Electronic Supplementary Material (ESI) for Molecular BioSystems.

Salivary Proteins exhibiting higher condition among subject groups			
Protein Name/Gene/Sequence ID	**W**	**T**	**Function**
Immunoglobulin J Chain (IGJ) P01591	H	H	Serves to link two monomer units of either IgM or IgA. In the case of IgM, the J chain-joined dimer is a nucleating unit for the IgM pentamer, and in the case of IgA it induces larger polymers. It also helps to bind these immunoglobulins to secretory component.
Uteroglobin (UTER) P11684	H	H, S3	Binds phosphatidylcholine, phosphatidylinositol, polychlorinated biphenyls (PCB) and weakly progesterone, potent inhibitor of phospholipase A2.
Carbonic anhydrase 6 (CAH6) P23280	H	H, S3	Reversible hydration of carbon dioxide. Its role in saliva is unknown.
Lysozyme C (LYSC) P23280	H	H	Lysozymes have primarily a bacteriolytic function; those in tissues and body fluids are associated with the monocyte-macrophage system and enhance the activity of immunoagents.
Beta-2-microglobulin (B2MG) P61769	H	H, S3	Component of the class I major histocompatibility complex (MHC). Involved in the presentation of peptide antigens to the immune system.
Uncharacterized protein UNQ773/PRO1567 (YP003) Q96DR5	H	H	No known function.
Short palate, lung and nasal epithelium carcinoma-associated protein 2 (SPLC2) Q96DR5	H	H, S3	Involved in host defense response against bacteria. Found in upper respiratory track.[40, 41]

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Polymeric immunoglobulin receptor (PIGR) P01833	H, S2	H, S2	This receptor binds polymeric IgA and IgM at the basolateral surface of epithelial cells. The complex is then transported across the cell to be secreted at the apical surface. During this process a cleavage occurs that separates the extracellular (known as the secretory component) from the transmembrane segment.
Ig alpha-1 chain C region (IGHA1) P01876	H, S2	H, S3	Ig alpha is the major immunoglobulin class in body secretions. It may serve both to defend against local infection and to prevent access of foreign antigens to the general immunologic system.
Zinc-alpha-2-glycoprotein (ZA2G) P25311	H, S2	H	Stimulates lipid degradation in adipocytes and causes the extensive fat losses associated with some advanced cancers. May bind polyunsaturated fatty acids.
Lipocalin-1 (LCN1) P31025	H, S2	H, S2	Could play a role in taste reception. Could be necessary for the concentration and delivery of sapid molecules in the gustatory system. Can bind various ligands, with chemical structures ranging from lipids and retinoids to the macrocyclic antibiotic rifampicin and even to microbial siderophores. Exhibits an extremely wide ligand pocket.
Alpha-amylase 1 (AMY1) P04745	H, S3	H, S3	Breaks down carbohydrates.
Submaxillary gland androgen-regulated protein 3B (SMR3B) P02814	S2	S2	No known function
Kallikren-1 (KLK1) P06870	S2	H, S2	Glandular kallikreins cleave Met-Lys and Arg-Ser bonds in kininogen to release Lys-bradykinin.

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Thioredoxin (THIO) P10599	S2	S2, S3	Common protein that acts as reducing agent in electron transfer function.[42]
Neutrophil gelatinase-associated lipocalin (NGAL) P80188	S2	S2, S3	Iron-trafficking protein involved in multiple processes such as apoptosis, innate immunity and renal development. Binds iron through association with 2,5-dihydroxybenzoic acid (2,5-DHBA), a siderophore that shares structural similarities with bacterial enterobactin, and delivers or removes iron from the cell, depending on the context. Iron-bound form (holo-24p3) is internalized following binding to the SLC22A17 (24p3R) receptor, leading to release of iron and subsequent increase of intracellular iron concentration. In contrast, association of the iron-free form (apo-24p3) with the SLC22A17 (24p3R) receptor is followed by association with an intracellular siderophore, iron chelation and iron transfer to the extracellular medium, thereby reducing intracellular iron concentration. Involved in apoptosis due to interleukin-3 (IL3) deprivation: iron-loaded form increases intracellular iron concentration without promoting apoptosis, while iron-free form decreases intracellular iron levels, inducing expression of the proapoptotic protein BCL2L11/BIM, resulting in apoptosis. Involved in innate immunity, possibly by sequestrating iron, leading to limit bacterial growth
Alpha-1-antitrypsin (A1AT) P01009	S2, S3	S3	Inhibitor of serine proteases. Its primary target is elastase, but it also has a moderate affinity for plasmin and thrombin. Irreversibly inhibits trypsin, chymotrypsin and plasminogen activator. The aberrant form inhibits insulin-induced NO synthesis in platelets, decreases coagulation time and has proteolytic activity against insulin and plasmin.

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Alpha-1-macroglobulin (A2MG) P01023	S2, S3	S3	Is able to inhibit all four classes of proteinases by a unique 'trapping' mechanism. This protein has a peptide stretch, called the 'bait region' which contains specific cleavage sites for different proteinases. When a proteinase cleaves the bait region, a conformational change is induced in the protein which traps the proteinase. The entrapped enzyme remains active against low molecular weight substrates (activity against high molecular weight substrates is greatly reduced). Following cleavage in the bait region a thioester bond is hydrolyzed and mediates the covalent binding of the protein to the proteinase.
Complement C3 (CO3) P01024	S2, S3	S3	C3 plays a central role in the activation of the complement system. Its processing by C3 convertase is the central reaction in both classical and alternative complement pathways. After activation C3b can bind covalently, via its reactive thioester, to cell surface carbohydrates or immune aggregates. Derived from proteolytic degradation of complement C3, C3a anaphylatoxin is a mediator of local inflammatory process. It induces the contraction of smooth muscle, increases vascular permeability and causes histamine release from mast cells and basophilic leukocytes.
Cystatin-SN (CYTN) P01037	S2, S3	S3	Human saliva appears to contain several cysteine proteinase inhibitors that are immunologically related to cystatin S but that differ in their specificity due to amino acid sequence differences. Cystatin SN, with a pI of 7.5, is a much better inhibitor of papain and dipeptidyl peptidase I than is cystatin S, although both inhibit ficin equally well.
Ig lambda chain C regions (LAC) P01842	S2, S3	H, S3	Part of humoral mediated B cell immune response.

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Ig gamma-1 chain C region (IGHG1) P01857	S2, S3	S3	Part of humoral mediated B cell immune response.
Ig gamma-2 chain C region (IGHG2) P01859	S2, S3	S3	Part of humoral mediated B cell immune response.
Ig alpha-2 chain C region (IGHA2) P01877	S2, S3	H, S3	Part of humoral mediated B cell immune response.
Alpha-1-acid glycoprotein 1 (A1AG1) P02763	S2, S3	S3	Functions as transport protein in the blood stream. Binds various ligands in the interior of its beta-barrel domain. Also binds synthetic drugs and influences their distribution and availability in the body. Appears to function in modulating the activity of the immune system during the acute-phase reaction.
Lactotransferrin (TRFL) P02788	S2, S3	S3	Lactotransferrin is a major iron-binding and multifunctional protein found in exocrine fluids such as breast milk and mucosal secretions. Has antimicrobial activity, which depends on the extracellular cation concentration. Antimicrobial properties include bacteriostasis, which is related to its ability to sequester free iron and thus inhibit microbial growth, as well as direct bactericidal properties leading to the release of lipopolysaccharides from the bacterial outer membrane. Can also prevent bacterial biofilm development in P.aeruginosa infection. Has weak antifungal activity against C.albicans.
Hemopexin (HEMO) P02790	S2, S3	S3	Binds heme and transports it to the liver for breakdown and iron recovery, after which the free hemopexin returns to the circulation.

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Cystatin-SA (CYTT) P09228	S2, S3	S3	Thiol protease inhibitor. Expressed in submandibular and sublingual saliva but not in parotid saliva (at protein level). Expressed in submandibular gland and parotid gland.
Prolactin-inducible protein (PIP) P12273	S2, S3	H, S3	The protein has a physiological function in regulation of water transport mainly in apocrine glands in the axilla, vulva, eyelid, and ear canal serous cells of the submandibular salivary gland, serous cells of the submucosal glands of the bronchi, and accessory lacrimal glands as well as cutaneous eccrine glands.[43] PIP has the ability to bind immunoglobulin G (IgG), IgG-Fc, CD4-T cell receptor suggesting a wide range of immunological functions.[44,45] PIP can bind different species of bacteria showing highest affinity to sterptococci thus playing a role in non-immune defense of the body aginst pathogenic bacterial strains.[46,47]
Cystatin-D (CYTD) P28325	S2, S3	S3	Cysteine proteinase inhibitor that possibly plays a protective role against proteinases present in the oral cavity.
Hemoglobin subunit beta (HBB) P68871	S2, S3	S3	Involved in oxygen transport from the lung to the various peripheral tissues
Hemoglobin subunit alpha (HBA) P69905	S2, S3	S3	Involved in oxygen transport from the lung to the various peripheral tissues
Fatty acid-binding protein, epidermal (FABP5) Q01469	S2, S3	S3	High specificity for fatty acids. Highest affinity for C18 chain length. Decreasing the chain length or introducing double bonds reduces the affinity. May be involved in keratinocyte differentiation.

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Bactericidal/permeability-increasing protein-like 1 (BPIL1) Q8N4F0	S2, S3	S2	Anti-bacterial protein that is involved in innate immune response.
Ig kappa chain C region (IGKC) P01834	S3	S3	Part of humoral mediated B cell immune response.
Ig gamma-3 chain C region (IGHG3) P01834	S3	S3	Part of humoral mediated B cell immune response.
Apolipoprotein A-I (APOA1) P02647	S3	S3	Participates in the reverse transport of cholesterol from tissues to the liver for excretion by promoting cholesterol efflux from tissues and by acting as a cofactor for the lecithin cholesterol acyltransferase (LCAT). As part of the SPAP complex, activates spermatozoa motility.
Serum Albumin (ALBU) P02768	S3	S3	Serum albumin, the main protein of plasma, has a good binding capacity for water, Ca2+, Na+, K+, fatty acids, hormones, bilirubin and drugs. Its main function is the regulation of the colloidal osmotic pressure of blood. Major zinc transporter in plasma, typically binds about 80% of all plasma zinc.
Vitamin D-binding protein (VTDB) P02774	S3	S3	Multifunctional protein found in plasma, ascitic fluid, cerebrospinal fluid, and urine and on the surface of many cell types. In plasma, it carries the vitamin D sterols and prevents polymerization of actin by binding its monomers. DBP associates with membrane-bound immunoglobulin on the surface of B-lymphocytes and with IgG Fc receptor on the membranes of T-lymphocytes.

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Serotransferrin (TRFE) P02787	S3	S3	Transferrins are iron binding transport proteins which can bind two Fe3+ ions in association with the binding of an anion, usually bicarbonate. It is responsible for the transport of iron from sites of absorption and heme degradation to those of storage and utilization. Serum transferrin may also have a further role in stimulating cell proliferation.

W=WaterSnap System; T=ThermoObitrap System
H = healthy; S2 = Stomatitis type II; S3 = Stomatitis type III
ANOVA cutoff range $p < 0.01$. All function information presented is obtained from UniProt Protein Database, except for protein information indicated as referenced from an additional source.