasma-EVs of naked mole-rat and in harbour seal (Magnadottir et al., 2020b). Deimination of GAPDH identified here in fin whale may contribute to its multifaceted physiological functions.

Haptoglobin is an acute phase plasma protein and is in mammals involved in protection of oxidative damage by binding to haemoglobin (Andersen et al., 2017; Redmond et al., 2018). Haptoglobin has been described in a range of whales and dolphins, with some specific features identified (Travis et al., 1971; Yim et al., 2014). In aquatic animals it has been found to have roles in anti-viral immunity (Cordero et al., 2017). Haptoglobin was here found to be deiminated in minke whale serum and has

previously been identified as deiminated in nurse shark (Criscitiello et al., 2019), possibly adding to some of its functional diversity throughout phylogeny.

Heat shock protein 90 (Hsp90) was here found to be deiminated in minke whale. Hsp90 is a phylogenetically highly conserved chaperone protein involved in protein folding, the stabilisation of proteins against heat stress and aids in protein degradation (Buchner 1999; Picard, 2002). Hsp90 also stabilizes a number of proteins required for tumour growth and is therefore important in anti-cancer drug investigations (Goetz et al., 2003). Hsp90 is responsible for most of the ATPase activity of the proteasome (Imai et al., 2003) and has an ATP binding region, which also is the main binding site of drugs, including anti-tumour drugs, that can be used to target Hsp90 (Chiosis et al., 2006). Hsp90 has previously been described to be post-translationally deiminated in rheumatoid arthritis, allowing deimination-induced shifts in protein structure to generate cryptic epitopes capable of bypassing B cell tolerance (Travers et al., 2016). HSP90 has also been verified as a deimination candidate in camelids (Criscitiello et al., 2020). Finding post-translational deimination of this protein throughout phylogeny supports translational investigations between species to further current understanding of HSP90 function, both in physiology and pathologies.

Hemopexin is a plasma glycoprotein and scavenger protein of haemoglobin and a predominant heme binding protein, which contributes to heme homeostasis (Smith and McCulloh, 2015; Immenschuh et al., 2017). Hemopexin also associates with high density lipoproteins (HDL), influencing their inflammatory properties (Mehta and Reddy, 2015). In relation to aquatic animals, hemopexin has been associated with physiological stresses, including increased water temperature, immune response and heavy metal exposure in fish (Kwon and Ghil, 2017; Diaz-Rosales et al., 2014). Here, hemopexin was found deiminated in minke whale serum. Previously, deimination of hemopexin has been found in teleost fish (Magnadottir et al., 2019a), in elasmobranch shark (Criscitiello et al., 2019), in naked mole-rat (Pamenter et al., 2019) and in camelid (Criscitiello et al., 2020). While hemopexin is a known glycoprotein, little is known regarding post-translational deimination for its function.

Immunoglobulin (Ig) proteins were identified here as being deiminated in minke whale serum. Ig's are key molecules in adaptive immunity and have been studied in whales (Andrésdóttir et al., 1987; Nollens et al., 2008). Furthermore, serum immunoglobulin levels have been associated with more active immune defences in free ranging bottlenose dolphins (*Tursiops truncatus*) compared to managed dolpins (Ruiz et al., 2009). Ig quantification assays have also been developed to assess immune function in orca (Taylor et al., 2002). Post-translational deimination of Ig's and roles in Ig

function have hitherto received little attention. In patients with bronchiectasis and RA, post-translational deimination of the IgG Fc region has been identified (Hutchinson et al., 2017). Deimination of Ig's in a range of taxa has recently been described by our group including teleost fish (Magnadottir et al., 2019a), elasmobranchs (Criscitiello et al., 2019), camelid (Criscitiello et al., 2020) and peglagic seabirds (Phillips et al., 2020). Given the increased interest in furthering understanding of Ig diversity throughout phylogeny (Dooley and Flajnik, 2006; Smith et al., 2012; Zhang et al., 2013; de los Rios et al., 2015; Zhang et al., 2016; Zhang et al., 2017; Stanfield et al., 2018) our current finding of deimination of whale Ig's highlights a novel concept of diversification of their function via post-translational deimination.

Isocitrate dehydrogenase 1 (IDH1) was here identified to be deiminated in fin whale only. It is found in the cytosol and in peroxisomes and involved in a major pathway for cellular NADPH generation (Golub et al., 2019). Mutations in IDH have been associated with cancer, leading to development of targeted cancer therapeutics (Golub et al., 2019), while post-translational deimination has, to our knowledge, not been described in any species before.

Keratins were here identified as deiminated in minke whale serum. Keratin cytoskeleton evolution has been extensively studied, including in marine mammals and whales (Sun et al., 2017; Ehrlich et al., 2019), with cetaceans displaying impaired terminal keratinocyte differentiation (Lopes-Marques et al., 2018). Baleen keratin is furthermore of some interested as a bioengineering material (Wang et al., 2019). In aquatic animals, roles for keratin in anti-bacterial defences have been shown in skin mucus, as keratin has pore-forming abilities. Keratin also serves as a first barrier to injury as a cytoskeletal protein (Molle et al., 2011). Downregulation of keratin II has for example been observed in *vibrio* infected fish (Rajan et al., 2013), while deiminated keratin was recently identified in teleost fish mucus (Magnadottir et al., 2018a), in birds (Phillips et al., 2020), naked mole-rat (Pamenter et al., 2019) and camelids (Criscitiello et al., 2020). In mammals, deimination of keratin is important including in skin physiology associated to cutaneous diseases (Chavanas et al., 2006; Ying et al., 2009); deimination indeed seems a phylogenetically conserved mechanism for faclilitation of moonlighting functions of keratin.

Kininogen forms part of the acute phase response, has been described in whales (Semba et al., 2000) and was here identified to be deiminated in minke whale serum. Kininogen has been previously found to be deiminated in teleost fish (Magadottir et al., 2019a), Antarctic birds (Phillips et al., 2020), camelid (Criscitiello et al., 2020) and naked mole-rat (Pamenter et al., 2019). In mammals, elevated levels of

kininogen are linked to sepsis (Hofman et al., 2018) and inflammatory and oxidative stress pathways in type I diabetes (Al Hariri et al., 2017). To what extent kininogen function is dependent on post-translational deimination remains to be further investigated.

Myoglobin was identified as deiminated in humpback whale (*Megaptera novaeangliae*) and Cuvier's beaked whale (*Ziphius cavirostris*), while ***hemoglobin*** was identified as deiminated in minke whale. Both haemoglobin and myoglobin are key molecules in molecular oxygen transport in the bloodstream and for its storage in skeletal muscle. In diving cetaceans they contribute to hypoxia tolerance (Tian et al., 2016; Fago et al., 2017). Hemoglobin has furthermore been found to be a major binding protein for methylmercury in the liver of dolphins (Zayas et al., 2014). Myoglobin is found at higher concentrations in myocytes of deep diving animals compared to terrestrial animals and has been described in a range of whales (Isogai et al., 2018; Iwanami et al., 2006; Jones et al., 1979), including in humpback whale (Lehman et al., 1978), finback whale (DiMarchi et al., 1978) and minke whale (Lehman et al., 1977). The diving capacity of mammals is related to the myoblobin concentration in their myocytes. A more positive net surface charges of myoglobin are seen in diving animals compared to terrestrial animals, possibly to cause electrostatic repulsion among myoglobin molecules and to prevent their aggregation and maintain high protein concentration (Mirceta et al., 2013; Isogai et al., 2018). Therefore, post-translational deimination of myoglobin identified here in whales may be of considerable interest in relation to their physiological adaption to deep-diving. This correlates also with our recent findings of deiminated myoglobin and hemoglobin in pinnipeds, possibly playing roles in their adaption to hypoxic conditions (Magnadottir et al., 2020b).

Plakoglobin (γ-catenin) was here found to be deiminated in minke whale serum. It forms part of the Wnt signalling pathway, is a component of adherens junctions and desmosomes and plays therefore a vital role in the regulation of cell-cell adhesion (Aktary et al., 2017). Plakoglobin is also involved in the regulation of tomourigenesis and metastasis (Aktary et al., 2017). Plakoglobin is important in heart development and regeneration (Piven and Winata, 2017). Mutations in plakoglobin are for example linked to cardiomyopathies and Naxos disease (Li et al., 2018). Phosphorylation of plakoglobin has been described, through which it associates with cadherins (Shibata et al., 1994), and deimination of plakoglobin (junction plakoglobin) was recently identified in the naked mole-rat (Pamenter et al., 2019). Therefore its deimination identified here in whales, also long-lived and cancer-resisitant animals, may be of some interest and further understanding of such post-translational changes contributing to plakoglobin functional diversity.

Protein S100 was here identified as deiminated in minke whale. The S100 family of proteins in vertebrates participate in a variety of intracellular and extracellular functions. This includes regulation of protein phosphorylation and transcription factors, regulation of enzyme activities, cell growth and differentiation and inflammatory responses, including as damage associated molecular patterns (DAMPs) (Donato, 2003; Marenholz et al., 2004). In whales, S100B, a calcium-binding stress protein with pleiotropic function, has been found to be significantly enriched in the brain transcriptome compared to terrestrial mammals, possibly contributing to hypoxia tolerance (Fabrizius et al., 2016). Deimination of S100 proteins, as identified here, may indeed contribute to their pleiotropic functions throughout phylogeny.

14-3-3 protein epsilon isoform X1 was here identified as deiminated in minke whale serum. 14-3-3 protein are a conserved family of regulatory molecules, involved in signalling via binding to a range of kinases, transmembrane receptors and phosphatases (Bridges and Moorhead., 2005). 14-3-3 proteins are involved in a range of pathologies and linked to cancer, age-related neurodegenerative diseases and ageing (Fan et al., 2019). Furthermore, 14-3-3 proteins play roles in immunoglobulin class switch recombination and are therefore important for the immune response (Xu et al., 2012; Lam et al., 2013; Li et al., 2017). 14-3-3 proteins act also via conformational change (Bridges and Moorhead, 2005) and therefore the identification of post-translational deimination here may be of considerable interest.

Recombination activating protein 1 (RAG1) was here identified as deiminated in Cuvier's beaked whale (*Ziphius cavirostris*) only. It is involved in immunoglobulin V-D-J recombination, which facilitates the generation of diverse repertoires of antigen receptors (Rodgers, 2017). RAG proteins are therefore critical for adaptive immune responses and are believed to have evolved from a mobile DNA element into a tightly controlled DNA recombinase in lymphocytes (Fugmann, 2010). In humans, mutation in RAG genes are related to a range of pathologies related to immune dysregulation (Notarangelo et al., 2016). In cetaceans, RAG1 has been identified in a range of species (McGowen et al., 2009). Post-translational deimination of RAG1 has not been identified in any species before to our knowledge and may possibly contribute to the diversification of adaptive immunity throughout phylogeny.

Rootletin, also known as ciliary rootlet coiled-coil protein (CROCC), was here identified as deiminated in minke whale. It is a protein that is required for centrosome cohesion and therefore plays important roles in mitosis (Bahe et al., 2005; Graser et al., 2007). Rootletin has been shown to be phosphorylated and to have the ability to form centriole-associated fibers, suggesting a dynamic model for centrosome cohesion based on entangling filaments (Bahe et al., 2005). Deletion of rootletin in mouse models

causes photoreceptor degeneration and impaired mucociliary clearance, supporting its key function in rootlet structures (Yang et al., 2005). Rootlets have been studied in the development of the nervous terminalis in toothed whales (Oelschläger et al., 1987) and baleen whales (Oelschläger, 1989). Rootletin was recently identified to be deiminated in camelid serum (Criscitiello et al., 2020) and its deimination also identified here in minke whale may provide novel insights into its dynamic functions via such post-translational modification.

Selenoprotein P (Sepp1) is a plasma glycoprotein, mainly secreted from liver but also other tissues and contains most of the selenium in plasma (Mosert, 2000; Persson-Mochos, 2000; Burk and Hill, 2009). It has antioxidant properties (Mosert, 2000) and serves in homeostasis and distribution of selenium (Burk and Hill, 2009). Phylogenetically Sepp1 is believed to have appeared in early metazoan species and terrestrial animals have fewer selenoproteins than marine animals, which may be reflected in different functions (Lobanov et al., 2008). While Sepp1 is known to be glycosylated, other post-translational changes have not been studied. Besides its identification here as a protein candidate for post-translational deimination, deimination was recently reported in Sepp1 in Antarctic seabirds (Phillips et al., 2020).

Serotransferrin was here identified as deiminated in minke whale serum. It acts as an antimicrobial agent and is at the frontier in innate immune mechanisms in some aquatic animals (Stafford and Belosevic, 2003; Mohd-Padil et al., 2013). In bottlenose dolphins (*Tursiops truncatus*), differences in transferrin levels of managed versus wild dolphins has been observed (Mazzaro et al., 2012), while in fish increased serotransferrin is found in response to toxins (Kiriake et al., 2016). Serotransferrin was recently identified to be deiminated in teleost fish (Magnadottir et al., 2018a), as well as in the naked mole-rat (Pamenter et al., 2019).

STE20-like serine/threonine-protein kinase isoform X2 was here found deiminated in minke whale serum. STE20-like kinases form part of the Hippo signalling pathway which regulates the balance between cell proliferation and apoptosis and is therefore involved in controlling organ size and tissue homeostasis (Bae and Luo, 2018). It is for example involved in liver size control and regeneration, as well as in tumourigenesis (Hong et al., 2015). Its deimination is here described for the first time to our knowledge.

Triose phosphate isomerase (TPI) was here identified as deiminated in minke whale serum. TPI plays an important role in glycolysis and is essential for efficient energy production. Besides roles in

glycolysis, TPI is linked to lipid metabolism and is involved in ageing, metabolism and a range of human diseases (Olivares-Illana et al., 2017). Other moonlighting functions identified for TPI are in sperm-egg interactions (Petit et al., 2014). Deimination of TPI has not been described before to our knowledge.

Vitamin D-binding protein (VDBP) is a multifaceted protein mainly produced in the liver, where its regulation is influenced by estrogen, glucocorticoids and inflammatory cytokines (Bikle and Schwartz, 2019). It is secreted into the blood circulation and is able to bind the various forms of vitamin D (Verboven et al., 2002; Norman, 2008). It transports vitamin D metabolites between skin, liver and kidney, as well as various target tissues (Norman, 2008). In minke whale, VDBP has been identified in the liver transcriptome, is negatively correlated with polychlorinated biphenyl levels and therefore may be a putative toxicology marker (Niimi et al., 2014). In humans, VDBP has been tested as an anti-cancer agent via activation of macrophages against cancer cells (Yamamoto et al., 2008). Some association has also been made between polymorphisms of VDBP and the risk of coronary artery disease (Tarighi et al., 2017). Post-translational modifications of VDBP have been associated with multiple sclerosis (MS) (Perga et al., 2015), although it remains to be exactly identified which these post-translational modifications are. On the other hand, protein deimination is well known to be associated with MS (Moscarello et al., 2013), while a link to VDBP has not been made in MS. VDBP has previously been identified to be glycosylated (Kilpatrick and Phinney, 2017) and was found to be deiminated in camelids (Criscitiello et al., 2020). Here it was identified as a deiminiation candidate in minke whale. Post-translational deimination may contribute to various functions of VDBP in physiological as well as pathophysiological processes.

Vitronectin (VTN) is a glycoprotein of the hemopexin family which is abundantly found in serum, the extracellular matrix and in bone. VTN is identified as a key controller of mammalian tissue repair and remodelling activity (Leavesley et al., 2013). It promotes cell adhesion and spreading. It also inhibits the membrane-damaging effect of the terminal cytolytic complement pathway and binds to several serine protease inhibitors (Felding-Habermann and Cheresh, 1993). VTN is also involved in haemostasis and tumour malignancy (Preissner and Seiffert, 1998; Hurt et al., 2009). Deimination of VTN has recently been desribed in wandering albatross (*Diomedea exulans*) plasma (Phillips et al., 2020) and was here identified in minke whale, possibly contributing to some of its pleiotropic functions throughout phylogeny.

Xaa-Pro dipeptidase, also known as prolidase, was here identified as deiminated in minke whale serum. Post-translational modifications of prolidase have been shown to regulate its enzymatic

abilities and in humans, deficiency in prolidase can cause a range of chronic, debilitating health conditions (Viglio et al., 2006; Kitchener et al., 2012). Increased serum proloidase activity has also been associated with oxidative stress in humans in relation to obesity (Aslan et al., 2017). Increased levels of prolidase activity are associated to some cancers, leading to the development of proline prodrugs (Mittal et al., 2005). Serum prolidase enzyme activity is also currently being explored as a biomarker for diseases including chronic hepatitis B and liver fibrosis (Duygu et al., 2013; Şen et al., 2014; Stanfliet et al., 2015). Phosphorylation of prolidase has been shown to increase its activity while dephosphorylation leads to a decrease in enzyme activity. Post-translational deimination of prolidase has recently been described in the llama (Criscitiello et al., 2020), a species adapted to high altitude and therefore tolerant of low oxygen levels. Studies into post-translational deimination of Xaa-Pro dipeptidase may add to current understanding of how this enzyme is regulated.

MicroRNAs (miRs) are highly conserved small non-coding RNAs that control gene expression and regulate biological processes by targeting messenger RNAs (mRNAs). MiRs can inhibit post-transcriptional translation of mRNA or enhance mRNA degradation (Bavelloni et al., 2017). Hitherto no studies have been carried out on miRs in whales, while some expression profiling has been carried out in dolphins with the aim to identify health related biomarkers in relation to organ injury (Segawa et al., 2016). Diving animals, such as whales and orca, undergo physiological and morphological changes needed for life in an aquatic environment, which are marked by resistance to physiological stresses caused by a lack of oxygen, increased amounts of reactive oxygen species and high salt levels (Yim et al., 2014). MiR210 has previously been identified as a major miR induced under hypoxia and has important roles in mitochondrial metabolism, DNA damage response, cell proliferation and apopotosis (Bavelloni et al., 2017). MiR210 has a role in regulating mitochondrial metabolism (Chen et al., 2010) and cell glycolytic activity and is also linked to inflammation (Volobоueva et al., 2017). MiR210 is also involved in angiogenesis and vascular remodelling (Fasanaro et al., 2008); for example, mesenchymal stem cell derived EVs have been identified to be enriched in miR210 and to promote angiogenesis in ischemic myocardium (Wang et al., 2017). MiR210 has been identified as a regulator of the hypoxia pathway and to have pro-apoptotic functions under normal oxygen conditions, but anti-apoptotic effects under hypoxic conditions (Favaro et al., 2010; Huang et al., 2010). In the current study, miR210 was found to be highest expressed in orca, followed by humpback whale, Cuvier's beaked whale, fin whale and minke whale and this may possibly reflect physiological differences between these species in relation to mitochondrial metabolism and oxygen transport.

MiR21 is strongly conserved throughout evolution, is a main immunoregulatory and onco-related miR and is also associated to chronic diseases (Musso et al., 2016, Juźwik et al., 2019; Li et al., 2019). While

many experimentally verified targets of miR21 are tumour suppressors, miR21 is also linked to cardiac disease and oxidative stress (Xu et al., 2019). In the current study miR21 was found to be highly expressed in humpback EVs, followed by minke whale EVs, but at lower levels in the other three species, with lowest levels detected in Cuvier's beaked whale. Whether this difference is innate to the whale's and orca's normal physiology, or due to differences in immune and health status of the individual animals, remains to be further investigated as this could not be assessed in the current study due to only one individual used per species. Roles for miR21 in immune responses of aquatic animals have previously been identified in teleost fish, where miR21 was found to be up-regulated after immune stimulation and to inhibit the expression of cytokines via regulation of Toll-like receptor signalling (Bi et al., 2017).

In mammals, miR155 is known to be a major inflammatory related miR, linked to inflammatory and stress responses (Xiaoyan et al., 2017). In the current study miR155 was by far most highly expressed in minke whale EVs, while fin whale, humpback whale and orca showed similar levels of miR155 and lowest levels were seen in Cuvier's beaked whale. As no previous studies have been carried out on these two miRs in cetaceans it remains to be fully understood which specific functions these have in whale physiology. Furthermore, both miR21 and miR155 have been associated to viral infections in fish (Andreassen and Høyheim, 2017), been found to be upregulated in fish exposed to chronic $[C_8mim]Br$ induced inflammation (Ma et al., 2019) and related to changes in sea temperature in teleost fish (Magnadottir et al., 2020a). Interspecies differences in miR expression observed here may indicate that levels of these miRs vary between species, depending on their habitat and metabolic activity. This may though also reflect different health status of the 5 animals used. As only one animal per species was assessed in this pilot study, such species-specific differences need to be further evaluated in larger sample cohorts.

This is the first study to assess EV profiles and PAD-mediated protein deimination in cetaceans, while recent studies on other pelagic animals such as teleost and elasmobranch fish as well as pinnipeds and seabirds have recently been carried out (Iliev et al., 2018; Magnadottir et al., 2019b; 2020a; 2020b; Criscitiello et al., 2019; Phillips et al., 2020), as well as on other mammals with unusual metabolism (Pamenter et al., 2019; Criscitiello et al., 2020). Roles for PADs and EVs in have also been described in parasite host-pathogen interactions (Gavinho et al., 2019), but remain to be further investigated for parasite infections and other zoonotic diseases in aquatic mammals. Furthermore, we identified here post-translational deimination of key immune factors of innate and adaptive immunity, as well as in metabolism of the cetaceans assessed in the current study. These findings highlight novel aspects of protein moonlighting functions of these immune proteins in sea mammals via post-translational

deimination. Due to the limited annotation of the whale and orca genomes, the hits identified in this study may though underestimate the amount of deiminated protein targets present in their sera, although this was compensated for to some extent using a wider search by assessing protein targets against a larger cetacean database, revealing a number of common KEGG pathways. Roles for miRs in gene regulation, including in stress responses due to environmental changes, toxicology and infection, are increasingly acknowledged and as miRs are known to be exported via EVs, changes in such EV cargo may be of considerable interest. An important finding of the current study is that EVs were a better source for miR analysis compared to whole sera, with EVs posing as better diagnostic markers than whole serum.

Findings of the current study touch upon a hugely understudied and emerging field of EV research in diverse taxa, in relation to sea mammal health and for the development of EV-related biomarkers to assess health status of wild sea animals in response to pollution, opportunistic infections as well as in response to changing sea temperatures and shift in habitat due to global warming. Orcas are for example among the world's most PCB-contaminated marine mammals, raising concerns about implications for their health (Buckman et al., 2011). Furthermore, findings in long-lived mammals that display cancer resistance, including cetaceams, may be of considerable translational value for furthering understanding of mechanisms underlying cancer resistance for improved development of human cancer therapies (Seluanov et al., 2018) and novel insights into potentially unique non-age-related mechanisms of carcinogenesis across species (Pesavento et al., 2018). Such comparative studies furthermore provide translational value for mechanisms involved insulin resistance (Tsagkogeorga et al., 2015), as well as revealing molecular signatures of longevity (Ma and Gladyshev, 2017).

In continuation of the current pilot study, further assessment of changes in deiminated proteins, EV profile and miR expression will be of great interest to assess health status of wild sea mammals in response to infection, environmental temperature and toxicology. In addition, wider sampling within and between populations would enable comparisons with normal physiological protein deimination status and EV-profiles. This would be particularly valuable for assessing natural and anthropogenic stresses in cetaceans in general, many of which face increasing threats related to changing climate. While the current study lays a base-line for these novel biomarkers, future studies will need to further refine and develop these markers as an applicable tool in the evaluation of cetacean health status.

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Credit Author Statement

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PU-O: Formal analysis; Resources; Validation; Visualisation, Writing - review & editing.

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SL: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Validation; Visualization; Writing - original draft; Writing - review & editing.

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Figure legends

Fig. 1. Extracellular vesicles (EVs) isolated from sera of whales and orca. Nanoparticle tracking analysis (NTA), Western blotting (WB) and transmission electron microscopy (TEM) for characterisation of EVs from: **A.** Minke whale (*Balaenoptera acutorostrata*); **B.** Fin whale

(*Balaenoptera physalus*); **C.** Humpback whale (*Megaptera novaeangliae*); **D.** Cuvier's beaked whale (*Ziphius cavirostris*); **E.** Orca (*Orcinus orca*). For all profiles, a poly-dispersed population of EVs in the size range of mainly 50-400 nm is seen, with main peaks of EV sizes differing between species, as seen in the individual NTA profiles. Analysis of EVs from whale serum by TEM confirms size and typical morphology of EVs; scale bar (100 nm) is indicated in all figures.

Fig. 2. EV yield and modal size of EVs from whale and orca sera. **A.** Total yield of EVs from whale sera varied between the sera from the 5 species under study. Highest levels of EV were seen in orca (*O. orca*) and Cuvier's beaked whale (*Z. cavi*), while the lowest EV serum yield was found in humpback whale (*M. Nova*). Similar EV yield was observed in minke (*B. acut*) and fin whale (*B. phys*). **B.** Modal size of EVs isolated from sera of the five cetacean species varied somewhat within an overall range of 100-170 nm. Minke whale showed larger EV modal size compared to the other whale species.

Fig. 3. Western blotting of deiminated proteins and PAD in whale and orca sera. **A.** PAD homologues were identified in whale sera at the expected size of approximately 70-75 kDa, using human PAD2 and PAD3 specific antibodies. The presence of deiminated histone H3 (citH3), representative of (neutrophil) extracellular traps (NET/ETs) was also identified, at approximately 20 kDa. **B.** Total deiminated proteins were identified in EVs from whale sera, using the F95 pan-deimination specific antibody. **C.** Western blotting confirmed the presence of deiminated proteins in total sera from whales and orca, as assessed by immunoprecipition of deiminated proteins from whole sera using the F95 pan-deimination antibody.

Fig. 4 Protein-protein interaction networks of deiminated protein hits identified in serum of minke whale (*Balaenoptera acutorostrata*). Reconstruction of protein-protein interactions based on known and predicted interactions using STRING analysis and the minke whale protein database in STRING. **A. KEGG pathways relating physiological pathways** are highlighted as follows: red=complement and coagulation cascade; blue=renin-angiotensin system; light green=oestrogen signalling; yellow=cholesterol metabolism; pink=vitamin digestion and absorption; dark green=glycolysis/gluconeogenesis; light blue=biosynthesis of amino acids; orange=fat digestion and absorption. **B. KEGG pathways relating to immunity**: red=*Staphylococcus aureus* infection; blue=SLE; light green=amoebiasis; yellow=ferroptosis; pink=phagosome; dark green=necroptosis. Coloured lines indicate whether protein interactions are identified via known interactions (curated databases, experimentally determined), predicted interactions (gene neighbourhood, gene fusion, gene co-

occurrence) or via text mining, co-expression or protein homology (see the colour key for connective lines included in the figure). PPI enrichment p-value: $p < 1.0 \times 10\text{-}16$

Fig. 5 Protein-protein interaction networks of deiminated protein hits identified in serum of fin whale (*Balaenoptera physalus*). Reconstruction of protein-protein interactions based on known and predicted interactions using STRING analysis and the orca protein database in STRING. **A. KEGG pathways relating physiological pathways** are highlighted as follows: red=complement and coagulation cascade; blue=metabolic pathways; light green=oestrogen signalling; yellow=cholesterol metabolism; pink=vitamin digestion and absorption; dark green=glycolysis/gluconeogenesis; light blue=biosynthesis of amino acids; orange=fat digestion and absorption; purple=carbon metabolism; brown=ECM-receptor interaction. **B. KEGG pathways relating to immunity**: red=*Staphylococcus aureus* infection; blue=SLE; light green=amoebiasis; yellow=prion diseases; pink=pertussis; dark green=proteoglycans in cancer; orange=metabolism of xenobiotics by cytochrome P450; light blue=human papillomavirus infection; purple=focal adhesion. Coloured lines indicate whether protein interactions are identified via known interactions (curated databases, experimentally determined), predicted interactions (gene neighbourhood, gene fusion, gene co-occurrence) or via text mining, co-expression or protein homology (see the colour key for connective lines included in the figure). PPI enrichment p-value: $p < 1.0 \times 10\text{-}16$

Fig. 6 Protein-protein interaction networks of deiminated protein hits identified in serum of humpback whale (*Megaptera novaeangliae*). Reconstruction of protein-protein interactions based on known and predicted interactions using STRING analysis and the orca protein database in STRING. **A. KEGG pathways relating physiological pathways** are highlighted as follows: red=complement and coagulation cascade; blue=metabolic pathways; light green=oestrogen signalling; yellow=cholesterol metabolism; pink=HIF-1 signalling pathway; dark green=glycolysis/gluconeogenesis; light blue=biosynthesis of amino acids; orange=carbon metabolsim; purple=nitrogen metabolism; brown=pentose phosphate pathway. **B. KEGG pathways relating to immunity**: red=complement and coagulation cascade; blue=*Staphylococcus aureus* infection. Coloured lines indicate whether protein interactions are identified via known interactions (curated databases, experimentally determined), predicted interactions (gene neighbourhood, gene fusion, gene co-occurrence) or via text mining, co-expression or protein homology (see the colour key for connective lines included in the figure). PPI enrichment p-value: $p < 1.0 \times 10\text{-}16$.

Fig. 7 Protein-protein interaction networks of deiminated protein hits identified in serum of Cuvier's beaked whale (*Ziphius cavirostris*). Reconstruction of protein-protein interactions based on known and predicted interactions using STRING analysis and the orca protein database in STRING. **A. KEGG pathways relating physiological pathways** are highlighted as follows: red=complement and coagulation cascade; blue=metabolic pathways; light green=mineral absorption; yellow=thyroid hormone synthesis; pink=HIF-1 signalling pathway; dark green=glycolysis/gluconeogenesis; light blue=biosynthesis of amino acids; orange=carbon metabolism; purple=nitrogen metabolism; brown=proximal tubule bicarbonate reclamation. **B. KEGG pathways relating to immunity (and metabolism)**: red=African trypanosomiasis; pink= ferroptosis; blue=pentose phosphate pathway; light green=fructose and mannose metabolism; yellow=pyruvate metabolism. Coloured lines indicate whether protein interactions are identified via known interactions (curated databases, experimentally determined), predicted interactions (gene neighbourhood, gene fusion, gene co-occurrence) or via text mining, co-expression or protein homology (see the colour key for connective lines included in the figure). PPI enrichment p-value: $p < 1.0 \times 10\text{-}16$

Fig. 8 Protein-protein interaction networks of deiminated protein hits identified in serum of orca (*Orcinus orca*). Reconstruction of protein-protein interactions based on known and predicted interactions using STRING analysis and the orca protein database in STRING. **A. KEGG pathways relating physiological pathways** are highlighted as follows: red=complement and coagulation cascade; blue=fat digestion and absorption; light green=cholesterol metabolism; yellow=vitamin digestion and absorption. **B. KEGG pathways relating to immunity**: red=*Staphylococcus aureus* infection; blue=SLE; light green=pertussis; yellow=prion diseases; pink=Chagas disease (American trypanosomiasis); dark green=African trypanosomiasis; light blue=ferroptosis. Coloured lines indicate whether protein interactions are identified via known interactions (curated databases, experimentally determined), predicted interactions (gene neighbourhood, gene fusion, gene co-occurrence) or via text mining, co-expression or protein homology (see the colour key for connective lines included in the figure). PPI enrichment p-value: $p < 1.0 \times 10\text{-}16$

Fig. 9. Venn diagram for physiological and immunological KEGG pathways in cetaceans. A. Deiminated KEGG protein pathways identified in STRING for the 5 cetaceans under study reveal a number of common/shared and species-specific pathways relating to physiological functions. **B.** Deiminated KEGG protein pathways immune functions, identified in STRING for the 5 cetaceans under study, reveal a number of common/shared and species-specific pathways.

Fig. 10. MicroRNA expression in whale and orca sera and serum-derived EVs. A-B. MiR21, miR155 and miR210 relative expression was assessed for key inflammatory and metabolic miRs respectively, in whale and orca sera and serum derived EVs. **A.** MiR21 expression was compared in EVs and sera of the 5 species under study, with highest levels found in EVs of humpback whale and minke whale; **B.** MiR155 expression was compared in EVs and sera of the 4 whales and orca, with the highest levels observed in minke whale; **C.** MiR210 expression was compared in EVs and sera of whales and orca, showing highest relative levels in orca EVs.

Supplementary Fig. 1. Phylogenetic tree for PAD isozymes in cetacea. Neighbour-joining phylogeny derived using the conditions of the Poisson distance correction model in MEGAX (Kumar et al., 2018), showing the relationships of cetacea and *Hippopotamus amphibius* PADs. Bootstrap values > 50 based on 1000 replicates are shown as nodal support. PADs for the 4 whales and orca focused on in this study, northern minke whale (*Balaenoptera acutorostrata*), fin whale (*Balaenoptera physalus*), humpback whale (*Megaptera novaeangliae*), Cuvier's beaked whale (*Ziphius cavirostris*) and orca (*Orcinus orca*), are highlighted by silhouettes.

Supplementary Fig. 2. Protein-protein interaction networks of deiminated protein hits identified in serum of minke whale (*Balaenoptera acutorostrata*). Reconstruction of protein-protein interactions based on known and predicted interactions using STRING analysis. As not all target proteins are present in STRING for minke whale, 85 minke whale proteins could be used for this analysis. KEGG pathways relating to the identified proteins and reported in STRING are highlighted as follows: red=complement and coagulation cascade; light blue=*Staphylococcus aureus* infection; orange=systemic lupus erythematosus (SLE); dark blue=cholesterol metabolism; pink=ECM receptor interaction; dark green=amoebiasis; yellow=estrogen signalling pathway; light green=glycolysis. Coloured lines indicate whether protein interactions are identified via known interactions (curated databases, experimentally determined), predicted interactions (gene neighbourhood, gene fusion, gene co-occurrence) or via text mining, co-expression or protein homology (see the colour key for connective lines included in the figure).

Supplementary Fig. 3. Protein-protein interaction networks of adiponectin in orca (*Orcinius orca*). Reconstruction of protein-protein interactions of orca adiponectin, based on known and predicted interactions using STRING analysis. **A.** Coloured nodes represent query proteins and first shell of interactors (ADIPOQ=adiponectin and highlighted in red). **B.** KEGG pathways related to adiponectin (ADIPOQ) and interacting proteins, reported in STRING and highlighted as follows: Yellow=non-

alcoholic fatty liver disease (NAFLD); pink=AMPK signalling pathway; dark green=longevity regulating pathway; red=adipocytokine signalling pathway; light blue=PPAR signalling pathway; orange=type II diabetes mellitus; purple=regulation of lipolysis in adipocytes; light green=HIF-1 signalling pathway; dark blue=insulin resistance; brown=FoxO signalling pathway. Coloured nodes represent query protein (adiponectin=ADIPOQ) and first shell of interactors, white nodes are second shell of interactors. Coloured lines indicate whether protein interactions are identified via known interactions (curated databases, experimentally determined), predicted interactions (gene neighbourhood, gene fusion, gene co-occurrence) or via text mining, co-expression or protein homology (see colour key for connective lines shown in the figure).

Supplementary Table 1. A summary on data available for the individual cetaceans from which serum samples were utilised in this study.

Supplementary Table 2. Deiminated proteins identified by F95 enrichment in serum of Northern minke whale (*Balaenoptera acutorostrata*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Peptide hits scoring with the cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues) are shown. Species hit names and total scores are shown.

Supplementary Table 3. Deiminated proteins identified by F95 enrichment in serum of fin whale (*Balaenoptera physalus*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Peptide hits scoring with the cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues) are shown. Species hit names and total scores are shown.

Supplementary Table 4. Deiminated proteins identified by F95 enrichment in serum of humpback whale (*Megaptera novaeangliae*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Peptide hits scoring with the cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues) are shown. Species hit names and total scores are shown.

Supplementary Table 5. Deiminated proteins identified by F95 enrichment in serum of Cuvier's beaked whale (*Ziphius cavirostris*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Peptide hits scoring with the cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues) are shown. Species hit names and total scores are shown.

Supplementary Table 6. Deiminated proteins identified by F95 enrichment in serum of orca (*Orcinus orca*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Peptide hits scoring with the cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues) are shown. Species hit names and total scores are shown.

Fig. 1

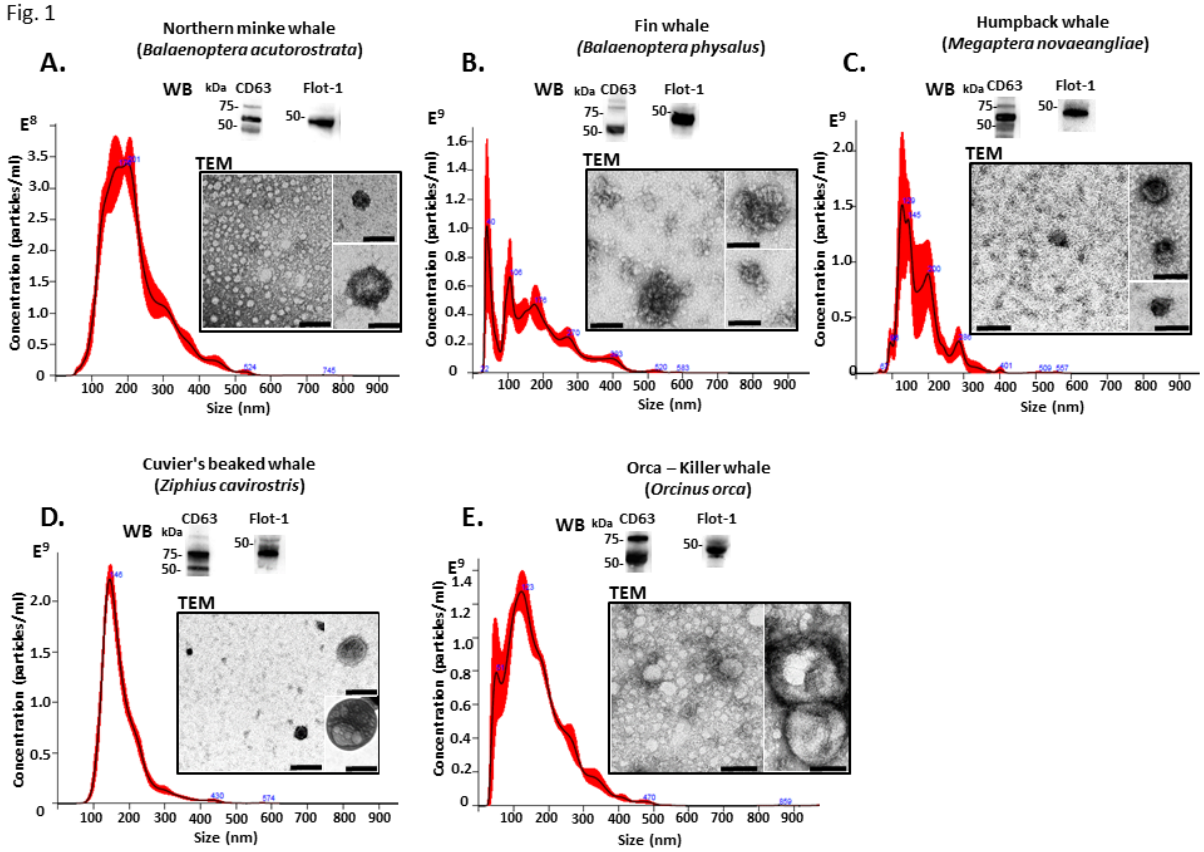

Fig. 2

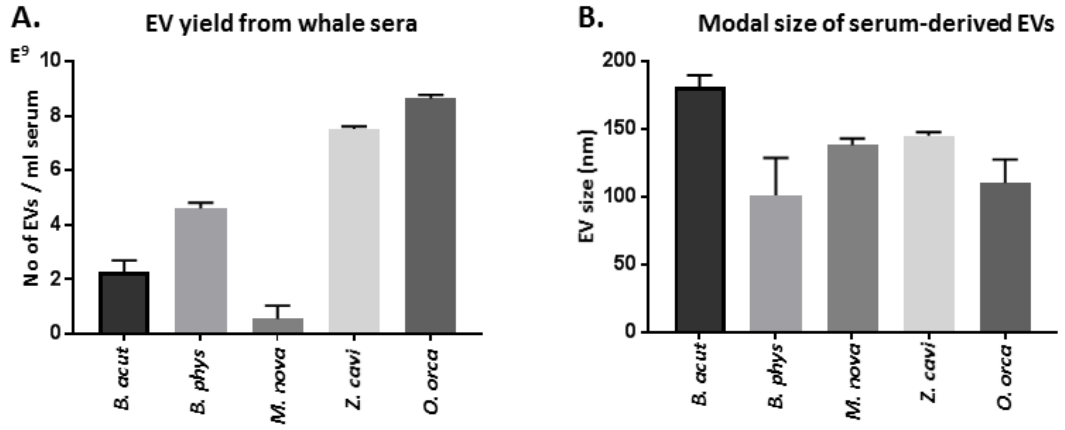

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Fig. 3

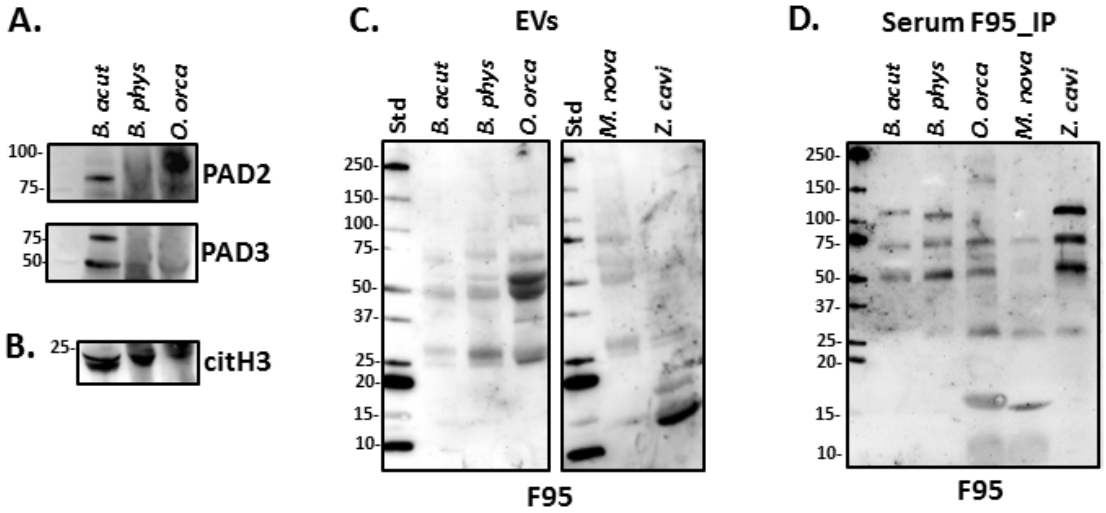

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Fig. 4. Minke whale (*Balaenoptera acutorostrata*)

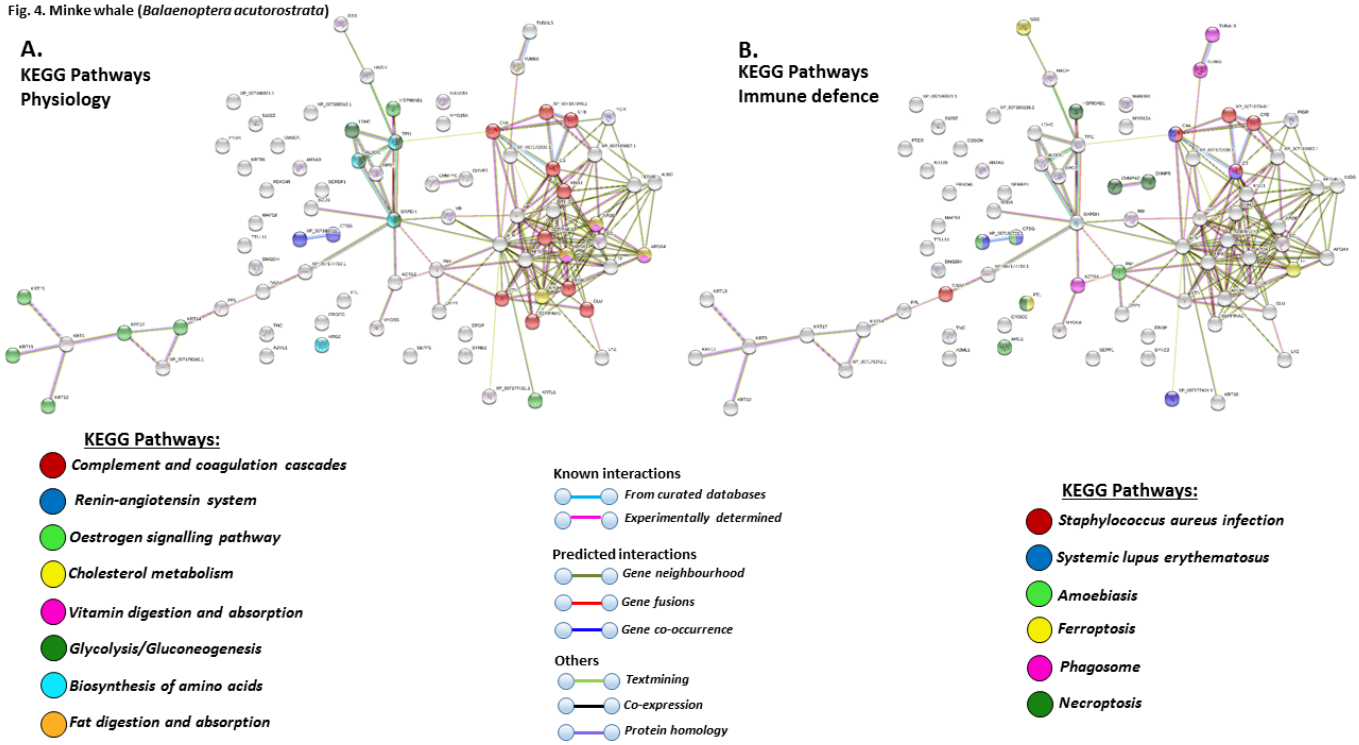

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Fig. 5. Fin whale (*Balaenoptera physalus*)

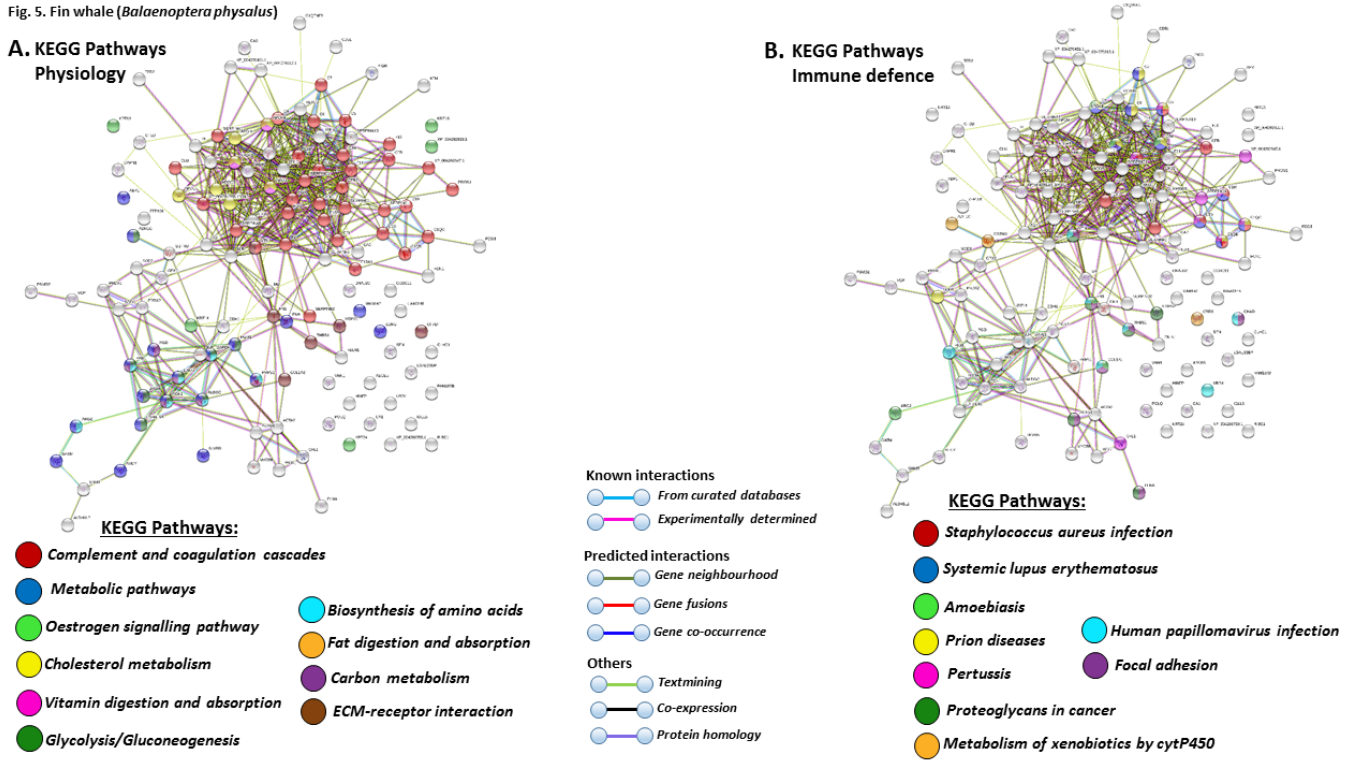

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Fig. 6. Humpback whale (*Megaptera novaeangliae*)

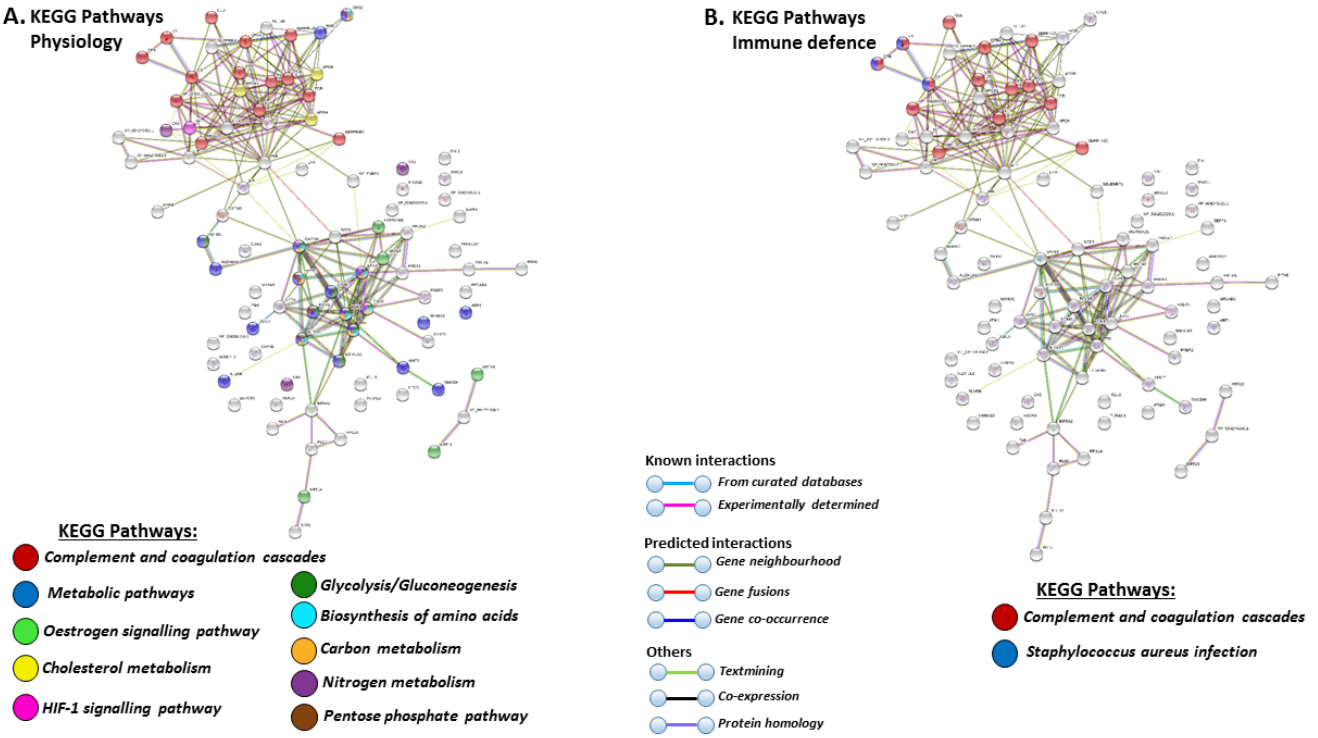

Fig. 7. Cuvier's beaked whale (*Ziphius cavirostris*)

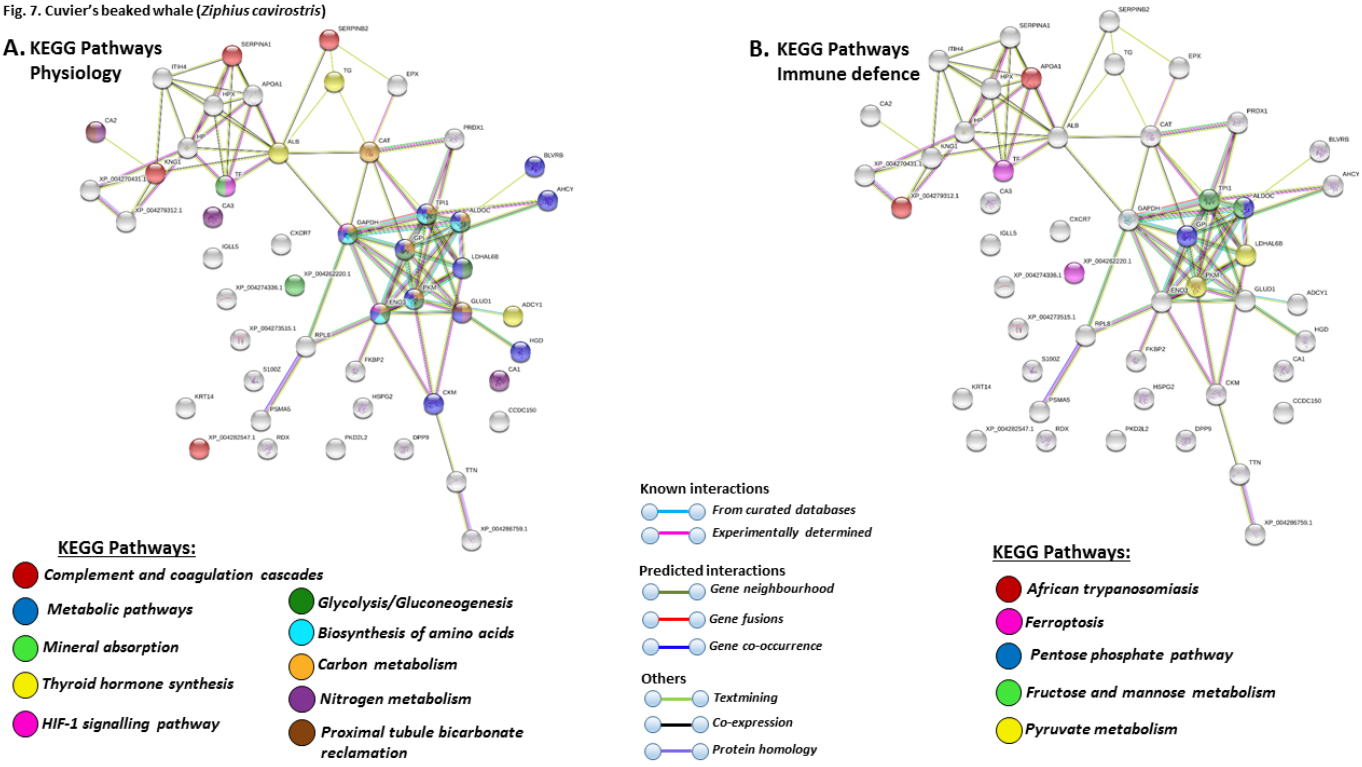

Fig. 8. Orca (*Orcinus orca*)

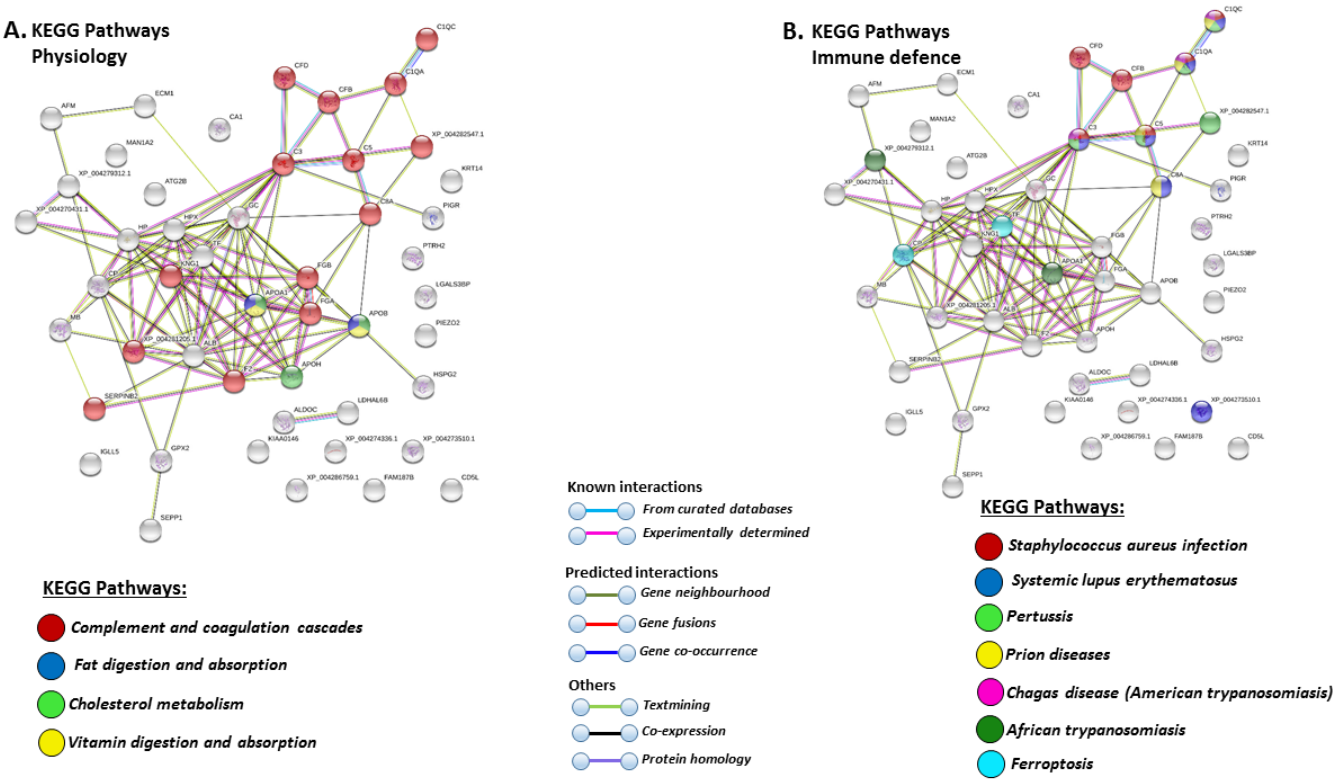

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Fig. 9.

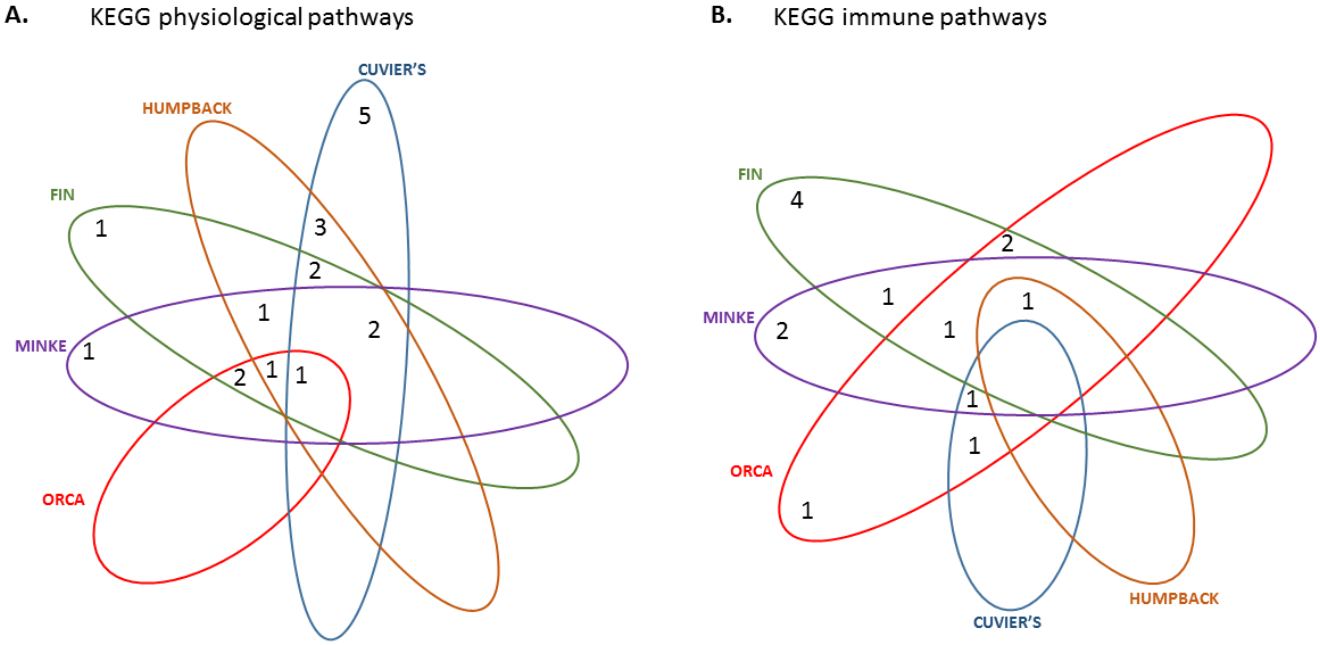

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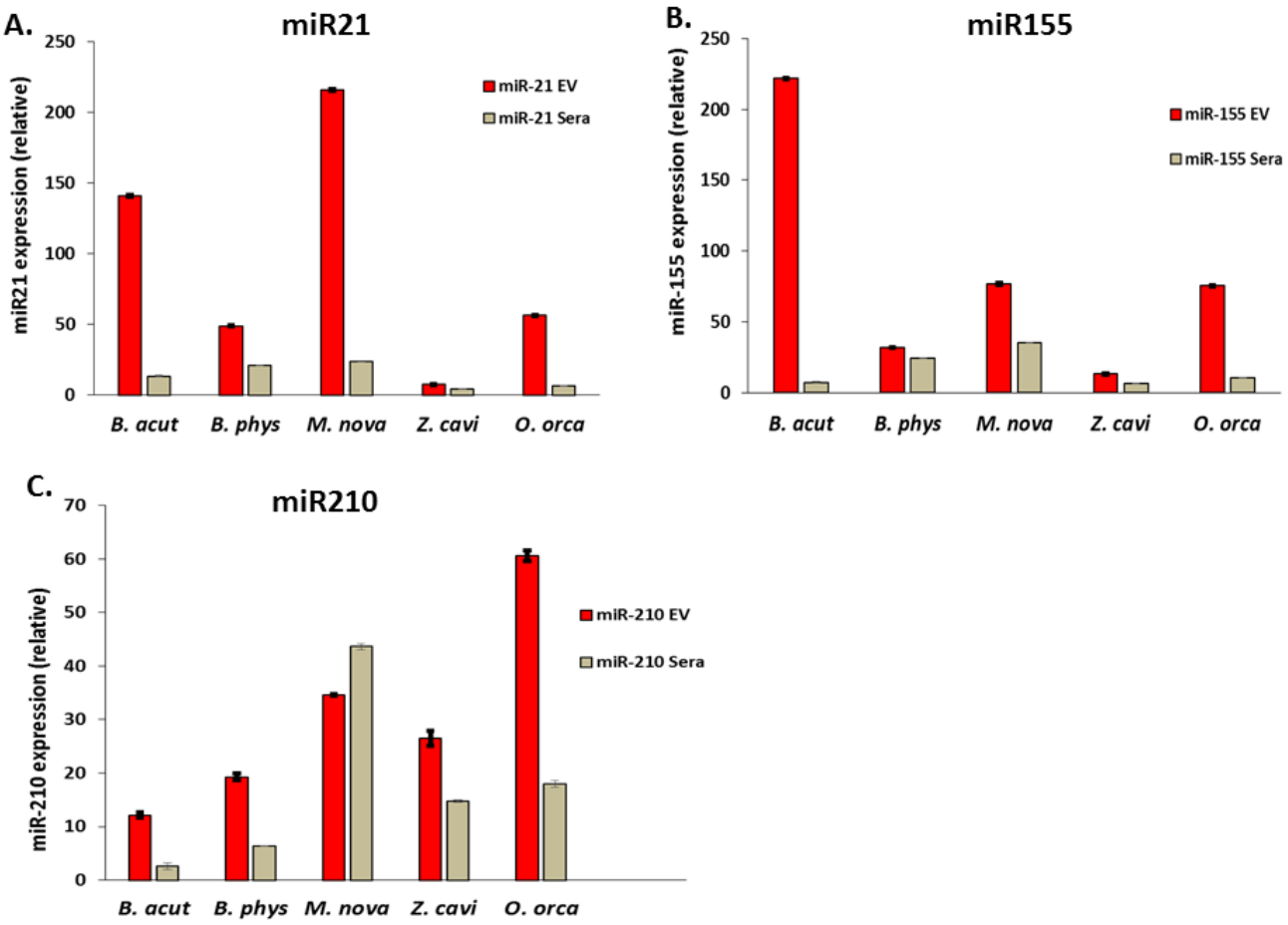
Fig. 10



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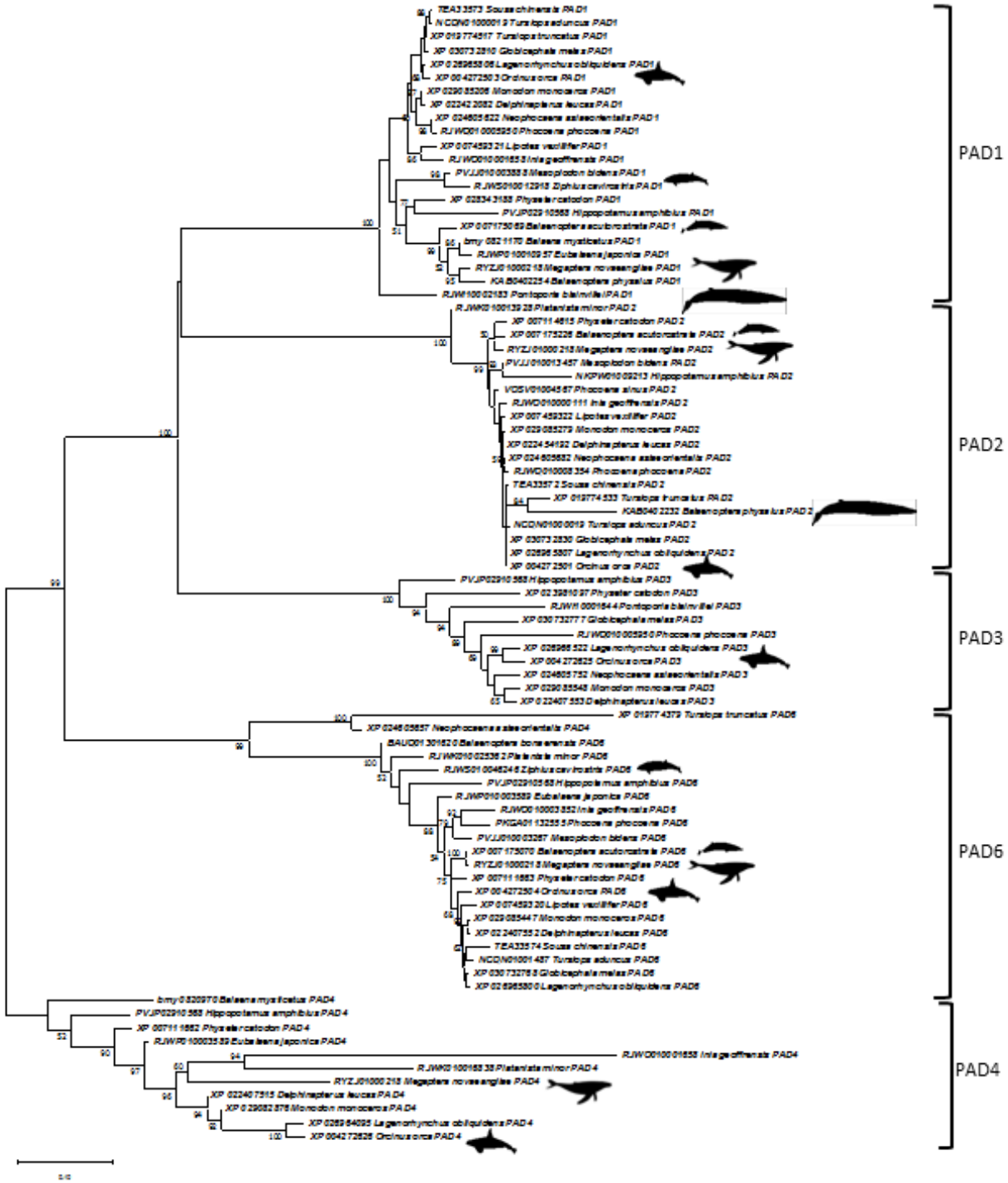
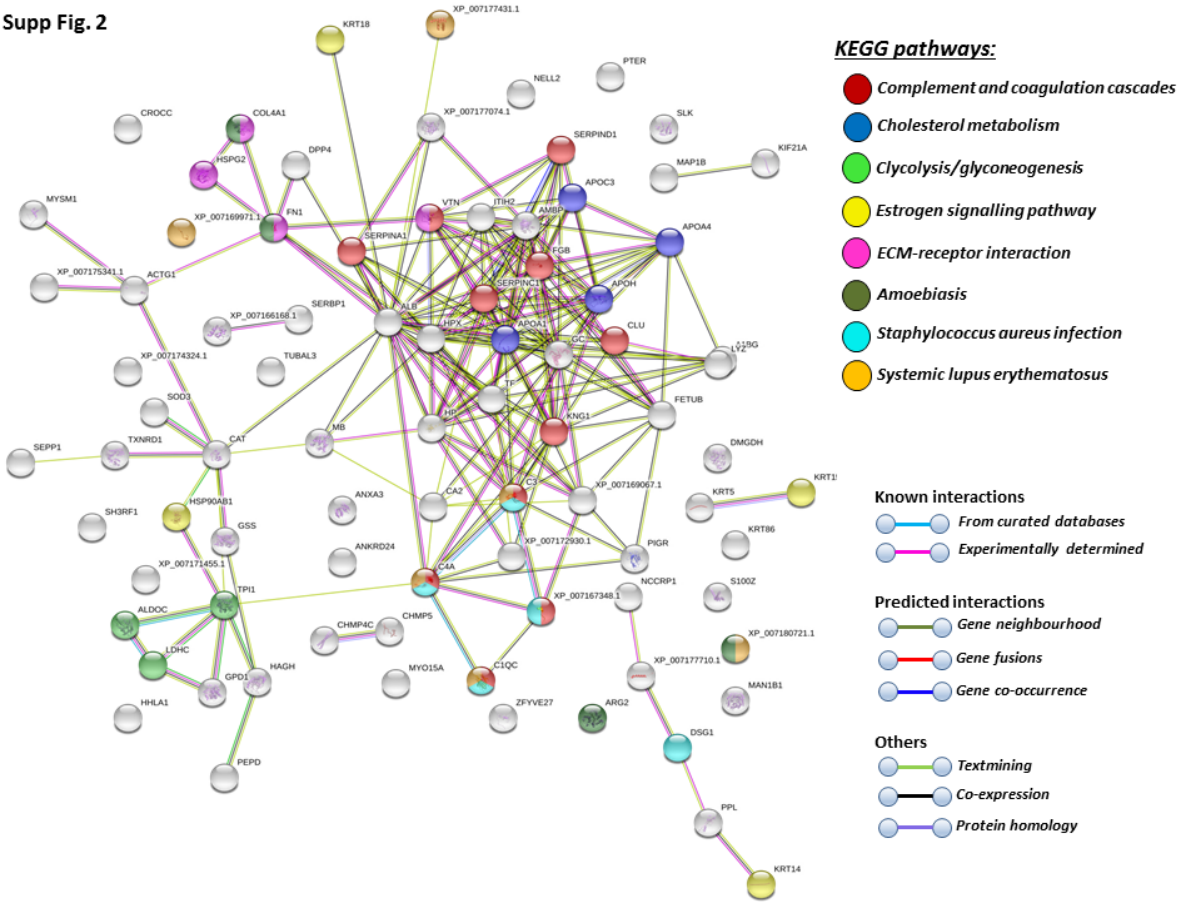
Supp. Fig. 1



Supp Fig. 2



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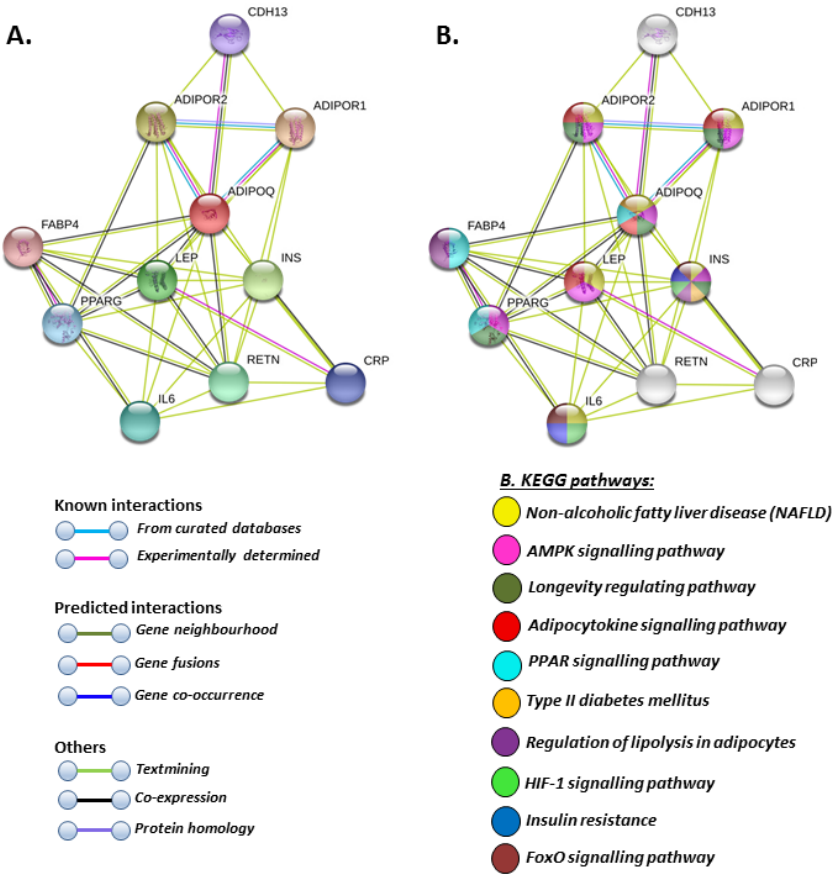
Supp. Fig. 3



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2692 **Supplementary Table 1.** Data summary for the individual cetaceans used in this study.

Common name	Species name	Sex	Maturity	Age (yrs)	Length /weight recorded	Location
Minke whale	*Balaenoptera acutorostrata*	male	mature	Not assessed	813 cm	South-Western Iceland (free ranging)
Fin whale	*Balaenoptera physalus*	female	anoestrous	33	2100 cm	South-Western Iceland (free ranging)
Humpback whale	*Megaptera novaeangliae*	female	immature	Not assessed	880 cm	South-Western Iceland (stranded)
Cuvier's beaked whale	*Ziphius cavirostris*	female	immature	Not assessed	605 cm	South-Eastern Iceland (stranded)
Orca	*Orcinus orca*	male	mature	22	5440 kg	South Iceland (captive)

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Supplementary Table 2. Deiminated proteins identified by F95 enrichment in serum of Northern minke whale (*Balaenoptera acutorostrata*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot . Peptide hits scoring with the cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues) are shown. Species hit names and total scores are shown.

Protein name	Species name	Common name	Total score (p<0.05)[‡]
A0A452CHV5_BALAS ***apolipoprotein B-100***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	3805
A0A384B912_BALAS ***alpha-2-macroglobulin isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	3144
A0A2P4TBI3_BAMTH ***apolipoprotein B-100***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	2503
A0A383Z2B4_BALAS ***complement C3***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	2339
A0A383ZXR0_BALAS ***serum albumin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	2314
A0A2Y9NK15_DELLE ***alpha-2-macroglobulin isoform X3***	*Delphinapterus leucas*	Beluga whale	2152
A0A2U4AKU7_TURTR ***alpha-2-macroglobulin-like***	*Tursiops truncatus*	Common bottlenose dolphin	2037
A0A4U1FPV0_MONMO ***Uncharacterized protein***	*Monodon monoceros*	Narwhal	2033
A0A384ALG4_BALAS ***ceruloplasmin isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1968
A0A455BHA9_PHYMC ***alpha-2-macroglobulin-like***	*Physeter macrocephalus*	Sperm whale	1848
A0A383Z5R5_BALAS ***serotransferrin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1707
A0A341C5T8_9CETA ***serum albumin***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	1640
A0A2U3V5M2_TURTR ***serum albumin isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	1610
A0A340XNP3_LIPVE ***complement C3***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	1548
A0A384B6G0_BALAS ***kininogen-1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1145
A0A383ZCJ5_BALAS ***Hemopexin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1094
A0A2F0B3C5_ESCRO ***Keratin, type II cytoskeletal 5***	*Eschrichtius robustus*	Gray whale	1092
A0A2Y9MM41_DELLE ***fibronectin isoform X6***	*Delphinapterus leucas*	Beluga whale	1047
A0A2Y9EED2_PHYMC ***fibronectin isoform X5***	*Physeter macrocephalus*	Sperm whale	1045
A0A340XBS1_LIPVE ***fibronectin***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	1022
A0A384ALK4_BALAS ***fibronectin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1016
A0A2F0B042_ESCRO ***Hemopexin***	*Eschrichtius robustus*	Gray whale	944
A0A383YWT8_BALAS	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	929

complement factor H-like isoform X1			
A0A383Z8T4_BALAS ***C4b-binding protein alpha chain isoform X7***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	864
APOA1_BALAS ***Apolipoprotein A-I***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	856
A0A384BF87_BALAS ***Haptoglobin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	722
A0A2Y9N2V9_DELLE ***kininogen-1 isoform X1***	*Delphinapterus leucas*	Beluga whale	707
A0A341CEB0_9CETA ***Hemopexin***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	674
0A484GXQ7_SOUCH ***Hemopexin***	*Sousa chinensis*	Indo-Pacific humpbacked dolphin	625
A0A4U1EQC8_MONMO ***apolipoprotein A-IV***	*Monodon monoceros*	Narwhal	623
A0A2Y9SJP9_PHYMC ***keratin, type II cytoskeletal 6A***	*Physeter macrocephalus*	Sperm whale	586
A0A383ZI56_BALAS ***inter-alpha-trypsin inhibitor heavy chain H4 isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	584
A0A140GN64_BALAC ***Hemoglobin subunit beta***	*Balaenoptera acutorostrata*	Northern minke whale	583
A0A340Y1E6_LIPVE ***keratin, type I cytoskeletal 14***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	569
AV1_ESCRO ***Keratin, type I cytoskeletal 14***	*Eschrichtius robustus*	Gray whale	517
A0A2Y9F6Z4_PHYMC ***kininogen-1 isoform X1***	*Physeter macrocephalus*	Sperm whale	504
A0A383ZST7_BALAS ***complement C5 isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	493
A0A384BAA9_BALAS ***apolipoprotein A-IV***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	491
A0A140GN67_MESDE ***Hemoglobin subunit beta***	*Mesoplodon densirostris*	Blainville's beaked whale	466
A0A383Z9Z9_BALAS ***Alpha-mannosidase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	456
A0A2F0BP97_ESCRO ***Ig mu heavy chain disease protein***	*Eschrichtius robustus*	Gray whale	439
A0A4U1FIN2_MONMO ***keratin, type I cytoskeletal 13***	*Monodon monoceros*	Narwhal	435
A0A383ZV20_BALAS ***alpha-1-antitrypsin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	431
A0A340XV96_LIPVE ***keratin, type I cytoskeletal 17***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	409
A0A383ZWF6_BALAS ***keratin, type II cytoskeletal 6A-like isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	388
A0A2Y9P8E6_DELLE ***desmoplakin isoform X1***	*Delphinapterus leucas*	Beluga whale	376
28_PONBL ***Apolipoprotein B***	*Pontoporia blainvillei*	La Plata dolphin	373
A0A140GN13_BALAC	*Balaenoptera acutorostrata*	Northern minke whale	365

Hemoglobin subunit alpha			
A0A384A3E4_BALAS ***hemoglobin subunit alpha isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	346
A0A384AZC9_BALAS ***Clusterin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	338
A0A384B1Q0_BALAS ***vitamin D-binding protein***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	328
A0A384A7N6_BALAS ***dipeptidyl peptidase 4***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	
A0A2Y9LVR1_DELLE ***keratin, type I cytoskeletal 15***	*Delphinapterus leucas*	Beluga whale	299
A0A2F0B4J5_ESCRO ***Hemoglobin subunit alpha***	*Eschrichtius robustus*	Gray whale	280
A0A383ZRY6_BALAS ***junction plakoglobin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	275
A0A2Y9P876_DELLE ***Tubulin beta chain***	*Delphinapterus leucas*	Beluga whale	272
A0A384AFQ0_BALAS ***Plasminogen***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	262
A0A140GN07_MESDE ***Hemoglobin subunit alpha***	*Mesoplodon densirostris*	Blainville's beaked whale	257
A0A2U4AUY5_TURTR ***dimethylglycine dehydrogenase, mitochondrial***	*Tursiops truncatus*	Common bottlenose dolphin	257
A0A140GN06_TURTR ***Hemoglobin subunit alpha***	*Tursiops truncatus*	Common bottlenose dolphin	248
A0A340YDD2_LIPVE ***xaa-Pro dipeptidase isoform X2***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	240
A0A2U4AU60_TURTR ***alpha-1B-glycoprotein***	*Tursiops truncatus*	Common bottlenose dolphin	216
A0A140GN09_KOGSI ***Hemoglobin subunit alpha***	*Kogia sima*	Dwarf sperm whale	214
A0A2Y9S2C1_PHYMC ***alpha-1B-glycoprotein***	*Physeter macrocephalus*	Sperm whale	203
A0A340WU44_LIPVE ***immunoglobulin lambda-like polypeptide 5***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	192
A0A2F0BAH8_ESCRO ***Complement factor B***	*Eschrichtius robustus*	Gray whale	191
A0A2F0BNF0_ESCRO ***Ig alpha-1 chain C region***	*Eschrichtius robustus*	Gray whale	186
A0A384B2W1_BALAS ***complement C4***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	181
A0A484GJZ6_SOUCH ***IF rod domain-containing protein***	*Sousa chinensis*	Indo-Pacific humpbacked dolphin	171
A0A384B7A3_BALAS ***selenoprotein P***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	160
A0A2F0BDQ6_ESCRO ***Keratin, type I cytoskeletal 18***	*Eschrichtius robustus*	Gray whale	155
A0A452C4G6_BALAS ***Lysozyme***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	154

A0A2U4BA07_TURTR ***Tubulin alpha chain***	*Tursiops truncatus*	Common bottlenose dolphin	153
A0A452C7H9_BALAS ***Ferritin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	144
A0A340X0S0_LIPVE ***desmoglein-1***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	142
A0A340YAH5_LIPVE ***Triosephosphate isomerase***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	141
A0A2U4BSU8_TURTR ***actin, cytoplasmic 2***	*Tursiops truncatus*	Common bottlenose dolphin	141
A0A2Y9F6J0_PHYMC ***antithrombin-III***	*Physeter macrocephalus*	Sperm whale	136
A0A384AFN8_BALAS ***Superoxide dismutase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	130
A0A452CDN2_BALAS ***keratin, type I cytoskeletal 12***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	120
A0A340XYI8_LIPVE ***keratin, type I cytoskeletal 42-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	120
A0A340WNM5_LIPVE ***obscurin-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	118
A0A384AEC5_BALAS ***beta-2-glycoprotein 1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	111
A0A2U3V0A2_TURTR ***Arginase***	*Tursiops truncatus*	Common bottlenose dolphin	109
A0A2F0B5A8_ESCRO ***Fetuin-B***	*Eschrichtius robustus*	Gray whale	108
A0A4U1EJD5_MONMO ***TAF domain-containing protein***	*Monodon monoceros*	Narwhal	108
A0A2U4CQQ1_TURTR ***heat shock protein HSP 90-alpha***	*Tursiops truncatus*	Common bottlenose dolphin	108
A0A2F0B5X4_ESCRO ***Heat shock protein HSP 90-beta***	*Eschrichtius robustus*	Gray whale	102
A0A2F0B035_ESCRO ***Fructose-bisphosphate aldolase***	*Eschrichtius robustus*	Gray whale	101
A0A2U4B6K7_TURTR ***inter-alpha-trypsin inhibitor heavy chain H2***	*Tursiops truncatus*	Common bottlenose dolphin	93
A0A384A960_BALAS ***alpha-2-antiplasmin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	90
A0A383ZWG2_BALAS ***keratin, type II cuticular Hb6***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	82
A0A2U4BFU2_TURTR ***unconventional myosin-Vb***	*Tursiops truncatus*	Common bottlenose dolphin	82
A0A2F0B3N0_ESCRO ***Vitronectin***	*Eschrichtius robustus*	Gray whale	80
A0A2F0BB48_ESCRO ***Phosphotriesterase-related protein***	*Eschrichtius robustus*	Gray whale	76
A0A452CPB6_BALAS ***complement component C9***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	76
A0A2Y9MHA0_DELLE	*Delphinapterus leucas*	Beluga whale	75

unconventional myosin-XV			
A0A2Y9PGE3_DELLE ***protein dopey-1 isoform X4***	*Delphinapterus leucas*	Beluga whale	74
A0A2U4APV3_TURTR ***L-lactate dehydrogenase***	*Tursiops truncatus*	Common bottlenose dolphin	74
A0A4U1EAQ3_MONMO ***Ig-like domain-containing protein***	*Monodon monoceros*	Narwhal	73
A0A2U4ANF3_TURTR ***14-3-3 protein epsilon***	*Tursiops truncatus*	Common bottlenose dolphin	68
A0A384A061_BALAS ***cathepsin G-like***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	66
A0A2F0BHJ5_ESCRO ***Cathepsin G***	*Eschrichtius robustus*	Gray whale	66
A0A2U4BPE6_TURTR ***nuclear mitotic apparatus protein 1 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	65
A0A2U4BAA2_TURTR ***protein kinase C-binding protein NELL2 isoform X3***	*Tursiops truncatus*	Common bottlenose dolphin	64
A0A340X2W3_LIPVE ***C-type lectin domain family 4 member K***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	63
A0A2F0BF69_ESCRO ***Heparin cofactor 2***	*Eschrichtius robustus*	Gray whale	62
A0A2F0AY08_ESCRO ***Glutathione synthetase***	*Eschrichtius robustus*	Gray whale	60
A0A2F0BHF1_ESCRO ***Annexin***	*Eschrichtius robustus*	Gray whale	59
A0A341ACJ2_9CETA ***charged multivesicular body protein 4c***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	58
A0A2U3V9U9_TURTR ***charged multivesicular body protein 5***	*Tursiops truncatus*	Common bottlenose dolphin	57
A0A383Z9P7_BALAS ***polymeric immunoglobulin receptor***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	56
A0A484GZC1_SOUCH ***Ferritin***	*Sousa chinensis*	Indo-Pacific humpbacked dolphin	56
A0A2U3V9D2_TURTR ***heterogeneous nuclear ribonucleoproteins A2/B1 isoform X4***	*Tursiops truncatus*	Common bottlenose dolphin	56
A0A340WWE6_LIPVE ***periplakin***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	56
A0A383ZLI1_BALAS ***microtubule-associated protein 1B***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	54
A0A2U4AKU6_TURTR ***Glyceraldehyde-3-phosphate dehydrogenase***	*Tursiops truncatus*	Common bottlenose dolphin	54
A0A4U1ETF4_MONMO ***Uncharacterized protein***	*Monodon monoceros*	Narwhal	54
A0A2F0AUI6_ESCRO ***Ferritin***	*Eschrichtius robustus*	Gray whale	53

A0A2U4C9F5_TURTR ***allergen Fel d 4-like***	*Tursiops truncatus*	Common bottlenose dolphin	52
A0A2U3V6F1_TURTR ***tenascin isoform X2***	*Tursiops truncatus*	Common bottlenose dolphin	51
A2U4BRW1_TURTR ***terminal uridylyltransferase 7 isoform X4***	*Tursiops truncatus*	Common bottlenose dolphin	51
A0A2U4AU11_TURTR ***insulin-like growth factor 2 mRNA-binding protein 3***	*Tursiops truncatus*	Common bottlenose dolphin	48
A0A2U4B3V1_TURTR ***E3 ubiquitin-protein ligase SH3RF1 isoform X2***	*Tursiops truncatus*	Common bottlenose dolphin	47
A0A2F0B098_ESCRO ***Hydroxyacylglutathione hydrolase, mitochondrial***	*Eschrichtius robustus*	Gray whale	46
A0A2Y9P0R0_DELLE ***F-box only protein***	*Delphinapterus leucas*	Beluga whale	46
A0A2F0AZL3_ESCRO ***Histone H2B***	*Eschrichtius robustus*	Gray whale	45
A0A2U3V4Z9_TURTR ***fibrinogen beta chain***	*Tursiops truncatus*	Common bottlenose dolphin	45
A0A340Y9E7_LIPVE ***tubulin polyglutamylase TTLL11***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	44
A0A2F0BHB3_ESCRO ***Glycerol-3-phosphate dehydrogenase [NAD(+)]***	*Eschrichtius robustus*	Gray whale	44
A0A2Y9MUL0_DELLE ***nesprin-2 isoform X1***	*Delphinapterus leucas*	Beluga whale	44
A0A2Y9LTS8_DELLE ***complement C3-like isoform X1***	*Delphinapterus leucas*	Beluga whale	43
A0A2F0B9E6_ESCRO ***Trypsin***	*Eschrichtius robustus*	Gray whale	43
rootletin	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	43
A0A2Y9FI42_PHYMC ***coiled-coil domain-containing protein 190***	*Physeter macrocephalus*	Sperm whale	43
A0A341BVR7_9CETA ***developmental pluripotency-associated protein 2-like***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	42
A0A2F0B364_ESCRO ***Protein S100***	*Eschrichtius robustus*	Gray whale	42
A0A2Y9LCY9_DELLE ***basement membrane-specific heparan sulfate proteoglycan core protein isoform X3***	*Delphinapterus leucas*	Beluga whale	42

[ǂ]Ions score is -10*Log(P), where P is the probability that the observed match is a random event. Individual ions scores > 41 indicated identity or extensive homology ($p < 0.05$). Protein scores were derived from ions scores as a non-probabilistic basis for ranking protein hits. Cut-off was set at Ions score 20.

Supplementary Table 3. Deiminated proteins identified by F95 enrichment in serum of fin whale (*Balaenoptera physalus*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Peptide hits scoring with the cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues) are shown. Species hit names and total scores are shown.

Protein name	Species name	Common name	Total score ($p<0.05$)[‡]
A0A384B912_BALAS ***alpha-2-macroglobulin isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	3650
A0A383ZXR0_BALAS ***serum albumin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	3062
A0A452CHV5_BALAS ***apolipoprotein B-100***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	2952
A0A383Z2B4_BALAS ***complement C3***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	2699
A0A341C5T8_9CETA ***serum albumin***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	2447
A0A384ALG4_BALAS ***ceruloplasmin isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	2325
A0A341AGH0_9CETA ***alpha-2-macroglobulin-like isoform X2***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	2262
A0A4U1FPV0_MONMO ***Uncharacterized protein***	*Monodon monoceros*	Narwhal	2249
A0A2U3V5M2_TURTR ***serum albumin isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	2203
A0A340XUI9_LIPVE ***apolipoprotein B-100***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	2193
A0A2U4AKU7_TURTR ***alpha-2-macroglobulin-like***	*Tursiops truncatus*	Common bottlenose dolphin	2181
A0A340Y7Z8_LIPVE ***serum albumin***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	2155
A0A383Z5R5_BALAS ***serotransferrin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	2141
A0A340XNP3_LIPVE ***complement C3***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	2106
A0A384AFQ0_BALAS ***Plasminogen***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	2090
A0A340YAE1_LIPVE ***alpha-2-macroglobulin-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	2014
A0A2Y9TJG8_PHYMC ***complement C3***	*Physeter macrocephalus*	Sperm whale	1908
A0A384ALK4_BALAS ***fibronectin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1871
A0A2U4BMT3_TURTR ***fibronectin isoform X4***	*Tursiops truncatus*	Common bottlenose dolphin	1842
A0A2Y9EED2_PHYMC ***fibronectin isoform X5***	*Physeter macrocephalus*	Sperm whale	1703
A0A383YWT8_BALAS ***complement factor H-like isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1662
A0A383Z1U4_BALAS ***complement C3-like isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1571

A0A384B2W1_BALAS ***complement C4***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1479
A0A384B6G0_BALAS ***kininogen-1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1364
A0A383ZST7_BALAS ***complement C5 isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1362
A0A452C585_BALAS ***pregnancy zone protein-like***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1272
P0DMA6|APOA1_BALAS ***Apolipoprotein A-I***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1269
A0A384BF87_BALAS ***Haptoglobin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1176
A0A340Y8V6_LIPVE ***alpha-2-macroglobulin-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	1169
A0A2U4CNJ2_TURTR ***Plasminogen***	*Tursiops truncatus*	Common bottlenose dolphin	1127
A0A140GN64_BALAC ***Hemoglobin subunit beta***	*Balaenoptera acutorostrata*	Northern minke whale	1078
A0A341CUQ2_9CETA ***complement C5***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	1062
A0A340XE64_LIPVE ***complement factor H-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	1061
A0A2Y9FIB4_PHYMC ***complement C5***	*Physeter macrocephalus*	Sperm whale	1045
A0A340XK77_LIPVE ***complement C4-A***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	1038
A0A4U1EQC8_MONMO ***Uncharacterized protein***	*Monodon monoceros*	Narwhal	1012
A0A2F0B042_ESCRO ***Hemopexin***	*Eschrichtius robustus*	Gray whale	966
A0A341ATW9_9CETA ***complement factor H isoform X2***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	901
A0A384AY37_BALAS ***complement component C6***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	888
A0A2Y9N2V9_DELLE ***kininogen-1 isoform X1***	*Delphinapterus leucas*	Beluga whale	869
A0A2F0BAH8_ESCRO ***Complement factor B***	*Eschrichtius robustus*	Gray whale	832
A0A384B1Q0_BALAS ***vitamin D-binding protein***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	831
A0A383ZI56_BALAS ***inter-alpha-trypsin inhibitor heavy chain H4 isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	824
A0A2Y9NIU7_DELLE ***complement factor H isoform X1***	*Delphinapterus leucas*	Beluga whale	821
A0A2Y9FDR4_PHYMC ***inter-alpha-trypsin inhibitor heavy chain H2***	*Physeter macrocephalus*	Sperm whale	812
A0A384B2P9_BALAS ***complement factor B***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	812
A0A384AGF6_BALAS ***Fructose-bisphosphate aldolase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	804

A0A383YX88_BALAS ***inter-alpha-trypsin inhibitor heavy chain H2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	801
A0A2F0B6R6_ESCRO ***Apolipoprotein A-IV***	*Eschrichtius robustus*	Gray whale	782
A0A4U1EEK0_MONMO ***complement factor B***	*Monodon monoceros*	Narwhal	764
A0A341C7J1_9CETA ***vitamin D-binding protein***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	750
A0A384A1L0_BALAS ***Prothrombin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	747
A0A383Z8T4_BALAS ***C4b-binding protein alpha chain isoform X7***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	740
A0A383ZI29_BALAS ***inter-alpha-trypsin inhibitor heavy chain H1 isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	737
A0A383ZCJ5_BALAS ***Hemopexin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	734
A0A341CEB0_9CETA ***Hemopexin***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	728
A0A340YB71_LIPVE ***complement component C6***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	719
A0A384BAA9_BALAS ***apolipoprotein A-IV***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	713
A0A384AEC5_BALAS ***beta-2-glycoprotein 1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	685
A0A383YNL2_BALAS ***complement component C8 alpha chain***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	662
A0A2Y9F6Z4_PHYMC ***kininogen-1 isoform X1***	*Physeter macrocephalus*	Sperm whale	656
A0A383ZG27_BALAS ***coagulation factor XI***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	654
A0A140GN67_MESDE ***Hemoglobin subunit beta***	*Mesoplodon densirostris*		653
A0A2Y9PXE8_DELLE ***Prothrombin***	*Delphinapterus leucas*	Beluga whale	645
A0A4V5P7Z3_MONMO ***inter-alpha-trypsin inhibitor heavy chain H3***	*Monodon monoceros*	Narwhal	638
A0A384AYR3_BALAS ***complement component C7 isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	630
A0A340WSC2_LIPVE ***keratin, type II cytoskeletal 5 isoform X1***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	626
A0A2F0BBI0_ESCRO ***Pregnancy zone protein***	*Eschrichtius robustus*	Gray whale	622
A0A484GV34_SOUCH ***Uncharacterized protein***	*Sousa chinensis*		604
A0A2U4AP99_TURTR ***complement factor B***	*Tursiops truncatus*	Common bottlenose dolphin	572
A0A2U4B948_TURTR ***serotransferrin***	*Tursiops truncatus*	Common bottlenose dolphin	568
A0A2Y9Q9H8_DELLE	*Delphinapterus leucas*	Beluga whale	559

complement component C7			
A0A383ZYJ4_BALAS ***carbonic anhydrase 1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	553
A0A383ZJG1_BALAS ***basement membrane-specific heparan sulfate proteoglycan core protein***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	549
A0A383ZSR9_BALAS ***gelsolin isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	542
A0A2F0AYW0_ESCRO ***Ig lambda-6 chain C region***	*Eschrichtius robustus*	Gray whale	534
A0A452CPB6_BALAS ***complement component C9***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	533
A0A340YCM8_LIPVE ***C4b-binding protein alpha chain-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	523
A0A340XC23_LIPVE ***serotransferrin***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	522
A0A340Y1E6_LIPVE ***keratin, type I cytoskeletal 14***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	498
A0A2Y9FI53_PHYMC ***gelsolin isoform X4***	*Physeter macrocephalus*	Sperm whale	497
A0A2Y9Q2M0_DELLE ***betaine-homocysteine S-methyltransferase 1***	*Delphinapterus leucas*	Beluga whale	492
A0A140GN13_BALAC ***Hemoglobin subunit alpha***	*Balaenoptera acutorostrata*	Northern minke whale	481
A0A2U4AKU6_TURTR ***Glyceraldehyde-3-phosphate dehydrogenase***	*Tursiops truncatus*	Common bottlenose dolphin	465
A0A2F0BP97_ESCRO ***Ig mu heavy chain disease protein***	*Eschrichtius robustus*	Gray whale	456
A0A344X2S6_GLOME ***Hemoglobin subunit beta***	*Globicephala melas*		454
A0A383ZV20_BALAS ***alpha-1-antitrypsin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	440
A0A383Z9Z9_BALAS ***Alpha-mannosidase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	437
A0A384A3E4_BALAS ***hemoglobin subunit alpha isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	436
A0A140GN07_MESDE ***Hemoglobin subunit alpha***	*Mesoplodon densirostris*		421
A0A2F0B7Q7_ESCRO ***Antithrombin-III***	*Eschrichtius robustus*	Gray whale	421
A0A140GN06_TURTR ***Hemoglobin subunit alpha***	*Tursiops truncatus*	Common bottlenose dolphin	421
A0A2Y9T858_PHYMC ***keratin, type I cytoskeletal 14 isoform X1***	*Physeter macrocephalus*	Sperm whale	420
A0A340XIR2_LIPVE ***complement component C9***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	415
A0A2F0B6I5_ESCRO ***Alpha-1-antitrypsin***	*Eschrichtius robustus*	Gray whale	395

A0A383ZRG8_BALAS ***keratin, type I cytoskeletal 15***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	393
A0A2F0BAV1_ESCRO ***Keratin, type I cytoskeletal 14***	*Eschrichtius robustus*		386
A0A384BCE5_BALAS ***Fructose-bisphosphate aldolase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	378
A0A2U3V780_TURTR ***carbonic anhydrase 2***	*Tursiops truncatus*	Common bottlenose dolphin	368
A0A383ZSX3_BALAS ***protein AMBP***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	368
A0A383ZA42_BALAS ***CD5 antigen-like isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	364
A0A2F0B6G6_ESCRO ***CD5 antigen-like***	*Eschrichtius robustus*	Gray whale	360
A0A2U4BSU8_TURTR ***actin, cytoplasmic 2***	*Tursiops truncatus*	Common bottlenose dolphin	358
A0A383ZRJ1_BALAS ***keratin, type I cytoskeletal 14***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	355
A0A140GN14_PHYMC ***Hemoglobin subunit alpha***	*Physeter macrocephalus*	Sperm whale	352
A0A340WLD3_LIPVE ***fibrinogen beta chain isoform X2***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	351
A0A2Y9SF59_PHYMC ***L-lactate dehydrogenase***	*Physeter macrocephalus*	Sperm whale	350
A0A383ZYR5_BALAS ***carbonic anhydrase 3***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	349
A0A452C7C8_BALAS ***complement component C8 beta chain***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	345
A0A384AET4_BALAS ***galectin-3-binding protein***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	340
A0A383ZI45_BALAS ***inter-alpha-trypsin inhibitor heavy chain H3 isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	338
A0A383ZNV5_BALAS ***fibrinogen gamma chain isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	336
A0A383ZHT1_BALAS ***apolipoprotein R-like***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	335
A0A455B568_PHYMC ***C4b-binding protein alpha chain***	*Physeter macrocephalus*	Sperm whale	324
A0A383ZWF6_BALAS ***keratin, type II cytoskeletal 6A-like isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	322
A0A384AUG3_BALAS ***pantetheinase isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	315
A0A384A960_BALAS ***alpha-2-antiplasmin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	311
A0A2F0AVP5_ESCRO ***Apolipoprotein E***	*Eschrichtius robustus*	Gray whale	307
A0A2Y9ELN5_PHYMC ***complement component C8 beta chain***	*Physeter macrocephalus*	Sperm whale	306

A0A2U4ANE4_TURTR ***alpha-2-antiplasmin***	*Tursiops truncatus*	Common bottlenose dolphin	297
D3TTK4_DELDE ***Hemoglobin beta5 chain***	*Delphinus delphis*		289
A0A2Y9MHB6_DELLE ***filamin-A isoform X1***	*Delphinapterus leucas*	Beluga whale	287
APOE_BALAS ***Apolipoprotein E***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	286
A0A340WU44_LIPVE ***immunoglobulin lambda-like polypeptide 5***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	286
A0A2F0B376_ESCRO ***Actin, aortic smooth muscle***	*Eschrichtius robustus*	Gray whale	281
A0A340X0E0_LIPVE ***alpha-enolase isoform X1***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	280
A0A2F0B4J5_ESCRO ***Hemoglobin subunit alpha***	*Eschrichtius robustus*	Gray whale	276
A0A383Z577_BALAS ***complement C1r subcomponent***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	273
A0A2F0BHT3_ESCRO ***Kininogen-2***	*Eschrichtius robustus*	Gray whale	270
A0A2U4A275_TURTR ***selenium-binding protein 1 isoform X2***	*Tursiops truncatus*	Common bottlenose dolphin	269
A0A341CXM1_9CETA ***heparin cofactor 2***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	269
A0A384A1C5_BALAS ***inhibitor of carbonic anhydrase isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	269
A0A2Y9MKT1_DELLE ***complement factor I***	*Delphinapterus leucas*	Beluga whale	264
A0A4U1FST8_MONMO ***complement C1q subcomponent subunit C***	*Monodon monoceros*	Narwhal	258
A0A2Y9N8Q0_DELLE ***keratin, type II cytoskeletal 6A-like***	*Delphinapterus leucas*	Beluga whale	257
A0A340XVX6_LIPVE ***complement factor I***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	253
A0A2F0B1I9_ESCRO ***Beta-enolase***	*Eschrichtius robustus*	Gray whale	251
A0A2Y9FPJ2_PHYMC ***Clusterin***	*Physeter macrocephalus*	Sperm whale	244
A0A383YVI2_BALAS ***flavin reductase (NADPH)***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	244
A0A2F0B3N0_ESCRO ***Vitronectin***	*Eschrichtius robustus*	Gray whale	241
A0A2Y9NWC0_DELLE ***complement component C8 gamma chain isoform X1***	*Delphinapterus leucas*	Beluga whale	230
A0A2Y9T005_PHYMC ***complement C1q subcomponent subunit C***	*Physeter macrocephalus*	Sperm whale	225
A0A384B6M8_BALAS ***fetuin-B***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	224

A0A2Y9EH60_PHYMC ***vitamin K-dependent protein S***	*Physeter macrocephalus*	Sperm whale	214
A0A2U3V7Z3_TURTR ***peroxiredoxin-1***	*Tursiops truncatus*	Common bottlenose dolphin	211
Q9GL90_BALMY ***Transferrin***	*Balaena mysticetus*		210
A0A383Z9P7_BALAS ***polymeric immunoglobulin receptor***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	208
A0A2F0AYU0_ESCRO ***Ig lambda chain V-III region SH***	*Eschrichtius robustus*	Gray whale	208
A0A383ZRC7_BALAS ***keratin, type I cytoskeletal 13***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	208
A0A2F0B2V1_ESCRO ***Glutathione peroxidase***	*Eschrichtius robustus*	Gray whale	202
A0A2Y9LPM6_DELLE ***immunoglobulin lambda-1 light chain-like***	*Delphinapterus leucas*	Beluga whale	194
A0A2U4CLI2_TURTR ***Adenosylhomocysteinase***	*Tursiops truncatus*	Common bottlenose dolphin	189
A0A2F0AXA3_ESCRO ***Pyruvate kinase***	*Eschrichtius robustus*	Gray whale	188
A0A2Y9NH97_DELLE ***L-lactate dehydrogenase***	*Delphinapterus leucas*	Beluga whale	187
A0A2Y9TCY0_PHYMC ***keratin, type I cytoskeletal 42-like***	*Physeter macrocephalus*	Sperm whale	186
A0A2U4B8X2_TURTR ***Amine oxidase***	*Tursiops truncatus*	Common bottlenose dolphin	179
A0A2Y9FE50_PHYMC ***inhibitor of carbonic anhydrase isoform X2***	*Physeter macrocephalus*	Sperm whale	176
A0A383Z4U0_BALAS ***complement C1s subcomponent isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	175
A0A383ZXQ7_BALAS ***afamin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	173
A0A0N9DSI7_BALOM ***C1Q and collagen domain containing adiponectin***	*Balaenoptera omurai*	Omura's whale (dwarf fin whale)	170
A0A2F0BMU1_ESCRO ***Fibrinogen alpha chain***	*Eschrichtius robustus*	Gray whale	169
A0A383ZJ84_BALAS ***complement C1q subcomponent subunit B***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	164
A0A452C5K2_BALAS ***plasma protease C1 inhibitor***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	156
A0A340XEE1_LIPVE ***alpha-1B-glycoprotein-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	155
A0A2U4BFU2_TURTR ***unconventional myosin-Vb***	*Tursiops truncatus*	Common bottlenose dolphin	148
A0A340XVM8_LIPVE ***keratin, type I cytoskeletal 15***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	147

A0A340WNM5_LIPVE ***obscurin-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	144
A0A383YWX2_BALAS ***coagulation factor XIII B chain***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	144
A0A2Y9P2W5_DELLE ***Glycine N-methyltransferase***	*Delphinapterus leucas*	Beluga whale	135
A0A2F0BNF0_ESCRO ***Ig alpha-1 chain C region***	*Eschrichtius robustus*	Gray whale	129
A0A2F0B6Y0_ESCRO ***Superoxide dismutase [Cu-Zn]***	*Eschrichtius robustus*	Gray whale	129
A0A2F0BBD2_ESCRO ***Glutathione S-transferase***	*Eschrichtius robustus*	Gray whale	128
Q0KIY9|MYG_INDPC ***Myoglobin***	*Indopacetus pacificus*	Tropical bottlenose whale	125
A0A2Y9MM08_DELLE ***carbamoyl-phosphate synthase [ammonia], mitochondrial isoform X2***	*Delphinapterus leucas*	Beluga whale	125
A0A452C3Q2_BALAS ***ficolin-1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	124
A0A2U3V999_TURTR ***ribose-phosphate pyrophosphokinase 1***	*Tursiops truncatus*	Common bottlenose dolphin	122
A0A383ZZD6_BALAS ***thrombospondin-1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	119
A0A2F0B025_ESCRO ***Peroxiredoxin-2***	*Eschrichtius robustus*	Gray whale	118
A0A2Y9EQK7_PHYMC ***transketolase isoform X1***	*Physeter macrocephalus*	Sperm whale	117
A0A2Y9LYW0_DELLE ***apolipoprotein C-III***	*Delphinapterus leucas*	Beluga whale	115
A0A2Y9Q8L6_DELLE ***selenoprotein P isoform X1***	*Delphinapterus leucas*	Beluga whale	114
A0A2Y9NVG6_DELLE ***phosphoglucomutase-1 isoform X1***	*Delphinapterus leucas*	Beluga whale	112
A0A2Y9F8B3_PHYMC ***fibrinogen alpha chain***	*Physeter macrocephalus*	Sperm whale	111
A0A2Y9FDN7_PHYMC ***14-3-3 protein sigma***	*Physeter macrocephalus*	Sperm whale	109
A0A452CCB0_BALAS ***immunoglobulin kappa light chain-like***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	109
A0A384A668_BALAS ***10-formyltetrahydrofolate dehydrogenase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	107
A0A2U3VAA7_TURTR ***alcohol dehydrogenase E chain***	*Tursiops truncatus*	Common bottlenose dolphin	106
A0A2F0BNZ5_ESCRO ***Fibrinogen gamma-B chain***	*Eschrichtius robustus*	Gray whale	106
A0A4U1ECF0_MONMO ***Ig-like domain-containing protein***	*Monodon monoceros*	Narwhal	105

A0A383YWU0_BALAS ***complement factor H isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	105
A0A341D7J4_9CETA ***collagen alpha-2(I) chain***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	104
A0A2Y9NGE0_DELLE ***ficolin-2-like isoform X2***	*Delphinapterus leucas*	Beluga whale	104
A0A2F0BEE8_ESCRO ***Apolipoprotein A-II***	*Eschrichtius robustus*	Gray whale	103
A0A384BES7_BALAS ***cadherin-1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	102
A0A2F0BQ50_ESCRO ***Extracellular superoxide dismutase [Cu-Zn]***	*Eschrichtius robustus*	Gray whale	102
A0A383ZHH6_BALAS ***keratin, type II microfibrillar-like***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	98
A0A2U3V9F2_TURTR ***Phosphoglycerate kinase***	*Tursiops truncatus*	Common bottlenose dolphin	91
A0A2Y9PJV8_DELLE ***calpain-1 catalytic subunit***	*Delphinapterus leucas*	Beluga whale	84
A0A2U4BAA2_TURTR ***protein kinase C-binding protein NELL2 isoform X3***	*Tursiops truncatus*	Common bottlenose dolphin	83
A0A2F0BAE6_ESCRO ***Cofilin-1***	*Eschrichtius robustus*	Gray whale	83
A0A2F0B4Y4_ESCRO ***Glycine amidinotransferase, mitochondrial***	*Eschrichtius robustus*	Gray whale	81
A0A2U3V6Z1_TURTR ***complement C1q tumor necrosis factor-related protein 3 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	80
A0A383Z8S9_BALAS ***apolipoprotein R-like isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	76
A0A2F0BPF2_ESCRO ***Angiotensinogen***	*Eschrichtius robustus*	Gray whale	74
A0A341B799_9CETA ***WD repeat-containing protein 1***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	72
A0A2Y9FNF4_PHYMC ***xaa-Pro dipeptidase isoform X3***	*Physeter macrocephalus*	Sperm whale	68
A0A2U4BCI8_TURTR ***zinc finger protein 106 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	64
A0A340XJB2_LIPVE ***E3 ubiquitin-protein ligase UBR4***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	62
A0A2U3V2I2_TURTR ***Histone H4***	*Tursiops truncatus*	Common bottlenose dolphin	61
A0A2Y9FLP7_PHYMC ***Fumarylacetoacetase***	*Physeter macrocephalus*	Sperm whale	61
A0A2Y9MHQ5_DELLE	*Delphinapterus leucas*	Beluga whale	61

nuclear mitotic apparatus protein 1 isoform X2			
A0A4U1EB65_MONMO ***Ig-like domain-containing protein***	*Monodon monoceros*	Narwhal	60
A0A2F0BPQ3_ESCRO ***Bisphosphoglycerate mutase***	*Eschrichtius robustus*	Gray whale	59
A0A2F0B2T1_ESCRO ***Ig heavy chain V region 3-6***	*Eschrichtius robustus*	Gray whale	59
A0A2F0BQ37_ESCRO ***Coagulation factor XIII A chain***	*Eschrichtius robustus*	Gray whale	58
A0A2U4AEQ4_TURTR ***Alpha-1,4 glucan phosphorylase***	*Tursiops truncatus*	Common bottlenose dolphin	57
A0A2Y9LWI5_DELLE ***junction plakoglobin***	*Delphinapterus leucas*	Beluga whale	56
A0A2Y9TGE0_PHYMC ***ATP-binding cassette sub-family B member 5***	*Physeter macrocephalus*	Sperm whale	56
A0A452CFC8_BALAS ***zinc finger protein 845-like***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	56
A0A2U4AKS5_TURTR ***complement C1s subcomponent***	*Tursiops truncatus*	Common bottlenose dolphin	55
A0A2F0B2N3_ESCRO ***Cathepsin B***	*Eschrichtius robustus*	Gray whale	54
A0A2Y9LYJ2_DELLE ***chondroadherin***	*Delphinapterus leucas*	Beluga whale	53
A0A2U4BYK3_TURTR ***Clathrin heavy chain linker domain-containing protein 1***	*Tursiops truncatus*	Common bottlenose dolphin	52
A0A2U3V0A2_TURTR ***Arginase***	*Tursiops truncatus*	Common bottlenose dolphin	52
A0A2F0BFV3_ESCRO ***Protein Z-dependent protease inhibitor***	*Eschrichtius robustus*	Gray whale	51
A0A2U4C129_TURTR ***RIB43A-like with coiled-coils protein 1***	*Tursiops truncatus*	Common bottlenose dolphin	51
A0A340XZH6_LIPVE ***coiled-coil domain-containing protein 11***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	51
A0A2F0B5J9_ESCRO ***Transitional endoplasmic reticulum ATPase***	*Eschrichtius robustus*	Gray whale	51
A0A2F0B6H3_ESCRO ***Coagulation factor X***	*Eschrichtius robustus*	Gray whale	50
A0A383ZRF2_BALAS ***keratin, type I cytoskeletal 24***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	49
A0A2Y9TDN0_PHYMC ***IgGFc-binding protein***	*Physeter macrocephalus*	Sperm whale	49
A0A2F0B8P2_ESCRO ***DnaJ subfamily B member 2***	*Eschrichtius robustus*	Gray whale	49
A0A384A3I0_BALAS ***DNA polymerase theta***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	

A0A2Y9MAX2_DELLE ***stromelysin-1-like***	*Delphinapterus leucas*	Beluga whale	46
A0A2U4AZR9_TURTR ***6-phosphogluconate dehydrogenase, decarboxylating***	*Tursiops truncatus*	Common bottlenose dolphin	46
A0A2U4ASA8_TURTR ***NEDD4-binding protein 2 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	45
A0A2F0B7K3_ESCRO ***26S proteasome non-ATPase regulatory subunit 2***	*Eschrichtius robustus*	Gray whale	45
A0A2Y9Q0K2_DELLE ***Fibulin-1***	*Delphinapterus leucas*	Beluga whale	44
A0A383ZV79_BALAS ***plasma serine protease inhibitor***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	44
A0A2U4B9G6_TURTR ***U2 snRNP-associated SURP motif-containing protein isoform X2***	*Tursiops truncatus*	Common bottlenose dolphin	44
A0A384AEK3_BALAS ***fas-binding factor 1 isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	44
A0A2F0B9R0_ESCRO ***Carbonyl reductase [NADPH] 3***	*Eschrichtius robustus*	Gray whale	43
A0A341CAB3_9CETA ***N-alpha-acetyltransferase 11-like isoform X2***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	41
A0A2U4BFX5_TURTR ***carboxypeptidase B2***	*Tursiops truncatus*	Common bottlenose dolphin	41
A0A2F0B6A6_ESCRO ***Dual serine/threonine and tyrosine protein kinase***	*Eschrichtius robustus*	Gray whale	40

[ǂ]Ions score is -10*Log(P), where P is the probability that the observed match is a random event. Individual ions scores > 40 indicated identity or extensive homology ($p < 0.05$). Protein scores were derived from ions scores as a non-probabilistic basis for ranking protein hits. Cut-off was set at Ions score 20.

Supplementary Table 4. Deiminated proteins identified by F95 enrichment in serum of humpback whale (*Megaptera novaeangliae*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Peptide hits scoring with the cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues) are shown. Species hit names and total scores are shown.

Protein name	Species name	Common name	Total score (p<0.05)[‡]
A0A384B912_BALAS ***alpha-2-macroglobulin isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	2926
A0A455BHA9_PHYMC ***alpha-2-macroglobulin-like***	*Physeter macrocephalus*	Sperm whale	2174
A0A2Y9NK15_DELLE ***alpha-2-macroglobulin isoform X3***	*Delphinapterus leucas*	Beluga whale	2132
A0A4U1FPV0_MONMO ***Uncharacterized protein***	*Monodon monoceros*	Narwhal	2020
A0A2U4AKU7_TURTR ***alpha-2-macroglobulin-like***	*Tursiops truncatus*	Common bottlenose dolphin	1993
A0A340YAE1_LIPVE ***alpha-2-macroglobulin-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	1907
A0A383Z2B4_BALAS ***complement C3***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1900
A0A383ZXR0_BALAS ***serum albumin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1848
A0A340XNP3_LIPVE ***complement C3***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	1345
A0A2Y9TJG8_PHYMC ***complement C3***	*Physeter macrocephalus*	Sperm whale	1286
A0A341C5T8_9CETA ***serum albumin***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	1270
A0A452C585_BALAS ***pregnancy zone protein-like***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1181
A0A384ALG4_BALAS ***ceruloplasmin isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1163
A0A2Y9M6G0_DELLE ***complement C3 isoform X2***	*Delphinapterus leucas*	Beluga whale	1132
A0A140GN64_BALAC ***Hemoglobin subunit beta***	*Balaenoptera acutorostrata*	Northern mine whale	1022
A0A383Z5R5_BALAS ***serotransferrin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	978
A0A340Y8V6_LIPVE ***alpha-2-macroglobulin-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	960
P0DMA6|APOA1_BALAS ***Apolipoprotein A-I***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	663
A0A2Y9PL94_DELLE ***Fructose-bisphosphate aldolase***	*Delphinapterus leucas*	Beluga whale	646
A0A384BF87_BALAS ***Haptoglobin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	556
A0A140GN67_MESDE ***Hemoglobin subunit beta***	*Mesoplodon densirostris*	Blainville's beaked whale	549
A0A384B6G0_BALAS ***kininogen-1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	518
A0A2F0B042_ESCRO	*Eschrichtius robustus*	Gray whale	480

Hemopexin			
A0A140GN13_BALAC ***Hemoglobin subunit alpha***	*Balaenoptera acutorostrata*	Northern mine whale	439
A0A2Y9F931_PHYMC ***carbonic anhydrase 2 isoform X1***	*Physeter macrocephalus*	Sperm whale	423
A0A384A3E4_BALAS ***hemoglobin subunit alpha isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	412
A0A2F0B3C5_ESCRO ***Keratin, type II cytoskeletal 5***	*Eschrichtius robustus*	Gray whale	387
A0A383ZLC8_BALAS ***betaine-homocysteine S-methyltransferase 1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	387
A0A384B1Q0_BALAS ***vitamin D-binding protein***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	356
A0A4U1FNC5_MONMO ***Hemoglobin subunit alpha***	*Monodon monoceros*	Narwhal	351
A0A2Y9SJP9_PHYMC ***keratin, type II cytoskeletal 6A***	*Physeter macrocephalus*	Sperm whale	341
A0A140GN07_MESDE ***Hemoglobin subunit alpha***	*Mesoplodon densirostris*	Blainville's beaked whale	338
A0A340XC23_LIPVE ***serotransferrin***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	333
A0A2F0BK75_ESCRO ***Glyceraldehyde-3-phosphate dehydrogenase***	*Eschrichtius robustus*	Gray whale	330
A0A2U4AKU6_TURTR ***Glyceraldehyde-3-phosphate dehydrogenase***	*Tursiops truncatus*	Common bottlenose dolphin	328
A0A383ZID2_BALAS ***L-lactate dehydrogenase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	322
Q06YY0_STECO ***Beta-actin***	*Stenella coeruleoalba*	Striped dolphin	312
A0A383Z8T4_BALAS ***C4b-binding protein alpha chain isoform X7***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	307
A0A4U1FI99_MONMO ***IF rod domain-containing protein***	*Monodon monoceros*	Narwhal	293
A0A4U1FIN2_MONMO ***Keratin, type I cytoskeletal***	*Monodon monoceros*	Narwhal	291
A0A2U3V5B8_TURTR ***antithrombin-III isoform X2***	*Tursiops truncatus*	Common bottlenose dolphin	275
A0A2Y9SF59_PHYMC ***L-lactate dehydrogenase***	*Physeter macrocephalus*	Sperm whale	274
A0A383ZYJ4_BALAS ***carbonic anhydrase 1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	271
A0A140GN68_KOGSI ***Hemoglobin subunit beta***	*Kogia sima*	Dwarf sperm whale	271
A0A384B2W1_BALAS ***complement C4***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	268
A0A383YRF9_BALAS ***Amine oxidase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	260

A0A2U3V7Z3_TURTR ***peroxiredoxin-1***	*Tursiops truncatus*	Common bottlenose dolphin	260
A0A384A7N6_BALAS ***dipeptidyl peptidase 4***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	259
A0A2F0AYW0_ESCRO ***Ig lambda-6 chain C region***	*Eschrichtius robustus*	Gray whale	258
A0A2Y9PHY7_DELLE ***Amine oxidase***	*Delphinapterus leucas*	Beluga whale	249
A0A384AFQ0_BALAS ***Plasminogen***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	244
A0A2F0BP97_ESCRO ***Ig mu heavy chain disease protein***	*Eschrichtius robustus*	Gray whale	243
A0A2F0BAV1_ESCRO ***Keratin, type I cytoskeletal 14***	*Eschrichtius robustus*	Gray whale	238
A0A2U3VAA7_TURTR ***alcohol dehydrogenase E chain***	*Tursiops truncatus*	Common bottlenose dolphin	235
A0A2U4CBA9_TURTR ***keratin, type II cytoskeletal 6A-like***	*Tursiops truncatus*	Common bottlenose dolphin	234
A0A383ZWF6_BALAS ***keratin, type II cytoskeletal 6A-like isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	226
A0A2F0B434_ESCRO ***Cytosolic 10-formyltetrahydrofolate dehydrogenase***	*Eschrichtius robustus*	Gray whale	223
A0A2F0B4J5_ESCRO ***Hemoglobin subunit alpha***	*Eschrichtius robustus*	Gray whale	219
A0A2U4B5X8_TURTR ***flavin reductase (NADPH)***	*Tursiops truncatus*	Common bottlenose dolphin	215
A0A1K0FUJ2_TURTR ***Globin B1***	*Tursiops truncatus*	Common bottlenose dolphin	214
A0A384B6I8_BALAS ***L-lactate dehydrogenase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	205
A0A383ZYR5_BALAS ***carbonic anhydrase 3***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	190
A0A384AL46_BALAS ***carbamoyl-phosphate synthase [ammonia], mitochondrial***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	186
A0A340WU44_LIPVE ***immunoglobulin lambda-like polypeptide 5***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	180
A0A384BCE5_BALAS ***Fructose-bisphosphate aldolase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	173
A0A4U1ECY9_MONMO ***Uncharacterized protein***	*Monodon monoceros*	Narwhal	169
A0A2U4A337_TURTR ***selenium-binding protein 1 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	166
A0A484GJZ6_SOUCH ***IF rod domain-containing protein***	*Sousa chinensis*	Indo-Pacific humpbacked dolphin	165

A0A2F0BAH8_ESCRO ***Complement factor B***	*Eschrichtius robustus*	Gray whale	163
A0A383ZNS6_BALAS ***fibrinogen beta chain***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	161
A0A384AFN8_BALAS ***Superoxide dismutase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	156
A0A2U4AUY5_TURTR ***dimethylglycine dehydrogenase, mitochondrial***	*Tursiops truncatus*	Common bottlenose dolphin	156
A0A2F0B025_ESCRO ***Peroxiredoxin-2***	*Eschrichtius robustus*	Gray whale	155
A0A340YDD2_LIPVE ***xaa-Pro dipeptidase isoform X2***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	150
A0A2F0BB82_ESCRO ***Glycerol-3-phosphate dehydrogenase [NAD(+)]***	*Eschrichtius robustus*	Gray whale	146
A0A383ZRC7_BALAS ***keratin, type I cytoskeletal 13***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	146
A0A2F0B5C3_ESCRO ***Factor XIIa inhibitor (Fragment)***	*Eschrichtius robustus*	Gray whale	145
A0A383ZPB5_BALAS ***fibrinogen alpha chain***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	136
A0A2Y9FBW7_PHYMC ***selenoprotein P***	*Physeter macrocephalus*	Sperm whale	134
A0A384A1C5_BALAS ***inhibitor of carbonic anhydrase isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	131
A0A452C7H9_BALAS ***Ferritin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	123
A0A340YEK8_LIPVE ***keratin 16***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	121
A0A383ZI56_BALAS ***inter-alpha-trypsin inhibitor heavy chain H4 isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	121
A0A341BLI5_9CETA ***apolipoprotein B-100***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	118
A0A2Y9FIB4_PHYMC ***complement C5***	*Physeter macrocephalus*	Sperm whale	111
A0A0N9DSI7_BALOM ***C1Q and collagen domain containing adiponectin***	*Balaenoptera omurai*	Omura's whale (dwarf fin whale)	111
A0A383ZHI2_BALAS ***four and a half LIM domains protein 1 isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	111
A0A2Y9Q8L6_DELLE ***selenoprotein P isoform X1***	*Delphinapterus leucas*	Beluga whale	109
A0A2Y9NVG6_DELLE ***phosphoglucomutase-1 isoform X1***	*Delphinapterus leucas*	Beluga whale	109
A0A2F0BG39_ESCRO ***Eosinophil peroxidase***	*Eschrichtius robustus*	Gray whale	107
A0A2F0B5X4_ESCRO	*Eschrichtius robustus*	Gray whale	102

Heat shock protein HSP 90-beta			
A0A2Y9M0C5_DELLE ***nesprin-1 isoform X9***	*Delphinapterus leucas*	Beluga whale	99
A0A2F0BF69_ESCRO ***Heparin cofactor 2***	*Eschrichtius robustus*	Gray whale	99
A0A2F0B1I9_ESCRO ***Beta-enolase***	*Eschrichtius robustus*	Gray whale	98
A0A2Y9S2C1_PHYMC ***alpha-1B-glycoprotein***	*Physeter macrocephalus*	Sperm whale	97
A0A383YWT8_BALAS ***complement factor H-like isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	96
A0A2F0B6Y0_ESCRO ***Superoxide dismutase [Cu-Zn]***	*Eschrichtius robustus*	Gray whale	96
A0A383Z9Z9_BALAS ***Alpha-mannosidase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	93
A0A2U3ZZ88_TURTR ***alpha-1-antitrypsin-like***	*Tursiops truncatus*	Common bottlenose dolphin	93
A0A2U3V1L4_TURTR ***alpha-enolase***	*Tursiops truncatus*	Common bottlenose dolphin	90
A0A2F0AUI6_ESCRO ***Ferritin***	*Eschrichtius robustus*	Gray whale	87
A0A2Y9F7I5_PHYMC ***fetuin-B isoform X1***	*Physeter macrocephalus*	Sperm whale	85
A0A2F0BBD2_ESCRO ***Glutathione S-transferase***	*Eschrichtius robustus*	Gray whale	85
A0A384AAI3_BALAS ***heat shock-related 70 kDa protein 2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	84
A0A4V5P683_MONMO ***Histone H2B***	*Monodon monoceros*	Narwhal	84
A0A2F0B3E9_ESCRO ***Superoxide dismutase***	*Eschrichtius robustus*	Gray whale	81
A0A2F0AVC4_ESCRO ***Fatty acid-binding protein, epidermal***	*Eschrichtius robustus*	Gray whale	80
A0A2Y9MBI0_DELLE ***keratin, type II cytoskeletal 8-like***	*Delphinapterus leucas*	Beluga whale	77
A0A340WNM5_LIPVE ***obscurin-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	75
A0A340XVM8_LIPVE ***keratin, type I cytoskeletal 15***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	75
A0A2U4BYT9_TURTR ***GTP-binding nuclear protein Ran***	*Tursiops truncatus*	Common bottlenose dolphin	73
A0A2F0B364_ESCRO ***Protein S100***	*Eschrichtius robustus*	Gray whale	70
A0A2Y9PGE3_DELLE ***protein dopey-1 isoform X4***	*Delphinapterus leucas*	Beluga whale	70
A0A2U3V4G0_TURTR ***PITH domain-containing protein 1***	*Tursiops truncatus*	Common bottlenose dolphin	69
A0A2U4CEL7_TURTR ***importin-7 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	69

A0A384AEC5_BALAS ***beta-2-glycoprotein 1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	68
A0A2U3V8D9_TURTR ***Peptidyl-prolyl cis-trans isomerase***	*Tursiops truncatus*	Common bottlenose dolphin	68
A0A2F0BDE3_ESCRO ***Carboxypeptidase B2***	*Eschrichtius robustus*	Gray whale	68
A0A2U4ANF3_TURTR ***14-3-3 protein epsilon***	*Tursiops truncatus*	Common bottlenose dolphin	67
A0A2U3V999_TURTR ***ribose-phosphate pyrophosphokinase 1***	*Tursiops truncatus*	Common bottlenose dolphin	67
A0A340XWI8_LIPVE ***Adenosylhomocysteinase***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	67
A0A2F0BI77_ESCRO ***Clusterin***	*Eschrichtius robustus*	Gray whale	67
Q0KIY1|MYG_BALBO ***Myoglobin***	*Balaenoptera borealis*	Sei whale	64
A0A2Y9EU52_PHYMC ***Triosephosphate isomerase***	*Physeter macrocephalus*	Sperm whale	63
A0A341BER1_9CETA ***homeobox protein Hox-B4***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	63
A0A2F0BB48_ESCRO ***Phosphotriesterase-related protein***	*Eschrichtius robustus*	Gray whale	62
A0A383ZHH6_BALAS ***keratin, type II microfibrillar-like***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	62
A0A340XTH9_LIPVE ***plectin***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	61
A0A2F0BAJ8_ESCRO ***Eukaryotic translation initiation factor 5A***	*Eschrichtius robustus*	Gray whale	60
A0A2F0B748_ESCRO ***Homogentisate 1,2-dioxygenase***	*Eschrichtius robustus*	Gray whale	57
A0A384A960_BALAS ***alpha-2-antiplasmin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	57
A0A341AVJ1_9CETA ***EF-hand calcium-binding domain-containing protein 6***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	56
A0A2F0BHS2_ESCRO ***Inter-alpha-trypsin inhibitor heavy chain H1***	*Eschrichtius robustus*	Gray whale	56
A0A2Y9MWF5_DELLE ***protocadherin Fat 1 isoform X1***	*Delphinapterus leucas*	Beluga whale	54
A0A2U4BA07_TURTR ***Tubulin alpha chain***	*Tursiops truncatus*	Common bottlenose dolphin	53
A0A2U4BFU2_TURTR ***unconventional myosin-Vb***	*Tursiops truncatus*	Common bottlenose dolphin	53
A0A2F0BDR3_ESCRO ***Calpain-1 catalytic subunit***	*Eschrichtius robustus*	Gray whale	52
A0A2U4BFQ3_TURTR ***Diacylglycerol kinase***	*Tursiops truncatus*	Common bottlenose dolphin	52

A0A452C841_BALAS ***ankyrin repeat domain-containing protein 24***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	49
A0A2U4C9K2_TURTR ***unconventional myosin-Va isoform X2***	*Tursiops truncatus*	Common bottlenose dolphin	49
A0A2U4AHH7_TURTR ***40S ribosomal protein S14***	*Tursiops truncatus*	Common bottlenose dolphin	49
A0A2F0BPQ3_ESCRO ***Bisphosphoglycerate mutase***	*Eschrichtius robustus*	Gray whale	48
A0A2F0B3N0_ESCRO ***Vitronectin***	*Eschrichtius robustus*	Gray whale	48
A0A455BTV8_PHYMC ***echinoderm microtubule-associated protein-like 1 isoform X2***	*Physeter macrocephalus*	Sperm whale	47
A0A2F0AVI7_ESCRO ***EF-hand domain-containing protein***	*Eschrichtius robustus*	Gray whale	47
A0A4U1F4C5_MONMO ***SAC domain-containing protein***	*Monodon monoceros*	Narwhal	47
A0A2F0BJB3_ESCRO ***Prothrombin***	*Eschrichtius robustus*	Gray whale	47
A0A2U4C8L6_TURTR ***protein KIBRA***	*Tursiops truncatus*	Common bottlenose dolphin	46
A0A2Y9MWH7_DELLE ***pericentriolar material 1 protein isoform X5***	*Delphinapterus leucas*	Beluga whale	46
A0A2Y9PYI9_DELLE ***fer-1-like protein 4***	*Delphinapterus leucas*	Beluga whale	46
A0A455AIA8_PHYMC ***eIF-2-alpha kinase activator GCN1 isoform X2***	*Physeter macrocephalus*	Sperm whale	46
A0A2U4C9F5_TURTR ***allergen Fel d 4-like***	*Tursiops truncatus*	Common bottlenose dolphin	45
A0A340X7R4_LIPVE ***leucine-rich repeat-containing protein 69***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	44
A0A384B088_BALAS ***uncharacterized protein C3orf20 homolog***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	43
A0A340XGD2_LIPVE ***matrix-remodeling-associated protein 5***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	42
A0A2F0BBC1_ESCRO ***Retinal dehydrogenase 1***	*Eschrichtius robustus*	Gray whale	42
A0A2F0BPS3_ESCRO ***Phosphoglycerate kinase***	*Eschrichtius robustus*	Gray whale	41

[ǂ]Ions score is -10*Log(P), where P is the probability that the observed match is a random event. Individual ions scores > 41 indicated identity or extensive homology ($p < 0.05$). Protein scores were derived from ions scores as a non-probabilistic basis for ranking protein hits. Cut-off was set at Ions score 20.

Supplementary Table 5. Deiminated proteins identified by F95 enrichment in serum of Cuvier's beaked whale (*Ziphius cavirostris*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot. Peptide hits scoring with the cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues) are shown. Species hit names and total scores are shown.

Protein name	Species name	Common name	Total score ($p<0.05$)[‡]
A0A383ZXR0_BALAS ***serum albumin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1159
A0A341C5T8_9CETA ***serum albumin***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	1156
A0A2U3V5M2_TURTR ***serum albumin***	*Tursiops truncatus*	Common bottlenose dolphin	1088
A0A140GN64_BALAC ***Hemoglobin subunit beta***	*Balaenoptera acutorostrata*	Northern minke whale	1003
A0A384AGF6_BALAS ***Fructose-bisphosphate aldolase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	970
A0A384B912_BALAS ***alpha-2-macroglobulin isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	932
A0A140GN67_MESDE ***Hemoglobin subunit beta***	*Mesoplodon densirostris*	Blainville's beaked whale	847
A0A2Y9NE67_DELLE ***alpha-2-macroglobulin isoform X2***	*Delphinapterus leucas*	Beluga whale	736
A0A344X2S6_GLOME ***Hemoglobin subunit beta***	*Globicephala melas*	Long-finned pilot whale	714
P02182|MYG_ZIPCA ***Myoglobin***	*Ziphius cavirostris*	Cuvier's beaked whale	696
A0A140GN07_MESDE ***Hemoglobin subunit alpha***	*Mesoplodon densirostris*	Blainville's beaked whale	637
A0A2Y9NWW8_DELLE ***L-lactate dehydrogenase***	*Delphinapterus leucas*	Beluga whale	559
A0A2Y9EHS1_PHYMC ***hemoglobin subunit beta-1/2 isoform X2***	*Physeter macrocephalus*	Sperm whale	520
A0A140GN06_TURTR ***Hemoglobin subunit alpha***	*Tursiops truncatus*	Common bottlenose dolphin	447
A0A140GN13_BALAC ***Hemoglobin subunit alpha***	*Balaenoptera acutorostrata*		445
A0A140GN14_PHYMC ***Hemoglobin subunit alpha***	*Physeter macrocephalus*	Sperm whale	403
A0A340WLD3_LIPVE ***fibrinogen beta chain isoform X2***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	390
A0A140GN09_KOGSI ***Hemoglobin subunit alpha***	*Kogia sima*	Dwarf sperm whale	364
A0A140GN68_KOGSI ***Hemoglobin subunit beta***	*Kogia sima*	Dwarf sperm whale	348
A0A4U1FNC5_MONMO ***Uncharacterized protein***	*Monodon monoceros*	Narwhal	346
A0A2U4AKU6_TURTR ***glycine amidinotransferase, mitochondrial isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	269
A0A2Y9EYT5_PHYMC ***Catalase***	*Physeter macrocephalus*	Sperm whale	269

A0A340WJU5_LIPVE ***alpha-1-antitrypsin isoform X2***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	269
A0A2U4AKU6_TURTR ***Glyceraldehyde-3-phosphate dehydrogenase***	*Tursiops truncatus*	Common bottlenose dolphin	260
A0A383ZV20_BALAS ***alpha-1-antitrypsin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	246
A0A341AN91_9CETA ***Haptoglobin***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	244
A0A4U1EJD5_MONMO ***TAF domain-containing protein***	*Monodon monoceros*	Narwhal	243
A0A2F0AZL3_ESCRO ***Histone H2B***	*Eschrichtius robustus*	Gray whale	238
A0A2F0AXA3_ESCRO ***Pyruvate kinase***	*Eschrichtius robustus*	Gray whale	237
A0A2F0B4J5_ESCRO ***Hemoglobin subunit alpha***	*Eschrichtius robustus*	Gray whale	235
A0A2F0BMF7_ESCRO ***Histone H2B***	*Eschrichtius robustus*	Gray whale	231
A0A340Y1E6_LIPVE ***keratin, type I cytoskeletal 14***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	226
A0A2Y9FPM0_PHYMC ***phosphoglucomutase-1 isoform X2***	*Physeter macrocephalus*	Sperm whale	220
A0A2F0BAV1_ESCRO ***Keratin, type I cytoskeletal 14***	*Eschrichtius robustus*	Gray whale	206
A0A2U4AC17_TURTR ***homogentisate 1,2-dioxygenase***	*Tursiops truncatus*	Common bottlenose dolphin	198
A0A2U4AM45_TURTR ***carbonic anhydrase 3***	*Tursiops truncatus*	Common bottlenose dolphin	186
A0A2F0B1I9_ESCRO ***Beta-enolase***	*Eschrichtius robustus*	Gray whale	184
A0A2U4CBF1_TURTR ***keratin, type II cytoskeletal 5***	*Tursiops truncatus*	Common bottlenose dolphin	168
A0A383ZJG1_BALAS ***basement membrane-specific heparan sulfate proteoglycan core protein***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	164
A0A2Y9EU52_PHYMC ***Triosephosphate isomerase***	*Physeter macrocephalus*	Sperm whale	163
A0A2Y9MCX1_DELLE ***Hemopexin***	*Delphinapterus leucas*	Beluga whale	163
A0A383Z5R5_BALAS ***serotransferrin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	163
A0A2U3V7Z3_TURTR ***peroxiredoxin-1***	*Tursiops truncatus*	Common bottlenose dolphin	159
A0A340XVL6_LIPVE ***Ferritin***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	158
A0A2U3V0H1_TURTR ***betaine-homocysteine S-methyltransferase 1***	*Tursiops truncatus*	Common bottlenose dolphin	157
A0A384BCE5_BALAS ***Fructose-bisphosphate aldolase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	156
A0A2F0B042_ESCRO ***Hemopexin***	*Eschrichtius robustus*	Gray whale	150

A0A341AG71_9CETA ***titin***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	148
A0A2Y9N3W5_DELLE ***keratin, type II cytoskeletal 5-like***	*Delphinapterus leucas*	Beluga whale	143
A0A2U4BKU4_TURTR ***protein 4.1 isoform X5***	*Tursiops truncatus*	Common bottlenose dolphin	136
A0A2U4B9J5_TURTR ***ceruloplasmin isoform X2***	*Tursiops truncatus*	Common bottlenose dolphin	135
A0A2Y9M110_DELLE ***complement C3 isoform X1***	*Delphinapterus leucas*	Beluga whale	134
A0A2F0AYW0_ESCRO ***Ig lambda-6 chain C region***	*Eschrichtius robustus*	Gray whale	127
A0A2U3V5S9_TURTR ***kininogen-1 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	122
A0A2Y9F6G6_PHYMC ***fibrinogen gamma chain isoform X2***	*Physeter macrocephalus*	Sperm whale	115
A0A384ANK3_BALAS ***thyroglobulin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	112
A0A2F0AYR9_ESCRO ***Glucose-6-phosphate isomerase***	*Eschrichtius robustus*	Gray whale	96
A0A383YWT8_BALAS ***complement factor H-like isoform X1***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	89
A0A2U3VA32_TURTR ***Protein S100***	*Tursiops truncatus*	Common bottlenose dolphin	87
A0A2U3V321_TURTR ***four and a half LIM domains protein 1 isoform X2***	*Tursiops truncatus*	Common bottlenose dolphin	86
A0A2U4B948_TURTR ***serotransferrin***	*Tursiops truncatus*	Common bottlenose dolphin	76
A0A340WU44_LIPVE ***immunoglobulin lambda-like polypeptide 5***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	75
A0A2Y9M0C5_DELLE ***nesprin-1 isoform X9***	*Delphinapterus leucas*	Beluga whale	73
A0A2Y9F931_PHYMC ***carbonic anhydrase 2 isoform X1***	*Physeter macrocephalus*	Sperm whale	73
A0A2F0BGI8_ESCRO ***Prelamin-A/C***	*Eschrichtius robustus*	Gray whale	70
A0A2U4CLI2_TURTR ***Adenosylhomocysteinase***	*Tursiops truncatus*	Common bottlenose dolphin	70
A0A2F0BP97_ESCRO ***Ig mu heavy chain disease protein***	*Eschrichtius robustus*	Gray whale	69
A0A2U3VA11_TURTR ***carbonic anhydrase 1***	*Tursiops truncatus*	Common bottlenose dolphin	64
A0A2U4AJY5_TURTR ***glutamate dehydrogenase 1, mitochondrial***	*Tursiops truncatus*	Common bottlenose dolphin	64
A0A2F0BN89_ESCRO ***Inter-alpha-trypsin inhibitor heavy chain H4***	*Eschrichtius robustus*	Gray whale	63

A0A2U3V937_TURTR ***Proteasome subunit alpha type***	*Tursiops truncatus*	Common bottlenose dolphin	62
APOA1_BALAS ***Apolipoprotein A-I***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	61
A0A2F0BG39_ESCRO ***Eosinophil peroxidase***	*Eschrichtius robustus*	Gray whale	60
A0A0N7EHN7_DELCA ***C1Q and collagen domain containing adiponectin***	*Delphinus capensis*	Long-beaked common dolphin	60
A0A340WNM5_LIPVE ***obscurin-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	57
A0A384AT03_BALAS ***coiled-coil domain-containing protein 150***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	57
A0A2Y9EWF4_PHYMC ***Alpha-1,4 glucan phosphorylase***	*Physeter macrocephalus*	Sperm whale	55
A0A2U4BQ96_TURTR ***adenylate cyclase type 1***	*Tursiops truncatus*	Common bottlenose dolphin	55
A0A2F0BCJ0_ESCRO ***Complement C4-B***	*Eschrichtius robustus*	Gray whale	54
A0A383ZUH3_BALAS ***DNA excision repair protein ERCC-6 isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	53
A0A2F0BKF1_ESCRO ***60S ribosomal protein L8***	*Eschrichtius robustus*	Gray whale	52
A0A340YCM8_LIPVE ***C4b-binding protein alpha chain-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	48
A0A2Y9P779_DELLE ***creatine kinase M-type***	*Delphinapterus leucas*	Beluga whale	45
A0A2U4BWA9_TURTR ***radixin isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	45
A0A2U4B5X8_TURTR ***flavin reductase (NADPH)***	*Tursiops truncatus*	Common bottlenose dolphin	44
A0A2U4B008_TURTR ***cilia- and flagella-associated protein 45 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	43
A0A340X7S9_LIPVE ***Plasminogen***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	42
A0A2F0AV78_ESCRO ***Dipeptidyl peptidase 9***	*Eschrichtius robustus*	Gray whale	42
A0A2Y9FG23_PHYMC ***Peptidyl-prolyl cis-trans isomerase***	*Physeter macrocephalus*	Sperm whale	42
A0A2U3V024_TURTR ***C-C motif chemokine 17***	*Tursiops truncatus*	Common bottlenose dolphin	41

[ǂ]Ions score is -10*Log(P), where P is the probability that the observed match is a random event. Individual ions scores > 41 indicated identity or extensive homology ($p < 0.05$). Protein scores were derived from ions scores as a non-probabilistic basis for ranking protein hits. Cut-off was set at Ions score 20.

Supplementary Table 6. Deiminated proteins identified by F95 enrichment in serum of orca (*Orcinus orca*). Deiminated proteins were isolated by immunoprecipitation using the pan-deimination F95 antibody. The F95 enriched eluate was analysed by LC-MS/MS and peak list files were submitted to mascot . Peptide hits scoring with the cetacean database (CCP_Cetacea Cetacea_20191213; 252,001 sequences; 150,129,595 residues) are shown. Species hit names and total scores are shown.

Protein name	Species name	Common name	Total score (p<0.05)[‡]
A0A341C5T8_9CETA ***serum albumin***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	2358
A0A2U3V5M2_TURTR ***serum albumin isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	2336
A0A2U4B948_TURTR ***serotransferrin***	*Tursiops truncatus*	Common bottlenose dolphin	2322
A0A2Y9QJ69_DELLE ***serum albumin***	*Delphinapterus leucas*	Beluga whale	2149
A0A383ZXR0_BALAS ***serum albumin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	2086
A0A2Y9NK15_DELLE ***alpha-2-macroglobulin isoform X3***	*Delphinapterus leucas*	Beluga whale	1928
A0A4U1FPV0_MONMO ***Uncharacterized protein***	*Monodon monoceros*	Narwhal	1883
A0A2U3V5S9_TURTR ***kininogen-1 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	1880
A0A384B912_BALAS ***alpha-2-macroglobulin isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	1800
A0A2U4AKU7_TURTR ***alpha-2-macroglobulin-like***	*Tursiops truncatus*	Common bottlenose dolphin	1763
A0A340Y7Z8_LIPVE ***serum albumin***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	1762
A0A2Y9P4F8_DELLE ***serotransferrin-like***	*Delphinapterus leucas*	Beluga whale	1703
A0A2Y9N2V9_DELLE ***kininogen-1 isoform X1***	*Delphinapterus leucas*	Beluga whale	1590
A0A2U4CD99_TURTR ***fibronectin isoform X4***	*Tursiops truncatus*	Common bottlenose dolphin	1374
A0A455BHA9_PHYMC ***alpha-2-macroglobulin-like***	*Physeter macrocephalus*	Sperm whale	1290
A0A341DCM8_9CETA ***kininogen-1 isoform X2***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	1173
A0A2U4CD99_TURTR ***hemopexin***	*Tursiops truncatus*	Common bottlenose dolphin	1046
A0A484GXQ7_SOUCH ***Hemopexin***	*Sousa chinensis*	Indo-Pacific humpbacked dolphin	1039
A0A340WVC6_LIPVE ***kininogen-1 isoform X1***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	867
A0A341CEB0_9CETA ***Hemopexin***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	801
A0A387L946_PSECS ***Complement component 4A***	*Pseudorca crassidens*	False killer whale	750
A0A140GN64_BALAC ***Hemoglobin subunit beta***	*Balaenoptera acutorostrata*	Northern minke whale	748
A0A2Y9MCX1_DELLE ***Hemopexin***	*Delphinapterus leucas*	Beluga whale	741

A0A2Y9MIR4_DELLE ***complement C4-like isoform X1***	*Delphinapterus leucas*	Beluga whale	712
A0A340XNP3_LIPVE ***complement C3***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	707
A0A2F0B042_ESCRO ***Hemopexin***	*Eschrichtius robustus*	Gray whale	694
A0A2Y9M110_DELLE ***complement C3 isoform X1***	*Delphinapterus leucas*	Beluga whale	670
A0A341BIQ3_9CETA ***complement C3***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	612
A0A2U3V5U9_TURTR ***complement factor H isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	565
A0A140GN67_MESDE ***Hemoglobin subunit beta***	*Mesoplodon densirostris*	Blainville's beaked whale	546
A0A383Z5R5_BALAS ***serotransferrin***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	534
A0A2U4CNJ3_TURTR ***Plasminogen***	*Tursiops truncatus*	Common bottlenose dolphin	531
A0A2U4CQ05_TURTR ***C4b-binding protein alpha chain***	*Tursiops truncatus*	Common bottlenose dolphin	472
A0A455BL00_PHYMC ***ceruloplasmin***	*Physeter macrocephalus*	Sperm whale	445
A0A383Z9Z9_BALAS ***Alpha-mannosidase***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	437
A0A4U1ETI6_MONMO ***Alpha-mannosidase***	*Monodon monoceros*	Narwhal	435
A0A2Y9N1N7_DELLE ***inter-alpha-trypsin inhibitor heavy chain H4 isoform X4***	*Delphinapterus leucas*	Beluga whale	434
A0A484GU10_SOUCH ***Uncharacterized protein***	*Sousa chinensis*	Indo-Pacific humpbacked dolphin	428
A0A2U4B9J5_TURTR ***ceruloplasmin isoform X2***	*Tursiops truncatus*	Common bottlenose dolphin	401
A0A340XE64_LIPVE ***complement factor H-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	397
A0A2Y9MD96_DELLE ***CD5 antigen-like***	*Delphinapterus leucas*	Beluga whale	393
A0A344X2S6_GLOME ***Hemoglobin subunit beta***	*Globicephala melas*	Long-finned pilot whale	389
A0A2Y9TJG8_PHYMC ***complement C3***	*Physeter macrocephalus*	Sperm whale	382
A0A484GS12_SOUCH ***Haptoglobin***	*Sousa chinensis*	Indo-Pacific humpbacked dolphin	357
A0A140GN13_BALAC ***Hemoglobin subunit alpha***	*Balaenoptera acutorostrata*	Northern minke whale	309
A0A341BX82_9CETA ***C4b-binding protein alpha chain isoform X2***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	302
A0A384ALG4_BALAS ***ceruloplasmin isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	299
A0A2U4C0C1_TURTR ***apolipoprotein B-100***	*Tursiops truncatus*	Common bottlenose dolphin	287

A0A2U4AL13_TURTR ***pregnancy zone protein-like***	*Tursiops truncatus*	Common bottlenose dolphin	272
A0A140GN07_MESDE ***Hemoglobin subunit alpha***	*Mesoplodon densirostris*	Blainville's beaked whale	270
A0A2F0AYW0_ESCRO ***Ig lambda-6 chain C region***	*Eschrichtius robustus*	Gray whale	265
A0A4U1FNC5_MONMO ***Uncharacterized protein***	*Monodon monoceros*	Narwhal	264
A0A340WU44_LIPVE ***immunoglobulin lambda-like polypeptide 5***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	261
A0A2U4B4R7_TURTR ***vitamin D-binding protein***	*Tursiops truncatus*	Common bottlenose dolphin	251
A0A140GN68_KOGSI ***Hemoglobin subunit beta***	*Kogia sima*	Dwarf sperm whale	251
A0A2Y9LCY9_DELLE ***basement membrane-specific heparan sulfate proteoglycan core protein isoform X3***	*Delphinapterus leucas*	Beluga whale	244
A0A2F0B4J5_ESCRO ***Hemoglobin subunit alpha***	*Eschrichtius robustus*	Gray whale	243
A0A341CUQ2_9CETA ***complement C5***	*Neophocaena asiaeorientalis asiaeorientalis*	Yangtze finless porpoise	235
A0A2Y9NPG1_DELLE ***pregnancy zone protein-like***	*Delphinapterus leucas*	Beluga whale	235
A0A2U4BJL8_TURTR ***basement membrane-specific heparan sulfate proteoglycan core protein***	*Tursiops truncatus*	Common bottlenose dolphin	228
A0A2U3V9T1_TURTR ***fibrinogen alpha chain***	*Tursiops truncatus*	Common bottlenose dolphin	218
A0A2Y9LZH5_DELLE ***apolipoprotein A-I***	*Delphinapterus leucas*	Beluga whale	213
A0A383Z8T4_BALAS ***C4b-binding protein alpha chain isoform X7***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	212
A0A2U4CBF1_TURTR ***keratin, type II cytoskeletal 5***	*Tursiops truncatus*	Common bottlenose dolphin	206
A0A383ZRJ1_BALAS ***keratin, type I cytoskeletal 14***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	201
A0A140GN09_KOGSI ***Hemoglobin subunit alpha***	*Kogia sima*	Dwarf sperm whale	188
A0A340WSC2_LIPVE ***keratin, type II cytoskeletal 5 isoform X1***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	186
A0A2U4AXD6_TURTR ***selenoprotein P***	*Tursiops truncatus*	Common bottlenose dolphin	164
A0A2F0BAV1_ESCRO ***Keratin, type I cytoskeletal 14***	*Eschrichtius robustus*	Gray whale	162
A0A2Y9F6G6_PHYMC ***fibrinogen gamma chain isoform X2***	*Physeter macrocephalus*	Sperm whale	156
P0DMA6|APOA1_BALAS ***Apolipoprotein A-I***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	152
A0A2U3V4Z9_TURTR ***fibrinogen beta chain***	*Tursiops truncatus*	Common bottlenose dolphin	151

A0A2Y9F6G0_PHYMC ***fibrinogen beta chain isoform X1***	*Physeter macrocephalus*	Sperm whale	150
A0A484H0L9_SOUCH ***Uncharacterized protein***	*Sousa chinensis*	Indo-Pacific humpbacked dolphin	136
A0A340WCV4_LIPVE ***alpha-1-antitrypsin isoform X1***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	125
A0A340WNM5_LIPVE ***obscurin-like***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	118
A0A340WNM5_LIPVE ***Fructose-bisphosphate aldolase***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	114
A0A4U1EB65_MONMO ***Ig-like domain-containing protein***	*Monodon monoceros*	Narwhal	109
A0A484H0M4_SOUCH ***IGv domain-containing protein***	*Sousa chinensis*	Indo-Pacific humpbacked dolphin	109
A0A2Y9PG29_DELLE ***Glutathione peroxidase***	*Delphinapterus leucas*	Beluga whale	100
A0A2F0BP97_ESCRO ***Ig mu heavy chain disease protein***	*Eschrichtius robustus*	Gray whale	98
A0A2U3V1T4_TURTR ***complement C1q subcomponent subunit A***	*Tursiops truncatus*	Common bottlenose dolphin	98
A0A2U4BME2_TURTR ***galectin-3-binding protein***	*Tursiops truncatus*	Common bottlenose dolphin	91
A0A4U1ECF0_MONMO ***Ig-like domain-containing protein***	*Monodon monoceros*	Narwhal	85
A0A2U4APV3_TURTR ***L-lactate dehydrogenase***	*Tursiops truncatus*	Common bottlenose dolphin	82
A0A2U3V4E2_TURTR ***beta-2-glycoprotein 1 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	81
A0A2F0AY95_ESCRO ***Complement C1q subcomponent subunit C***	*Eschrichtius robustus*	Gray whale	76
A0A2F0BAH8_ESCRO ***Complement factor B***	*Eschrichtius robustus*	Gray whale	69
A0A2U3V982_TURTR ***immunoglobulin J chain isoform X2***	*Tursiops truncatus*	Common bottlenose dolphin	65
A0A2U4AGU1_TURTR ***RNA-binding protein 27 isoform X1***	*Tursiops truncatus*	Common bottlenose dolphin	56
Q0KIY9|MYG_INDPC ***Myoglobin***	*Indopacetus pacificus*	Tropical bottlenose whale	52
A0A2Y9NX77_DELLE ***Piezo-type mechanosensitive ion channel component***	*Delphinapterus leucas*	Beluga whale	51
A0A2U4BAA2_TURTR ***protein kinase C-binding protein NELL2 isoform X3***	*Tursiops truncatus*	Common bottlenose dolphin	51

A0A2U3VA11_TURTR ***carbonic anhydrase 1***	*Tursiops truncatus*	Common bottlenose dolphin	49
A0A2F0AZJ9_ESCRO ***Histone H2A***	*Eschrichtius robustus*	Gray whale	49
A0A2Y9SDE6_PHYMC ***SEC14-like protein 3***	*Physeter macrocephalus*	Sperm whale	49
A0A4U1EBP7_MONMO ***IGv domain-containing protein***	*Monodon monoceros*	Narwhal	48
A0A2F0B5R5_ESCRO ***Complement component C8 alpha chain***	*Eschrichtius robustus*	Gray whale	48
A0A340WK61_LIPVE ***autophagy-related protein 2 homolog B***	*Lipotes vexillifer*	Baiji (white-finned dolphin)	47
A0A2U3V609_TURTR ***afamin***	*Tursiops truncatus*	Common bottlenose dolphin	47
A0A2Y9MDP5_DELLE ***extracellular matrix protein 1 isoform X1***	*Delphinapterus leucas*	Beluga whale	45
A0A2Y9FWE7_PHYMC ***complement factor D***	*Physeter macrocephalus*	Sperm whale	43
A0A2Y9QED7_DELLE ***huntingtin-interacting protein 1-related protein isoform X2***	*Delphinapterus leucas*	Beluga whale	43
A0A2Y9Q1L2_DELLE ***polymeric immunoglobulin receptor***	*Delphinapterus leucas*	Beluga whale	42
A0A0N7EHN7_DELCA ***C1Q and collagen domain containing adiponectin***	*Delphinus capensis*	Long-beaked common dolphin	42
A0A383ZKS2_BALAS ***DENN domain-containing protein 5B isoform X2***	*Balaenoptera acutorostrata scammoni*	Scammon's minke whale	41
A0A2F0BJB3_ESCRO ***Prothrombin***	*Eschrichtius robustus*	Gray whale	41
A0A2F0BL32_ESCRO ***Peptidyl-tRNA hydrolase 2, mitochondrial***	*Eschrichtius robustus*	Gray whale	41

[ǂ]Ions score is -10*Log(P), where P is the probability that the observed match is a random event. Individual ions scores > 41 indicated identity or extensive homology ($p < 0.05$). Protein scores were derived from ions scores as a non-probabilistic basis for ranking protein hits. Cut-off was set at Ions score 20.