



Experimental design considerations for studies of human tear proteins

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ABSTRACT

Purpose: Human tears contain abundant, diverse sets of proteins that may serve as biomarkers of ocular surface health. There is a need for reproducible methods that consider multiple factors influencing the tear proteome, in addition to the variable of interest. Here we examined a workflow for proteomic analysis of tear proteins without the need to pool tear samples from multiple individuals, thus allowing for analyses based on individual factors, and increasing opportunities for protein biomarker discovery.

Methods: Tears were collected by Schirmer strip following topical ocular anesthetic application then individually stored at -80°C prior to processing for proteomics. Tear proteins were extracted from Schirmer strips, digested using suspension trapping spin columns (S-Trap), and labeled with high multiplicity tandem mass tags (TMT). Peptide digests were then extensively fractionated by two-dimensional chromatography and analyzed by mass spectrometry to identify and measure changes in protein abundance in each sample. Analysis of select samples was performed to test protocols and to compare the impact of clinically relevant parameters. To facilitate comparison of separate TMT experiments, common pool samples were included in each TMT instrument run and internal reference scaling (IRS) was performed.

Results: Differences in subsets of tear proteins were noted for: geographic site of tear collection, contact lens use, and differences in tear fluid volume among individuals.

Conclusion: These findings demonstrate that proteomic analysis of human tear proteins can be performed without the need to pool samples, and that development of analytic workflows must consider factors that may affect outcomes in studies focused on diverse clinical samples.

1. Introduction

Human tears are critical in the maintenance of ocular surface homeostasis and exhibit differential composition in states of health and disease. A healthy tear film bathes the cornea and conjunctival tissues to provide constant hydration, supply oxygen and nutrients, and maintain a smooth refractive surface. Tears also impart physical, antimicrobial, and environmental protection; their secretion and content change dynamically in response to local, systemic, and even emotional

stimulation. Tear fluid has a relatively high protein content and proteins within the tear fluid arise primarily from the main lacrimal gland, but proteins have also been traced to serum and infiltrating immune cells [1]. With advancements in proteomic analysis techniques, patterns of change within the tear proteome have been identified in association with conditions ranging from dry eye disease and contact lens use to diabetes and Alzheimer's disease [2–5].

The non-invasive nature of sample collection and insight into physiologic and pathologic processes make tears an attractive source for

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biomarker discovery [6]. However, proteomic analysis of tear fluid presents challenges. Individual sample volumes are small, particularly when collected from participants with aqueous-deficient dry eye disease. Consequently, many early tear proteome studies relied on sample pooling from multiple individuals with particular conditions or attributes. Given the wide range of factors influencing the proteome, pooling participant samples based on one factor of interest may confound data analysis. In addition, high abundance proteins predominate in the composition of human tear fluid and can suppress detection of lower abundance proteins, which may also vary in expression levels between individuals and conditions [7]. Recent technical advances have increased the capacity for rapid protein identification and quantification [8]. However, in the absence of standardized protocols to improve reproducibility in proteomic techniques and data analysis, investigators face challenges in interpreting results across studies.

In the present study, we used isobaric labeling of samples with tandem mass tags (TMT) and subsequent fractionation to allow for parallel processing of individual tear samples and deeper sampling of the proteome, producing quantitative tear protein data with minimal missing values. Differential abundances of tear proteins are elucidated using data analytic pipelines for protein identification and quantification, extensive quality control analysis, and robust statistical comparisons. These methods were applied to compare the degree of influence of three different factors on human tear proteomes: Schirmer strip wetted length, geographic site of tear collection, and contact lens (CL) use.

2. Methods

2.1. Study workflow

Fig. 1 illustrates the workflow for the sample collection and proteomic analysis of human tear proteins. Tear samples were placed in tubes on dry ice for no more than 2 h prior to transfer to -80°C for storage. Other steps in the workflow are described in detail below.

2.2. Participants

Healthy individuals with no known ocular disease were recruited from two geographic sites to answer questionnaires and donate tear samples. The protocols used in this study have been approved by the Institutional Review Boards at both sites: Casey Eye Institute at the Oregon Health & Science University (OHSU) in Portland, Oregon (OR) and Bascom Palmer Eye Institute at the University of Miami in Miami, Florida (FL). The study was conducted in accordance with the principles of the Declaration of Helsinki and complied with the requirements of the United States Health Insurance Portability and Accountability Act. Written informed consent was obtained from all participants prior to any study activities unless only deidentified data were collected. Samples

were collected between November 2020 and January 2021.

2.3. Symptom questionnaires

Individual participants completed validated ocular symptom questionnaires including the 5-Item Dry Eye Questionnaire (DEQ5) and the Ocular Surface Disease Index (OSDI), and provided demographic information including sex, age, and CL use [9,10].

2.4. Tear collection

Tears were collected with Schirmer strips (Diagnostic Schirmer Tear Strips, Sports World Vision, Ireland) placed in both eyes simultaneously and left in place for 5 min. Standard clinical protocol was followed with Schirmer strips placed in the lateral aspect of the inferior conjunctival cul de sac [11]. The experimenter wore nitrile gloves when handling strips to minimize contamination. Most participants received topical anesthetic (0.5% proparacaine hydrochloride ophthalmic solution, Alcon Laboratories, Fort Worth, TX, NDC 61314-016-01, or Bausch and Lomb, Tampa, FL, NDC 24208-730-06) in both eyes 30 s prior to tear collection (see Results for participant details). Schirmer strips were removed from the eyes and the wetted length of the strip was recorded to the nearest millimeter (mm). Strips were then placed in individual sterile 2 ml polypropylene tubes (Thermo Fisher Scientific (TFS), cat # 346911, Waltham, MA, or Sarstedt, Inc., cat # 72.694.006, Newton, NC) and stored at -80°C until further processing.

For a control experiment examining the analytical effect of tear volume on the proteome (see 3.4), tears were collected by polystyrene capillary tube from 10 additional volunteers (5 females, 5 males) distinct from the participants described in 2.1. Capillary tubes were held on the tear meniscus near the lateral canthus for up to 5 min, or until additional movement of fluid up the capillary had stopped.

2.5. Sample preparation

2.5.1. Protein extraction, assay, and digestion

The proteomics workflow for this study is illustrated in Fig. 1. Schirmer strips were removed from -80°C storage, cut into approximately 3 mm square pieces using dissecting scissors (Fisher Scientific, cat # 08–940) and placed directly into 1.5 ml Eppendorf Lo-Bind tubes (cat # 022431081). Different tear sample collection and processing protocols have been shown to affect the proteins recovered for proteomic analysis [12]. To reduce potential sources of sample variation, both clinic sites used the same study materials, including Schirmer strips and sterile storage tubes from the same lot of a single manufacturer.

Tear proteins were extracted from Schirmer strips using 5% SDS in 100 mM HEPES buffer (pH 8). Aliquots were removed for bicinchoninic (BCA) assay (Pierce BCA assay kit, TFS, cat # 23225) to determine total

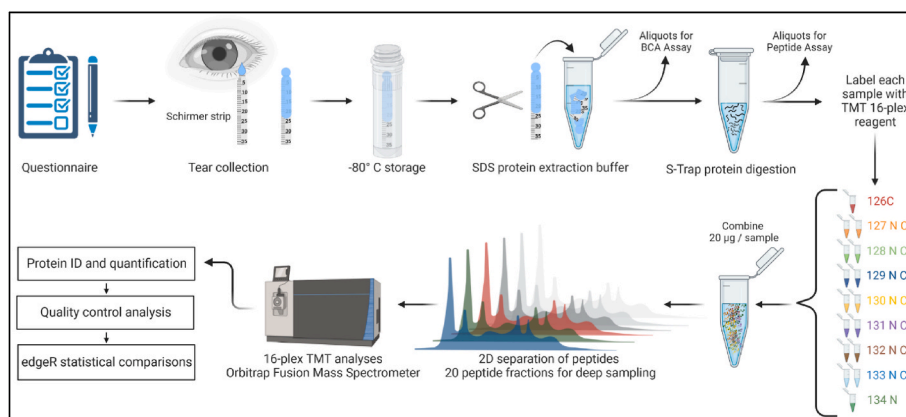


Fig. 1. Tandem mass tag (TMT) workflow for collection and analysis of human tear fluids. Created with BioRender.com.

protein recovered from the Schirmer strips [13]. Tear proteins were then applied to suspension-trapping (S-Trap) micro spin columns (Protifi, cat #C02-micro) for trypsin digestion using the manufacturer's recommended protocol and sequencing grade modified trypsin (ProMega, cat #V5111) [14,15]. The Pierce Quantitative Colorimetric Peptide Assay (TFS cat # 23275) was used to determine the amount of recovered peptides in each sample.

2.5.2. Common pool samples

To allow quantitative comparisons between TMT runs, a common pool of tears was created and included in each instrument run. The pool was created with Schirmer strips from at least one eye of 22 different individuals, and BCA protein assays were performed on individual extracts as described above. A total of 2.5 mg of combined tear proteins was then digested using S-Trap Midi columns (ProtiFi, C02-mini) with sequencing grade modified trypsin (as above). A Pierce peptide assay determined a yield of 2.3 mg of peptide, which was aliquoted and frozen at -80°C for use as an internal reference standard for the TMT analyses (see 2.6.3 below) [16].

2.5.3. Isobaric labeling and mass spectrometry analysis

For each instrument run, tears from up to 14 different samples (20 μg) were trypsin-digested and labeled using the TMTpro™ 16plex label reagents as per the manufacturer's protocol (TFS, A44522). Two channels per run were reserved for the common pool tear digest used for internal reference scaling. Samples were analyzed to identify and quantify the relative abundance of tear proteins using LC/MS analysis as described previously [16]. Briefly, following an initial small-scale mixing and analysis to normalize summed TMT reporter ion intensities, adjusted volumes of each labeled sample were mixed and multiplexed peptides separated by automated two-dimensional liquid chromatography. The first-dimension chromatography step separated the peptides into 20 fractions, and each of these was further separated using a 140 min nano reverse-phase chromatographic run interfaced to an Orbitrap Fusion Tribrid Mass Spectrometer (Thermo Scientific). Peptide identification used MS2 spectra, while quantification of TMT reporter ions for each peptide was performed using MS3 scans, which include additional fragmentation events [17].

2.6. Comparative analysis

2.6.1. Data processing

Peptide sequences associated with specific tear proteins were identified using the Comet search engine (version 2016.03) and proteomic analysis workflow pipeline as previously described using an UniProt protein sequence database (UP000005640, human, taxon ID 9606) containing 20,603 canonical protein sequences plus common contaminants. False discovery for peptide identification was below 1% [18,19]. Identified peptides were assembled into protein lists [20]. Proteins with 3 or more peptide spectral matches (PSMs) were considered to be confidently measured. Jupyter notebooks with an R kernel were used for data visualization and quality control testing.

2.6.2. Within-run comparisons of replicate samples

To test the reproducibility of the workflow and protocol, we collected Schirmer strips from 7 individuals, then cut each strip lengthwise for a total of 14 samples. The 14 half-strip samples were then processed through the workflow, as shown in Fig. 1.

2.6.3. Differential protein comparisons within groups

Statistical analyses were performed on all proteins with at least 3 PSMs using the Bioconductor package edgeR [21]. Additional criteria applied to analysis of candidate proteins for differential abundance included an uncorrected edgeR p value of <0.05 and a linear fold change of at least ± 1.5 [22,23]. Since these experiments were modestly sized and considered pilot studies, we opted a priori to focus on p-values and

magnitude of fold changes, and to not apply overly conservative adjustments for multiple comparisons at this stage of the analysis.

2.6.4. Internal reference scaling (IRS) normalization across studies of CL comparisons

Datasets from three smaller experiments were combined to compare the tear proteomes of CL users to those who do not use CLs. The combined dataset included samples from both tear collection sites (Casey Eye Institute, Portland, OR and Bascom Palmer Eye Institute, Miami, FL) and used internal reference scaling (IRS) normalization to achieve quantification across multiple TMT runs [16]. The common pool sample was used as the internal reference standard (see above 2.5.2). In this comparison, we used Benjamini-Hochberg adjustment to define a false discovery rate (FDR) for differential protein abundance. We used an FDR <0.1 as the criterion to identify differentially abundant proteins between the CL groups (users vs non-users).

2.6.5. Data visualizations

Volcano plots with color-coding were used to visualize proteins measured in each comparison (2.6.2), and proteins differentially expressed between CL and non-CL users. In each plot, x-axis values are the \log_2 fold changes and y-axis values are the \log_{10} uncorrected edgeR exact test p-values. Red and blue dots represent proteins that met PSM criteria, uncorrected edge R exact p value < 0.05 , and demonstrated an absolute fold change of 1.5 or more (>1.5 red, < -1.5 blue). For ease of comparison across studies, the volcano plot scales were identical. The MA plot (also known as Bland-Altman plot) was used to visualize comparisons between CL users and non-users in the combined study (2.6.3). In the MA plot, the x-axis values are the \log_{10} average intensity of the proteins and the y-axis values are \log_2 fold change, with red and blue dots representing proteins that meet the more rigorous statistical criteria detailed above and demonstrate an increase (red) or decrease (blue) in intensity in CL users as compared to non-CL users. Data visualizations were performed in R 3.6.2. Correlation data was visualized using Sigmaplot 14.5 (Inpixon, Palo Alto, CA).

3. Results

3.1. Participant characteristics

A total of 50 healthy individuals without known pre-existing ocular disease were recruited from two geographic sites (Casey Eye Institute, Portland, OR, and Bascom Palmer Eye Institute, Miami, FL) for this study (Table 1). Individual samples included in proteomic analyses were balanced within experiments for demographics and characteristics outside of the condition(s) being compared, when possible (Fig. 2).

3.2. Within-run comparisons of replicate samples for reproducibility

There were 3057 proteins detected in all 14 samples, and only 0.6% (19 proteins) met our criteria (see 2.6.1) for differential relative abundance between the half-strip replicates (Fig. 3A). These results demonstrate the high reproducibility of this workflow for tear sample preparation and proteomic analysis.

3.3. Within-subject comparisons: left eye versus right eye

We tested the degree of tear protein variation between the right and left eyes of participants, using protein extracted from 8 strips collected from 4 individuals at a single time point. This analysis identified 1987 proteins that were detected in all 8 samples. There was only 1 differentially abundant protein, representing 0.05% of total proteins that met our criteria of at least 3 PSMs, an uncorrected edgeR p-value of <0.05 , and a fold change of ± 1.5 . These results demonstrate a uniform protein expression between the two eyes of each healthy individual and further support the reproducibility of the study methods (Fig. 3B).

Table 1
Participant characteristics.

	Casey Eye Institute Portland, OR	Bascom Palmer Eye Institute Miami, FL
N	22	28
Sex	12 Females, 10 Males	19 Females, 9 Males
Age (years; Mean ± SEM)	35.9 ± 2.1	34.8 ± 1.9
Race	5 Asian, 0 Black, 15 White, 2 Other	2 Asian, 3 Black, 14 White, 9 Other
Ethnicity ^a	2 Hispanic, 13 Non-Hispanic	10 Hispanic, 17 Non-Hispanic
Soft Contact Lens (CL) use (% of participants)	43%	27%
OSDI Score (Mean ± SEM)	4.7 ± 1.1	3.4 ± 0.9
DEQ5 (Mean ± SEM)	6.1 ± 0.7	4.3 ± 0.9

^a Not answered by all participants.

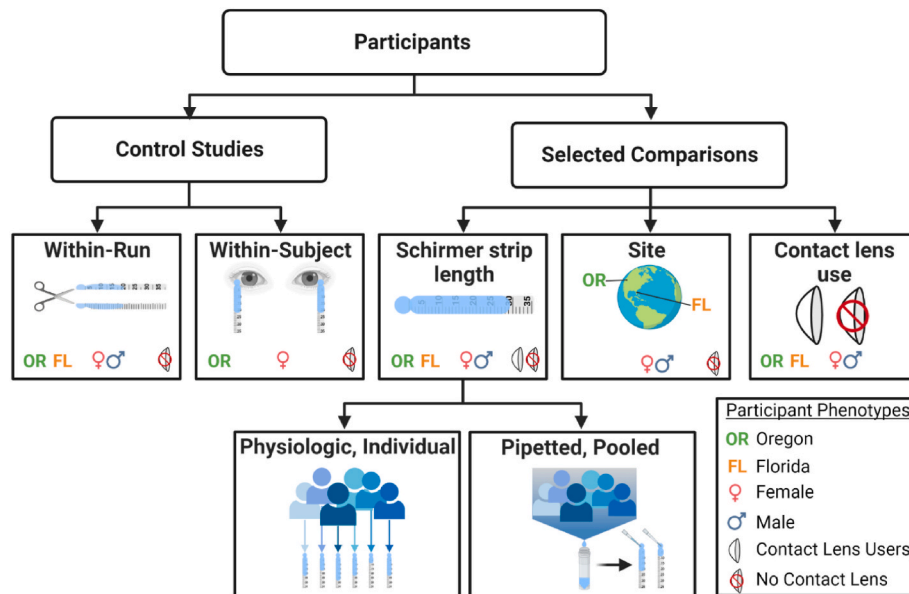


Fig. 2. Summary of proteomic control and selected comparisons and participant phenotypes within each comparison. Created with BioRender.com.

3.4. Proteomic changes related to tear volume

Study participants presented with a wide range of tear volumes as measured by Schirmer strip wetted length over a 5-min period. There was a moderate, but statistically significant trend to recover more protein from strips with higher wetted length (Linear regression: $R = 0.390$, $P = 0.007$) (Fig. 4), although there was a large variation in the total amount of tear protein recovered between individuals, suggesting the concentration of protein in tears of individuals varied substantially.

Given this variation in tear strip wetting and protein recovery, we investigated to what extent tear volume contributes to differential protein abundance across samples by conducting two comparisons. First, we

performed TMT analysis on 14 samples from individuals with large differences in tear volume. Samples designated as “short” had Schirmer tear strip wetted lengths of less than 10 mm (mean ± SEM: 8.1 ± 0.3 mm) and samples designated as “long” had Schirmer tear strip wetted lengths of 20 mm or greater (mean ± SEM: 31.4 ± 2.4 mm). A total of 2901 proteins were detected in all of these samples and 424 (14.6%) were differentially abundant based on our criteria (Methods 2.6.2.). A volcano plot demonstrates the number of proteins that were differentially abundant in the “long” tear strip samples compared to the “short” tear strip samples (Fig. 5A). Many proteins were more abundant in the long tear strips (348 proteins, red dots), and some proteins (76, blue dots) were less abundant in long tear strips compared to short tear strips.

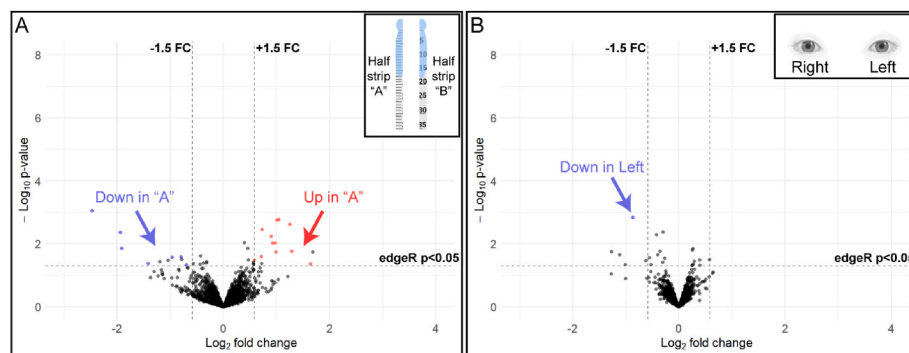


Fig. 3. Volcano plots of relative protein abundance in (A) replicates of strips cut in half ($n = 7$ eyes, 2 half-strips/eye, 14 half strips, inset) and (B) left and right eyes of the same individual ($n = 4$ people, 8 eyes, inset). X-axis values are the log₂ fold changes (FC) and y-axis values are the log₁₀ uncorrected edgeR exact test p-values. There were very few proteins that demonstrated an increase (red) or decrease (blue) in relative abundance in (A) half strip “A” as compared to half strip “B”. There was only 1 protein in the left eye (B) that demonstrated decreased (blue) relative abundance when compared to the right eye of the same participant. A complete list of differentially expressed proteins in the above comparisons can be found in Appendix Tables A.1 and A.2. Insets created with BioRender.com.

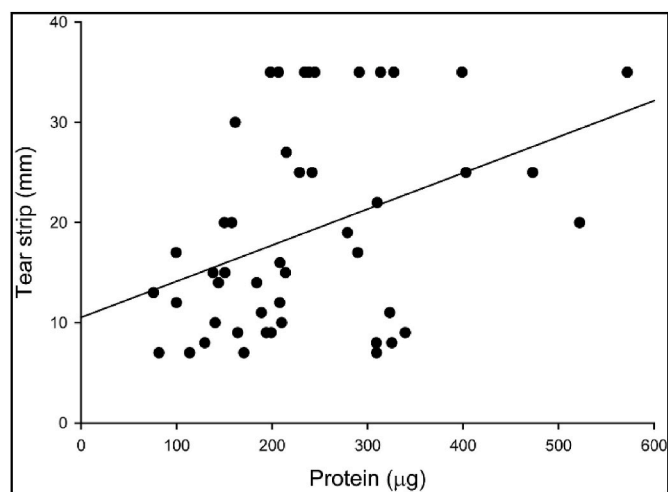


Fig. 4. Tear protein recovery increases with Schirmer strip wetted length across individual eyes, although there is wide variation. The total amount of protein (μg) recovered from each tear strip was plotted versus the Schirmer strip wetted length (mm). Each data point represents one sample from one eye. Some samples were collected from different eyes of the same participant; therefore, some individuals are represented more than once ($n = 47$ samples from 37 individuals).

Although equal amounts of recovered peptides were used for TMT labeling within each TMT analysis, differences in collected tear volumes and overall greater amounts of extracted protein in some tear strips (Fig. 4) could have altered the abundance of some proteins in the extracts. To examine the degree of variability in protein abundance based on volume alone, tear fluid from a pool of tears were pipetted onto Schirmer strips to create short and long Schirmer strip wetted lengths. Tears from 10 individuals were collected using polystyrene capillary tubes and pooled into a single volume. One of two different fixed amounts of volume (5 or 15 μl) from the pooled sample was pipetted onto 7 Schirmer strips, yielding an average wetted length of 8 mm (“short”) and 20 mm (“long”), respectively. The total amount of protein recovered from “long” strips (mean \pm SEM = $112.0 \pm 2.0 \mu\text{g}$) was significantly more than the amount of protein recovered from “short” strips (mean \pm SEM = $30.1 \pm 1.6 \mu\text{g}$; t -test, $P < 0.001$). The short ($n = 3$) and long ($n = 4$) Schirmer strips were then processed using the TMT workflow (Fig. 1). The TMT detected 1536 proteins in all of the samples, 2.2% ($n = 33$) of which were differentially abundant between the short and long tear strips (Fig. 5B). Most differentially detected proteins were

more abundant in the pipetted “short” strips, in contrast to the trend seen in tears from physiologically-determined strip lengths, i.e., the wetted length collected from a participant through standard 5-min clinical Schirmer testing (Fig. 5A). Thus, both the number and the direction of differential protein abundance in the pooled study (Fig. 5B) were distinct from the differences seen between individual participants with either high or low tear volumes (Fig. 5A).

3.5. Proteomic differences between geographic sites

The tear proteome was compared between samples collected at two geographic sites: Casey Eye Institute in Portland, OR, and Bascom Palmer Eye Institute in Miami, FL. Based on the significant impact of Schirmer strip wetted length on the tear proteome (Fig. 5A), we restricted between-site comparisons to a subgroup from each site that had similar Schirmer strip wetted lengths (10–14 mm). Of the 3498 total proteins detected (Fig. 6), 129 proteins (3.7%) were differentially abundant. There were both increased (51) and decreased (78) proteins detected in the Oregon (OR) samples ($n = 2$) as compared to the Florida (FL) samples ($n = 4$). While this study was not powered for rigorous statistical comparisons, it suggests that tear collection site should be considered a potential factor that can influence outcomes when designing multi-site tear proteome studies.

3.6. Tear proteome changes with soft contact lens (CL) use

To compare differences in tear proteins with CL use, samples from soft CL users at both geographic sites were compared to participants who did not use CL. In our first analysis (CL Experiment 1), 3156 proteins were detected and 183 (5.8%) met our criteria for differential abundance in CL users ($n = 9$) compared to individuals who do not use CLs ($n = 5$; Fig. 7A). However, individuals in the CL group had a wide range of Schirmer wetted lengths (range 7–35 mm), while most individuals in the non-CL group had a smaller range of Schirmer wetted lengths (9–12 mm; with one sample at 25 mm) (Fig. 7A, inset). Based on our prior study demonstrating the effect of Schirmer strip wetting on the tear proteome (Fig. 5A), we conducted another analysis (CL Experiment 2) on participants that did ($n = 5$) or did not ($n = 5$) use CLs, but analyzed only samples within a restricted range of Schirmer length (15–22 mm). In this analysis, 2516 proteins were detected and 79 proteins (3.1%) were differentially abundant (Fig. 7B). These findings suggest that Schirmer strip wetted length, in addition to CL use, contributed to the larger protein variation in the first analysis that compared participants based only on CL use (Fig. 7A).

The two CL experiments (Fig. 7), revealed 23 proteins that were

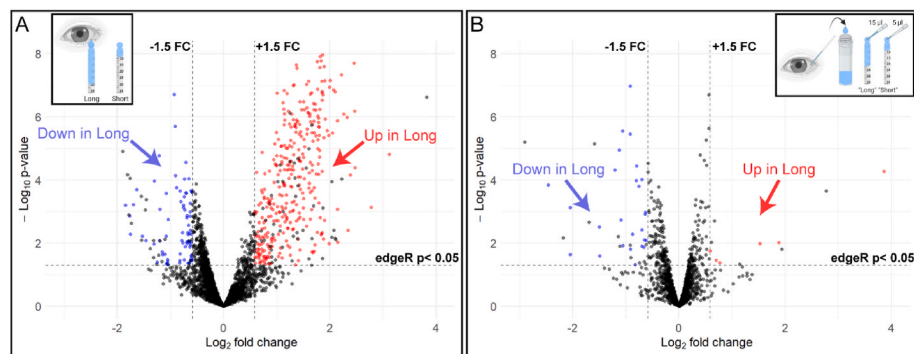


Fig. 5. Effect of Schirmer strip wetted length on the tear proteome. (A) Individuals that naturally produce long Schirmer strip wetted length (inset) show extensive differential abundance of tear proteins as compared to those that produce short Schirmer strip wetted length. (B) Pipetted application of different fluid amounts from pooled tear samples (inset) causes some differential relative abundance of proteins in the pipetted “Long” Schirmer group as compared to the pipetted “Short” group, although not to the extent seen in individuals that naturally produce long Schirmer strip wetted lengths (A). Many proteins demonstrated an increased relative abundance in Long strips (A, red) when compared to Short strips with fewer proteins demonstrating a decrease in relative abundance in Long strips (blue) versus Short strips. The opposite was true in the pipetted samples

with very few proteins demonstrating an increase in relative abundance in pipetted “Long” strips (B, red) compared to pipetted “Short” strips and more proteins demonstrating decreased relative abundance in pipetted “Long” strips (blue) compared to pipetted “Short” strips. Due to volcano plot scale standardization, 20 proteins for panel A and 3 proteins for panel B exceeded the scale and are not shown. A complete list of differentially expressed proteins in the above comparisons can be found in Appendix Tables A.3 and A.4. Insets created with BioRender.com.

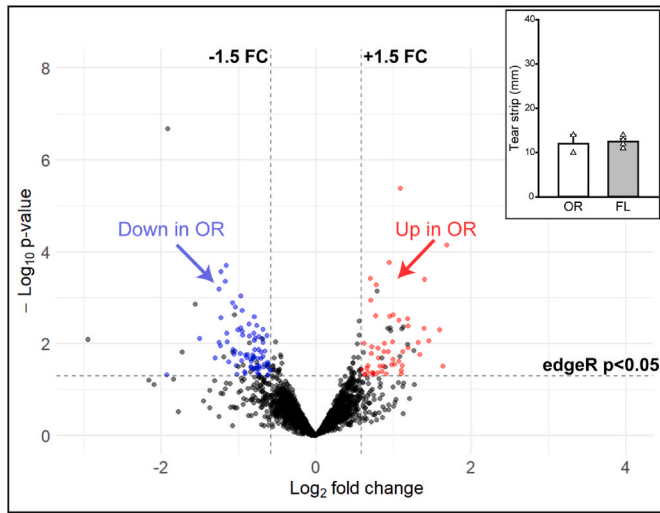


Fig. 6. Volcano plot of differentially abundant proteins by tear collection site. Oregon (OR) samples demonstrate differential abundance of proteins as compared to Florida (FL) samples. Inset is a graph of Schirmer strip wetted length for OR and FL samples included in this comparison. Even when Schirmer strip wetted length was controlled, there were proteins that were increased (red) or decreased (blue) in relative abundance in OR samples as compared to FL samples. There was one protein that exceeded the standardized scales set for these volcano plots and is not shown. A complete list of differentially expressed proteins in the above comparisons can be found in Appendix Table A.5. *Inset:* Mean tear strip length \pm SEM. White triangles represent individual sample values within each group.

differentially abundant according to our criteria in both experiments. Most of these proteins ($n = 22$) were upregulated with CL use (Table 2), but one protein (Cystatin-SA) showed changes in direction, i.e., upregulated versus downregulated, and different magnitudes of fold change across the two experiments. Most of the proteins that were altered in abundance in both experiments are involved in immune pathways or keratinization and cell-cell adhesion based on Gene Ontology (GO) term analyses. These studies suggest that there is consistency in the proteins that differ by CL use/non-use.

3.7. Combination of multiple TMT experiments to increase sample size for CL use comparison

The use of samples from the same common tear pool on each TMT run allowed us to combine 3 smaller experiments and use IRS normalization (Methods 2.6.3.) to increase sample sizes in the CL and no CL groups. Two samples were used on two different TMT runs for CL analyses but were only included once in the IRS analysis. In two cases, samples from left and right eyes of the same individual were included in

Table 2
Differentially abundant proteins across contact lens (CL) experiments.

Protein	Gene name	Fold changes in CL users	
		CL Expt 1	CL Expt 2
Beta-1,3-galactosyl-O-glycosyl-glycoprotein beta-1,6-N-acetylglucosaminyltransferase 3	GCNT	+1.9	+1.6
Corneodesmosin	CDSN	+2.1	+1.9
Cystatin-SA	CST2	+11.3	-2.6
Desmocollin-1	DSC1	+2.1	+1.9
Desmoglein-1	DSG1	+2.0	+1.7
Desmoplakin	DSP	+2.2	+1.6
Loricrin	LRN	+2.0	+2.4
Mesothelin, cleaved form	MSLN	+1.9	+1.7
Polymeric immunoglobulin receptor	PIGR	+1.8	+2.3
Immunoglobulins, 14	See below ^a	+1.6 to +2.5	+1.8 to +2.9

Differential abundance was determined using the uncorrected edgeR p values in these CL analyses. CL Experiment 1 included a wide range of Schirmer strip wetted length, while CL Experiment 2 included samples from a restricted range of Schirmer strip wetted length. Bolded gene names represent proteins that were also elevated in a larger CL comparison with restricted Schirmer strip wetted length using IRS normalization (described below).

^a 14 specific Immunoglobulins were more abundant with CL use: **IGHA1, IGHV3-11, IGHV3-49, IGHV3-53, IGHV3-7, IGHV3-74, IGHV4-28, IGHV5-51, IGHV6-1, IGKV1-27, IGKV3-11, IGLV1-44, IGLV3-19, IGLL5.**

two separate TMT runs, which could potentially reduce variability between TMT runs. Schirmer tear strip wetted length was balanced between the two groups (Fig. 8, inset). Data from 17 samples from 14 CL users and 19 samples from 16 non-users were compared and differentially expressed proteins were determined. This analysis revealed that of 2596 proteins detected, 58 proteins (2.2%) were differentially abundant between the CL users and non-users (Fig. 8). Fifty-five proteins had a higher relative abundance (Up, red dots, Fig. 8) and 3 proteins had a lower relative abundance (Down, blue dots, Fig. 8) in CL users as compared to non-users. Of these total 58 proteins, there were 12 proteins that were in common with the differential proteins found in the small CL studies (Table 2, bolded).

4. Discussion

Obtaining quantitative, reproducible, and clinically relevant data on the human tear proteome demands careful consideration of experimental design, methodology, and data analytical methods. We have demonstrated consistent results using TMT analysis of tear proteins from individual participants, thus increasing opportunities for protein biomarker discovery based on individual tear samples and participant characteristics. We found minimal within-person variability using these methods in healthy individuals when comparing tears from left and right

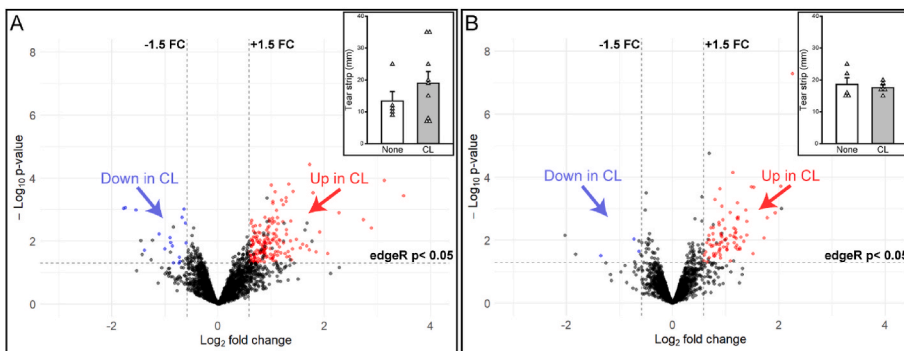


Fig. 7. Volcano plots of differentially abundant proteins with soft contact lens (CL) use for (A) individuals with a wide range of Schirmer strip wetted length or (B) individuals with more restricted Schirmer length. Both panels depict the number of proteins that increase (red) or decrease (blue) in relative abundance in CL users as compared to those participants who do not use CLs. One protein exceeded the standardized scales and was not shown in figure (A). Insets are Schirmer strip wetted lengths from CL users (CL, gray bar) and those who do not use CLs (None, white bar) for each experiment. A complete list of differentially expressed proteins in the above comparisons can be found in Appendix Tables A.6 and A.7. *Insets:* Mean tear strip lengths \pm SEM. White triangles represent individual sample values within each group.

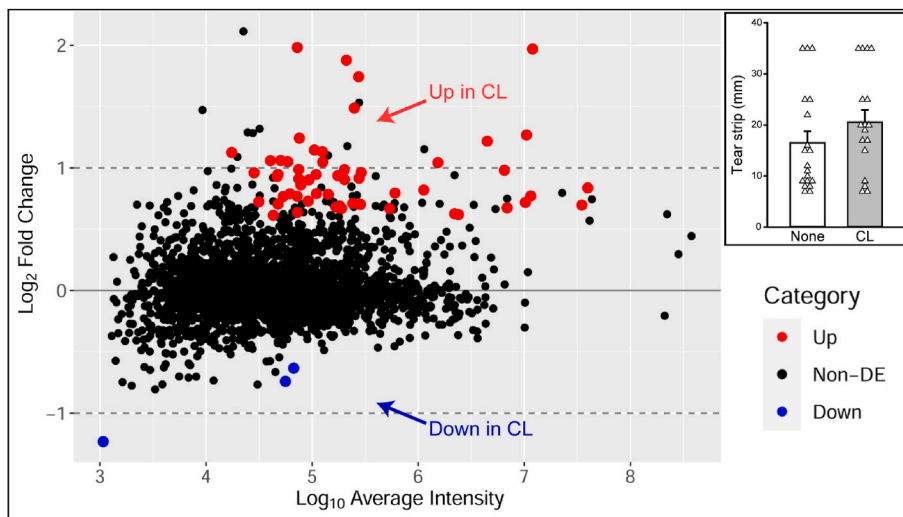


Fig. 8. Visual representation of the 2596 total proteins detected in the combined contact lens (CL) analysis of differentially abundant proteins in CL users as compared to CL non-users. Proteins that met criteria for differential abundance are color-coded by those that had increased (red) and decreased (blue) abundance in CL users. Proteins that were not differentially expressed (Non-DE) between the two groups are shown in black. *Inset:* Schirmer tear strip wetted lengths are balanced between the CL group (CL, gray bar) and non-user group (None, white bar) with a wide variation in strip lengths. *Inset:* Bars indicate mean strip lengths \pm SEM. White triangles represent individual sample values within each group.

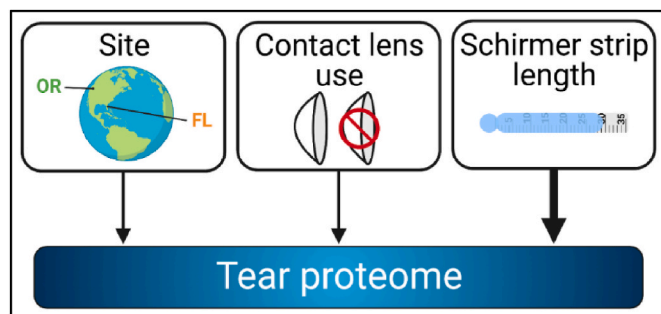


Fig. 9. Various factors may influence an individual's tear proteome and should be taken into consideration when designing and conducting tear proteomic studies. Geographic site and soft contact lens use contributed modestly to changes in the tear proteome, while tear volume (Schirmer tear strip wetted length) contributed most significantly to changes in the tear proteome in our experiments. Created with BioRender.com.

eyes collected on the same day. We also detected changes in tear proteins with soft CL use. Other factors that contributed most extensively to changes in the tear proteome were geographic site and tear volume as assessed by Schirmer tear strip wetted length (Fig. 9).

4.1. Numbers of detected proteins and percentage of differential candidates differ across experiments

4.1.1. Greater tear volume correlates with more differential protein expression

Similar to the findings in this study, previous studies have demonstrated correlations between total protein content and increased Schirmer tear strip wetted lengths [24,25]. The increasing number of abundant proteins with higher tear volume potentially confounds analyses of differential abundance with comparison of other covariates. To test the influence of tear sample volume (as measured by wetted tear strip length) on the analytical method, we generated a pooled tear sample and pipetted set volumes onto Schirmer strips to achieve "short" and "long" wetted lengths (Methods 3.4). In this pooled sample study, there were far fewer differential candidates (Table 3, 2.1%) than the number of candidates detected when comparing short versus long wetted strips from individual participants (Table 3, 14.6%). Since there were more differential candidates when comparing individual subjects with different Schirmer tear strip wetted lengths, this appears to be a real biological difference that is not due to methodological differences when analyzing short versus long strips. There is controversy

Table 3

Total proteins meeting differential abundance criteria in each experiment.

Experiment description	Total proteins detected	Proteins meeting criteria	
		Number	% of total
Within-run replicate samples	3057	19	0.6%
Within-subject left vs right eye	1987	1	0.05%
Natural Long vs Short Schirmer	2901	424	14.6%
Pipetted Long vs Short Schirmer	1536	33	2.1%
Geographic site comparison	3498	129	3.7%
CL experiment 1	3156	183	5.8%
CL experiment 2	2516	79	3.1%

Criteria for all studies included 3 peptide spectral matches (PSMs), an uncorrected edgeR *p* value of <0.05 , and a fold change of at least ± 1.5 .

surrounding whether Schirmer strip collection under topical anesthesia measures basal tearing, reflex tearing caused by irritative contact with the ocular surface, or a mixture of both [26]. While the significance of specific proteins that are elevated in individuals with long wetted strips is unknown, this knowledge should inform future study design and data interpretation.

4.1.2. The number of detected proteins varies between different TMT experiments

The total number of detected proteins in individual experiments ranged from 1536 to 3498 (Table 3). Proteins that were not present in the experiments with fewer detected proteins may reflect relatively low abundance. While some of this variation in abundance may be due to changes in instrument sensitivity between runs, an additional contribution could be due to the composition of tears analyzed within each TMT experiment. Proteins are detected from the MS2 spectra assigned to individual proteins within each TMT experiment, and each MS2 spectrum is generated from a composite of all multiplexed tear digests within in each experiment. If some multiplexed samples contain a greater proportion of highly abundant tear proteins than others, this could suppress the detection of less abundant tear proteins within that run. Thus, the numbers of proteins detected in some experiments may have had fewer detected proteins overall, emphasizing the value of balancing biological factors within each instrument run.

4.2. Geographic site influences the tear proteome

Our results illustrate differences between the tear proteomes of individuals in Miami, FL and those in Portland, OR. This is consistent with

the finding that climate, allergens, and other regional factors can influence symptoms, tearing, and ocular surface proteins [27]. These findings reinforce the importance of documenting all information available regarding sample collection, including environment, to allow differential analyses of all factors that may influence the outcome of human clinical studies.

4.3. CL use alters the tear proteome

Most proteins differentially expressed in CL users that we identified belong to the immunoglobulin family and proteins related to cell adhesion. Previous studies, though varying in magnitude and direction of changes, support these findings. As CL use alters structural and functional aspects of the ocular surface [28], understanding differences in the tear proteome of CL users may inform the study of CL use-related complications including microbial keratitis, dry eye disease, and chronic discomfort [29,30]. Several proteins were consistently altered in CL users across the studies presented, showing that with rigorous methods, a small number of samples can provide insights into factors that may influence individual tear proteomes.

4.4. Limitations and technical considerations

One limitation of protein studies on tear samples collected from Schirmer strips is the efficiency of extracting and digesting proteins off of the strips. While not shown in this study, we tested different protocols and identified S-Trap digestion as the method that gave the highest peptide yield following digestion. Our methods included the strong protein solubilizing detergent SDS and avoided solid phase extraction steps that can lower peptide yields. While it is still possible that recovery of different proteins will vary using SDS, this should not impact the results if the proportional loss of proteins is consistent across strips. However, it is possible that the protocol was unable to elute all proteins on the strips.

For quantitative comparisons, one distinct feature of the TMT method is that quantitative results are obtained for each protein across

every sample in a multiplexed run. This means there is no ‘missing’ data for identified proteins within each TMT run. Furthermore, due to the extensive data collection afforded by the two-dimensional liquid chromatography separation, the number of missing proteins across TMT runs was minimized.

5. Conclusions

We present a method for the analysis of human tear proteins using standard clinical protocols and a reproducible workflow for sample collection and proteomic analysis. We found factors that altered the tear proteome between individuals that were expected (geographic site, soft CL use) and unexpected (Schirmer wetted length). Effect sizes (fold changes) observed in these studies were relatively modest which may be due to small sample sizes and/or the fact that tears from healthy individuals were examined. These studies support the need to consider a range of factors in addition to the biological or clinical feature of interest when performing tear protein studies. In addition, biostatistical methods will be required to differentiate these factors from other patient characteristics in clinical biomarker discovery studies.

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Conflict of interest disclosures

The authors report no conflicts of interest.

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APPENDIX

A total of 7 separate lists of differentially expressed proteins that met our criteria of at least 3 PSMs, an uncorrected edgeR p-value of <0.05, and a fold change of +1.5, are attached below for each volcano plot figure. Summary statistics are also provided for each protein.

Click on the bullet triangle points to expand each table.

Table A.1
Differentially expressed proteins between the half-strip replicates (first half and second half) – see Fig. 3A

Accession	PSMs	LogFC	FC	PValue	mean_first	mean_second	SD_first	SD_second	CV_first	CV_second	direction
sp P04279 SEMG1_HUMAN	4	-2.47	-5.53	0.001	20858	3774	37252	1522	1.79	0.40	down
sp Q13443 ADAM9_HUMAN	4	-1.94	-3.83	0.004	1317	344	850	416	0.65	1.21	down
sp Q53LP3 SWAHC_HUMAN	3	-1.91	-3.77	0.014	1833	486	936	847	0.51	1.74	down
sp Q7Z6J4 FGD2_HUMAN	4	-1.41	-2.66	0.043	893	336	656	403	0.73	1.20	down
sp Q08554 DSC1_HUMAN	12	-0.97	-1.95	0.027	47172	24150	40369	9732	0.86	0.40	down
sp P15924 DESP_HUMAN	131	-0.80	-1.74	0.026	1309162	754195	935169	201334	0.71	0.27	down
sp O14979 HNRDL_HUMAN	3	-0.69	-1.62	0.047	15758	9737	11357	2524	0.72	0.26	down
sp P80723 BASP1_HUMAN	28	0.59	1.50	0.033	56671	85092	14297	38079	0.25	0.45	up
sp P11215 ITAM_HUMAN	16	0.72	1.65	0.026	36165	59493	10439	36684	0.29	0.62	up
sp P08567 PLEK_HUMAN	3	0.73	1.66	0.004	8046	13356	2074	5327	0.26	0.40	up
sp P05164 PERM_HUMAN	37	0.90	1.87	0.006	288511	538775	90228	353705	0.31	0.66	up
sp P08246 ELNE_HUMAN	20	0.93	1.90	0.009	221136	420538	93052	256240	0.42	0.61	up
sp P08311 CATG_HUMAN	25	0.98	1.97	0.009	115956	228323	41688	170627	0.36	0.75	up
sp P24158 PRTN3_HUMAN	16	0.99	1.99	0.018	186373	370206	102625	256786	0.55	0.69	up
sp P49913 CAMP_HUMAN	10	1.01	2.01	0.002	50608	101835	19802	56970	0.39	0.56	up
sp P10153 RNAS2_HUMAN	5	1.05	2.06	0.002	12517	25827	4504	16278	0.36	0.63	up
sp P20160 CAP7_HUMAN	36	1.25	2.38	0.002	100092	238155	33802	202738	0.34	0.85	up
sp P59665 DEF1_HUMAN (+1)	17	1.29	2.44	0.017	104310	254952	68169	245646	0.65	0.96	up
sp P32320 CDD_HUMAN	5	1.64	3.11	0.043	457	1423	826	864	1.81	0.61	up

Table A.2
Differentially expressed proteins between left eye and right eye (reference) – see Fig. 3B

Accession	PSMs	LogFC	FC	PValue	mean_left	mean_right	SD_left	SD_right	CV_left	CV_right	direction
sp O60841 IF2P_HUMAN	3	-0.86	-1.82	0.001	230072	126412	127720	18894	0.56	0.15	down

Table A.3
Differentially expressed proteins between long schirmer strip and short schirmer strip (reference) – see Fig. 5A

Accession	PSMs	logFC	FC	PValue	mean_short	mean_long	SD_short	SD_long	CV_short	CV_long	direction
sp Q96176 MMS19_HUMAN	3	-1.85	-3.60	0.001	2344	651	589	747	0.25	1.15	down
sp Q13325 IFIT5_HUMAN	5	-1.76	-3.40	0.001	4659	1372	1103	1220	0.24	0.89	down
sp Q9UBC2 EP15R_HUMAN	3	-1.75	-3.37	0.005	2096	622	1074	593	0.51	0.95	down
sp Q9Y508 RN114_HUMAN	7	-1.69	-3.23	0.001	2372	733	423	618	0.18	0.84	down
sp P27482 CALL3_HUMAN	9	-1.63	-3.10	0.000	21015	6772	12274	3498	0.58	0.52	down
sp Q9HC07 TM165_HUMAN	5	-1.53	-2.88	0.006	1782	619	688	618	0.39	1.00	down
sp Q9HB21 PKHA1_HUMAN	5	-1.46	-2.75	0.008	2767	1008	308	1044	0.11	1.04	down
sp P45983 MK08_HUMAN	4	-1.31	-2.48	0.011	2720	1098	617	803	0.23	0.73	down
sp Q9BQE3 TBA1C_HUMAN	6	-1.30	-2.46	0.000	13781	5599	3538	2763	0.26	0.49	down
sp Q9Y2W1 TR150_HUMAN	3	-1.25	-2.38	0.041	1636	689	1003	741	0.61	1.08	down
sp P30838 AL3A1_HUMAN	85	-1.21	-2.31	0.000	2227718	964452	754334	357045	0.34	0.37	down
sp Q8WVJ2 NUDC2_HUMAN	5	-1.20	-2.30	0.008	3463	1503	763	957	0.22	0.64	down
sp Q14002 CEAM7_HUMAN	9	-1.20	-2.29	0.001	66936	29188	32777	7880	0.49	0.27	down
sp Q9UJW0 DCTN4_HUMAN	3	-1.15	-2.22	0.019	1349	606	408	561	0.30	0.93	down
sp Q03519 TAP2_HUMAN	4	-1.15	-2.21	0.023	8940	4038	4797	2673	0.54	0.66	down
sp P07738 PMGE_HUMAN	4	-1.10	-2.15	0.023	6248	2909	2352	1807	0.38	0.62	down
sp P23381 SYWC_HUMAN	33	-1.08	-2.11	0.000	313385	148582	200257	28251	0.64	0.19	down
sp Q9BPW9 DHRS9_HUMAN	5	-1.08	-2.11	0.006	31051	14727	18033	4713	0.58	0.32	down
sp Q9Y2B0 CNPY2_HUMAN	4	-1.07	-2.10	0.045	1633	778	668	726	0.41	0.93	down
sp Q6IQ22 RAB12_HUMAN	3	-1.06	-2.09	0.045	2871	1372	512	1089	0.18	0.79	down
sp Q93009 UBP7_HUMAN	3	-1.05	-2.08	0.038	1786	860	353	756	0.20	0.88	down
sp P10398 ARAF_HUMAN	3	-1.05	-2.08	0.047	1935	932	425	1027	0.22	1.10	down
sp Q03518 TAP1_HUMAN	6	-1.05	-2.07	0.033	8072	3897	4375	2380	0.54	0.61	down
sp Q9BQE5 APOL2_HUMAN	5	-1.04	-2.05	0.002	27362	13321	14090	5573	0.51	0.42	down
sp P42574 CASP3_HUMAN	15	-0.93	-1.90	0.000	89932	47265	13751	9466	0.15	0.20	down
sp P30740 ILEU_HUMAN	142	-0.91	-1.88	0.000	2828144	1507176	720565	138989	0.25	0.09	down
sp P80217 IN35_HUMAN	7	-0.90	-1.86	0.000	60865	32653	12437	9830	0.20	0.30	down
sp Q01469 FABP5_HUMAN	60	-0.88	-1.84	0.000	706868	383370	245743	76312	0.35	0.20	down
sp Q9NZ32 ARP10_HUMAN	4	-0.83	-1.77	0.043	5537	3122	1107	1498	0.20	0.48	down
sp P22528 SPR1B_HUMAN	6	-0.82	-1.77	0.036	210407	119038	126197	64795	0.60	0.54	down
sp P42224 STAT1_HUMAN	46	-0.81	-1.76	0.000	502295	285576	160456	58596	0.32	0.21	down
sp P10321 HLAC_HUMAN	4	-0.81	-1.76	0.022	9374	5340	2629	3202	0.28	0.60	down
sp P15104 GLNA_HUMAN	34	-0.80	-1.75	0.000	386724	221453	134158	58995	0.35	0.27	down
sp Q8WTS6 SETD7_HUMAN	3	-0.78	-1.72	0.008	5527	3207	1001	1522	0.18	0.47	down
sp Q9NZN3 EHD3_HUMAN	7	-0.77	-1.70	0.005	16365	9601	6014	3396	0.37	0.35	down
sp Q86YS7 C2CD5_HUMAN	4	-0.76	-1.70	0.010	3403	2002	1270	338	0.37	0.17	down
sp P09914 IFIT1_HUMAN	7	-0.75	-1.69	0.001	51913	30777	18149	5077	0.35	0.16	down
sp P43405 KSYK_HUMAN	8	-0.75	-1.68	0.001	17229	10248	1626	3923	0.09	0.38	down
sp Q99805 TM9S2_HUMAN	7	-0.74	-1.67	0.034	16148	9658	1750	6134	0.11	0.64	down
sp O60841 IF2P_HUMAN	6	-0.74	-1.67	0.000	8696	5222	1442	829	0.17	0.16	down
sp Q14879 IFIT3_HUMAN	13	-0.73	-1.65	0.001	17245	10428	4270	2635	0.25	0.25	down
sp P21980 TGM2_HUMAN	280	-0.72	-1.64	0.013	3418228	2078435	1265972	792628	0.37	0.38	down
sp P52209 PGD_HUMAN	110	-0.71	-1.64	0.000	1897556	1159852	275889	205190	0.15	0.18	down
sp Q9UN36 NDRG2_HUMAN	29	-0.71	-1.64	0.000	555504	339649	159140	51075	0.29	0.15	down
sp P50454 SERPH_HUMAN	6	-0.70	-1.63	0.000	38348	23543	8876	4664	0.23	0.20	down
sp Q6IA69 NADE_HUMAN	7	-0.69	-1.61	0.002	14620	9077	2131	3105	0.15	0.34	down
sp Q15847 ADIRF_HUMAN	5	-0.69	-1.61	0.009	13236	8223	3833	3039	0.29	0.37	down
sp P20591 MX1_HUMAN	32	-0.68	-1.61	0.001	205266	127680	56772	26215	0.28	0.21	down
sp Q16625 OCLN_HUMAN	3	-0.68	-1.60	0.010	7240	4513	1463	1832	0.20	0.41	down
sp Q16719 KYNU_HUMAN	28	-0.67	-1.59	0.005	667361	419734	233742	86430	0.35	0.21	down
sp Q13885 TBB2A_HUMAN	3	-0.67	-1.59	0.044	21038	13266	12337	4226	0.59	0.32	down
sp Q9H0P0 SNT3A_HUMAN	6	-0.66	-1.59	0.009	37171	23445	10565	6305	0.28	0.27	down
sp Q9GZP8 IMUP_HUMAN	5	-0.66	-1.59	0.005	166288	104913	26756	33884	0.16	0.32	down
sp P32456 GBP2_HUMAN	11	-0.66	-1.58	0.003	118697	75318	41675	12560	0.35	0.17	down
sp Q96KP4 CNDP2_HUMAN	92	-0.65	-1.57	0.000	808707	514609	97461	105435	0.12	0.20	down
sp Q13075 BIRC1_HUMAN	3	-0.65	-1.57	0.043	7122	4538	3141	1840	0.44	0.41	down
sp Q9NXA8 SIR5_HUMAN	3	-0.65	-1.57	0.009	6551	4180	1758	1062	0.27	0.25	down
sp P01903 DRA_HUMAN (+1)	8	-0.64	-1.56	0.005	169523	108803	43268	30163	0.26	0.28	down
sp P31947 1433S_HUMAN	33	-0.63	-1.55	0.013	260296	167768	107672	12086	0.41	0.07	down
sp O15327 INP4B_HUMAN	6	-0.63	-1.55	0.010	11564	7472	2866	2331	0.25	0.31	down
sp P21964 COMT_HUMAN	30	-0.63	-1.55	0.001	521168	336894	117033	62206	0.22	0.18	down
sp P30044 PRDX5_HUMAN	79	-0.63	-1.55	0.001	764121	493973	202710	62715	0.27	0.13	down
sp P28838 AMPL_HUMAN	55	-0.63	-1.54	0.001	1196015	774179	250638	135293	0.21	0.17	down
sp Q9UL46 PSME2_HUMAN	27	-0.62	-1.54	0.012	287833	187335	95773	36148	0.33	0.19	down
sp P29728 OAS2_HUMAN	16	-0.62	-1.53	0.004	113308	73822	39344	9543	0.35	0.13	down

(continued on next page)

Table A.3 (continued)

Accession	PSMs	logFC	FC	PValue	mean_short	mean_long	SD_short	SD_long	CV_short	CV_long	direction
sp P33241 LSP1_HUMAN	14	-0.61	-1.53	0.035	70212	45949	27538	15927	0.39	0.35	down
sp Q9ULC6 PAD11_HUMAN	6	-0.61	-1.53	0.035	32638	21377	12377	8394	0.38	0.39	down
sp O43396 TXNL1_HUMAN	24	-0.61	-1.52	0.000	115042	75455	12637	15074	0.11	0.20	down
sp O43169 CYB5B_HUMAN	6	-0.61	-1.52	0.009	14073	9236	2571	2886	0.18	0.31	down
sp Q8NBX0 SCPD_L_HUMAN	4	-0.61	-1.52	0.031	46737	30700	16246	11434	0.35	0.37	down
sp P19971 TYPH_HUMAN	47	-0.60	-1.52	0.024	402469	265066	146398	78972	0.36	0.30	down
sp P84085 ARF5_HUMAN	5	-0.60	-1.52	0.026	9939	6549	1214	2719	0.12	0.42	down
sp O43399 TPD54_HUMAN	6	-0.60	-1.52	0.005	10842	7150	2265	1902	0.21	0.27	down
sp Q9NQW7 XPP1_HUMAN	33	-0.59	-1.51	0.000	317858	210759	33062	38478	0.10	0.18	down
sp P07195 LDHB_HUMAN	20	-0.59	-1.51	0.000	388204	257436	55064	46862	0.14	0.18	down
tr A0A0G2JQ6 A0A0G2JQ6_HUMAN	11	-0.59	-1.51	0.035	64425	42738	23435	16812	0.36	0.39	down
sp P23284 PPIB_HUMAN	20	0.59	1.50	0.006	629881	947769	150974	265554	0.24	0.28	up
sp Q9H4G4 GAPR1_HUMAN	4	0.59	1.51	0.028	8677	13068	2302	5459	0.27	0.42	up
sp Q6YP21 KAT3_HUMAN	5	0.59	1.51	0.017	19430	29262	5598	9463	0.29	0.32	up
sp O60826 CCD22_HUMAN	10	0.59	1.51	0.001	7428	11214	1142	1987	0.15	0.18	up
sp Q9NTJ4 MA2C1_HUMAN	3	0.60	1.52	0.001	17014	25862	3611	5116	0.21	0.20	up
sp P13987 CD59_HUMAN	12	0.61	1.52	0.044	104779	159478	26431	98122	0.25	0.62	up
sp Q15582 BGH3_HUMAN	7	0.62	1.53	0.028	20327	31155	8138	10561	0.40	0.34	up
sp P61086 UBE2K_HUMAN	14	0.62	1.54	0.000	43664	67177	6430	9388	0.15	0.14	up
sp Q9BRG2 SH23A_HUMAN	7	0.62	1.54	0.001	11437	17622	372	4904	0.03	0.28	up
sp P0C870 JMD7_HUMAN	3	0.62	1.54	0.006	2997	4617	503	978	0.17	0.21	up
sp O14787 TNPO2_HUMAN	5	0.63	1.55	0.020	30111	46641	5283	26730	0.18	0.57	up
sp O00468 AGRIN_HUMAN	16	0.64	1.56	0.010	9794	15292	2238	5554	0.23	0.36	up
sp Q9NZL4 HPBP1_HUMAN	3	0.65	1.57	0.015	4950	7748	1648	2675	0.33	0.35	up
sp Q9H3S4 TPK1_HUMAN	8	0.65	1.57	0.020	16556	26006	2947	14451	0.18	0.56	up
sp P39060 COIA1_HUMAN	4	0.66	1.58	0.004	4844	7632	1005	1929	0.21	0.25	up
sp P41227 NAA10_HUMAN	5	0.66	1.58	0.006	25991	41088	5085	16669	0.20	0.41	up
sp P01715 LV301_HUMAN	7	0.66	1.58	0.025	29108	46131	12878	17118	0.44	0.37	up
sp Q9NUP9 LIN7C_HUMAN	3	0.67	1.59	0.016	7383	11728	2099	4627	0.28	0.39	up
sp Q16348 S15A2_HUMAN	3	0.67	1.59	0.001	7542	11993	1566	2341	0.21	0.20	up
sp O95671 ASML_HUMAN	11	0.67	1.59	0.002	18934	30120	3604	10149	0.19	0.34	up
sp P54803 GALC_HUMAN	3	0.67	1.59	0.011	17165	27320	3376	11736	0.20	0.43	up
sp P04839 CY24B_HUMAN	6	0.67	1.59	0.024	11300	17995	3629	8051	0.32	0.45	up
sp O60271 JIP4_HUMAN	12	0.67	1.60	0.031	19626	31326	1341	22855	0.07	0.73	up
sp O60573 IF4E2_HUMAN	3	0.69	1.61	0.043	8922	14349	1534	11001	0.17	0.77	up
sp P84095 RHOG_HUMAN	6	0.69	1.61	0.007	11562	18608	2313	7078	0.20	0.38	up
sp Q96QA5 GSDMA_HUMAN	6	0.69	1.62	0.041	55605	89806	33503	30421	0.60	0.34	up
sp Q9BUJ2 HNRL1_HUMAN	3	0.69	1.62	0.022	7550	12220	1883	6727	0.25	0.55	up
sp Q8N1F7 NUP93_HUMAN	6	0.70	1.63	0.001	20926	34084	2448	11021	0.12	0.32	up
sp P62312 LSM6_HUMAN	3	0.71	1.64	0.011	6899	11291	1989	4169	0.29	0.37	up
sp Q8IV08 PLD3_HUMAN	4	0.71	1.64	0.000	7984	13092	1883	1769	0.24	0.14	up
sp O00479 HMGN4_HUMAN	3	0.72	1.65	0.015	7908	13052	3105	5652	0.39	0.43	up
sp A0A0B4J1V2 HV226_HUMAN	8	0.73	1.65	0.037	71979	119104	21264	65708	0.30	0.55	up
sp Q10471 GALT2_HUMAN	12	0.73	1.66	0.002	60160	99640	12958	34965	0.22	0.35	up
sp P12821 ACE_HUMAN	8	0.73	1.66	0.004	32673	54154	12807	17251	0.39	0.32	up
sp O75882 ATRN_HUMAN	26	0.73	1.66	0.000	114009	189026	12924	41342	0.11	0.22	up
sp Q92542 NICA_HUMAN	4	0.73	1.66	0.006	5461	9063	882	4295	0.16	0.47	up
sp A0A0J9YXX1 HV5X1_HUMAN	3	0.73	1.66	0.018	35774	59463	7894	30019	0.22	0.50	up
sp P42785 PCP_HUMAN	4	0.74	1.67	0.000	18877	31456	3972	7971	0.21	0.25	up
sp P00748 FA12_HUMAN	11	0.74	1.67	0.010	23650	39465	10403	13669	0.44	0.35	up
sp Q5EBM0 CMPK2_HUMAN	4	0.75	1.68	0.027	3958	6669	1026	4442	0.26	0.67	up
sp P21926 CD9_HUMAN	10	0.76	1.69	0.002	117982	199535	20252	83636	0.17	0.42	up
sp P11215 ITAM_HUMAN	8	0.76	1.70	0.007	20077	34049	6657	12589	0.33	0.37	up
sp P04062 GLCM_HUMAN	5	0.77	1.70	0.000	27311	46498	6670	13928	0.24	0.30	up
sp P32321 DCTD_HUMAN	5	0.77	1.70	0.000	12620	21488	1462	7354	0.12	0.34	up
sp A0A0C4DH34 HV428_HUMAN	14	0.77	1.70	0.041	235302	400907	95578	218745	0.41	0.55	up
sp Q9H269 VPS16_HUMAN	3	0.77	1.70	0.000	9589	16344	820	5372	0.09	0.33	up
sp P09455 RET1_HUMAN	13	0.77	1.71	0.031	124072	211696	49761	130458	0.40	0.62	up
sp P17900 SAP3_HUMAN	6	0.77	1.71	0.017	127533	218128	84047	77729	0.66	0.36	up
sp P11279 LAMP1_HUMAN	6	0.78	1.71	0.000	84427	144723	11197	44335	0.13	0.31	up
sp P10253 LYAG_HUMAN	10	0.78	1.72	0.003	35189	60385	6554	27891	0.19	0.46	up
sp A0A0C4DH72 KV106_HUMAN	17	0.78	1.72	0.027	35791	61461	11187	37535	0.31	0.61	up
sp P54105 ICLN_HUMAN	3	0.79	1.73	0.005	3976	6870	968	2693	0.24	0.39	up
sp P01700 LV147_HUMAN	11	0.79	1.73	0.047	29239	50570	10770	35338	0.37	0.70	up
sp P01033 TIMP1_HUMAN	14	0.80	1.74	0.033	140357	243822	90394	107460	0.64	0.44	up
sp Q96TC7 RMD3_HUMAN	3	0.80	1.74	0.002	6778	11794	2103	3638	0.31	0.31	up
sp Q8N163 CCAR2_HUMAN	3	0.81	1.75	0.029	4184	7327	794	5496	0.19	0.75	up
sp P13688 CEAM1_HUMAN	7	0.82	1.76	0.030	64274	113145	16544	95981	0.26	0.85	up
sp P49257 LMAN1_HUMAN	17	0.82	1.76	0.001	59032	104025	21076	27159	0.36	0.26	up
sp P12107 COBA1_HUMAN	8	0.82	1.77	0.006	6770	11961	2154	5026	0.32	0.42	up
sp Q9Y394 DHRS7_HUMAN	3	0.83	1.77	0.011	13193	23400	4237	15621	0.32	0.67	up
sp O43657 TSN6_HUMAN	3	0.83	1.78	0.026	2607	4631	1189	2197	0.46	0.47	up
sp O43291 SPIT2_HUMAN	4	0.83	1.78	0.005	6371	11340	1403	5615	0.22	0.50	up
sp O94985 CSTN1_HUMAN	8	0.83	1.78	0.000	13751	24529	3698	7665	0.27	0.31	up
sp P07339 CATD_HUMAN	53	0.84	1.79	0.001	345864	619970	73801	244441	0.21	0.39	up

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Table A.3 (continued)

Accession	PSMs	logFC	FC	PValue	mean_short	mean_long	SD_short	SD_long	CV_short	CV_long	direction
sp P14923 PLAK_HUMAN	35	0.85	1.80	0.001	228229	410904	74841	159603	0.33	0.39	up
sp P04433 KV311_HUMAN	22	0.85	1.80	0.013	59460	107101	22910	55764	0.39	0.52	up
sp P60891 PRPS1_HUMAN	4	0.86	1.82	0.000	22198	40421	2698	13062	0.12	0.32	up
sp Q9HC84 MUC5B_HUMAN	7	0.86	1.82	0.021	5627	10247	2832	4812	0.50	0.47	up
sp Q9UI42 CBPA4_HUMAN	4	0.87	1.82	0.045	4473	8150	2192	5641	0.49	0.69	up
sp P49788 TIG1_HUMAN	14	0.87	1.82	0.028	100750	183716	38441	117578	0.38	0.64	up
sp Q9NZ08 ERAP1_HUMAN	31	0.87	1.83	0.000	201537	368099	76046	90141	0.38	0.24	up
sp P01040 CYTA_HUMAN	12	0.87	1.83	0.015	106646	194786	47589	114156	0.45	0.59	up
sp P53367 ARFP1_HUMAN	3	0.87	1.83	0.000	4466	8162	1029	2572	0.23	0.32	up
sp Q9H477 RBSK_HUMAN	4	0.88	1.84	0.001	4442	8176	879	3135	0.20	0.38	up
sp A6NI72 NCF1B_HUMAN (+1)	3	0.89	1.85	0.044	42329	78438	29228	52483	0.69	0.67	up
sp P05186 PPBT_HUMAN	23	0.89	1.86	0.001	114297	212289	52249	57878	0.46	0.27	up
sp P00450 CERU_HUMAN	252	0.90	1.86	0.001	2132715	3969034	811314	1059440	0.38	0.27	up
sp Q9NQ79 CRAC1_HUMAN	8	0.90	1.87	0.013	7720	14407	2793	8919	0.36	0.62	up
sp P15924 DESP_HUMAN	117	0.90	1.87	0.008	634671	1185087	323755	567783	0.51	0.48	up
sp P10619 PPGB_HUMAN	5	0.91	1.88	0.000	25728	48285	8762	16414	0.34	0.34	up
sp P51688 SPHM_HUMAN	4	0.91	1.88	0.007	15486	29064	4607	15544	0.30	0.53	up
sp Q99523 SORT_HUMAN	4	0.91	1.88	0.009	9246	17366	5413	6792	0.59	0.39	up
sp O75635 SPB7_HUMAN	3	0.91	1.88	0.012	4418	8324	1819	4809	0.41	0.58	up
sp P04066 FUCO_HUMAN	13	0.93	1.90	0.001	58786	111778	10757	56096	0.18	0.50	up
sp O60613 SEP15_HUMAN	3	0.94	1.92	0.007	11027	21169	1831	13923	0.17	0.66	up
sp O00754 MA2B1_HUMAN	6	0.94	1.92	0.000	29679	57117	4181	21422	0.14	0.38	up
sp P24592 IBP6_HUMAN	3	0.95	1.93	0.002	16275	31360	5621	16614	0.35	0.53	up
sp O00391 QSOX1_HUMAN	46	0.95	1.93	0.001	301254	580850	141028	188021	0.47	0.32	up
sp Q92896 GSLG1_HUMAN	44	0.95	1.93	0.000	205466	397571	59373	143598	0.29	0.36	up
sp P00918 CAH2_HUMAN	7	0.97	1.95	0.000	28415	55520	7706	15536	0.27	0.28	up
sp O43493 TGON2_HUMAN	7	0.97	1.96	0.008	6212	12158	1546	7828	0.25	0.64	up
sp P08962 CD63_HUMAN	6	0.97	1.96	0.000	43405	85106	10851	29358	0.25	0.34	up
sp Q9GZ44 BSSP4_HUMAN	6	0.99	1.98	0.002	7408	14695	2901	7708	0.39	0.52	up
sp P21333 FLNA_HUMAN	32	0.99	1.98	0.001	85924	170550	30181	79430	0.35	0.47	up
sp Q9HAT2 SIAE_HUMAN	10	1.00	1.99	0.000	34461	68728	7440	26148	0.22	0.38	up
sp Q14435 GALT3_HUMAN	8	1.00	1.99	0.000	34422	68652	4167	25734	0.12	0.37	up
sp P16278 BGAL_HUMAN	5	1.00	2.00	0.000	12985	25948	2762	9655	0.21	0.37	up
sp P16070 CD44_HUMAN	6	1.00	2.00	0.000	54429	108912	14424	35656	0.27	0.33	up
sp Q7Z7H5 TMED4_HUMAN	6	1.01	2.01	0.000	44637	89896	5247	26434	0.12	0.29	up
sp Q08188 TGM3_HUMAN	15	1.02	2.03	0.001	27361	55440	10688	24603	0.39	0.44	up
sp P10909 CLUS_HUMAN	109	1.03	2.04	0.002	929056	1895940	433416	849357	0.47	0.45	up
sp P17050 NAGAB_HUMAN	6	1.03	2.04	0.000	3324	6791	785	2236	0.24	0.33	up
sp P53634 CATC_HUMAN	13	1.04	2.05	0.000	128683	264064	30323	84784	0.24	0.32	up
sp Q9Y337 KLK5_HUMAN	4	1.04	2.05	0.005	18948	38886	9342	21722	0.49	0.56	up
sp Q9UBT3 DKK4_HUMAN	12	1.04	2.05	0.027	44521	91380	36896	42920	0.83	0.47	up
sp P05089 ARGH1_HUMAN	12	1.05	2.07	0.001	76718	159186	30769	81741	0.40	0.51	up
sp P15144 AMPN_HUMAN	41	1.06	2.08	0.000	177523	368962	71925	121116	0.41	0.33	up
sp P25774 CATS_HUMAN	14	1.06	2.08	0.000	50804	105728	17244	47435	0.34	0.45	up
sp Q9Y295 DRG1_HUMAN	4	1.06	2.08	0.021	1618	3368	551	1723	0.34	0.51	up
sp Q9UHL4 DPP2_HUMAN	12	1.06	2.09	0.001	73777	153857	20344	89477	0.28	0.58	up
sp P10586 PTPRF_HUMAN	20	1.06	2.09	0.000	13365	27937	3692	10718	0.28	0.38	up
sp O75629 CREG1_HUMAN	3	1.07	2.09	0.003	3548	7430	1312	4051	0.37	0.55	up
sp P21589 5NTD_HUMAN	11	1.07	2.10	0.014	15636	32879	5726	27515	0.37	0.84	up
sp Q8N4A0 GALT4_HUMAN	14	1.08	2.12	0.000	53064	112437	12148	44249	0.23	0.39	up
sp O43866 CD5L_HUMAN	14	1.09	2.12	0.000	22808	48444	6032	13764	0.26	0.28	up
sp Q01130 SRSF2_HUMAN	5	1.09	2.13	0.000	10615	22628	2269	7863	0.21	0.35	up
sp Q865F2 GALT7_HUMAN	25	1.09	2.14	0.000	161845	345647	40995	137046	0.25	0.40	up
sp P22392 NDKB_HUMAN	10	1.10	2.14	0.001	816988	1747486	127896	840822	0.16	0.48	up
sp O14657 TOR1B_HUMAN	4	1.10	2.14	0.000	14239	30465	3059	13723	0.21	0.45	up
sp P12724 ECP_HUMAN	4	1.10	2.15	0.030	13567	29114	7419	22771	0.55	0.78	up
sp Q13724 MOGS_HUMAN	8	1.10	2.15	0.000	11114	23874	3367	12639	0.30	0.53	up
sp P36222 CH3L1_HUMAN	7	1.11	2.16	0.001	5161	11138	2973	3581	0.58	0.32	up
sp Q5JWF2 GNAS1_HUMAN	5	1.12	2.17	0.001	27102	58850	6356	42510	0.23	0.72	up
sp P08240 SRPRA_HUMAN	8	1.12	2.18	0.000	28649	62359	5608	20691	0.20	0.33	up
sp Q14766 LTBP1_HUMAN	11	1.13	2.19	0.000	10104	22113	3340	8166	0.33	0.37	up
sp Q15166 PON3_HUMAN	3	1.13	2.19	0.005	7532	16489	3287	8884	0.44	0.54	up
sp Q10472 GALT1_HUMAN	6	1.13	2.20	0.000	13007	28559	3017	9060	0.23	0.32	up
sp Q5T749 KPRP_HUMAN	7	1.14	2.20	0.000	11549	25381	3806	12214	0.33	0.48	up
sp O95793 STAU1_HUMAN	7	1.14	2.20	0.000	25741	56690	4846	17452	0.19	0.31	up
sp Q7Z2W4 ZCCHV_HUMAN	3	1.14	2.20	0.000	19015	41885	9139	14889	0.48	0.36	up
sp P15309 PPAP_HUMAN	10	1.14	2.20	0.000	47426	104527	11017	39333	0.23	0.38	up
sp Q9BTY2 FUCO2_HUMAN	12	1.14	2.20	0.000	51235	112949	12965	48444	0.25	0.43	up
sp Q9Y662 HS3SB_HUMAN (+1)	3	1.15	2.21	0.000	4948	10948	970	4128	0.20	0.38	up
sp Q14697 GANAB_HUMAN	84	1.15	2.22	0.000	612672	1357078	128849	492640	0.21	0.36	up
sp Q9NZP8 C1RL_HUMAN	9	1.15	2.22	0.000	30745	68110	10224	27498	0.33	0.40	up
sp P07996 TSP1_HUMAN	44	1.15	2.22	0.001	125875	279476	51428	149226	0.41	0.53	up
sp O15439 MRP4_HUMAN	5	1.15	2.23	0.000	6019	13393	1187	8282	0.20	0.62	up
sp Q9Y4L1 HYOU1_HUMAN	46	1.15	2.23	0.000	203039	452107	50930	165486	0.25	0.37	up
sp Q8NFL0 B3GN7_HUMAN	6	1.16	2.23	0.002	29422	65635	17335	33035	0.59	0.50	up
sp Q04609 FOLH1_HUMAN	20	1.17	2.25	0.001	99285	223740	21117	165161	0.21	0.74	up

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Table A.3 (continued)

Accession	PSMs	logFC	FC	PValue	mean_short	mean_long	SD_short	SD_long	CV_short	CV_long	direction
sp Q11517 CDSN_HUMAN	7	1.18	2.26	0.001	16118	36466	8597	18897	0.53	0.52	up
sp Q12841 FSTL1_HUMAN	5	1.18	2.27	0.001	6840	15539	1893	10028	0.28	0.65	up
sp Q9UKY7 CDV3_HUMAN	7	1.18	2.27	0.009	15883	36097	4975	38868	0.31	1.08	up
sp P09237 MMP7_HUMAN	8	1.19	2.28	0.000	43045	97959	9005	50856	0.21	0.52	up
sp P11717 MPRI_HUMAN	18	1.19	2.28	0.000	19831	45153	7924	14846	0.40	0.33	up
sp Q9UN19 DAPP1_HUMAN	3	1.19	2.28	0.002	2499	5695	849	3557	0.34	0.62	up
sp Q93100 KPBB_HUMAN	5	1.19	2.28	0.000	20855	47557	5626	20023	0.27	0.42	up
sp Q8NES3 LFNG_HUMAN	8	1.19	2.29	0.000	17320	39647	3835	11699	0.22	0.30	up
sp P61225 RAP2B_HUMAN	3	1.20	2.29	0.002	2722	6236	1379	3360	0.51	0.54	up
sp Q60568 PLOD3_HUMAN	6	1.20	2.29	0.000	8187	18783	2533	8542	0.31	0.45	up
sp Q75153 CLU_HUMAN	5	1.20	2.30	0.003	13188	30300	1312	29837	0.10	0.98	up
sp Q75888 TNF13_HUMAN	3	1.20	2.30	0.000	21275	49000	2582	24052	0.12	0.49	up
sp Q8WWY8 LIPH_HUMAN	5	1.21	2.31	0.000	11037	25456	3599	11688	0.33	0.46	up
sp Q02413 DSG1_HUMAN	21	1.21	2.31	0.012	88434	204257	66927	159174	0.76	0.78	up
sp P0DTE7 AMY1B_HUMAN (+2)	50	1.22	2.32	0.003	450720	1046365	225225	470567	0.50	0.45	up
sp Q7Z6J0 SH3R1_HUMAN	3	1.22	2.33	0.000	7843	18303	2902	3727	0.37	0.20	up
sp P43251 BTD_HUMAN	13	1.23	2.35	0.000	129099	303663	42223	142931	0.33	0.47	up
sp P61916 NPC2_HUMAN	20	1.24	2.36	0.000	152162	358561	40805	178349	0.27	0.50	up
sp Q9Y6W3 CAN7_HUMAN	6	1.24	2.36	0.000	4030	9503	1228	4679	0.30	0.49	up
sp Q60513 B4GT4_HUMAN	3	1.24	2.36	0.000	8911	21057	2580	8645	0.29	0.41	up
sp P17405 ASM_HUMAN	3	1.24	2.37	0.000	8481	20078	2118	7559	0.25	0.38	up
sp Q5JRA6 TGO1_HUMAN	4	1.25	2.37	0.014	1748	4148	922	1573	0.53	0.38	up
sp Q96SW2 CRBN_HUMAN	3	1.25	2.38	0.000	4082	9704	818	4052	0.20	0.42	up
sp P0DJ18 SAA1_HUMAN	4	1.25	2.38	0.001	12258	29214	6130	14598	0.50	0.50	up
sp P05090 APOD_HUMAN	34	1.26	2.39	0.024	165460	395334	152550	274688	0.92	0.69	up
sp P33908 MA1A1_HUMAN	11	1.26	2.39	0.002	82179	196501	39144	141911	0.48	0.72	up
sp Q9Y2C3 B3GT5_HUMAN	6	1.26	2.40	0.000	20208	48505	3310	35457	0.16	0.73	up
sp Q00115 DNS2A_HUMAN	6	1.26	2.40	0.000	21688	52114	6679	20778	0.31	0.40	up
sp Q14773 TPP1_HUMAN	20	1.27	2.41	0.000	82586	199087	15401	89769	0.19	0.45	up
sp Q9Y6E0 STK24_HUMAN	7	1.28	2.42	0.000	17817	43199	6455	20589	0.36	0.48	up
sp Q9NQ84 GPC5C_HUMAN	6	1.28	2.43	0.000	12354	29963	5896	12057	0.48	0.40	up
sp Q96BQ1 FAM3D_HUMAN	9	1.28	2.43	0.000	27369	66414	7485	36922	0.27	0.56	up
sp P40199 CEAM6_HUMAN	13	1.28	2.43	0.000	262694	639531	69209	285816	0.26	0.45	up
sp Q5JSH3 WDR44_HUMAN	3	1.28	2.44	0.000	14371	35015	6746	11603	0.47	0.33	up
sp Q43490 PROM1_HUMAN	24	1.29	2.44	0.000	83187	203048	34539	122483	0.42	0.60	up
sp P15289 ARSA_HUMAN	8	1.29	2.45	0.001	11912	29190	5233	18104	0.44	0.62	up
sp Q5SGD2 PPM1L_HUMAN	5	1.30	2.47	0.001	7095	17517	1718	13616	0.24	0.78	up
sp P06865 HEXA_HUMAN	15	1.30	2.47	0.000	61350	151539	19524	82709	0.32	0.55	up
sp Q9HBR0 S38AA_HUMAN	7	1.31	2.47	0.004	6317	15610	4594	9491	0.73	0.61	up
sp P40818 UBP8_HUMAN	3	1.31	2.49	0.004	4730	11766	2560	8428	0.54	0.72	up
sp Q96P63 SPB12_HUMAN	12	1.32	2.49	0.000	42183	104957	16708	53334	0.40	0.51	up
sp Q9UBR2 CATZ_HUMAN	6	1.32	2.49	0.000	51619	128600	17541	47206	0.34	0.37	up
sp Q15293 RCN1_HUMAN	33	1.32	2.49	0.000	200890	500693	25168	209362	0.13	0.42	up
sp Q13421 MSLN_HUMAN	75	1.32	2.49	0.001	1717903	4281750	787743	2346185	0.46	0.55	up
sp P16035 TIMP2_HUMAN	15	1.32	2.50	0.000	46671	116653	14287	64485	0.31	0.55	up
sp Q95967 FBLN4_HUMAN	4	1.33	2.51	0.000	1713	4302	657	2110	0.38	0.49	up
sp P54802 ANAG_HUMAN	10	1.33	2.51	0.000	27379	68787	7152	23592	0.26	0.34	up
sp P26572 MGAT1_HUMAN	11	1.33	2.52	0.000	50918	128113	22514	47841	0.44	0.37	up
sp P07686 HEXB_HUMAN	22	1.34	2.53	0.000	154630	391289	48613	167850	0.31	0.43	up
sp Q16769 QPCT_HUMAN	7	1.35	2.54	0.000	28353	72141	8569	31881	0.30	0.44	up
sp P16144 ITB4_HUMAN	4	1.35	2.55	0.049	1570	4008	832	6496	0.53	1.62	up
sp Q75976 CBPD_HUMAN	10	1.36	2.57	0.000	20031	51481	7117	19172	0.36	0.37	up
sp Q8NB7 SUMF2_HUMAN	7	1.36	2.57	0.000	43049	110838	7482	64070	0.17	0.58	up
sp Q92520 FAM3C_HUMAN	7	1.36	2.58	0.000	20506	52812	5525	26811	0.27	0.51	up
sp P14314 GLU2B_HUMAN	29	1.37	2.58	0.000	140380	362029	26748	141685	0.19	0.39	up
sp Q14656 TOR1A_HUMAN	3	1.37	2.58	0.001	3531	9121	1283	6682	0.36	0.73	up
sp P60033 CD81_HUMAN	4	1.37	2.59	0.000	7693	19925	2747	4105	0.36	0.21	up
sp Q9UGM3 DMBT1_HUMAN	578	1.37	2.59	0.002	2514580	6515970	1032182	5511229	0.41	0.85	up
sp P15907 SIAT1_HUMAN	11	1.38	2.60	0.000	37897	98639	14172	33881	0.37	0.34	up
sp P02649 APOE_HUMAN	28	1.39	2.62	0.000	164595	430592	57058	125933	0.35	0.29	up
sp P50591 TNF10_HUMAN	12	1.40	2.63	0.000	34810	91709	12917	36091	0.37	0.39	up
sp A0A0B4J1V0 HV315_HUMAN	14	1.40	2.64	0.008	64961	171778	30104	162883	0.46	0.95	up
sp Q16706 MA2A1_HUMAN	14	1.41	2.65	0.000	43467	115292	15071	61965	0.35	0.54	up
sp Q8IVD9 NUDC3_HUMAN	3	1.41	2.65	0.036	525	1393	447	1058	0.85	0.76	up
sp P21741 MK_HUMAN	10	1.41	2.66	0.002	45936	122211	27098	100096	0.59	0.82	up
sp Q77M9 GALT5_HUMAN	18	1.41	2.67	0.000	69639	185658	25204	93013	0.36	0.50	up
sp Q13232 NDK3_HUMAN	10	1.42	2.68	0.000	46884	125626	9605	46295	0.20	0.37	up
sp Q9GZM7 TINAL_HUMAN	9	1.43	2.69	0.000	17708	47624	8129	14362	0.46	0.30	up
sp Q9Y2E5 MA2B2_HUMAN	3	1.43	2.69	0.000	4433	11941	1669	6186	0.38	0.52	up
sp Q13835 PKP1_HUMAN	8	1.43	2.69	0.000	8515	22937	3542	11231	0.42	0.49	up
sp Q95395 GCNT3_HUMAN	11	1.43	2.70	0.000	66208	178435	40849	62683	0.62	0.35	up
sp P23490 LORI_HUMAN	3	1.43	2.70	0.000	13931	37549	5813	16639	0.42	0.44	up
sp P13866 SC5A1_HUMAN	5	1.43	2.70	0.001	5259	14182	2171	13382	0.41	0.94	up
sp P08571 CD14_HUMAN	20	1.43	2.70	0.000	170746	461166	56591	214307	0.33	0.46	up
sp P31944 CASPE_HUMAN	17	1.44	2.71	0.002	96906	262780	60799	207640	0.63	0.79	up
sp Q96EU7 C1GLC_HUMAN	8	1.44	2.71	0.000	38937	105672	12978	41357	0.33	0.39	up

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Table A.3 (continued)

Accession	PSMs	logFC	FC	PValue	mean_short	mean_long	SD_short	SD_long	CV_short	CV_long	direction
sp Q99935 PROL1_HUMAN	51	1.44	2.72	0.017	791475	2150059	908090	1160766	1.15	0.54	up
sp P51993 FUT6_HUMAN	4	1.45	2.73	0.000	7626	20823	2788	13659	0.37	0.66	up
sp Q16270 IBP7_HUMAN	7	1.45	2.73	0.000	44600	121791	19131	64671	0.43	0.53	up
sp Q99519 NEUR1_HUMAN	11	1.45	2.73	0.000	27906	76320	9589	35960	0.34	0.47	up
sp Q06828 FMOD_HUMAN	12	1.45	2.74	0.000	34544	94603	16612	50399	0.48	0.53	up
sp P20062 TCO2_HUMAN	5	1.47	2.76	0.000	15650	43245	5571	22601	0.36	0.52	up
sp P15291 B4GT1_HUMAN	10	1.47	2.78	0.000	68461	190187	20793	88897	0.30	0.47	up
sp P09668 CATH_HUMAN	12	1.49	2.81	0.000	137778	387091	62159	192914	0.45	0.50	up
sp O00560 SDCB1_HUMAN	11	1.49	2.81	0.000	35762	100510	14491	57669	0.41	0.57	up
sp P01034 CYTC_HUMAN	45	1.49	2.82	0.000	516163	1453298	439091	467925	0.85	0.32	up
sp Q15782 CH3L2_HUMAN	25	1.50	2.83	0.001	271042	767953	133044	432518	0.49	0.56	up
sp O43505 B4GA1_HUMAN	7	1.51	2.84	0.000	23470	66667	6446	34007	0.27	0.51	up
sp Q9GZZ8 LACRT_HUMAN	105	1.51	2.84	0.002	12549765	35686160	8128507	24562203	0.65	0.69	up
sp P01036 CYTS_HUMAN	171	1.51	2.85	0.000	697686	1986288	420767	765334	0.60	0.39	up
sp P00264 PGRC1_HUMAN	3	1.51	2.85	0.000	6092	17355	1415	11861	0.23	0.68	up
sp P45877 PPIC_HUMAN	8	1.52	2.86	0.000	58883	168289	17750	101628	0.30	0.60	up
sp P19021 AMD_HUMAN	15	1.52	2.87	0.000	59416	170397	22418	71649	0.38	0.42	up
sp P20933 ASPG_HUMAN	7	1.52	2.87	0.000	10439	30000	3535	20222	0.34	0.67	up
sp P06280 AGAL_HUMAN	6	1.53	2.89	0.000	5005	14447	2168	6949	0.43	0.48	up
sp O75787 RENH_HUMAN	5	1.57	2.96	0.000	24604	72936	7584	33421	0.31	0.46	up
sp Q8TAX7 MUC7_HUMAN	7	1.57	2.97	0.003	78010	231350	51415	188400	0.66	0.81	up
sp P50897 PPT1_HUMAN	7	1.57	2.97	0.000	27136	80533	7021	44986	0.26	0.56	up
sp Q86X29 LSR_HUMAN	20	1.57	2.98	0.000	50101	149066	20220	68849	0.40	0.46	up
sp Q15041 SEM3E_HUMAN	12	1.58	2.99	0.000	28953	86462	9917	46307	0.34	0.54	up
sp Q02487 DSC2_HUMAN	5	1.59	3.01	0.000	25709	77332	9832	39534	0.38	0.51	up
sp P12830 CADH1_HUMAN	20	1.60	3.03	0.000	117183	355328	40794	148145	0.35	0.42	up
sp Q14515 SPRL1_HUMAN	43	1.60	3.03	0.000	317659	963904	172876	299159	0.54	0.31	up
sp Q96596 PEBP4_HUMAN	14	1.61	3.04	0.000	479705	1460336	186728	963234	0.39	0.66	up
sp Q8IWU5 SULF2_HUMAN	8	1.61	3.06	0.000	29015	88792	12851	54130	0.44	0.61	up
sp P28799 GRN_HUMAN	21	1.62	3.07	0.000	210658	646158	79443	551525	0.38	0.85	up
sp P22352 GPX3_HUMAN	11	1.62	3.08	0.000	63864	196593	24278	87430	0.38	0.44	up
sp Q9UNW1 MINP1_HUMAN	11	1.63	3.09	0.000	54520	168731	18951	90596	0.35	0.54	up
sp Q8WVQ1 CANT1_HUMAN	9	1.63	3.10	0.000	46405	143783	21818	94890	0.47	0.66	up
sp Q8NB14 GOLM1_HUMAN	29	1.63	3.10	0.000	169581	526026	53261	243358	0.31	0.46	up
sp P20061 TCO1_HUMAN	101	1.63	3.10	0.000	1091808	3388691	499410	2508065	0.46	0.74	up
sp Q4KMQ2 ANO6_HUMAN	5	1.64	3.11	0.002	6262	19451	2345	24635	0.37	1.27	up
sp Q9H173 SIL1_HUMAN	14	1.64	3.11	0.000	71074	221384	43842	66994	0.62	0.30	up
sp Q8NCH0 CHSTE_HUMAN	3	1.66	3.16	0.000	2377	7510	406	3741	0.17	0.50	up
sp Q14050 CO9A3_HUMAN	9	1.66	3.16	0.001	14240	45064	9897	27530	0.69	0.61	up
sp P12931 SRC_HUMAN	4	1.66	3.17	0.019	3475	11017	867	18344	0.25	1.67	up
sp Q92820 GGH_HUMAN	4	1.67	3.17	0.000	40105	127230	12666	82167	0.32	0.65	up
sp P61769 B2MG_HUMAN	38	1.67	3.18	0.000	447608	1423211	255938	740603	0.57	0.52	up
sp O75503 CLN5_HUMAN	6	1.67	3.18	0.000	59363	188913	22968	122231	0.39	0.65	up
sp P14555 PA2GA_HUMAN	130	1.67	3.19	0.000	3131419	9994110	2260554	4157828	0.72	0.42	up
sp Q08380 LG3BP_HUMAN	73	1.68	3.21	0.000	540635	1733318	232571	859455	0.43	0.50	up
sp Q16378 PROL4_HUMAN	71	1.68	3.21	0.020	4223305	13544435	4914916	14254993	1.16	1.05	up
sp P07858 CATB_HUMAN	49	1.68	3.21	0.000	463614	1487861	154599	1002083	0.33	0.67	up
sp Q9Y646 CBPQ_HUMAN	11	1.69	3.22	0.000	37031	119080	11665	44894	0.32	0.38	up
sp P34096 RNAS4_HUMAN	16	1.70	3.25	0.000	435081	1411986	185985	665233	0.43	0.47	up
sp Q11201 SIA4A_HUMAN	10	1.71	3.26	0.000	54429	177519	24784	75278	0.46	0.42	up
sp Q01459 DIAC_HUMAN	11	1.71	3.26	0.000	98269	320518	40578	148929	0.41	0.46	up
sp Q9UM07 PADI4_HUMAN	6	1.71	3.27	0.018	2615	8558	2254	7515	0.86	0.88	up
sp Q08431 MFGM_HUMAN	39	1.71	3.27	0.000	184138	602828	90499	245739	0.49	0.41	up
sp Q86Y38 XYLT1_HUMAN	5	1.71	3.27	0.000	11122	36411	4064	24584	0.37	0.68	up
sp Q86YZ3 HORN_HUMAN	8	1.72	3.29	0.012	1022	3364	839	2835	0.82	0.84	up
sp Q9H8J5 MANS1_HUMAN	3	1.72	3.30	0.000	2621	8641	831	9460	0.32	1.09	up
sp Q14118 DAG1_HUMAN	11	1.73	3.31	0.000	74759	247815	25411	136816	0.34	0.55	up
sp P48723 HSP13_HUMAN	11	1.74	3.34	0.000	40086	133778	17941	64116	0.45	0.48	up
sp P12273 PIP_HUMAN	514	1.74	3.34	0.000	15010691	50129511	9226837	16291842	0.61	0.32	up
sp P12645 BMP3_HUMAN	4	1.74	3.35	0.000	6030	20196	1698	18346	0.28	0.91	up
sp Q13162 PRDX4_HUMAN	14	1.76	3.39	0.000	66916	226739	27524	82957	0.41	0.37	up
sp Q8WXG9 AGRV1_HUMAN	3	1.76	3.39	0.005	14481	49126	14256	27361	0.98	0.56	up
sp P35475 IDUA_HUMAN	5	1.77	3.40	0.000	7460	25387	2808	11550	0.38	0.45	up
sp Q15375 EPAH7_HUMAN	3	1.77	3.42	0.000	3400	11618	976	6136	0.29	0.53	up
sp P02788 TRFL_HUMAN	3706	1.78	3.42	0.000	114945168	393460755	57418908	201361732	0.50	0.51	up
sp Q02818 NUCB1_HUMAN	29	1.78	3.43	0.000	110822	380068	38672	234619	0.35	0.62	up
sp Q95841 ANGL1_HUMAN	15	1.78	3.43	0.000	73303	251559	36637	128800	0.50	0.51	up
sp Q9UHD0 IL19_HUMAN	3	1.78	3.44	0.000	25956	89237	13174	45015	0.51	0.50	up
sp Q13438 OS9_HUMAN	28	1.79	3.46	0.000	54065	186883	32095	80282	0.59	0.43	up
sp Q5XXA6 ANO1_HUMAN	12	1.79	3.46	0.000	52889	182952	19625	192909	0.37	1.05	up
sp Q92743 HTRA1_HUMAN	30	1.79	3.46	0.000	141505	489701	67167	242003	0.47	0.49	up
sp Q96MK3 FA20A_HUMAN	7	1.79	3.46	0.000	11690	40505	4799	20345	0.41	0.50	up
sp Q95968 SG1D1_HUMAN	127	1.80	3.48	0.001	1951395	6788253	1346841	4121333	0.69	0.61	up
sp Q95084 PRS23_HUMAN	7	1.80	3.49	0.000	20634	71953	8024	44548	0.39	0.62	up
sp Q13217 DNJC3_HUMAN	60	1.80	3.49	0.000	340495	1189610	202968	564516	0.60	0.47	up
sp Q8N474 SFRP1_HUMAN	44	1.81	3.50	0.000	760107	2657660	295280	2056785	0.39	0.77	up

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Table A.3 (continued)

Accession	PSMs	logFC	FC	PValue	mean_short	mean_long	SD_short	SD_long	CV_short	CV_long	direction
sp P07602 SAP_HUMAN	56	1.81	3.50	0.000	971809	3398532	501805	2304753	0.52	0.68	up
sp Q9BRK5 CAB45_HUMAN	17	1.81	3.51	0.000	126130	443317	46421	258555	0.37	0.58	up
sp P25311 ZA2G_HUMAN	499	1.82	3.52	0.000	12010383	42318551	5491790	15839132	0.46	0.37	up
sp P49458 SRP09_HUMAN	7	1.82	3.53	0.002	58167	205240	26500	226948	0.46	1.11	up
sp O00462 MANBA_HUMAN	25	1.82	3.53	0.000	94413	333218	24695	169102	0.26	0.51	up
sp Q02809 PLOD1_HUMAN	31	1.82	3.53	0.000	113013	399175	38617	192830	0.34	0.48	up
sp P30533 AMRP_HUMAN	4	1.84	3.57	0.005	10058	35942	1206	62509	0.12	1.74	up
sp Q13444 ADA15_HUMAN	3	1.84	3.57	0.000	5722	20453	1898	9683	0.33	0.47	up
sp P84243 H33_HUMAN	3	1.85	3.60	0.005	6327	22774	2332	37891	0.37	1.66	up
sp Q14393 GAS6_HUMAN	12	1.85	3.61	0.000	19174	69166	6301	38213	0.33	0.55	up
sp Q9NRJ3 CCL28_HUMAN	4	1.86	3.62	0.000	62147	224944	38032	169646	0.61	0.75	up
sp P6PCB0 VWA1_HUMAN	10	1.86	3.63	0.000	60389	219072	22232	113334	0.37	0.52	up
sp P03950 ANGI_HUMAN	11	1.86	3.63	0.000	130173	472772	55448	253618	0.43	0.54	up
sp O43852 CALU_HUMAN	34	1.86	3.63	0.000	269575	979546	96886	558636	0.36	0.57	up
sp P41214 EIF2D_HUMAN	4	1.86	3.63	0.005	989	3594	758	2789	0.77	0.78	up
sp Q99574 NEUS_HUMAN	20	1.87	3.64	0.000	103235	376250	46786	150888	0.45	0.40	up
sp Q99538 LGMN_HUMAN	9	1.87	3.66	0.000	16736	61178	7114	30668	0.43	0.50	up
sp Q13296 SG2A2_HUMAN	4	1.89	3.70	0.007	25605	94648	19361	150142	0.76	1.59	up
sp Q75094 SLIT3_HUMAN	32	1.89	3.70	0.000	60621	224225	25672	166454	0.42	0.74	up
sp O43405 COCH_HUMAN	9	1.90	3.73	0.000	39372	146670	12021	79959	0.31	0.55	up
sp Q9Y2I8 WDR37_HUMAN	3	1.90	3.74	0.002	5431	20308	788	33457	0.15	1.65	up
sp Q8NCL4 GALT6_HUMAN	17	1.91	3.75	0.000	50586	189664	16663	112883	0.33	0.60	up
sp P27487 DPP4_HUMAN	25	1.91	3.77	0.000	163788	617059	62270	500755	0.38	0.81	up
sp O00584 RNT2_HUMAN	27	1.92	3.77	0.000	289905	1093670	117438	452742	0.41	0.41	up
sp Q9UJJ9 GNPTG_HUMAN	13	1.95	3.86	0.000	24154	93255	10408	46887	0.43	0.50	up
sp P55058 PLTP_HUMAN	58	1.96	3.88	0.000	583422	2262147	304563	1414120	0.52	0.63	up
sp P12259 FA5_HUMAN	61	1.98	3.95	0.000	233543	921762	173399	479702	0.74	0.52	up
sp P01037 CYTN_HUMAN	121	1.99	3.97	0.011	622973	2474580	942964	1933569	1.51	0.78	up
sp Q9UBX1 CATF_HUMAN	12	1.99	3.98	0.000	22092	87966	8277	52738	0.37	0.60	up
sp P07711 CATL1_HUMAN	11	2.01	4.02	0.000	69453	278925	31628	136999	0.46	0.49	up
sp P12109 CO6A1_HUMAN	21	2.04	4.12	0.000	29092	119855	8013	53212	0.28	0.44	up
sp P03973 SLPI_HUMAN	146	2.05	4.14	0.000	966886	4005439	364541	3659686	0.38	0.91	up
sp Q6UXI9 NPNT_HUMAN	8	2.07	4.21	0.000	21366	89911	11187	50398	0.52	0.56	up
sp Q9NRA1 PDGFC_HUMAN	12	2.11	4.30	0.000	29032	124900	10826	83990	0.37	0.67	up
sp Q9UL18 AGO1_HUMAN	4	2.14	4.42	0.001	4161	18389	999	30229	0.24	1.64	up
sp P80303 NUCB2_HUMAN	64	2.15	4.42	0.000	579257	2562499	317692	1595970	0.55	0.62	up
sp Q9H336 CRLD1_HUMAN	3	2.15	4.45	0.009	1256	5589	915	7105	0.73	1.27	up
sp Q86UD1 OAF_HUMAN	11	2.22	4.65	0.000	40753	189659	21139	68182	0.52	0.36	up
sp P58499 FAM3B_HUMAN	5	2.22	4.67	0.000	9609	44829	3595	31413	0.37	0.70	up
sp Q9BWS9 CHID1_HUMAN	20	2.24	4.73	0.000	69311	327609	22571	185496	0.33	0.57	up
sp P98160 PGBM_HUMAN	418	2.26	4.80	0.000	1834748	8812277	546782	6494029	0.30	0.74	up
sp Q9UBS3 DNJB9_HUMAN	5	2.26	4.81	0.000	13362	64222	9942	27537	0.74	0.43	up
sp P61626 LYSC_HUMAN	1385	2.31	4.97	0.000	75221412	373685183	31487163	183899286	0.42	0.49	up
sp P31025 LCN1_HUMAN_family	1587	2.32	5.01	0.000	50310517	251985844	34956864	99720435	0.69	0.40	up
sp Q9P2M7 CING_HUMAN	6	2.35	5.09	0.004	19878	101093	3613	211771	0.18	2.09	up
sp Q9BQ16 TICN3_HUMAN	14	2.39	5.24	0.000	29169	152784	15164	159289	0.52	1.04	up
sp Q92838 EDA_HUMAN	3	2.41	5.33	0.000	1815	9666	922	4965	0.51	0.51	up
sp P09958 FURIN_HUMAN	5	2.42	5.34	0.000	8707	46461	2633	32986	0.30	0.71	up
sp Q6UXB2 CXL17_HUMAN	10	2.46	5.50	0.000	132829	730425	72766	429055	0.55	0.59	up
sp Q9BXJ1 C1QT1_HUMAN	3	2.47	5.54	0.000	6623	36677	4132	25772	0.62	0.70	up
sp P21246 PTN_HUMAN	13	2.47	5.56	0.000	26051	144832	12325	157128	0.47	1.08	up
sp P22079 PERL_HUMAN	75	2.51	5.70	0.000	539345	3075435	218249	1419452	0.40	0.46	up
sp Q96DA0 ZG16B_HUMAN	102	2.59	6.02	0.000	1323279	7964362	495272	6299434	0.37	0.79	up
sp Q95965 ITGBL_HUMAN	3	2.78	6.88	0.001	536	3688	819	2803	1.53	0.76	up
sp Q75556 SG2A1_HUMAN	167	3.12	8.69	0.000	2835732	24639065	1507206	35061575	0.53	1.42	up
sp Q8IXB1 DJC10_HUMAN	3	6.73	105.87	0.000	1420	150387	2017	361837	1.42	2.41	up

Table A.4

Differentially expressed proteins between pipetted long schirmer strip and short schirmer strip (reference) – see Fig. 5B

Accession	PSMs	logFC	FC	PValue	mean_short	mean_long	sd_short	sd_long	cv_short	cv_long	direction
sp Q12913 PTPRJ_HUMAN	3	-2.46	-5.50	0.000	3796	690	2378	374	0.63	0.54	down
sp P69905 HBA_HUMAN	17	-2.05	-4.13	0.001	1036139	250679	1204258	25426	1.16	0.10	down
sp Q04323 UBXN1_HUMAN	7	-2.04	-4.12	0.023	1165	283	1330	265	1.14	0.94	down
sp P46108 CRK_HUMAN	8	-1.50	-2.82	0.003	15864	5618	15635	660	0.99	0.12	down
sp P41236 IPP2_HUMAN (+1)	3	-1.49	-2.81	0.026	419	149	456	6	1.09	0.04	down
sp Q9HBR0 S38AA_HUMAN	5	-1.20	-2.30	0.000	5845	2543	541	943	0.09	0.37	down
sp Q99935 PROL1_HUMAN	40	-1.12	-2.17	0.000	5294362	2441034	2177847	315137	0.41	0.13	down
sp P00492 HPRT_HUMAN	3	-1.09	-2.13	0.002	3402	1599	1203	243	0.35	0.15	down
sp Q16531 DDB1_HUMAN	3	-1.06	-2.09	0.000	11794	5656	3339	890	0.28	0.16	down
sp P68871 HBB_HUMAN	12	-1.05	-2.08	0.012	389363	187570	325182	9301	0.84	0.05	down
sp Q9GZZ8 LACRT_HUMAN	101	-0.91	-1.88	0.000	41450019	22012306	11835300	2664648	0.29	0.12	down

(continued on next page)

Table A.4 (continued)

Accession	PSMs	logFC	FC	PValue	mean_short	mean_long	sd_short	sd_long	cv_short	cv_long	direction
sp P53004 BIEA_HUMAN	4	-0.91	-1.88	0.000	74617	39654	20255	2689	0.27	0.07	down
sp O75688 PPM1B_HUMAN	4	-0.91	-1.87	0.016	14930	7969	10584	1221	0.71	0.15	down
sp P61758 PFD3_HUMAN	3	-0.87	-1.82	0.005	5281	2895	1431	932	0.27	0.32	down
sp P02795 MT2_HUMAN (+2)	5	-0.82	-1.76	0.048	3436	1949	567	844	0.17	0.43	down
sp P02654 APOC1_HUMAN	6	-0.80	-1.75	0.000	67646	38746	19233	7128	0.28	0.18	down
sp Q9NVE7 PANK4_HUMAN	4	-0.79	-1.73	0.000	10496	6055	2083	803	0.20	0.13	down
sp A8K2U0 A2ML1_HUMAN	6	-0.75	-1.68	0.000	32593	19399	9965	1563	0.31	0.08	down
sp P02763 A1AG1_HUMAN	22	-0.71	-1.64	0.000	561742	343050	48871	29888	0.09	0.09	down
sp P81605 DCD_HUMAN	12	-0.70	-1.62	0.004	629786	389001	244675	38337	0.39	0.10	down
sp P58107 EPIPL_HUMAN	10	-0.69	-1.62	0.013	21631	13362	10563	1652	0.49	0.12	down
sp P24666 PPAC_HUMAN	7	-0.69	-1.62	0.000	13958	8623	2999	783	0.21	0.09	down
sp Q01082 SPTB2_HUMAN	5	-0.66	-1.58	0.014	4560	2891	763	593	0.17	0.21	down
sp O95747 OXSR1_HUMAN	3	-0.64	-1.56	0.008	6899	4420	1120	1177	0.16	0.27	down
sp O75368 SH3L1_HUMAN	4	-0.64	-1.55	0.001	21575	13888	5788	1462	0.27	0.11	down
sp O75351 VPS4B_HUMAN	3	-0.63	-1.54	0.001	9692	6278	1597	987	0.16	0.16	down
sp P31151 S10A7_HUMAN	10	-0.61	-1.53	0.008	1036679	678502	273715	170801	0.26	0.25	down
sp Q9P2J5 SYLC_HUMAN	3	0.59	1.51	0.018	2995	4514	49	954	0.02	0.21	up
sp P26640 SYVC_HUMAN	5	0.70	1.63	0.035	1692	2754	101	693	0.06	0.25	up
sp P05164 PERM_HUMAN	22	0.77	1.71	0.043	174898	298393	7704	192996	0.04	0.65	up
sp Q8NBJ7 SUMF2_HUMAN	3	1.53	2.88	0.010	5987	17270	150	15118	0.03	0.88	up
sp Q8WVY7 UBCP1_HUMAN	4	1.89	3.70	0.010	442	1634	497	416	1.12	0.25	up
sp Q9H4G4 GAPR1_HUMAN	3	3.86	14.56	0.000	152	2215	11	2035	0.07	0.92	up

Table A.5

Differentially expressed proteins between Portland site and Miami site (reference) – see Fig. 6

Accession	PSMs	logFC	FC	PValue	mean_miami	mean_portland	sd_miami	sd_portland	cv_miami	cv_portland	direction
tr A0A075B7B6 A0A075B7B6_HUMAN	4	-1.93	-3.80	0.048	10278	2707	10006	710	0.97	0.26	down
sp P24593 IBP5_HUMAN	10	-1.50	-2.83	0.008	63618	22488	32162	8407	0.51	0.37	down
sp O14815 CAN9_HUMAN	3	-1.30	-2.46	0.021	11758	4771	5807	447	0.49	0.09	down
sp P98088 MUC5A_HUMAN	224	-1.25	-2.38	0.010	3250990	1366096	1216103	789937	0.37	0.58	down
sp P35542 SAA4_HUMAN	6	-1.25	-2.38	0.001	331611	139483	107032	34336	0.32	0.25	down
sp P22891 PROZ_HUMAN	3	-1.23	-2.35	0.011	16946	7226	6595	3475	0.39	0.48	down
sp P43652 AFAM_HUMAN	50	-1.23	-2.34	0.003	848588	362492	281551	165197	0.33	0.46	down
sp P25815 S100P_HUMAN	6	-1.23	-2.34	0.000	15535	6644	2678	2448	0.17	0.37	down
sp P51159 RB27A_HUMAN	6	-1.17	-2.25	0.000	69483	30924	18337	1399	0.26	0.05	down
sp P02656 APOC3_HUMAN	6	-1.16	-2.23	0.000	21164	9481	3810	2913	0.18	0.31	down
sp O95716 RAB3D_HUMAN	9	-1.15	-2.22	0.006	78620	35458	30982	101	0.39	0.00	down
sp P0C0L5 CO4B_HUMAN_family	142	-1.14	-2.21	0.009	3081650	1395441	1162559	358875	0.38	0.26	down
sp P10620 MGST1_HUMAN	6	-1.12	-2.18	0.025	86057	39501	45044	11027	0.52	0.28	down
sp P07360 CO8G_HUMAN	8	-1.07	-2.11	0.001	86167	40918	24870	5178	0.29	0.13	down
sp Q96KN2 CNDP1_HUMAN	3	-1.07	-2.10	0.013	9684	4608	3395	1343	0.35	0.29	down
sp P08575 PTPRC_HUMAN	5	-1.06	-2.08	0.017	5945	2857	2497	176	0.42	0.06	down
tr A0A075B7D0 A0A075B7D0_HUMAN	5	-1.05	-2.07	0.015	12448	6028	3789	2792	0.30	0.46	down
sp P09455 RET1_HUMAN	14	-1.04	-2.05	0.002	157025	76580	46717	13567	0.30	0.18	down
sp Q8N118 CP4X1_HUMAN	3	-1.03	-2.04	0.030	11048	5418	4116	2512	0.37	0.46	down
sp P05090 APOD_HUMAN	26	-1.02	-2.03	0.047	264130	130339	117713	45938	0.45	0.35	down
sp Q9UBX7 K1K11_HUMAN	5	-1.01	-2.01	0.005	35616	17683	11165	406	0.31	0.02	down
sp P04217 A1BG_HUMAN	40	-0.98	-1.97	0.016	577457	293491	257547	40389	0.45	0.14	down
sp P08263 GSTA1_HUMAN_family	48	-0.97	-1.96	0.001	1329269	678884	345873	10550	0.26	0.02	down
sp P52895 AK1C2_HUMAN	12	-0.97	-1.96	0.005	231245	118178	81177	8983	0.35	0.08	down
sp P04004 VTNC_HUMAN	19	-0.96	-1.94	0.024	334782	172216	162304	6272	0.48	0.04	down
sp Q9BZQ8 NIBA1_HUMAN	33	-0.95	-1.94	0.005	744212	384224	233502	40621	0.31	0.11	down
sp P02647 APOA1_HUMAN	79	-0.95	-1.93	0.002	4089805	2113719	943388	316398	0.23	0.15	down
sp Q14520 HABP2_HUMAN	10	-0.95	-1.93	0.007	77797	40346	25111	1684	0.32	0.04	down
sp Q9BV36 MELPH_HUMAN	5	-0.92	-1.90	0.042	10812	5701	4411	1022	0.41	0.18	down
sp Q9H8H3 MET7A_HUMAN	6	-0.91	-1.88	0.044	132601	70454	60071	7543	0.45	0.11	down
sp P02790 HEMO_HUMAN	117	-0.91	-1.87	0.018	2751647	1468429	1083529	5900	0.39	0.00	down
sp P02649 APOE_HUMAN	18	-0.90	-1.86	0.020	171215	91886	36200	49606	0.21	0.54	down
sp P19823 TIH2_HUMAN	49	-0.88	-1.85	0.018	1219218	660399	483474	58480	0.40	0.09	down
sp Q8IXJ6 SIR2_HUMAN	3	-0.86	-1.82	0.004	18497	10160	2109	3509	0.11	0.35	down
sp O15195 VILL_HUMAN	8	-0.86	-1.81	0.007	52925	29164	12817	7161	0.24	0.25	down
sp Q9BS40 LXN_HUMAN	18	-0.84	-1.80	0.022	324644	180794	125092	3707	0.39	0.02	down
sp Q8IXB1 DJC10_HUMAN	4	-0.84	-1.79	0.032	7288	4072	2218	1308	0.30	0.32	down
sp P02765 FETUA_HUMAN	69	-0.84	-1.79	0.034	4482193	2504859	1819423	340960	0.41	0.14	down
sp Q9Y696 CLIC4_HUMAN	11	-0.84	-1.78	0.024	66140	37075	22049	7035	0.33	0.19	down
sp P00742 FA10_HUMAN	8	-0.82	-1.76	0.018	26211	14883	7848	1171	0.30	0.08	down
sp P22792 CPN2_HUMAN	10	-0.81	-1.76	0.022	66330	37703	22303	906	0.34	0.02	down

(continued on next page)

Table A.5 (continued)

Accession	PSMs	logFC	FC	PValue	mean_miami	mean_portland	sd_miami	sd_portland	cv_miami	cv_portland	direction
sp O43175 SERA_HUMAN	26	-0.81	-1.75	0.037	410474	234145	143823	73340	0.35	0.31	down
sp P00748 FA12_HUMAN	14	-0.80	-1.75	0.035	53633	30718	8167	17042	0.15	0.55	down
sp P28161 GSTM2_HUMAN	3	-0.80	-1.75	0.020	46424	26591	11829	8098	0.25	0.30	down
sp P01011 AACT_HUMAN	75	-0.80	-1.74	0.006	1339489	767783	340930	22766	0.25	0.03	down
sp P19827 ITIH1_HUMAN	34	-0.80	-1.74	0.020	535497	307781	184236	57527	0.34	0.19	down
sp O95994 AGR2_HUMAN	39	-0.79	-1.73	0.003	1102436	635636	204993	111040	0.19	0.17	down
sp P08962 CD63_HUMAN	4	-0.79	-1.73	0.009	82483	47632	16147	13434	0.20	0.28	down
sp P01042 KNG1_HUMAN	52	-0.79	-1.73	0.035	885227	511623	331263	21548	0.37	0.04	down
sp P02760 AMBP_HUMAN	24	-0.79	-1.73	0.014	196427	113537	58524	13394	0.30	0.12	down
sp O43866 CD5L_HUMAN	14	-0.78	-1.72	0.008	147992	86174	28269	22653	0.19	0.26	down
sp O95445 APOM_HUMAN	7	-0.77	-1.70	0.035	79036	46451	27286	1307	0.35	0.03	down
sp P05156 CFAI_HUMAN	24	-0.76	-1.70	0.004	280415	165282	58538	26828	0.21	0.16	down
sp O95881 TXD12_HUMAN	3	-0.76	-1.69	0.030	38028	22469	8747	7584	0.23	0.34	down
sp P49914 MTHFS_HUMAN	3	-0.75	-1.69	0.021	6572	3897	1450	262	0.22	0.07	down
sp P07357 CO8A_HUMAN	19	-0.75	-1.69	0.044	187679	111365	68676	10566	0.37	0.09	down
sp Q96AX2 RAB37_HUMAN	4	-0.75	-1.68	0.033	23570	14029	6086	3370	0.26	0.24	down
sp P03952 KLKB1_HUMAN	22	-0.74	-1.67	0.007	212667	127151	51155	4984	0.24	0.04	down
sp Q9NPH2 INO1_HUMAN	6	-0.74	-1.67	0.013	30094	18029	6547	2129	0.22	0.12	down
sp P23142 FBLN1_HUMAN	12	-0.74	-1.67	0.046	55763	33466	21246	3030	0.38	0.09	down
sp P02766 TTHY_HUMAN	76	-0.73	-1.66	0.031	1077992	649598	335454	12227	0.31	0.02	down
sp P18428 LBP_HUMAN	5	-0.73	-1.66	0.035	45692	27536	13983	5572	0.31	0.20	down
sp Q93084 AT2A3_HUMAN	8	-0.71	-1.64	0.015	19430	11874	4528	95	0.23	0.01	down
sp P17252 KPCA_HUMAN	8	-0.71	-1.63	0.021	25345	15531	6537	1819	0.26	0.12	down
sp Q5T5C0 STXB5_HUMAN	10	-0.69	-1.61	0.008	20014	12417	2887	1863	0.14	0.15	down
sp P30626 SORCN_HUMAN	6	-0.68	-1.60	0.009	61100	38069	11175	910	0.18	0.02	down
sp P01031 CO5_HUMAN	53	-0.68	-1.60	0.019	453061	282317	121190	6045	0.27	0.02	down
sp P47736 RPGP1_HUMAN	3	-0.68	-1.60	0.005	10747	6703	795	14	0.07	0.00	down
sp P08603 CFAH_HUMAN	91	-0.68	-1.60	0.033	1467607	918694	429809	116192	0.29	0.13	down
sp P05155 IC1_HUMAN	24	-0.67	-1.59	0.028	1068658	673773	274814	69916	0.26	0.10	down
sp Q8NBS9 TXND5_HUMAN	13	-0.66	-1.58	0.015	147491	93499	33885	87	0.23	0.00	down
sp Q6BCY4 NB5R2_HUMAN	9	-0.63	-1.55	0.007	38452	24837	4049	404	0.11	0.02	down
sp P55145 MANF_HUMAN	3	-0.62	-1.54	0.028	15765	10228	2025	2974	0.13	0.29	down
sp P00751 CFAB_HUMAN	72	-0.62	-1.54	0.048	1937722	1260085	471585	303696	0.24	0.24	down
sp O00194 RB27B_HUMAN	13	-0.62	-1.54	0.050	215493	140250	58059	9748	0.27	0.07	down
sp P35080 PROF2_HUMAN	6	-0.62	-1.54	0.025	21959	14300	3431	3251	0.16	0.23	down
sp O00391 QSOX1_HUMAN	39	-0.62	-1.53	0.031	337729	220029	70140	61506	0.21	0.28	down
sp P00734 THRB_HUMAN	59	-0.61	-1.53	0.028	577613	378114	146839	11882	0.25	0.03	down
sp Q9H299 SH3L3_HUMAN	11	-0.59	-1.51	0.038	37693	25011	7457	3367	0.20	0.13	down
sp O60268 K0513_HUMAN	3	-0.59	-1.50	0.037	16375	10885	2696	2440	0.16	0.22	down
sp P35637 FUS_HUMAN	4	0.59	1.51	0.036	33958	51144	6151	15203	0.18	0.30	up
sp P36578 RL4_HUMAN	11	0.62	1.54	0.010	94726	146088	17840	2860	0.19	0.02	up
sp Q15233 NONO_HUMAN	7	0.63	1.55	0.047	70176	108514	19310	16913	0.28	0.16	up
sp Q14195 DPYL3_HUMAN	9	0.63	1.55	0.049	42546	65885	12947	5470	0.30	0.08	up
sp P07711 CATL1_HUMAN	14	0.66	1.58	0.034	53519	84583	14275	19170	0.27	0.23	up
sp O43405 COCH_HUMAN	13	0.67	1.59	0.030	35982	57357	4351	26846	0.12	0.47	up
sp Q641Q2 WAC2A_HUMAN	6	0.68	1.60	0.042	3772	6023	943	561	0.25	0.09	up
sp P05387 RLA2_HUMAN	8	0.70	1.63	0.000	88705	144334	6877	4507	0.08	0.03	up
sp O60437 PEPL_HUMAN	100	0.71	1.64	0.001	1013398	1658749	149703	54161	0.15	0.03	up
sp A0A0C4DH67 KV108_HUMAN	7	0.72	1.65	0.016	2659	4374	217	585	0.08	0.13	up
sp P16989 YBOX3_HUMAN	5	0.72	1.65	0.012	7618	12551	1800	1320	0.24	0.11	up
sp O15344 TRI18_HUMAN	3	0.74	1.67	0.043	13332	22200	391	13982	0.03	0.63	up
sp Q8IW75 SPA12_HUMAN	5	0.74	1.67	0.048	20994	34962	7975	9107	0.38	0.26	up
sp Q6VY07 PACS1_HUMAN	12	0.74	1.67	0.044	84195	140898	11077	88592	0.13	0.63	up
sp Q09666 AHNK_HUMAN	144	0.77	1.71	0.002	1958183	3341649	275061	974845	0.14	0.29	up
sp P21397 AOFA_HUMAN	11	0.78	1.71	0.001	106288	182042	15292	23415	0.14	0.13	up
sp Q07002 CDK18_HUMAN	3	0.80	1.74	0.044	2199	3818	603	1332	0.27	0.35	up
sp Q9Y2W1 TR150_HUMAN	5	0.80	1.75	0.013	6395	11162	1679	684	0.26	0.06	up
sp Q9UBT3 DKK4_HUMAN	10	0.81	1.75	0.020	28217	49428	7162	22797	0.25	0.46	up
sp O94903 PLPHP_HUMAN	5	0.83	1.78	0.031	15850	28153	2281	18082	0.14	0.64	up
sp Q5D862 FILA2_HUMAN	24	0.86	1.81	0.040	260672	471928	137313	75107	0.53	0.16	up
sp Q8WVV4 POF1B_HUMAN	7	0.87	1.83	0.031	24754	45365	6557	27167	0.26	0.60	up
sp Q8N1A6 CD033_HUMAN	3	0.88	1.84	0.015	38600	71001	11338	28054	0.29	0.40	up
sp P47929 LEG7_HUMAN	10	0.88	1.84	0.010	84273	155371	15951	81177	0.19	0.52	up
sp A0A0A0MT36 KVD21_HUMAN	3	0.91	1.88	0.045	2237	4204	971	548	0.43	0.13	up
sp Q96QA5 GSDMA_HUMAN	7	0.94	1.91	0.015	101879	194918	47337	17437	0.46	0.09	up
sp P28907 CD38_HUMAN	5	0.95	1.93	0.000	29183	56202	3892	14171	0.13	0.25	up
sp O75635 SPB7_HUMAN	4	0.95	1.94	0.003	11116	21526	1613	9655	0.15	0.45	up
sp Q9UBG3 CRNN_HUMAN	11	0.98	1.97	0.029	103001	203318	31060	134861	0.30	0.66	up
sp Q96EN8 MOCOS_HUMAN	7	0.99	1.99	0.009	18121	36005	7033	6555	0.39	0.18	up
sp P14317 HCLS1_HUMAN	5	1.00	1.99	0.002	4138	8254	1154	469	0.28	0.06	up
sp P14923 PLAK_HUMAN	35	1.00	2.00	0.022	386468	771928	94730	558498	0.25	0.72	up
sp O75556 SG2A1_HUMAN	107	1.02	2.02	0.028	926984	1873386	430354	1014889	0.46	0.54	up
sp Q14050 CO9A3_HUMAN	7	1.07	2.10	0.003	18471	38858	6178	509	0.33	0.01	up
sp P48960 AGRES_HUMAN	3	1.07	2.10	0.024	1980	4165	814	1421	0.41	0.34	up

(continued on next page)

Table A.5 (continued)

Accession	PSMs	logFC	FC	PValue	mean_miami	mean_portland	sd_miami	sd_portland	cv_miami	cv_portland	direction
sp P0DTE7 AMY1B_HUMAN (+2)	43	1.09	2.13	0.000	317317	675085	60323	65500	0.19	0.10	up
sp P30511 HLAF_HUMAN	3	1.10	2.15	0.039	1621	3480	859	349	0.53	0.10	up
sp Q96P63 SPB12_HUMAN	14	1.10	2.15	0.045	63752	137080	34573	94486	0.54	0.69	up
sp Q13835 PKP1_HUMAN	12	1.11	2.17	0.031	53528	115935	2157	108615	0.04	0.94	up
sp P15924 DESP_HUMAN	144	1.12	2.18	0.015	884715	1924808	177379	1525616	0.20	0.79	up
sp Q08188 TGM3_HUMAN	20	1.19	2.27	0.003	81115	184488	28917	86506	0.36	0.47	up
sp P40394 ADH7_HUMAN	47	1.19	2.28	0.004	1193876	2720674	510930	484020	0.43	0.18	up
sp P13498 CY24A_HUMAN	3	1.19	2.28	0.012	20046	45743	8946	24224	0.45	0.53	up
sp Q02413 DSG1_HUMAN	32	1.32	2.50	0.010	118285	295824	34437	243907	0.29	0.82	up
sp Q86T26 TM11B_HUMAN	4	1.34	2.53	0.017	8630	21855	2980	19747	0.35	0.90	up
sp Q6UWP8 SBSN_HUMAN	4	1.40	2.64	0.005	21289	56101	5186	46621	0.24	0.83	up
sp P30838 AL3A1_HUMAN	104	1.40	2.64	0.000	2137012	5641749	885373	518327	0.41	0.09	up
sp A0A0C4DH33 HV124_HUMAN	3	1.46	2.75	0.009	2784	7643	36	7343	0.01	0.96	up
sp Q08554 DSC1_HUMAN	15	1.60	3.03	0.005	46485	140884	10555	137276	0.23	0.97	up
sp Q4351 S26A4_HUMAN	3	1.64	3.12	0.031	4027	12552	2547	13423	0.63	1.07	up
sp Q95968 SG1D1_HUMAN	63	1.69	3.23	0.000	3063467	9905511	889072	6416356	0.29	0.65	up

Table A.6

Differentially expressed proteins between contact lens user and non-user (reference) with a wide range of Schirmer strip wetted length – see Fig. 7A

Accession	PSMs	logFC	FC	PValue	mean_no	mean_yes	sd_no	sd_yes	cv_no	cv_yes	direction
sp P02795 MT2_HUMAN (+2)	6	-1.78	-3.43	0.001	1288	375	365	372	0.28	0.99	down
sp P02652 APOA2_HUMAN	5	-1.75	-3.35	0.001	83799	24985	125022	5036	1.49	0.20	down
sp Q8N6T3 ARFG1_HUMAN	3	-1.55	-2.92	0.001	954	326	156	288	0.16	0.88	down
sp O95965 ITGBL_HUMAN	6	-1.38	-2.61	0.020	58543	22431	96114	9833	1.64	0.44	down
sp P23141 EST1_HUMAN	11	-1.11	-2.15	0.006	91057	42325	50566	19170	0.56	0.45	down
sp Q9P2B2 FPRP_HUMAN	3	-1.00	-2.00	0.018	3318	1661	858	725	0.26	0.44	down
sp Q9NVA2 SEP11_HUMAN	3	-0.90	-1.87	0.008	3474	1862	268	705	0.08	0.38	down
sp Q05639 EF1A2_HUMAN	5	-0.89	-1.85	0.011	34702	18750	30254	5052	0.87	0.27	down
sp Q8TC07 TBC15_HUMAN	5	-0.86	-1.81	0.014	8115	4477	6819	1206	0.84	0.27	down
sp P02656 APOC3_HUMAN	4	-0.84	-1.79	0.049	14940	8342	16067	2837	1.08	0.34	down
sp O14936 CSKP_HUMAN	3	-0.73	-1.66	0.050	5046	3033	1926	1543	0.38	0.51	down
sp Q9BRF8 CPPED_HUMAN	16	-0.73	-1.66	0.033	204415	123386	94119	73696	0.46	0.60	down
sp Q14978 NOLC1_HUMAN	4	-0.71	-1.64	0.044	6937	4230	1800	2263	0.26	0.53	down
sp P49207 RL34_HUMAN	6	-0.67	-1.60	0.002	52764	33069	20200	6167	0.38	0.19	down
sp P51858 HDGF_HUMAN	11	-0.64	-1.56	0.001	54720	35163	12236	7497	0.22	0.21	down
sp P13073 COX41_HUMAN	7	-0.62	-1.53	0.003	140927	91918	34237	20023	0.24	0.22	down
sp Q9NXG2 THUM1_HUMAN	3	-0.60	-1.52	0.011	9438	6216	3064	1713	0.32	0.28	down
sp Q95523 SORT1_HUMAN	3	0.59	1.50	0.028	7571	11364	1936	3809	0.26	0.34	up
sp Q969Q5 RAB24_HUMAN	3	0.59	1.50	0.022	5503	8267	889	3241	0.16	0.39	up
sp Q9BTY2 FUOCO2_HUMAN	9	0.59	1.50	0.046	36799	55363	11273	22582	0.31	0.41	up
tr A0A075B7B8 A0A075B7B8_HUMAN	5	0.61	1.52	0.044	33788	51402	18365	14797	0.54	0.29	up
sp P00450 CERU_HUMAN	220	0.61	1.53	0.028	1504664	2298893	477572	778312	0.32	0.34	up
sp O75976 CBPD_HUMAN	13	0.62	1.53	0.028	23329	35748	5119	13155	0.22	0.37	up
sp Q9H9Q2 CSN7B_HUMAN	3	0.62	1.54	0.035	1385	2130	267	660	0.19	0.31	up
sp P01011 AACT_HUMAN	70	0.62	1.54	0.009	659007	1014941	152764	295550	0.23	0.29	up
sp P02775 CXCL7_HUMAN	3	0.62	1.54	0.014	27609	42531	9822	13741	0.36	0.32	up
sp P49257 LMAN1_HUMAN	15	0.62	1.54	0.003	59489	91666	10451	24205	0.18	0.26	up
sp P26572 MGAT1_HUMAN	8	0.62	1.54	0.041	30031	46299	8004	22559	0.27	0.49	up
sp O15173 PGRC2_HUMAN	3	0.63	1.54	0.015	2757	4258	396	1387	0.14	0.33	up
sp P00740 FA9_HUMAN	4	0.64	1.55	0.002	6587	10231	1426	2570	0.22	0.25	up
sp Q96BQ1 FAM3D_HUMAN	11	0.64	1.56	0.010	30536	47730	5758	17073	0.19	0.36	up
sp P50897 PPT1_HUMAN	3	0.64	1.56	0.013	8199	12821	2277	4101	0.28	0.32	up
sp B9A064 IGLL5_HUMAN	44	0.65	1.57	0.010	161314	252748	45826	82156	0.28	0.33	up
sp Q9N208 ERAP1_HUMAN	28	0.66	1.58	0.013	147924	233655	35359	86000	0.24	0.37	up
sp Q9H0P0 5NNT3A_HUMAN	6	0.66	1.58	0.003	26509	41909	4665	12639	0.18	0.30	up
sp Q02809 PLOD1_HUMAN	35	0.66	1.58	0.041	144287	228129	36802	113096	0.26	0.50	up
tr A0A075B7F0 A0A075B7F0_HUMAN	3	0.66	1.58	0.028	17651	27926	8911	8254	0.50	0.30	up
sp P20062 TCO2_HUMAN	11	0.66	1.58	0.007	18606	29479	3697	9767	0.20	0.33	up
sp Q8IZ07 AN13A_HUMAN	4	0.67	1.59	0.005	5831	9249	932	2920	0.16	0.32	up
sp Q13449 LSAMP_HUMAN	4	0.67	1.59	0.011	9501	15135	3114	4646	0.33	0.31	up
sp P04433 KV311_HUMAN	23	0.67	1.59	0.046	105558	168228	61888	50241	0.59	0.30	up
sp Q02818 NUCB1_HUMAN	22	0.68	1.60	0.044	151636	242649	47517	121053	0.31	0.50	up
sp Q9H173 SIL1_HUMAN	9	0.68	1.60	0.026	43065	69046	12651	31044	0.29	0.45	up
sp P01876 IGHA1_HUMAN	606	0.69	1.61	0.035	10300857	16565075	5623403	4603321	0.55	0.28	up
sp Q01459 DIAC_HUMAN	10	0.69	1.61	0.023	78864	127118	19026	59685	0.24	0.47	up
sp O75787 RENH_HUMAN	6	0.69	1.61	0.033	18670	30137	5402	14989	0.29	0.50	up
sp P01763 HV348_HUMAN_family	11	0.69	1.62	0.032	24811	40120	6099	18539	0.25	0.46	up
sp P10909 CLUS_HUMAN	113	0.70	1.62	0.008	954695	1547218	160571	539271	0.17	0.35	up
sp P01762 HV311_HUMAN	8	0.70	1.62	0.047	13124	21316	6679	8775	0.51	0.41	up

(continued on next page)

Table A.6 (continued)

Accession	PSMs	logFC	FC	PValue_	mean_no	mean_yes	sd_no	sd_yes	cv_no	cv_yes	direction
sp O75635 SPB7_HUMAN	6	0.70	1.62	0.048	24122	39189	6742	23342	0.28	0.60	up
sp Q12965 MYO1E_HUMAN	6	0.70	1.63	0.006	3997	6500	866	2217	0.22	0.34	up
sp O00560 SDCB1_HUMAN	15	0.70	1.63	0.003	19230	31293	3146	9428	0.16	0.30	up
sp P20061 TCO1_HUMAN	105	0.70	1.63	0.049	806307	1314187	330870	628191	0.41	0.48	up
sp Q16610 ECM1_HUMAN	5	0.71	1.63	0.026	15465	25233	3174	12190	0.21	0.48	up
sp P07711 CATL1_HUMAN	13	0.71	1.64	0.039	80386	131436	33434	65415	0.42	0.50	up
sp P10586 PTPRF_HUMAN	16	0.73	1.65	0.008	13483	22299	3359	8792	0.25	0.39	up
sp P01780 HV307_HUMAN	10	0.73	1.66	0.047	223618	371397	111108	179153	0.50	0.48	up
sp P48723 HSP13_HUMAN	8	0.74	1.67	0.007	30738	51201	10329	17793	0.34	0.35	up
sp O14657 TOR1B_HUMAN	3	0.74	1.67	0.020	4280	7131	982	3341	0.23	0.47	up
sp O60568 PLOD3_HUMAN	5	0.74	1.67	0.010	7280	12136	2125	4948	0.29	0.41	up
sp P35475 IDUA_HUMAN	7	0.74	1.67	0.026	13255	22181	3305	11943	0.25	0.54	up
sp Q96PP9 GBP4_HUMAN	7	0.75	1.68	0.046	17003	28528	1329	17951	0.08	0.63	up
sp Q9Y646 CBPQ_HUMAN	5	0.75	1.69	0.035	10450	17616	2649	10307	0.25	0.59	up
sp Q6VY07 PACS1_HUMAN	6	0.76	1.69	0.011	58439	98960	7847	47070	0.13	0.48	up
sp Q9UNW1 MINP1_HUMAN	10	0.77	1.70	0.005	45083	76697	10370	31529	0.23	0.41	up
sp Q14118 DAG1_HUMAN	5	0.77	1.70	0.011	40222	68574	8770	32173	0.22	0.47	up
sp P06280 AGAL_HUMAN	6	0.77	1.71	0.020	10074	17220	2606	9258	0.26	0.54	up
sp Q9UIV8 SPB13_HUMAN	3	0.78	1.72	0.023	2473	4261	245	2612	0.10	0.61	up
sp P05161 ISG15_HUMAN	5	0.79	1.73	0.003	3857	6670	1130	2196	0.29	0.33	up
sp A0A0B4J1U7 HV601_HUMAN	19	0.79	1.73	0.040	117956	204038	56746	94681	0.48	0.46	up
sp P45877 PPIC_HUMAN	4	0.79	1.73	0.006	16771	29017	2045	12311	0.12	0.42	up
sp P13284 GILT_HUMAN	5	0.79	1.73	0.009	11776	20408	2921	9484	0.25	0.46	up
sp A0A0B4J1V2 HV226_HUMAN	13	0.80	1.74	0.023	94387	163919	53269	63496	0.56	0.39	up
sp P03950 ANGI_HUMAN	16	0.80	1.74	0.023	151077	263135	50139	143841	0.33	0.55	up
sp P34096 RNAS4_HUMAN	16	0.81	1.75	0.024	346072	605216	89404	339328	0.26	0.56	up
sp P19021 AMD_HUMAN	20	0.81	1.75	0.013	90872	158943	22544	78485	0.25	0.49	up
sp P17900 SAP3_HUMAN	6	0.81	1.75	0.044	57834	101429	10177	74379	0.18	0.73	up
sp A8K2U0 A2ML1_HUMAN	13	0.82	1.76	0.019	14791	26099	2538	15315	0.17	0.59	up
sp P01833 PIGR_HUMAN	814	0.83	1.78	0.020	11759538	20925349	7092116	7049969	0.60	0.34	up
sp Q9UJ9 GNPTG_HUMAN	6	0.84	1.79	0.015	7346	13123	2490	6508	0.34	0.50	up
sp Q13162 PRDX4_HUMAN	8	0.85	1.80	0.021	35762	64324	11479	36672	0.32	0.57	up
sp O00584 RNT2_HUMAN	26	0.85	1.80	0.022	229206	412652	47758	250814	0.21	0.61	up
sp Q96AX2 RAB37_HUMAN	6	0.85	1.80	0.022	33782	60971	6911	40429	0.20	0.66	up
sp A0A0C4DH38 HV551_HUMAN_family	36	0.85	1.81	0.035	333289	602363	173496	280999	0.52	0.47	up
sp Q11201 SLA4A_HUMAN	11	0.86	1.81	0.013	54321	98297	13340	55290	0.25	0.56	up
sp P09972 ALDOC_HUMAN	11	0.86	1.82	0.007	85994	156228	15283	89742	0.18	0.57	up
sp P01714 LV319_HUMAN	18	0.86	1.82	0.015	109185	198394	54387	70075	0.50	0.35	up
sp P36980 FHR2_HUMAN	3	0.86	1.82	0.028	7544	13740	2069	7637	0.27	0.56	up
sp Q9H1E1 RNAS7_HUMAN	6	0.87	1.83	0.019	17933	32737	1735	18744	0.10	0.57	up
sp P22735 TGM1_HUMAN	19	0.87	1.83	0.017	87595	160119	9799	114635	0.11	0.72	up
sp P01019 ANGT_HUMAN	31	0.87	1.83	0.045	257340	470860	93727	305233	0.36	0.65	up
sp Q5XXA6 ANP1_HUMAN	6	0.87	1.83	0.010	12065	22096	2978	10926	0.25	0.49	up
sp P14923 PLAK_HUMAN	46	0.87	1.83	0.024	338159	620147	23631	471308	0.07	0.76	up
sp O00115 DNS2A_HUMAN	7	0.88	1.84	0.011	39433	72644	8520	43969	0.22	0.61	up
sp O95841 ANGL1_HUMAN	12	0.88	1.84	0.018	31282	57709	13488	30399	0.43	0.53	up
sp P01699 LV144_HUMAN	9	0.88	1.84	0.023	5727	10566	3410	5034	0.60	0.48	up
sp A0A075B6Q5 HV364_HUMAN	8	0.89	1.85	0.002	15112	27937	6657	7902	0.44	0.28	up
sp Q9BRK5 CAB45_HUMAN	17	0.89	1.85	0.018	255458	472424	81672	273905	0.32	0.58	up
sp P50591 TNF10_HUMAN	5	0.89	1.85	0.009	1834	3393	599	1328	0.33	0.39	up
sp O95395 GCNT3_HUMAN	7	0.89	1.85	0.013	28860	53515	13523	24859	0.47	0.46	up
sp Q08431 MPGM_HUMAN	28	0.89	1.86	0.011	88052	163506	32885	80947	0.37	0.50	up
sp Q9HBR0 S38AA_HUMAN	3	0.90	1.86	0.028	3807	7097	1703	3993	0.45	0.56	up
sp P80303 NUCB2_HUMAN	43	0.91	1.88	0.033	431033	809366	189583	513158	0.44	0.63	up
sp P61769 B2MG_HUMAN	23	0.91	1.88	0.016	328590	618350	48985	387682	0.15	0.63	up
tr A0A0J9YY99 A0A0J9YY99_HUMAN	7	0.92	1.89	0.007	14849	28005	6727	12000	0.45	0.43	up
sp O14638 ENPP3_HUMAN	9	0.92	1.89	0.004	5534	10455	2292	4461	0.41	0.43	up
sp P05089 ARGI1_HUMAN	14	0.93	1.90	0.031	75773	143985	22151	114228	0.29	0.79	up
sp Q99519 NEUR1_HUMAN	7	0.93	1.90	0.012	22694	43144	7871	22264	0.35	0.52	up
sp A0A0C4DH34 HV428_HUMAN	15	0.94	1.92	0.008	97397	186705	50526	77916	0.52	0.42	up
sp Q13421 MSLN_HUMAN	69	0.94	1.92	0.004	943612	1810780	303360	834807	0.32	0.46	up
sp Q8NBJ4 GOLM1_HUMAN	22	0.95	1.94	0.005	226143	437762	46348	217138	0.20	0.50	up
sp A0A0A0MS15 HV349_HUMAN	12	0.95	1.94	0.009	60242	116781	24482	52645	0.41	0.45	up
sp O43490 PROM1_HUMAN	16	0.96	1.94	0.003	70456	137003	23918	60136	0.34	0.44	up
sp P15907 SIAT1_HUMAN	9	0.97	1.95	0.002	26464	51713	10432	18397	0.39	0.36	up
sp Q9GZM7 TINAL_HUMAN	6	0.97	1.96	0.002	3438	6748	1209	2991	0.35	0.44	up
sp Q13217 DNJC3_HUMAN	33	0.98	1.97	0.012	303728	597837	99672	371792	0.33	0.62	up
sp Q9HC84 MUC5B_HUMAN	3	0.98	1.98	0.017	1688	3341	790	1510	0.47	0.45	up
sp O60784 TOM1_HUMAN	6	0.99	1.98	0.035	48220	95564	22169	65950	0.46	0.69	up
sp Q13438 OS9_HUMAN	27	0.99	1.98	0.012	74799	148295	20501	91629	0.27	0.62	up
sp Q9UBX5 FBLN5_HUMAN	3	0.99	1.99	0.026	1200	2386	691	731	0.58	0.31	up
sp Q9Y478 AAKB1_HUMAN	6	1.00	2.00	0.000	11175	22353	3118	7731	0.28	0.35	up
sp P0DTE7 AMY1B_HUMAN (+2)	39	1.02	2.02	0.037	265115	536343	68114	431833	0.26	0.81	up
tr A0A0G2JRO6 A0A0G2JRO6_HUMAN	7	1.02	2.03	0.009	9467	19240	5271	9027	0.56	0.47	up
sp Q9UBT3 DKK4_HUMAN	5	1.02	2.03	0.003	10416	21170	3661	10457	0.35	0.49	up
sp Q96P63 SPB12_HUMAN	12	1.03	2.04	0.002	34629	70660	4478	39210	0.13	0.55	up

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Table A.6 (continued)

Accession	PSMs	logFC	FC	PValue_	mean_no	mean_yes	sd_no	sd_yes	cv_no	cv_yes	direction
sp P23490 LORI_HUMAN	13	1.03	2.04	0.035	24037	49078	7463	37016	0.31	0.75	up
sp Q02413 DSGI_HUMAN	24	1.03	2.04	0.002	118048	241103	25751	134903	0.22	0.56	up
sp A0A075B6J9 LV218_HUMAN	8	1.03	2.05	0.010	31075	63676	15138	30197	0.49	0.47	up
sp O60911 CATL2_HUMAN	8	1.04	2.05	0.029	11106	22764	2538	20555	0.23	0.90	up
sp O15041 SEM3E_HUMAN	7	1.04	2.05	0.001	12676	25984	3353	11423	0.26	0.44	up
sp P01721 LV657_HUMAN	9	1.04	2.05	0.001	71853	147287	16857	65586	0.23	0.45	up
sp P42357 HUTH_HUMAN	5	1.04	2.05	0.042	22219	45625	5433	45122	0.24	0.99	up
sp Q51749 KPRP_HUMAN	10	1.04	2.06	0.006	14657	30140	1729	19141	0.12	0.64	up
sp Q08188 TGM3_HUMAN	28	1.04	2.06	0.033	40679	83866	13704	86141	0.34	1.03	up
sp Q15517 CDSN_HUMAN	5	1.06	2.08	0.008	26423	54933	8223	38262	0.31	0.70	up
sp Q5D862 FILA2_HUMAN	34	1.06	2.09	0.027	307238	642480	87770	537322	0.29	0.84	up
sp Q92485 ASM3B_HUMAN	3	1.07	2.09	0.002	23082	48349	14294	14700	0.62	0.30	up
sp P55058 PLTP_HUMAN	43	1.07	2.10	0.006	163033	342882	49210	192366	0.30	0.56	up
sp Q9NU19 TB22B_HUMAN	13	1.08	2.11	0.000	415854	878287	145128	327286	0.35	0.37	up
sp A0A0B4J1Y8 LV949_HUMAN	3	1.09	2.12	0.022	10720	22774	7706	12853	0.72	0.56	up
sp P05090 APOD_HUMAN	30	1.09	2.13	0.043	113748	242072	68817	195440	0.60	0.81	up
sp Q08554 DSC1_HUMAN	13	1.10	2.14	0.010	42644	91380	13316	67306	0.31	0.74	up
sp A0A0B4J2D9 KVD13_HUMAN (+1)	20	1.10	2.15	0.007	50203	107690	21904	55540	0.44	0.52	up
sp Q99574 NEUS_HUMAN	13	1.10	2.15	0.004	67315	144740	17524	90430	0.26	0.62	up
sp Q8NES3 LFNG_HUMAN	9	1.11	2.15	0.001	22749	48964	7367	22206	0.32	0.45	up
sp P15924 DESP_HUMAN	117	1.12	2.17	0.012	604610	1314267	93577	1142978	0.15	0.87	up
sp Q86UD1 OAF_HUMAN	7	1.12	2.17	0.028	21268	46241	12086	36658	0.57	0.79	up
sp P25311 ZA2G_HUMAN	426	1.12	2.18	0.002	11800269	25695154	3661638	13030147	0.31	0.51	up
sp Q96QA5 GSDMA_HUMAN	6	1.13	2.18	0.021	44229	96627	7767	95047	0.18	0.98	up
sp A0A0B4J1X5 HV374_HUMAN	9	1.13	2.20	0.003	269311	591351	189394	167645	0.70	0.28	up
sp Q51750 XP32_HUMAN	7	1.15	2.22	0.009	5165	11480	881	7596	0.17	0.66	up
sp P06831 HV434_HUMAN_family	5	1.16	2.23	0.015	60040	134156	42731	68496	0.71	0.51	up
sp Q06828 FMOD_HUMAN	6	1.16	2.24	0.010	15290	34284	7727	24279	0.51	0.71	up
sp P09958 FURIN_HUMAN	7	1.18	2.27	0.024	7072	16069	1423	15194	0.20	0.95	up
sp Q6UXI9 NPNT_HUMAN	6	1.19	2.29	0.001	7728	17684	2586	8274	0.33	0.47	up
sp P01034 CYTC_HUMAN	46	1.22	2.33	0.002	299461	697124	82827	431611	0.28	0.62	up
sp Q09328 MGT5A_HUMAN	4	1.23	2.34	0.001	3566	8346	804	3504	0.23	0.42	up
sp P01767 HV353_HUMAN	13	1.24	2.36	0.011	7376	17374	3368	13366	0.46	0.77	up
sp Q6UXB2 CXL17_HUMAN	10	1.27	2.41	0.025	51271	123527	27516	105035	0.54	0.85	up
sp P12273 PIP_HUMAN	396	1.28	2.43	0.001	11438567	27806049	4034273	15651254	0.35	0.56	up
sp Q04837 SSBP_HUMAN	3	1.28	2.44	0.000	1260	3069	355	1660	0.28	0.54	up
sp Q14515 SPRL1_HUMAN	35	1.29	2.44	0.004	253020	617991	150897	319965	0.60	0.52	up
sp Q9GZZ8 LACRT_HUMAN	85	1.29	2.45	0.006	5909023	14484550	3373433	8901467	0.57	0.61	up
sp P14138 EDN3_HUMAN	3	1.29	2.45	0.032	4409	10815	1784	13324	0.40	1.23	up
sp Q75556 SG2A1_HUMAN	100	1.32	2.50	0.021	557326	1395440	346821	1161660	0.62	0.83	up
sp P27487 DPP4_HUMAN	23	1.33	2.52	0.000	91904	231684	18562	123093	0.20	0.53	up
sp A0A075B6S5 KV127_HUMAN	10	1.34	2.54	0.031	24457	62079	16967	69124	0.69	1.11	up
sp P31025 LCN1_HUMAN	1079	1.36	2.57	0.010	52227172	134338658	27549695	122761267	0.53	0.91	up
sp Q8IW75 SPA12_HUMAN	3	1.37	2.59	0.002	22434	58181	8870	44611	0.40	0.77	up
sp P23381 SYWC_HUMAN	30	1.38	2.61	0.039	161690	421645	44192	592355	0.27	1.40	up
sp Q13336 UT1_HUMAN	3	1.40	2.65	0.018	3141	8312	2048	6102	0.65	0.73	up
sp P14555 PA2GA_HUMAN	88	1.42	2.67	0.000	1310891	3499307	400994	1929378	0.31	0.55	up
sp A2NJV5 KV229_HUMAN	16	1.48	2.78	0.009	13758	38302	10310	28728	0.75	0.75	up
sp Q95968 SG1D1_HUMAN	61	1.56	2.94	0.016	2454542	7212372	1979739	6262686	0.81	0.87	up
sp Q8WVV4 POF1B_HUMAN	10	1.59	3.02	0.013	10967	33113	1254	48058	0.11	1.45	up
sp P14902 I23O1_HUMAN	7	1.67	3.19	0.014	9738	31083	2238	33229	0.23	1.07	up
sp P47929 LEG7_HUMAN	5	1.72	3.30	0.019	55205	181966	13059	314222	0.24	1.73	up
sp A0A075B6K0 LV316_HUMAN	3	1.73	3.31	0.000	7518	24912	2378	13957	0.32	0.56	up
sp P01036 CYTS_HUMAN	121	1.79	3.45	0.000	171808	593182	84702	388392	0.49	0.65	up
sp Q15389 ANGP1_HUMAN	3	1.84	3.59	0.022	348	1249	501	788	1.44	0.63	up
sp P23280 CAH6_HUMAN	5	1.92	3.78	0.005	2408	9100	1055	10831	0.44	1.19	up
sp P20930 FILA_HUMAN	8	2.07	4.18	0.025	46914	196334	17052	413591	0.36	2.11	up
sp Q9UBS3 DNJB9_HUMAN	5	2.28	4.85	0.001	713	3453	564	2899	0.79	0.84	up
sp P01037 CYTN_HUMAN	142	2.74	6.67	0.002	224479	1497264	205871	1537742	0.92	1.03	up
sp P29034 S10A2_HUMAN	3	2.89	7.41	0.004	5029	37260	1135	83089	0.23	2.23	up
sp P28325 CYTD_HUMAN	13	3.13	8.76	0.000	14420	126281	5123	138570	0.36	1.10	up
sp P09228 CYTT_HUMAN	15	3.50	11.29	0.000	9505	107339	3967	182673	0.42	1.70	up

Table A.7

Differentially expressed proteins between contact lens user and non-user (reference) with restricted Schirmer strip length – see Fig. 7B

Accession	PSMs	logFC	FC	PValue	mean_yes	mean_no	sd_yes	sd_no	cv_yes	cv_no	direction
sp P09228 CYTT_HUMAN	18	-1.35	-2.55	0.031	40990	104660	17132	122968	0.42	1.17	down
sp P00746 CFAD_HUMAN	7	-0.73	-1.66	0.009	35632	59031	9615	23095	0.27	0.39	down
sp P41222 PTGDS_HUMAN	9	-0.63	-1.55	0.023	71734	111264	16706	46166	0.23	0.41	down
sp P01880 IGHD_HUMAN	12	0.59	1.50	0.046	52027	34579	23527	8592	0.45	0.25	up
sp P05186 PPBT_HUMAN	20	0.60	1.51	0.029	171522	113452	64392	28630	0.38	0.25	up
sp P10398 ARAF_HUMAN	4	0.62	1.54	0.024	15039	9784	5493	2533	0.37	0.26	up
sp P15924 DESP_HUMAN	96	0.65	1.57	0.012	743440	474280	327638	48025	0.44	0.10	up

(continued on next page)

Table A.7 (continued)

Accession	PSMs	logFC	FC	PValue	mean_yes	mean_no	sd_yes	sd_no	cv_yes	cv_no	direction
sp Q9H1E1 RNAS7_HUMAN	9	0.66	1.58	0.049	65419	41505	31619	10524	0.48	0.25	up
sp Q95395 GCNT3_HUMAN	10	0.69	1.61	0.007	98964	61471	33722	13751	0.34	0.22	up
sp P01619 KV320_HUMAN	36	0.69	1.61	0.010	307017	190562	121041	34171	0.39	0.18	up
sp Q9Y223 GLCNE_HUMAN	6	0.69	1.62	0.036	56557	34995	33905	8072	0.60	0.23	up
sp Q13459 MYO9B_HUMAN	3	0.71	1.64	0.014	4283	2615	1597	552	0.37	0.21	up
sp P30405 PPIF_HUMAN	3	0.72	1.65	0.004	39857	24140	16313	4444	0.41	0.18	up
sp P01040 CYTA_HUMAN	16	0.73	1.66	0.016	179829	108094	79648	25832	0.44	0.24	up
sp Q9UHD0 IL19_HUMAN	3	0.76	1.69	0.006	41462	24534	15854	2907	0.38	0.12	up
sp A0A0C4DH25 KVD20_HUMAN	4	0.76	1.69	0.015	143142	84583	70611	10399	0.49	0.12	up
sp Q02413 DSG1_HUMAN	18	0.76	1.70	0.004	182530	107422	68832	19030	0.38	0.18	up
sp Q13421 MSLN_HUMAN	87	0.77	1.71	0.027	2736224	1603541	1498027	275417	0.55	0.17	up
sp A0A0C4DH31 HV118_HUMAN	11	0.77	1.71	0.010	39873	23333	16514	4971	0.41	0.21	up
tr A0A075B7D0 A0A075B7D0_HUMAN	4	0.78	1.72	0.031	10887	6343	5474	1604	0.50	0.25	up
sp P22528 SPR1B_HUMAN	4	0.79	1.73	0.031	76094	44064	48700	7923	0.64	0.18	up
sp P01782 HV309_HUMAN (+1)	16	0.80	1.74	0.001	499678	287870	106608	75607	0.21	0.26	up
sp Q9H074 PAIP1_HUMAN	3	0.82	1.76	0.027	32121	18243	20812	4339	0.65	0.24	up
sp Q04609 FOLH1_HUMAN	10	0.82	1.77	0.014	77918	44110	40305	10279	0.52	0.23	up
sp A0A0B4J1Y9 HV372_HUMAN	4	0.87	1.83	0.024	20933	11445	13479	1979	0.64	0.17	up
sp A0A075B6K4 LV310_HUMAN	6	0.87	1.83	0.003	20553	11210	7517	2960	0.37	0.26	up
sp P01714 LV319_HUMAN	14	0.88	1.84	0.003	106111	57743	43259	9267	0.41	0.16	up
sp Q14894 CRYM_HUMAN	14	0.88	1.84	0.014	303154	164728	202194	31014	0.67	0.19	up
sp A0A0B4J1X8 HV343_HUMAN	6	0.89	1.85	0.020	37441	20271	18311	9592	0.49	0.47	up
sp P01700 LV147_HUMAN	7	0.89	1.86	0.019	40875	22033	24317	4467	0.59	0.20	up
sp Q15517 CDSN_HUMAN	6	0.89	1.86	0.000	28454	15317	9350	2687	0.33	0.18	up
sp B9A064 IGLL5_HUMAN	41	0.90	1.86	0.030	3874995	2083485	2577341	548387	0.67	0.26	up
tr S4R460 S4R460_HUMAN_family	11	0.90	1.86	0.012	53233	28615	30374	5474	0.57	0.19	up
sp A0A0C4DH32 HV320_HUMAN	11	0.90	1.87	0.037	63918	34153	49303	10678	0.77	0.31	up
sp Q86SQ4 AGRG6_HUMAN	5	0.91	1.88	0.006	7734	4122	3518	821	0.45	0.20	up
sp P16651 PRSS8_HUMAN	8	0.92	1.89	0.007	135804	71893	76430	11819	0.56	0.16	up
sp A0A075B6S5 KV127_HUMAN	12	0.93	1.90	0.008	142242	74862	74725	18102	0.53	0.24	up
sp Q08554 DSC1_HUMAN	7	0.93	1.90	0.001	114471	60210	45296	11998	0.40	0.20	up
sp A0A0C4DH38 HV551_HUMAN	20	0.93	1.91	0.011	105546	55378	60474	10074	0.57	0.18	up
sp A0A087WSY6 KVD15_HUMAN_family	25	0.94	1.92	0.002	293790	152652	138827	21367	0.47	0.14	up
sp P01824 HV439_HUMAN	5	0.96	1.95	0.016	9795	5026	5809	1332	0.59	0.27	up
sp P01706 LV211_HUMAN	22	0.98	1.98	0.010	230803	116807	133514	29402	0.58	0.25	up
sp P20020 AT2B1_HUMAN	4	0.98	1.98	0.004	24344	12304	12799	3019	0.53	0.25	up
sp P01876 IGHA1_HUMAN	686	1.01	2.01	0.009	42792417	21268469	25945307	3895347	0.61	0.18	up
sp A0A0C4DH72 KV106_HUMAN	8	1.01	2.02	0.016	21274	10530	13732	3906	0.65	0.37	up
sp P01593 KVD33_HUMAN (+1)	21	1.02	2.03	0.019	171696	84540	125858	32873	0.73	0.39	up
sp Q5VIR6 VPS53_HUMAN	4	1.02	2.03	0.021	145974	71847	96776	18686	0.66	0.26	up
sp P04433 KV311_HUMAN	11	1.04	2.06	0.013	413366	200942	220541	83673	0.53	0.42	up
sp A0A075B6S6 KVD30_HUMAN	17	1.08	2.12	0.007	72242	34062	45961	6685	0.64	0.20	up
sp A0A0A0MS15 HV349_HUMAN	8	1.09	2.12	0.001	126094	59364	59680	13125	0.47	0.22	up
sp A0A0B4J1V6 HV373_HUMAN	4	1.09	2.13	0.046	102727	48139	105982	21360	1.03	0.44	up
sp P01764 HV323_HUMAN	6	1.13	2.19	0.000	24842	11323	10485	2086	0.42	0.18	up
sp P01834 IGKC_HUMAN	473	1.15	2.22	0.008	22535364	10160772	14386632	3121415	0.64	0.31	up
sp P0DOY2 IGLC2_HUMAN_family	45	1.15	2.23	0.004	9872099	4434459	5974218	976070	0.61	0.22	up
sp P01699 LV144_HUMAN	12	1.16	2.24	0.012	50562	22602	41059	7359	0.81	0.33	up
sp P01911 DRB1_HUMAN	3	1.17	2.25	0.008	45816	20364	31028	9098	0.68	0.45	up
sp A0A075B6I0 LV861_HUMAN	4	1.18	2.26	0.006	106764	47223	69788	15633	0.65	0.33	up
sp P01762 HV311_HUMAN	3	1.18	2.27	0.005	55063	24273	31793	7966	0.58	0.33	up
sp P01871 IGHM_HUMAN	140	1.19	2.28	0.017	5382387	2363344	4501961	365308	0.84	0.15	up
sp P01591 IGJ_HUMAN	158	1.19	2.28	0.006	6247553	2738635	4221636	498022	0.68	0.18	up
sp P01701 LV151_HUMAN	20	1.20	2.29	0.009	138352	60317	100104	12559	0.72	0.21	up
tr A0A0J9Y99 A0A0J9Y99_HUMAN	10	1.21	2.31	0.015	78679	33998	58852	9711	0.75	0.29	up
sp P01833 PIGR_HUMAN	883	1.22	2.32	0.002	47207095	20329989	28873792	3022167	0.61	0.15	up
sp P01703 LV140_HUMAN	6	1.22	2.33	0.001	71572	30667	35135	8391	0.49	0.27	up
sp A0A0C4DH67 KV108_HUMAN	5	1.23	2.34	0.002	42530	18185	28773	4000	0.68	0.22	up
sp A0A075B6H9 LV469_HUMAN	3	1.23	2.34	0.020	255586	109060	189140	62586	0.74	0.57	up
sp A0A075B6P5 KV228_HUMAN (+3)	20	1.23	2.35	0.002	157119	66867	93410	18453	0.59	0.28	up
sp P23490 LORI_HUMAN	6	1.26	2.40	0.020	45329	18866	50187	4687	1.11	0.25	up
sp P01767 HV353_HUMAN	6	1.27	2.41	0.018	71603	29725	56567	13101	0.79	0.44	up
sp A0A0B4J1V0 HV315_HUMAN	25	1.28	2.43	0.008	791739	325548	604688	76852	0.76	0.24	up
sp P01718 LV327_HUMAN	5	1.34	2.53	0.011	27133	10712	22241	4732	0.82	0.44	up
sp P01780 HV307_HUMAN	5	1.38	2.59	0.001	327633	126291	202367	31549	0.62	0.25	up
sp P01597 KV139_HUMAN (+1)	7	1.40	2.63	0.003	151057	57330	125375	11474	0.83	0.20	up
sp A0A0B4J1U7 HV601_HUMAN	16	1.40	2.64	0.007	471213	178592	377067	63454	0.80	0.36	up
sp A0A0C4DH34 HV428_HUMAN	12	1.48	2.79	0.000	199183	71323	126199	17527	0.63	0.25	up
sp A0A075B6I9 LV746_HUMAN	3	1.52	2.86	0.027	87575	30605	95672	20896	1.09	0.68	up
sp A0A0B4J1X5 HV374_HUMAN	7	1.53	2.89	0.000	628830	217851	358042	59530	0.57	0.27	up
sp P42858 HD_HUMAN	5	1.72	3.30	0.009	12929	3913	12624	2542	0.98	0.65	up
sp P01877 IGHA2_HUMAN	262	1.78	3.44	0.002	5659330	1643335	5064017	563640	0.89	0.34	up
sp P04211 LV743_HUMAN	3	1.94	3.83	0.001	15517	4056	13524	2194	0.87	0.54	up
sp A0A0B4J1U3 LV136_HUMAN	6	2.04	4.11	0.000	26518	6459	24782	861	0.93	0.13	up
sp A0A0A0MS14 HV145_HUMAN	3	2.26	4.79	0.000	38054	7937	19464	3873	0.51	0.49	up

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