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Application of systems biology principles to protein biomarker discovery: Urinary exosomal proteome in renal transplantation

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Abstract

Purpose—In MS-based studies to discover urinary protein biomarkers, an important question is how to analyze the data to find the most promising potential biomarkers to be advanced to large-scale validation studies. Here, we describe a 'systems biology-based' approach to address this question.

Experimental design—We analyzed large-scale LC-MS/MS data of urinary exosomes from renal allograft recipients with biopsy-proven evidence of immunological rejection or tubular injury. We asked whether bioinformatic analysis of urinary exosomal proteins can identify protein groups that correlate with biopsy findings and whether the protein groups fit with general knowledge of the pathophysiological mechanisms involved.

Results—LC-MS/MS analysis of urinary exosomal proteomes identified more than 1000 proteins in each pathologic group. These protein lists were analyzed computationally to identify Biological Process and KEGG Pathway terms that are significantly associated with each pathological group. Among the most informative terms for each group were: "sodium ion transport" for tubular injury; "immune response" for all rejection; "epithelial cell differentiation" for cell-mediated rejection; and "acute inflammatory response" for antibody-mediated rejection. Based on these terms, candidate biomarkers were identified using a novel strategy to allow a dichotomous classification between different pathologic categories.

Conclusions and clinical relevance—The terms and candidate biomarkers identified make rational connections to pathophysiological mechanisms, suggesting that the described bioinformatic approach will be useful in advancing large-scale biomarker identification studies toward a validation phase.

Keywords

exosome; proteomics; rejection; transplant; urine

Conflict of interest statement

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Introduction

The main objective of the present study is to develop a bioinformatic strategy that can reveal exploitable patterns in protein mass spectrometry data from urinary samples. The question being addressed is how to proceed from mass spectrometry-generated lists of proteins to a choice of candidate biomarkers for future testing in validation clinical trials. Here we describe and illustrate an approach derived from the field of systems biology that uses computational tools to discover biologically meaningful differences among experimentally derived protein lists [1, 2]. This approach is based on the idea that the objective of biomarker discovery studies should be to identify *biological processes* that are deranged rather than to look for specific proteins that may stand out. The rationale has been presented previously [3]. Briefly, it is based on the idea that protein biomarkers that "make sense" from the perspective of pathophysiology are more likely to succeed in the clinical setting than randomly discovered proteins that have uncertain connection to the relevant disease mechanisms (see Discussion). In this study, as a 'proof of principle', we apply such an approach to proteins detected by LC-MS/MS (liquid chromatography-tandem mass spectrometry) analysis of urinary exosome samples from three groups of renal transplant patients with different pathologic findings in the allograft biopsy: tubular injury, cellmediated rejection, and antibody-mediated rejection. The bioinformatic approach outlined identified biological processes and candidate biomarkers associated with the different patient groups that fit with known pathophysiological mechanisms.

Materials and methods

Patients and samples

Urine samples were collected prospectively from adult renal transplant recipients followed at the Johns Hopkins Comprehensive Transplant Center. These patients underwent a kidney graft biopsy, either for cause (due to rise in baseline serum creatinine) or as protocol biopsy in patients with stable renal function. All patients received standard immunosuppressive treatment with prednisone, mycophenolate, and tacrolimus. Exclusion factors included combined transplantation of kidney and other organs, evidence of infection in the kidney (bacterial or viral such as BK/polyoma, CMV, or Herpes), primary glomerular disease (de novo or recurrent), post-transplant lymphoproliferative disorder (PTLD). Kidney graft biopsies were processed for routine studies as previously described including staining with hematoxilin-eosin (H&E), periodic acid-Schiff (PAS) methenamine silver, and Masson's trichrome for light microscopy examination [4]. C4d staining by immunofluorescence was routinely performed on frozen sections of transplant kidney biopsies (alternatively C4d immunoperoxidase-based stain was also available on sections from paraffin embedded tissue). Biopsies were graded for cellular- and antibody-mediated rejection according to the Banff score [5, 6]. Based on the graft biopsy findings, patients were assigned to four groups: Non-Specific Findings (N), mild to moderate Tubular Injury (TI), Cell-Mediated Rejection (CMR), or Antibody-Mediated Rejection (AMR). The study protocol was approved by the Johns Hopkins Medical Institutions Review Board.

Freshly voided urine (20-200 ml) was collected in the morning, before the biopsy (but was not the first morning urine sample), and was processed immediately to isolate urinary exosomes using the differential centrifugation procedure described by Gonzales et al [7]. Processed protein samples solubilized in Laemmli reagent were pooled for each pathological group for analysis by LC-MS/MS.

Sample processing and mass spectrometry analysis

Triplicate sets of 200 µg of urinary exosomal proteins pooled from each pathological group (7 TI, 6 CMR, 3 AMR, and 2 N, supporting Information Table S1) were separated by one dimensional SDS/PAGE electrophoresis using 10% polyacrylamide gels. After staining with Coomassie blue, the gels were de-stained, cut in multiple slices, dehydrated, reduced, alkylated, and subjected to trypsin digestion at 37°C overnight to obtain peptides, which were reconstituted in 0.1% formic acid for analysis as described [8]. LC-MS/MS was performed on triplicate aliquots of digested protein samples using LTQ Orbitrap XL (two runs) and LTQ Orbitrap Velos (one run) (Thermo Scientific, Waltham, MA). Reversedphase C18 chromatographic separation of trapped peptides was carried out on a prepacked Beta Basic C18 PicoFrit column (75 μ m i.d. \times 10 cm length; New Objective) at 300 nL/min using the following gradient: 2–5% solvent B for 2 min; 5–45% solvent B for 45 min; 45– 50% solvent B for 5 min; 50-95% solvent B for 5 min (solvent A: 0.1% formic acid in 98% water, 2% acetonitrile; solvent B: 0.1% formic acid in 100% acetonitrile). To identify peptide sequences, the MS data was searched against National Center for Biotechnology Information (NCBI) Reference Sequence human protein database (April 8, 2010, 38767 entries) which included a list of common contaminating proteins and scored using SEQUEST algorithm on Proteome Discoverer software (ver. 1.1, Thermo Scientific). Precursor ion tolerance was 50 ppm, while fragment ion tolerance was 1.0 Da. Two missed trypsin cleavage sites were allowed. Static modifications included carbamidomethylation of cysteine (+57.021 Da) and variable modifications included oxidation of methionine (+15.995 Da). The peptide false discovery rate was limited to < 2% for individual peptides using the target-decoy approach [9]. All MS spectral files associated with this manuscript may be downloaded from ProteomeCommons.org Tranche using the following hashes:

1. LTQ Orbitrap XL Data 1st set

p7DyXnHc+EyANszEZXPsThX/EzRPhJR0YmfDYGZJoRREeKgRm00/ jM47tDEH5Gh0wzO/Bk N5BcA0IQPCCN2QmJAWs4UAAAAAAAfow==

2. LTQ Orbitrap XL Data 2nd set

RD+8p8/vHKT7QhWVYe0hMsVKKEZitqPGBgv60DDvoGuOQ1ZaGz6Bpgmy +o/2FSOe+Y4v 1BfFtzlZcKEOJ43T7HwEVkUAAAAAAAiHg==

3. LTQ Orbitrap Velos Data

DlI2b2OfY46ui/

 $\label{eq:starseq} Fln5JivUyHW03ZxU4Pv5xapK4xl9FB4wdSyW1Ffo4gQ38tjNwZo4SehiBbar RU0k8QiwrOiS5phrYAAAAAAACyg==$

For the evaluation of relative abundance of exosomal proteins among groups, the spectral counts were normalized by dividing by the number of theoretical tryptic peptides detectable by LC-MS/MS (criteria for predicting a detectable tryptic peptide are as followed: theoretical m/z = 300-2000 for charge states +1 to +3, peptide length = 6-35, possible missed cleavage sites < 3). These values were further normalized by dividing by the median value for each group to account for potential differences in sample size.

Bioinformatic analysis

Identified proteins were classified as 'extrinsic to exosomes' if they possessed the *Gene Ontology Cellular Component* term of "extracellular space", but lacked the terms "anchor" and "cytosol". The remaining proteins were placed in the 'intrinsic to exosomes' subgroup. Protein lists were analyzed using the DAVID bioinformatic tool (Database for Annotation, Visualization and Integrated Discovery, NIAID, Bethesda, MD http://

david.abcc.niifcrf.gov/) [10] to determine what Gene Ontology Biological Process terms are

over-represented relative to the concatenated lists from all four conditions. The DAVID tool was also applied to determine what KEGG pathways (*Kyoto Encyclopedia of Genes and Genomes*) [11] are over-represented in each pathological group.

Results

Proteomes were profiled by LC-MS/MS in urinary exosome samples from renal allograft recipients with acute decrease in renal function and distinct biopsy findings: tubular injury (TI), cell-mediated rejection (CMR), and antibody-mediated rejection (AMR) (supporting Information Table S1). We also examined urinary exosomes of two allograft recipients with stable renal function undergoing "protocol" kidney graft biopsy, with non-specific findings (N). We selected cases that were stereotypical of each category, recognizing that real-world cases often display less distinct histology. Exosome samples were pooled within each histology class (supporting Information Table S1) and analyzed by LC-MS/MS. 1989 urine exosomal proteins were identified in renal transplant patients (false discovery rate < 2%, target-decoy analysis). This total exceeds the 1160 proteins reported in the Urinary Exosome Protein Database (http://dir.nhlbi.nih.gov/papers/lkem/exosome/). A list of all identified proteins along with associated median-normalized spectral counts, a measure of relative abundance (Materials and methods), can be accessed online through http://helixweb.nih.gov/ ESBL/Database/EXORT/ (username: clp, password: Esbl!@#\$, login to be removed upon acceptance of this paper). Each group had a large subset of uniquely identified proteins, TI: 353 proteins; CMR: 322 proteins; and AMR 165 proteins, with 1073 proteins present in more than one group.

We classified the identified proteins into one of two subgroups (*Materials and methods*): 'intrinsic to exosomes' or 'extrinsic to exosomes' (see the online database). The 'extrinsic' proteins are presumably plasma proteins that have crossed the glomerular filter and are nonspecifically associated with exosomes. The 'intrinsic' proteins were used for bioinformatic analysis. Overall, 92% of the proteins identified were classified as intrinsic, suggesting that they were a component of exosomes (or similar membranous structures) released from kidney cells.

Interestingly, there seems to be a higher proportion of extrinsic proteins in the transplanted control group than in the non-transplanted group (chi-square, p < 0.0001) when comparing the most abundant proteins (based on spectral counts) found in the group of transplant recipients with non-specific findings versus the most abundant proteins found in a group of healthy, non-transplanted volunteers that we studied previously [7], (supporting Information Table S2). Although these results need to be confirmed on a larger number of observations in transplanted patients without kidney pathology, they suggest that transplanted kidneys excrete higher levels of plasma proteins than non-transplanted kidneys even with no obvious pathological changes suggestive of tubular injury or rejection, and are also consistent with previously noted differences in the proteomic profile of urine from patients with transplanted or native kidneys [12, 13].

Identification of biological processes over-represented in groups

We analyzed the intrinsic exosomal proteins in each group to determine what characteristics distinguish the groups based on the biological processes that they take part in. This analysis was conducted with an online bioinformatic analysis tool called "DAVID" (*Materials and methods*), using the *Gene Ontology (GO) Database*, which attaches hierarchical descriptors to all annotated proteins coded by the human genome. We applied the *Biological Process GO* terms to identify which *Biological Process* terms are represented statistically more frequently in a list of exosomal proteins from a given patient group than from the entire set of exosomal proteins.

We asked whether any *GO Biological Process* terms are over-represented in the urinary exosomal proteins from kidneys of each patient group with abnormal biopsy findings (compared with the list of all proteins identified in transplanted kidneys). Table 1 shows the *GO Biological Processes* identified in each group with p < 0.05 (Fisher Exact). A comparison of Table 1A, 1B, and 1C reveals that several terms were enriched in more than one group. For example the term "immune response" is found in both graft rejection groups. Thus, proteins populating the "immune response" list can be deemed potential discriminators between rejection and tubular injury, but not between the two forms of rejection. supporting Information Table S3 shows proteins in this "immune response" list (cell-mediated and antibody-mediated rejection combined). Each pathological group in Table 1 is associated with at least one unique term (represented in **Bold**). As discussed below, most of these appear to be related to the underlying pathophysiology.

For the *Tubular Injury* group, the *Gene Ontology Biological Process* term "sodium ion transport" was the only unique term (Table 1A). This protein list (Table 2) includes a large number of transporters, many of them are sodium-coupled solute transporters expressed in the apical brush border membrane of the proximal tubule. Based on the transcriptomic databases of proximal tubule, medullary thick ascending limb, and inner medullary collecting duct [14], [15], 25 out of all 29 proteins (86%) in Table 2 were expressed with relatively high signal values in proximal tubule. This finding is presumably indicative of proximal tubule damage and therefore makes sense from a pathophysiological perspective.

In the *Cell-Mediated Rejection* group (Table 1B), there are several unique terms, including three similar terms: "actin filament based process", "actin cytoskeleton organization", and "cytoskeleton organization". The proteins in the former group are shown in supporting Information Table S4. An additional unique term in the *Cell-Mediated Rejection* group is "epithelial cell differentiation" (Table 3). These are predominantly proteins involved in intermediate filament organization and include four different uroplakin isoforms. The latter are expressed in the renal ureter and pelvis, and point to the possibility that the transitional epithelium of the urinary drainage system is a target tissue in cell-mediated allograft rejection.

In the *Antibody-Mediated Rejection* group (Table 1C), several unique terms appear, including three similar terms relevant to protein trafficking. The proteins in the "protein localization" group are listed in supporting Information Table S5. Additional unique terms in the *Antibody-Mediated Rejection* group are "response to unfolded protein" (supporting Information Table S6) and "acute inflammatory response" (Table 4). The latter category is dominated by components of the complement pathway. These categories refer to aspects of pathophysiology that appear logical in the context of current knowledge about antibody-mediated rejection (see *Discussion*).

Identification of KEGG biological pathways over-represented in pathological groups

We next analyzed the data to determine what characteristics distinguish the groups based on the KEGG biological pathways that they take part in, asking the question: "What KEGG pathways are represented statistically more frequently in a list of urinary exosomal proteins from a given patient group than in the list of all identified intrinsic exosomal proteins in all groups?"

The findings are summarized in Table 5. There were no unique KEGG pathways for exosomal proteins in the *Tubular Injury* group. One pathway was over-represented in the two Rejection groups, namely "endocytosis" (supporting Information Table S7 shows the "endocytosis" proteins combined from the two Rejection groups). Two KEGG pathways were uniquely over-represented in the list of exosomal proteins found in the *Cell-Mediated*

Rejection group, viz. "tight junction" (supporting Information Table S8) and "glutathione metabolism" (supporting Information Table S9). Interestingly the "tight junction" KEGG pathway with the *Cell-Mediated Rejection* group proteins include three proteins that are critically involved in epithelial polarization through PDZ interactions, viz. Crumbs3 (*CRB3*), PALS1 (*MPP5*), and PATJ (*INADL*) [16], and may be important in the recovery of tubular integrity damaged by "Tubulitis", a signature pathologic lesion in this type of rejection. Also as seen in Table 5, four KEGG pathways were uniquely over-represented in the *Antibody-Mediated Rejection* group, viz. "antigen processing and presentation" (Table 6), "neurotrophin signaling pathway", "pathways in cancer" and "pathogenic E. coli infection" (supporting Information Tables S10-S12). The "antigen processing and presentation" list is dominated by major histocompatibility complex proteins and heat shock proteins.

A strategy for identification of candidate biomarker proteins from *Biological Processprotein* lists

The approach described above selects groups of MS-identified proteins associated via *Gene Ontology Biological Process* terms or KEGG Pathways that relate to pathophysiological mechanisms in different patient groups. In full-scale biomarker studies, the next task would be to select candidate biomarkers from the protein groups that are predicted from the mass spectrometry data to have the potential to discriminate patient groups. In this study, we developed a strategy to identify candidate biomarkers from our 'proof-of-principle' data using the protein lists associated with the over-represented *Biological Processes* for each pathologic category (Tables 2-4 and supporting Information Tables S3-6). In this context, a first practical goal would be to identify pairs of proteins that will allow a dichotomous classification into *Rejection* vs. *Tubular Injury* categories (Figure 1). A second goal would be to choose protein pairs that allow samples to be categorized as *Antibody-Mediated Rejection* vs. *Cell-Mediated Rejection* (Figure 2). Selecting pairs of proteins that may have sufficient discriminating power between two different conditions, based on ratios of their abundance, would avoid the need of normalization factors, a main hurdle in optimizing assay conditions for urine biomarkers.

As rationalized in the Discussion, criteria for selection of candidate proteins from the Gene Ontology Biological Process lists obtained in the present study were: 1) maximization of the spectral count ratio between the two states being discriminated and 2) high absolute abundance based on spectral counts. Figure 1A shows a heat map representation of the dichotomous classification between All Rejection vs. Tubular Injury. The numbers for each pair of proteins are discrimination factors between the two conditions for a protein pair [Values are $\log_2(R_R/R_T)$, where R_R is the median-normalized spectral count ratio of the two proteins for All Rejection and R_{TI} is the ratio of the two proteins in Tubular Injury]. The best discrimination factors are the highest positive numbers. Figure 1B shows the same type of information for the comparison between Antibody-Mediated Rejection versus Tubular Injury and Figure 1C shows comparable information for Cell-Mediated Rejection versus Tubular Injury. Figure 2 shows the dichotomous classification between Antibody-Mediated Rejection and Cell-Mediated Rejection in which the median-normalized spectral count ratio between potential markers are represented in the same manner as in Figure 1. All proteins presented in Figures 1 and 2 were also selected from the *Biological Process* protein lists only if their absolute abundance levels in the pathologic category associated with a particular protein list were at least 2-fold above the median value for that pathologic category (mediannormalized spectral count values > 2).

Discussion

Typically biomarker development studies involve at least three distinct stages: discovery, validation, and implementation [17]. Here, we describe a bioinformatic approach to the analysis of discovery data. We used state-of-the-art mass spectrometry techniques for proteomic analysis of urinary exosomes from renal transplant recipients with renal dysfunction and biopsy-proven tubular injury, cell-mediated rejection, or antibody-mediated rejection. Although this approach was developed in the context of urinary proteomics data, it theoretically could be applied to analysis of data from other body fluids.

A central question addressed in this study is: "how best to analyze large-scale mass spectrometry data from urinary biomarker discovery studies to find proteins that have a meaningful connection to the pathophysiology of the disease process under study?" Optimally, candidate protein biomarkers must be sufficiently abundant to allow measurement in whole urine and should 'make sense' in terms of the pathophysiological processes involved [3]. The latter requirement is based on three considerations: a) measurements of biomarkers consistent with current pathophysiological knowledge will more readily be integrated with other types of results in future clinical studies; b) such biomarkers will be more readily acceptable and useful to the clinical nephrology community than those with no known connection to pathophysiology; and c) biomarkers that fit with recognized mechanisms are less likely to be false positives.

Because of the considerations outlined in the foregoing *Discussion*, we have devised a 'process-oriented' approach to bioinformatic interpretation of the protein mass spectrometry discovery data. Thus, we are not looking for specific proteins that are enriched in individual patient groups, but rather we wish to identify classes of proteins (involved in specific biological processes) that can be shown statistically to be associated with individual patient groups. To implement this approach, we used the online computer utility, DAVID (see *Materials and methods*), to identify either *Gene Ontology Biological Process* (GO-BP) terms or KEGG Pathway terms that are selectively associated with lists of proteins identified in urinary exosomes in each renal transplant subgroup. Based on this approach, we can summarize the key observations in our 'proof of principle' samples as follows:

- 1. The only GO-BP term significantly associated with the *Tubular Injury* exosomal protein list was "sodium ion transport" (Table 1A). The list of proteins in this group (Table 2) consists chiefly of transporter proteins characteristic of the proximal tubule brush border but also includes proteins from the thick ascending limb of Henle (*SLC12A1*) and distal convoluted tubule (*SLC12A3*). These findings are consistent with the idea that tubular injury is seen mainly in proximal tubule, thick ascending limb of Henle, and distal convoluted tubule, where ATP demand is high because of the energy cost of transpithelial solute transport. This study did not single out any of the proteins previously proposed to be associated with ischemic tubule injury such as KIM-1 [18], Hsp72 [19], klotho [20], IL-6 [21], NGAL [22], L-FABP [23], netrin-1 [24], or fetuin-A [25], presumably because the pathophysiology is dependent on the context (transplanted kidney with immunosuppression) and because our bioinformatic analysis focused on functional classes of proteins.
- 2. Proteins classified with the GO-BP term "immune response" were enriched in the two rejection groups but not the *Tubular Injury* group (Table 1). This classification makes sense in the context of the immunological nature of rejection. The proteins in this group are dominated by proteins of the major histocompatibility complex and complement components (supporting Information Table S3).

- **3.** The GO-BP term "epithelial cell differentiation" is uniquely associated with *Cell-Mediated Rejection* (Table 1B). Despite its name, this category is made up largely of proteins associated with stratified epithelia including the transitional epithelium of the pelvis and ureter (Table 3). For example, we identified four uroplakins, abundant proteins that form a large part of the surface area of the umbrella cells of transitional epithelia [26, 27]. This result is compatible with the hypothesis that cell-mediated rejection may affect multiple epithelial cells of the transplanted organ, including the pelvis and ureter that are not affected in the other two pathologies.
- 4. Several GO-BP terms are associated with proteins in the *Antibody-Mediated Rejection* group including "acute inflammatory response" (Table 1C). Several complement components were found in the "acute inflammatory response" category (Table 4), a finding that fits with the proposed roles for the complement pathway in the pathophysiology of antibody-mediated rejection, and with current efforts to devise therapies based on inhibition of terminal complement activation with targeted monoclonal antibodies [28].

In a full-blown discovery study, the ultimate objective would be the development and testing of immunoassays (or other assays) for selected biomarker proteins. A major problem in designing useful urinary assays is normalization. The need for normalization arises from the fact that water excretion is highly variable, depending on physiological factors, rendering measurement of the absolute concentrations of a given biomarker substance virtually useless for making practical comparisons. Much has been written about the use of various measures such as creatinine, osmolality, Tamm-Horsfall protein, etc., to normalize urinary measurements. Such normalizing factors add work and variability to the read-out. However, because many clinical problems (including the one described in this paper) involve the development of a dichotomous classification that distinguishes one state from another, the normalization problem may be obviated; it is theoretically sufficient to form ratios of measured biomarker abundances, thereby canceling out the normalization factor. In the example developed for this study, two dichotomies are seen: 1) between rejection and tubular injury and 2) between cell-mediated rejection and antibody-mediated rejection. Consequently, in such studies it is rational to identify pairs of biomarker proteins, which, when measured under arbitrary loading conditions, give a concentration ratio that correlates with disease state. If the assays are linear, the ratio should be independent of water excretion rate or sample size, and separate normalization should be unnecessary.

Given the above observations, we selected candidate biomarkers representative of the biological processes identified by bioinformatic analysis. Operationally, we identified pairs of candidate biomarker proteins that potentially could allow a dichotomous classification into *Rejection* vs. *Tubular Injury* (Figure 1) and, among those classified as Rejection, will allow samples to be categorized as *Antibody-Mediated* vs. *Cell-Mediated* (Figure 2). Among the proteins in Figures 1 and 2, *SERPING1* [29] and *S100A9* [30] have already been reported to be candidate biomarker proteins for acute rejection in renal allografts. Many membrane protein candidates were identified and have not been reported in the literatures associated with renal allograft rejection. This observation is likely to be due to the use of urinary exosomes in this study. Urinary exosomes are tiny (40–80 nm) membranous structures secreted by every renal tubule epithelial cell type, as well as podocytes and transitional epithelia from the urinary collecting system [31].

In summary, the object of this paper was to describe and illustrate an approach to bioinformatic analysis of biomarker discovery data in order to facilitate identification of candidate biomarkers for future testing in validation clinical trials. For this purpose, we prepared samples from a small number of actual renal transplant patients with different

pathological changes in the allograft. The primary goal of this study was <u>not</u> to validate protein biomarkers for different processes that could cause an elevation of serum creatinine in renal transplant patients. Optimally, such validation studies would warrant the analysis of larger numbers of samples than used here. Nevertheless, data presented here, when combined with results from other biomarker studies [12] [13] [32] [33] [34] [35], could be useful in the design of validation studies for a limited number of protein biomarker candidates that make pathophysiological sense.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Statement of clinical relevance

A rising serum creatinine concentration in renal transplant patients raises a diagnostic dilemma: Is the rise in creatinine due to rejection or to tubular injury? If the former is true, what is the pathophysiological basis of the rejection? Presently these questions are best answered by examination of tissue from renal biopsy, an invasive procedure that requires hours to provide a diagnosis. The ultimate long-term objective of the present line of investigation is to devise immunological assays that can predict the biopsy results, possibly allowing earlier start of appropriate therapeutic intervention pending biopsy findings. The question addressed in this paper is: "how best to analyze large-scale mass spectrometry data from urinary biomarker discovery studies to find proteins that have a meaningful connection to the pathophysiology of the disease process under study?" To address this, we used state-of-the-art mass spectrometry techniques for analysis of urinary exosomes from patients with renal transplants, including those with biopsy evidence of tubular injury, cell-mediated rejection, and antibody-mediated rejection. We have developed a 'process-oriented' approach to bioinformatic interpretation of the protein mass spectrometry discovery data that facilitates identification of candidate biomarkers for future testing in validation clinical trials.

Pisitkun et al.

		All De		GI No.	4502277	186910319	109659836	225637552	134254459	21361181	157671931	167466278	44680145	4507033	4506979	4507031
		All KA	vs. 11	Gene	ATP1B1	SLC12A3	SLC5A10	SLC13A2	SLC12A1	ATP1A1	SLC5A12	SLC5A8	SLC23A1	SLC5A2	SLC13A2	SLC5A1
		GI No.	Gene	SC	3.23	6.06	10.27	11.53	23.26	10.60	11.11	5.32	5.21	2.98	2.34	2.06
		34485711	RAB27A	2.50	6.29	6.29	6.29	6.29	6.29	6.29	6.29	6.29	6.29	6.29	6.29	6.29
		54607120	I TE	4.95	6.04	5.67	5.27	4.65	5.93	5.26	4.46	3.69	3.79	3.46	4.04	3.04
		4500007	47004	4.00	0.04	0.50	0.40	4.00	0.00	0.04	4.40	0.54	0.04	0.04	4.04	0.40
		4502337	AZGPT	26.39	2.90	2.52	2.12	1.51	2.03	2.01	1.31	0.54	0.64	0.31	0.63	-0.10
		32455266	PRDX1	4.05	1.95	2.11	2.17	1.56	1.03	1.00	0.82	0.58	0.68	0.36	-0.37	-0.05
		4557417	CD14	4.82	1.91	2.07	1.98	1.36	0.98	0.96	0.78	0.39	0.49	0.17	-0.42	-0.25
		148612842	IFITM3	10.39	1.58	1.75	1.81	2.00	0.66	0.64	0.46	1.81	0.51	0.00	-0.74	-0.22
		12025678	ACTN4	2.57	1.88	2.05	1.74	1.13	0.96	0.93	0.75	0.16	0.25	-0.07	-0.44	-0.48
		161702986	FZR	11 31	1.89	1.88	1.48	0.86	0.97	0.94	0.67	-0.11	-0.01	-0.33	-0.43	-0.74
		100002044	CTEC	45.04	4.00	4.40	4.45	4.00	0.34	0.04	0.01	4.45	0.46	0.05	4.00	0.50
	5	189083844	CISC	15.84	1.23	1.40	1.45	1.65	0.31	0.28	0.11	1.45	0.16	-0.35	-1.09	-0.58
	<u>e</u>	56682959	FTH1	4.93	1.22	1.39	1.44	1.34	0.30	0.27	0.10	0.37	0.15	-0.36	-1.10	-0.58
	Ū.	208973244	YWHAZ	5.76	1.35	1.52	1.49	0.87	0.43	0.40	0.22	-0.10	0.00	-0.32	-0.97	-0.74
	÷	4757952	CDC42	3.71	1.58	1.53	1.13	0.51	0.66	0.64	0.32	-0.46	-0.36	-0.68	-0.74	-1.09
	æ	89903012	CDC42	9.64	1.09	1.25	1.31	0.70	0.17	0.14	-0.04	-0.28	-0.18	-0.50	-1.23	-0.91
	Ξ	4502211	AREA	2 74	1 58	1 21	0.81	0.19	0.66	0.64	0.00	-0.78	-0.68	-1.00	-0.74	-1.42
	◄	55022 TT	00000	7.70	1.00	4.40	4.00	0.15	0.00	0.04	0.00	0.70	0.00	0.04	4.20	4.00
		55749525	SUCBP	1.12	1.03	1.19	1.00	0.39	0.10	0.08	-0.10	-0.58	-0.49	-0.81	-1.30	-1.22
		4827036	PGLYRP1	29.28	1.36	0.99	0.58	-0.03	0.44	0.41	-0.22	-1.00	-0.90	-1.22	-0.96	-1.64
		4758146	DEFA1	15.78	0.58	0.75	0.81	1.00	-0.34	-0.36	-0.54	0.22	-0.49	-1.00	-1.74	-1.22
		56243522	SDCBP	5.02	0.58	0.75	0.81	0.83	-0.34	-0.36	-0.54	-0.14	-0.49	-1.00	-1.74	-1.22
		22165433	ANXA11	5.17	0.65	0.81	0.87	0.38	-0.27	-0.30	-0.48	-0.59	-0.49	-0.94	-1.67	-1.23
		21264361	MASP2	51 14	0.57	0.74	0.79	0.48	.0 35	-0.38	-0.55	-0.49	-0.50	-1.01	-1.75	-1 24
		E4E4140	TECIOI	0.04	4.40	0.72	0.22	0.20	0.44	0.24	0.40	4.20	4.40	1.40	0.06	4.00
		5454140	136101	2.34	1.10	0.72	0.32	-0.29	0.44	0.31	-0.49	-1.26	-1.16	-1.49	-0.96	-1.90
		73858570	SERPING1	9.85	-0.16	-0.53	-0.93	-1.55	-0.59	-0.94	-1.74	-2.52	-2.42	-2.74	-2.16	-3.16
		21264363	MASP2	7.74	-1.04	-1.42	-1.82	-2.43	-1.44	-1.83	-2.62	-3.40	-3.30	-3.62	-3.04	-4.04
R										Tubula	r Iniury					
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		AMR	vs. TI	GI No.	4502277	134254459	186910319	109659836	21361181	225637552	157671931	4506979	44680145	167466278	4507033	4507031
		0.00		Gene	ATP1B1	SLC12A1	SLC12A3	SLC5A10	ATP1A1	SLC13A2	SLC5A12	SLC13A2	SLC23A1	SLC5A8	SLC5A2	SLC5A1
		GI No.	Gene	SCI	3.23	23.26	6.06	10.27	10.60	11.53	11.11	2.34	5.21	5.32	2.98	2.06
		166235903	C1QC	10.04	6,29	6.07	5,91	5.51	5,50	4.89	4,70	4.29	4.02	3.92	3.70	3.29
		4759000	RABID	6.91	5 39	5.18	5.02	4.61	4.60	4.00	3.81	3 30	3.13	3.03	2.81	2 30
		4103000	0100	0.91	0.39	0.10	0.02	4.01	4.00	4.00	3.61	3.39	3.13	3.03	2.01	2.39
		0/298828	CTQB	3.00	5.17	4.96	4.79	4.39	4.38	3.78	3.58	3.17	2.91	2.81	2.58	2.17
		50234889	RAB43	4.20	4.75	4.54	4.38	3.98	3.97	3.36	3.17	2.75	2.49	2.39	2.17	1.75
		166197660	C8G	9.39	4.70	4.49	4.32	3.92	3.91	3.31	3.12	2.70	2.44	2.34	2.12	1.70
		148612842	IFITM3	16.42	4.58	4.37	4.21	3.81	3.80	3.19	3.00	2.58	2.32	2.22	2.00	1.58
		19923750	RAB3B	7.31	4,49	4.28	4.12	3.71	3.70	3,10	2.91	2.49	2.23	2.13	1.91	1.49
		52426774	HLA-DRA	4 88	4 39	4.18	4.02	3.61	3.60	3.00	2.81	2 39	2 13	2.03	1.81	1 39
	5	24147512	DAD7A	11.14	4.24	4.42	2.06	2.50	2.55	2.05	2.75	2.24	2.09	4.09	4.75	4.24
	ō	3414/513	RAB/A	11.14	4.34	4.13	3.96	3.56	3.55	2.95	2.75	2.34	2.08	1.98	1.75	1.34
	5	189083844	CTSC	24.95	4.21	4.00	3.84	3.43	3.42	2.82	2.63	2.21	1.95	1.85	1.63	1.21
	ē	9966867	EIF5A2	2.15	4.17	3.96	3.79	3.39	3.38	2.78	2.58	2.17	1.91	1.81	1.58	1.17
	°,	19923483	RAB14	5.96	4.17	3.96	3.79	3.39	3.38	2.78	2.58	2.17	1.91	1.81	1.58	1.17
	-	208609962	RAB7L1	2.23	3.91	3.70	3.53	3.13	3.12	2.51	2.32	1.91	1.64	1.54	1.32	0.91
	ä	4506365	RAR2A	3.41	3.81	3.60	3.43	3.03	3.02	2 42	2 22	1.81	1.54	1.44	1 22	0.81
	at	7706563	DADOD	5.00	0.01	0.00	2.20	0.00	0.02	0.00	2.00	4.07	4.44	4.24	4.00	0.07
	9	7706563	RAB8B	5.28	3.67	3.46	3.30	2.89	2.88	2.28	2.09	1.67	1.41	1.31	1.09	0.67
	ě	13569962	RAB1B	6.07	3.58	3.37	3.21	2.81	2.80	2.19	2.00	1.58	1.32	1.22	1.00	0.58
	<u> </u>	4502503	C4BPA	2.02	3.58	3.37	3.21	2.81	2.80	2.19	2.00	1.58	1.32	1.22	1.00	0.58
	€	5803135	RAB35	6.00	3.39	3.18	3.02	2.61	2.60	2.00	1.81	1.39	1.13	1.03	0.81	0.39
	õ	16933567	RAB8A	6.60	3.28	3.07	2.90	2.50	2.49	1.88	1.69	1.28	1.01	0.91	0.69	0.28
	≝	4758988	RAR1A	6 10	3.22	3.01	2.85	2 44	2 43	1.83	1.64	1.22	0.96	0.86	0.64	0.22
	ŝ	050000000	DADIA	5.07	0.00	0.01	2.05	0.05	2.45	1.05	1.04	1.00	0.30	0.00	0.45	0.00
	•	230222019	NOAD TO	0.01	3.03	2.02	2.00	2.25	2.24	1.04	1.45	1.05	0.77	0.07	0.45	0.03
		32455266	PRDX1	3.92	2.95	2.74	2.57	2.17	2.16	1.56	1.36	0.95	0.68	0.58	0.36	-0.05
			AZGP1	17.68	2.90	2.69	2.52	2.12	2.11	1.51	1.31	0.90	0.64	0.54	0.31	-0.10
		4502337	DADSC	10.13	2.82	2.61	2.44	2.04	2.03	1.43	1.23	0.82	0.56	0.46	0.23	-0.18
		4502337 41393614	104000		0.04	2.60	2.43	2.03	2.02	1.42	1.00	0.04			0.00	
		4502337 41393614 66879662	ARF1	8.15	2.81	A			2.02	1.46	1.22	0.01	0.54	0.44	0.22	-0.19
		4502337 41393614 66879662 7705885	ARF1 VPS2R	8.15	2.81	2.57	2.40	2.00	1.99	1.39	1.22	0.78	0.54	0.44	0.22	-0.19
		4502337 41393614 66879662 7705885	ARF1 VPS28	8.15 3.03	2.81	2.57	2.40	2.00	1.99	1.39	1.22	0.78	0.54	0.44	0.19	-0.19
		4502337 41393614 66879662 7705885 4557417	ARF1 VPS28 CD14	8.15 3.03 4.42	2.81 2.78 2.75	2.57 2.54	2.40 2.38	2.00 1.98	1.99 1.97	1.39	1.22	0.78	0.54 0.51 0.49	0.44 0.42 0.39	0.19	-0.19 -0.22 -0.25
		4502337 41393614 66879662 7705885 4557417 56682959	ARF1 VPS28 CD14 FTH1	8.15 3.03 4.42 5.65	2.81 2.78 2.75 2.74	2.57 2.54 2.53	2.40 2.38 2.36	2.00 1.98 1.96	1.99 1.97 1.95	1.39 1.36 1.34	1.22 1.19 1.17 1.15	0.78 0.75 0.74	0.54 0.51 0.49 0.47	0.44 0.42 0.39 0.37	0.22 0.19 0.17 0.15	-0.19 -0.22 -0.25 -0.26
		4502337 41393614 66879662 7705885 4557417 56682959 189163485	ARF1 VPS28 CD14 FTH1 CTSA	8.15 3.03 4.42 5.65 4.65	2.81 2.78 2.75 2.74 2.70	2.57 2.54 2.53 2.49	2.40 2.38 2.36 2.32	2.00 1.98 1.96 1.92	2.02 1.99 1.97 1.95 1.91	1.39 1.36 1.34 1.31	1.22 1.19 1.17 1.15 1.12	0.81 0.78 0.75 0.74 0.70	0.54 0.51 0.49 0.47 0.44	0.44 0.42 0.39 0.37 0.34	0.22 0.19 0.17 0.15 0.12	-0.19 -0.22 -0.25 -0.26 -0.30
		4502337 41393614 66879662 7705885 4557417 56682959 189163485	ARF1 VPS28 CD14 FTH1 CTSA	8.15 3.03 4.42 5.65 4.65	2.81 2.78 2.75 2.74 2.70	2.57 2.54 2.53 2.49	2.40 2.38 2.36 2.32	2.00 1.98 1.96 1.92	2.02 1.99 1.97 1.95 1.91	1.39 1.36 1.34 1.31	1.22 1.19 1.17 1.15 1.12	0.81 0.78 0.75 0.74 0.70	0.54 0.51 0.49 0.47 0.44	0.44 0.42 0.39 0.37 0.34	0.22 0.19 0.17 0.15 0.12	-0.19 -0.22 -0.25 -0.26 -0.30
-		4502337 41393614 66879662 7705885 4557417 56682959 189163485	ARF1 VPS28 CD14 FTH1 CTSA	8.15 3.03 4.42 5.65 4.65	2.81 2.78 2.75 2.74 2.70	2.57 2.54 2.53 2.49	2.40 2.38 2.36 2.32	2.00 1.98 1.96 1.92	1.99 1.97 1.95 1.91	1.39 1.36 1.34 1.31	1.22 1.19 1.17 1.15 1.12	0.81 0.78 0.75 0.74 0.70	0.54 0.51 0.49 0.47 0.44	0.44 0.42 0.39 0.37 0.34	0.22 0.19 0.17 0.15 0.12	-0.19 -0.22 -0.25 -0.26 -0.30
С		4502337 41393614 66879662 7705885 4557417 56682959 189163485	ARF1 VPS28 CD14 FTH1 CTSA	8.15 3.03 4.42 5.65 4.65	2.81 2.78 2.75 2.74 2.70	2.57 2.54 2.53 2.49	2.40 2.38 2.36 2.32	2.00 1.98 1.96 1.92	1.99 1.97 1.95 1.91	1.39 1.36 1.34 1.31 Tubula	1.22 1.19 1.17 1.15 1.12 r Injury	0.81 0.78 0.75 0.74 0.70	0.54 0.51 0.49 0.47 0.44	0.44 0.42 0.39 0.37 0.34	0.22 0.19 0.17 0.15 0.12	-0.19 -0.22 -0.25 -0.26 -0.30
с		4502337 41393614 66879662 7705885 4557417 56682959 189163485	ARF1 VPS28 CD14 FTH1 CTSA	8.15 3.03 4.42 5.65 4.65 GI No.	2.81 2.78 2.75 2.74 2.70	2.57 2.54 2.53 2.49	2.40 2.38 2.36 2.32	2.00 1.98 1.96 1.92	2.02 1.99 1.97 1.95 1.91	1.39 1.36 1.34 1.31 Tubula 134254459	1.22 1.19 1.17 1.15 1.12 r Injury 21361181	0.81 0.78 0.75 0.74 0.70	0.54 0.51 0.49 0.47 0.44 157671931	0.44 0.42 0.39 0.37 0.34	0.22 0.19 0.17 0.15 0.12	-0.19 -0.22 -0.25 -0.26 -0.30
С		4502337 41393614 66879662 7705885 4557417 56682959 189163485 CMR	ARF1 VPS28 CD14 FTH1 CTSA vs. TI	8.15 3.03 4.42 5.65 4.65 GI No. Gene	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2	2.57 2.54 2.53 2.49 109659836 SLC5A10	2.40 2.38 2.36 2.32 167466278 SLC5A8	2.00 1.98 1.96 1.92 186910319 SLC12A3	2.02 1.99 1.97 1.95 1.91 4502277 ATP1B1	1.39 1.36 1.34 1.31 Tubula 134254459 SLC12A1	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 ATP1A1	0.81 0.78 0.75 0.74 0.70 44680145 SLC23A1	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12	0.44 0.42 0.39 0.37 0.34 4507033 SLC5A2	0.22 0.19 0.17 0.15 0.12 4507031 SLC5A1	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2
C		4502337 41393614 66879662 7705885 4557417 56682959 189163485 CMR GI No.	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2 11.53	2.57 2.54 2.53 2.49 109659836 <i>SLC5A10</i> 10.27	2.40 2.38 2.36 2.32 167466278 SLC5A8 5.32	2.00 1.98 1.96 1.92 186910319 SLC12A3 6.06	2.02 1.99 1.97 1.95 1.91 4502277 ATP1B1 3.23	1.32 1.39 1.36 1.34 1.31 Tubula 134254459 <i>SLC12A1</i> 23.26	1.22 1.19 1.17 1.15 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.13 1.12 1.15 1.12 1.10 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.12 1.15 1.15 1.12 1.15 1.15 1.12 1.15 1.15 1.12 1.15 1.15 1.15 1.15 1.15 1.12 1.15 1	0.81 0.78 0.75 0.74 0.70 44680145 SLC23A1 5.21	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11	0.44 0.42 0.39 0.37 0.34 4507033 SLC5A2 2.98	0.22 0.19 0.17 0.15 0.12 4507031 SLC5A1 2.06	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34
C		4502337 41393614 66879662 7705885 4557417 56682959 189163485 CMR GI No. 22538440	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2 11.53 8.02	2.57 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02	2.40 2.38 2.36 2.32 167466278 SLC5A8 5.32 8.02	2.00 1.98 1.96 1.92 186910319 SLC12A3 6.06 8.02	2.02 1.99 1.97 1.95 1.91 4502277 ATP1B1 3.23 8.02	1.39 1.36 1.34 1.31 Tubula 134254459 SLC12A1 23.26 8.02	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 <i>ATP1A1</i> 10.60 8.02	0.81 0.78 0.75 0.74 0.70 44680145 SLC23A1 5.21 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02	0.44 0.42 0.39 0.37 0.34 4507033 SLC5A2 2.98 8.02	0.22 0.19 0.17 0.15 0.12 4507031 <i>SLC5A1</i> 2.06 8,02	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02
C		4502337 41393614 66879662 7705885 4557417 56682959 189163485 CMR GI No. 22538440 26024195	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFN	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2 11.53 8.02 8.02	2.57 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02 8.02	2.40 2.38 2.36 2.32 167466278 SLC5A8 5.32 8.02 8.02	2.00 1.98 1.96 1.92 186910319 SLC12A3 6.06 8.02 8.02	2.02 1.99 1.97 1.95 1.91 4502277 ATP1B1 3.23 8.02 8.42	1.32 1.39 1.36 1.34 1.34 1.31 Tubula 134254459 SLC12A1 23.26 8.02 8.02	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 <i>ATP1A1</i> 10.60 8.02 8.02	0.81 0.78 0.75 0.74 0.70 44680145 <i>SLC23A1</i> 5.21 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02	0.44 0.42 0.39 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02	0.22 0.19 0.17 0.15 0.12 4507031 SLC5A1 2.06 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02
0		4502337 41393614 66879662 7705885 4557417 56682959 189163485 CMR GI No. 22538440 26024195 34485711	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFN BAB27A	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2 11.53 8.02 8.02 8.02	2.50 2.57 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02 8.02 8.02	2.40 2.38 2.36 2.32 167466278 SLC5A8 5.32 8.02 8.02 8.02	2.00 2.00 1.98 1.96 1.92 186910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02	2.02 1.99 1.97 1.95 1.91 4502277 ATP1B1 3.23 8.02 8.02 8.02	1.32 1.39 1.36 1.34 1.31 Tubula 134254459 <i>SLC12A1</i> 23.26 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.16 1.12 1.16 1.17 1.15 1.12 1.10 1.17 1.15 1.12 1.10 1.15 1.12 1.16 1.16 1.17 1.16 1.17 1.16 1.17 1.15 1.12 1.16 1.16 1.16 1.17 1.16 1	0.81 0.78 0.75 0.74 0.70 44680145 SLC23A1 5.21 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.34 4507033 <i>SLC5A2</i> 2.98 8.02 8.02 8.02	0.22 0.19 0.17 0.15 0.12 4507031 <i>SLC5A1</i> 2.06 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02
C		4502337 41393614 66879662 7705885 4557417 56682959 189163485 8189163485 CMR GI No. 22538440 26024195 34485711	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFN RAB27A	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56	2.81 2.78 2.77 2.74 2.70 225637552 SLC13A2 11.53 8.02 8.02 8.02	2.55 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02 8.02 8.02	2.40 2.38 2.36 2.32 167466278 SLC5A8 5.32 8.02 8.02 8.02 8.02	2.00 1.98 1.96 1.92 186910319 SLC12A3 6.06 8.02 8.02 8.02	2.02 1.99 1.97 1.95 1.91 4502277 ATP1B1 3.23 8.02 8.02 8.02 8.02	1.32 1.39 1.36 1.34 1.31 Tubula 134254459 <i>SLC12A1</i> 23.26 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.15 1.12 r Injury 21361181 <i>ATP1A1</i> 10.60 8.02 8.02 8.02 8.02	0.81 0.78 0.75 0.74 0.70 44680145 <i>SLC23A1</i> 5.21 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02 8.02 8.02	0.22 0.19 0.17 0.15 0.12 4507031 <i>SLC5A1</i> 2.06 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02
C		4502337 41393614 66879662 7705885 4557417 56682959 189163485 0004195 22538440 226024195 34485711 54607120	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFN RAB27A LTF	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56 8.54	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2 11.53 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02 8.02 8.02 8.02 7.83	2.40 2.38 2.36 2.32 167466278 SLC5A8 5.32 8.02 8.02 8.02 8.02 8.02 7.83	2.00 1.98 1.96 1.92 186910319 SLC12A3 6.06 8.02 8.02 8.02 8.02 7.77	2.02 1.99 1.97 1.95 1.91 4502277 <i>ATP1B1</i> 3.23 8.02 8.02 8.02 8.02	1.32 1.39 1.36 1.34 1.31 Tubula 134254459 <i>SLC12A1</i> 23.26 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.12 1.16 1.12 1.16 1.12 1.16 1.12 1.16 1.17 1.15 1.12 1.16 1.17 1.15 1.12 1.16 1.16 1.17 1.16 1	0.81 0.78 0.75 0.74 0.70 44680145 <i>SLC23A1</i> 5.21 8.02 8.02 8.02 8.02 6.54	0.54 0.51 0.49 0.47 0.44 157671931 <i>SLC5A12</i> 11.11 8.02 8.02 8.02 8.02 6.48	0.44 0.42 0.39 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02 8.02 8.02 8.02	0.22 0.19 0.17 0.15 0.12 4507031 <i>SLC5A1</i> 2.06 8.02 8.02 8.02 8.02 5.80	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02
С		4502337 41393614 66879662 7705885 4557417 56682959 189163485 189163485 CMR GI NO. 22538440 26024195 34485711 54607120 29788785	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFC CNFC RAB27A LTF TUBB	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56 8.54 3.21	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2 11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02 8.02 8.02 8.02 7.83 3.81	2.40 2.38 2.36 2.32 167466278 SLC5A8 5.32 8.02 8.02 8.02 8.02 7.83 3.81	2.00 1.98 1.96 1.92 186910319 SLC1243 6.06 8.02 8.02 8.02 8.02 7.77 3.75	2.02 1.99 1.97 1.95 1.91 4502277 ATP1B1 3.23 8.02 8.02 8.02 8.02 7.61 3.58	1.39 1.36 1.34 1.34 1.31 Tubula 134254459 <i>SLC12A1</i> 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 ATP1A1 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.81 0.78 0.75 0.74 0.70 44680145 <i>SLC23A1</i> 5.21 8.02 8.02 8.02 8.02 6.54 2.51	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 8.02 8.02 6.48 2.46	0.44 0.42 0.37 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02 8.02 8.02 8.02 2.00	0.22 0.19 0.17 0.15 0.12 4507031 <i>SLC5A1</i> 2.06 8.02 8.02 8.02 8.02 5.60 1.78	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02 8.02 5.29 1.26
C		4502337 41393614 66879662 7705885 4557417 56682950 189163485 189163485 189163485 24024195 34485711 54607120 29788785 4502101	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFN RAB27A LTF TUBB ANXA1	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56 8.554 3.21 16.17	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2 11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 109659836 <i>SLC5A10</i> 10.27 8.02 8.02 8.02 8.02 7.83 3.81 3.53	2.40 2.38 2.36 2.32 167466278 SLC5A8 5.32 8.02 8.02 8.02 8.02 7.83 3.81 3.53	2.00 1.98 1.96 1.92 186910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02 8.02 7.77 3.75 3.47	2.02 1.99 1.97 1.95 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.32 1.36 1.34 1.34 1.31 Tubula 134254459 <i>SLC12A1</i> 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 ATP1A1 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.75 0.75 0.74 0.70 44680145 5.21 8.02 8.02 8.02 8.02 6.54 2.51 2.24	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.37 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02 8.02 8.02 6.02 2.00 1.72	0.22 0.19 0.17 0.15 0.12 4507031 SLC5A1 2.06 8.02 8.02 8.02 8.02 5.80 1.78 1.50	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
0		4502337 41393614 66879662 7705885 4557417 56682959 189163485 189163485 CMR GI No. 22538440 26024195 34485711 24485711 29788785 4502101 5174735	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFM RAB27A LTF TUBB ANXA1 TUBB2C	8.15 3.03 4.42 5.65 4.65 GI No. Gene I SC 22.64 19.92 3.56 8.54 3.21 16.17 2.42	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2 11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02 8.02 8.02 7.83 3.81 3.53 3.39	2.40 2.38 2.36 2.32 167466278 SLC5A8 5.32 8.02 8.02 8.02 8.02 7.63 3.81 3.53 3.39	2.00 1.98 1.96 1.92 186910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02 7.77 3.75 3.47	2.02 1.99 1.97 1.95 1.91 4502277 ATP1B1 3.23 8.02 8.02 8.02 8.02 8.02 7.61 3.58 3.31 3.17	1.32 1.36 1.36 1.34 1.31 Tubula 134254459 SLC12A1 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 ATP1A1 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.78 0.78 0.75 0.74 0.70 44680145 <i>SLC23A1</i> 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 6.48 2.46 2.18 2.04	0.44 0.42 0.37 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02 8.02 8.02 8.02 6.02 2.00 1.72 2.00	0.22 0.19 0.17 0.15 0.12 4507031 SLC5A1 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 \$LC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
0		4502337 41393614 66879662 7705885 4557417 56682959 189163485 189163485 22538440 22538440 22538440 22538440 2253847 24602419 34485711 54607120 29788785 4502101 5174735	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFN RAB27A LITF TUBB ANXA1 TUBB27	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56 8.54 3.21 16.17 2.42 39.10	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2 11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 109659836 SLC5410 10.27 8.02 8.02 8.02 8.02 7.83 3.81 3.53 3.34	2.40 2.38 2.36 2.32 167466278 SLC5A8 5.32 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	2.00 1.98 1.96 1.92 186910319 SLC12A3 6.06 8.02 8.02 8.02 8.02 8.02 7.77 3.75 3.47 3.33 3.19	2.02 1.99 1.97 1.95 1.91 4502277 <i>ATP1B1</i> 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.32 1.33 1.36 1.34 1.31 Tubula 134254459 <i>SLC12A1</i> 23.26 8.02 8.03 8.03 8.25 8.55 8.5	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 <i>ATP1A1</i> 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.75 0.74 0.70 44680145 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLCSA12 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.34 4507033 <i>SLC5A2</i> 2.98 8.02 8.02 8.02 8.02 8.02 2.00 1.72 1.55	0.12 0.13 0.17 0.15 0.12 4507031 <i>SLC5A1</i> 2.06 8.02 8.02 8.02 8.02 8.02 1.78 1.50 1.38	-0.19 -0.22 -0.25 -0.26 -0.30 \$100000000000000000000000000000000000
C		4502337 41393614 66879662 7705885 4557417 566822650 189163485 189163485 189163485 26027120 22538440 26024195 344657120 29788785 45607120 29788785 4502337 5174735	ARF1 VPS28 CD14 FTH1 CTSA Vs. TI Gene CTSC CNFN RAB27A LTF TUBB ANXA1 TUBB2C AZGP1	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56 8.54 3.21 16.17 2.42 39.10	2.87 2.78 2.75 2.74 2.70 225637552 5.LC13A2 11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 109659836 <i>SLC5A10</i> 10.27 8.02 8.02 7.83 3.81 3.53 3.39 3.18 2.07	2.40 2.38 2.36 2.32 167466278 <i>SLC5A8</i> 5.32 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	2.00 1.98 1.96 1.92 186910319 SLC12A3 6.06 8.02 8.02 8.02 7.77 3.75 3.47 3.33 3.12 2.04	2.02 1.99 1.97 1.95 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.32 1.39 1.36 1.34 1.32 1.35 1.34	1.122 1.19 1.17 1.15 1.12 r Injury 21361181 ATP1A1 10.60 8.02	0.81 0.75 0.74 0.70 44680145 5.21 8.02 8.02 8.02 6.54 2.51 2.51 2.51 1.88 4.78	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 6.48 2.46 2.16 2.46 2.46 2.46 2.46 2.46	0.44 0.42 0.37 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02 8.02 8.02 8.02 8.02 1.72 1.58 1.37	0.12 0.19 0.17 0.15 0.12 4507031 <i>SLC5A1</i> 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.028.02 8.02 8.02 8.02 8.028.02 8.02 8.028.02 8.02 8.028.02 8.028.028.028.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
C		4502337 41393614 66879662 7705885 4557417 56682959 189163485 189163485 22538440 26024195 34485711 54607120 29788785 4502101 5174735 4502101	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFN RAB27A LTF TUBB ANXA1 TUBB27A LTF TUBB ANXA1 TUBB271 UPK2	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56 8.54 3.21 16.17 2.42 39.10 20.54	2.81 2.78 2.75 2.74 2.70 225637552 SLC13A2 11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 4.00 3.72 3.58 3.37 3.26	2.57 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02 8.02 8.02 8.02 7.83 3.81 3.53 3.39 3.18 3.07	2.40 2.38 2.36 2.32 167466278 5.32 8.02 8.02 8.02 8.02 8.02 7.83 3.81 3.53 3.81 3.53 3.18 3.07	2.00 1.98 1.96 1.92 186910319 SLC12A3 6.06 8.02 8.02 8.02 8.02 7.77 3.75 3.47 3.37 3.12 3.01	2.02 1.99 1.97 1.95 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.32 1.39 1.36 1.34 1.34 1.34 134254459 SLC12A1 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 <i>ATP1A1</i> 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.01 0.75 0.75 0.74 0.70 44680145 5.21 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLCSA12 11.11 8.02 8.02 8.02 8.02 6.46 2.46 2.46 2.46 2.48 2.46 1.83 1.72	0.44 0.42 0.39 0.37 0.34 4507033 SLC542 2.98 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.12 0.19 0.17 0.15 0.12 4507031 3LC5A1 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02 8.02 5.29 1.26 0.99 0.85 0.63 0.53
C	u	4502337 41393614 66879662 7705885 4557417 56682950 189163485 189163485 26024195 32485711 54607120 29788785 44502101 5174735 4502337 5603215 5031635	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFN RAB27A LTF TUBB2C ANXA1 TUBB2C ANXA1 TUBB2C AZGP1 UPK2 CFL1	8.15 3.03 4.42 5.65 4.65 GI No. Gene I SC 22.64 19.92 3.56 8.554 3.21 16.17 2.42 39.10 20.54 13.57	2.88 2.75 2.74 2.70 225637552 3.11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02 8.02 8.02 7.83 3.81 3.53 3.39 3.18 3.07 2.99	2.40 2.38 2.36 2.32 2.32 2.32 2.32 2.32 8.02 8.02 8.02 7.83 3.81 3.53 3.39 3.18 3.07 2.99	2.00 1.98 1.96 1.96 1.96 1.96 1.96 1.96 8.02 8.02 8.02 8.02 7.77 3.75 3.47 3.33 3.12 3.01 2.93	2.02 1.99 1.97 1.95 1.91 4502277 ATP181 3.23 8.02 8.02 7.61 3.58 8.02 7.61 3.53 3.31 3.17 2.96 2.85 2.77	1.32 1.39 1.36 1.34 1.34 1.34 1.34254459 SLC72A1 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12	0.81 0.75 0.74 0.70 44680145 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 81256712 11.11 8.02 8.02 8.02 8.48 2.46 2.48 2.48 2.48 2.48 2.48 2.04 1.83 1.72 2.04	0.44 0.42 0.39 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02 8.02 8.02 8.02 8.02 1.72 1.58 1.37 1.26 1.18	0.12 0.17 0.15 0.17 0.15 0.12 4507031 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
D	tion	4502337 41339614 41339614 41339614 4557417 56682959 189163485 189163485 28024195 34485711 54607120 29788785 4502101 5174735 4502215 5031635 5002155	ARF1 VPS28 CD14 FTH1 CTSA Vs. TI Gene CTSC CNFN RAB27A LIF TUBB ANXA1 TUBB2C AZGP1 UPK2 CFL1 UPK2 CFL1 UPK2 AUPK3A	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56 8.54 3.21 16.17 2.42 39.10 20.54 13.57 2.77	2.81 2.78 2.75 2.74 2.70 2.70 2.70 2.74 2.70 2.70 2.70 2.75 2.74 2.70 2.75 2.74 2.75 2.75 2.75 2.75 2.75 2.75 2.75 2.75	2.57 2.54 2.53 2.49 109659836 <i>SLC5A10</i> 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.03 8.03 8.03 8.03 8.03 8.03 8.03 8.03	2.40 2.38 2.36 2.32 32 32 3.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8	2.00 1.98 1.96 1.92 186910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02 8.02 7.77 3.75 3.47 3.37 3.12 3.01 2.93 2.75	2.02 1.99 1.97 1.95 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.32 1.33 1.36 1.34 1.34 1.34 134254459 SLC12A1 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 21361181 A77141 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.73 0.75 0.74 0.74 0.74 0.74 0.74 0.74 0.74 0.74	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02 8.02 8.02 2.00 1.72 8.02 2.00 1.75 8.02 1.55 1.37 1.26 1.37 1.26 1.18	0.12 0.19 0.17 0.15 0.12 4507031 3LC5A1 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
C	ection	4502337 41330614 66879662 7705885 4557417 56682359 189163485 189163485 2623240 22538440 26024195 34485711 54607120 29788785 450210 2178755 4502337 5602215 4502337 55031635 5502152	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFN RAB27A LTF TUBB ANXA1 TUBB2C AZGP1 UPK2 CFL1 UPK2 CFL1 UPK2	8.15 3.03 4.42 5.65 4.65 GI No. Gene. I SC 22.64 19.92 3.56 8.54 3.21 16.17 2.42 39.10 20.54 13.57 2.75	2.81 2.75 2.74 2.70 2.74 2.70 2.70 2.74 2.70 2.70 2.75 2.74 2.70 2.72 3.55 3.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8	2.57 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02 8.02 7.83 3.81 3.53 3.39 3.18 3.07 2.99 2.81 2.64	2.40 2.38 2.36 2.32 2.32 2.32 8.02 8.02 8.02 8.02 7.83 3.81 3.53 3.39 3.18 3.07 2.99 2.81 2.64	2.00 1.98 1.96 1.96 1.96 1.96 1.96 1.96 1.96 1.96	2.02 1.99 1.97 1.95 1.91 4502277 ATP1B1 3.23 8.02 8.02 7.61 3.58 8.02 7.61 3.53 3.31 3.17 2.96 2.85 2.77 2.58 2.42	1.32 1.36 1.36 1.34 1.34 1.34 134254459 5LC72A1 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12	0.81 0.75 0.74 0.70 44680145 5.21 8.02 8.02 8.02 6.54 2.51 8.02 8.02 6.54 2.51 8.02 8.02 8.02 6.54 2.51 1.78 1.70 1.51 1.34	0.54 0.51 0.49 0.47 0.44 157671931 54.05A12 11,11 8.02 8.02 8.02 6.46 2.46 2.46 2.48 2.04 1.83 2.04 1.83 1.72 1.64 1.46	0.44 0.42 0.39 0.37 0.34 4507033 <i>SLC5A2</i> 2.98 8.02 8.02 8.02 8.02 8.02 8.02 1.72 1.58 1.37 1.26 1.18 1.00 0.83	0.12 0.17 0.15 0.17 0.15 0.12 4507031 SLC5A1 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 -0.30 -0.30 -0.30 -0.30 -0.30 -0.30 -0.26 -0.30 -0.26 -0.30 -0.26 -0.30 -0.26 -0.30 -0.26 -0.26 -0.30 -0.26 -0.36 -0.26 -0.36 -0.26 -0.36 -0.35 -0.26 -0.35 -0.26 -0.35 -0.26 -0.35 -0.26
0	ejection	4502337 41339614 41339614 41339614 4557417 56682959 189163485 CMR GI No. 22538440 226024195 34485711 54607120 29788785 4502101 5174735 4502317 5031635 5031635 5032165	ARF1 ARF1 VP528 CD14 FTH1 CTSA Vs. TI Gene CTSC CNFN RAB27A LTF TUBB ANXA1 TUBB271 UPK2 CFL1 UPK3A YWHAZ WHVAZ RHOA	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56 8.54 3.21 16.17 2.42 39.10 20.54 13.57 2.77 5.75 9.12	2.81 2.78 2.75 2.74 2.70 2.5637552 3.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8	2.57 2.54 2.53 2.49 109659836 <i>SLC5A10</i> 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.03 8.03 8.03 8.03 8.03 8.03 8.03 8.03	2.40 2.38 2.36 2.32 32 32 32 8.02 8.02 8.02 8.02 8.02 7.63 3.81 3.53 3.39 3.18 3.07 2.99 2.81 2.64	2.00 1.98 1.96 1.92 186910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02 8.02 7.77 3.75 3.47 3.33 3.12 3.01 2.75 2.58 2.49	2.02 1.99 1.97 1.95 1.95 1.95 1.95 1.95 1.95 1.95 1.95	1.32 1.33 1.36 1.34 1.34 1.34 134254459 <i>SLC12A1</i> 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 21361181 A77141 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.75 0.74 0.75 0.74 0.74 0.74 0.74 0.74 0.74 0.74 0.74	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.12 0.17 0.17 0.15 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.12	-0.19 -0.22 -0.25 -0.26 -0.30 -0.30 -0.26 -0.30 SLC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
C	Rejection	4502337 41330814 66879662 7705885 4557417 56682359 189163485 189163485 2682245 26824195 34485711 54607120 29788785 4502110 5174735 45002337 5902215 45002337 5902215 45002337 59022152 4507252	ARE1 ARE1 VPS28 CD14 FTH1 CTSA Vs. TI Gene CTSC CNFN RAB27A LTF TUBB2C ANXA1 TUBB2C AXAX1 TUBB2C AXAX1 UPK2 CFL1 UPK2 CFL1 UPK2 CFL1 UPK2 RH0A	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 19.92 3.56 8.54 19.92 3.56 8.54 19.92 3.56 8.54 19.92 3.56 8.54 19.92 3.56 8.54 19.92 3.56 8.54 19.92 3.56 8.54 19.92 3.56 8.54 19.92 3.56 8.54 19.92 3.56 8.55 19.55	2.87 2.75 2.74 2.70 2.25637552 SLC13A2 11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 109659836 SLC5A10 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.40 2.38 2.36 2.32 32 32 32 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	2.00 1.98 1.96 1.92 186910319 SLC12A3 6.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.02 1.99 1.97 1.97 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.34 1.39 1.36 1.34 1.34 1.34 1.34 1.34 2.325 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 <i>ATP1A1</i> 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.75 0.75 0.74 0.70 0.70 0.70 0.70 0.70 0.70 0.70	0.54 0.51 0.49 0.47 0.44 157671931 <i>SLC5A12</i> 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.37 0.34 4507033 SLC542 2.98 8.02 8.02 8.02 8.02 8.02 8.02 1.58 8.02 1.58 1.37 1.26 1.18 1.00 0.83 0.63 0.63 0.63	0.12 0.17 0.17 0.12 4507031 <i>SLC5A1</i> 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 \$LC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
0	d Rejection	4502337 413303614 66879662 7705885 4557417 566822959 189163485 CMR GI NO. 22538440 26024195 34485711 54607120 29788785 44502101 5174735 44502315 5031635 5032155 5031635 5032155 10335049 10335049 10335049	ARF1 VPS28 CD14 FTH1 CTSA vs. TI Gene CTSC CNFN RAB27A LTF TUBB ANXA1 TUBB271 UPK2 CFL1 UPK3A YWHAZ WHAZ	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56 8.54 19.92 3.56 8.54 19.92 3.56 8.54 19.92 3.56 8.54 19.7 2.42 39.10 20.57 2.77 5.75 9.12 30.33	2.87 2.78 2.75 2.74 2.70 225637552 3.11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.54 2.49 109659836 5LC5A10 10.27 8.02 8.02 8.02 8.02 7.83 3.81 3.53 3.39 3.38 3.318 3.07 2.99 2.81 2.64 2.54 2.54 2.54	2.40 2.38 2.36 2.32 2.32 3.2 3.2 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.	2.00 1.98 1.96 1.92 186910319 5.LC12A3 6.06 8.02 8.02 8.02 8.02 7.77 3.75 3.47 3.33 3.12 3.01 2.93 3.01 2.93 2.75 2.58 2.49 2.41	2.02 1.99 1.97 1.97 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 7.61 3.58 3.31 3.58 3.31 2.96 2.85 2.77 2.58 2.42 2.58 2.42 2.52	1.34 1.33 1.34 1.34 1.34 1.34 1.34 1.34	1.22 1.19 1.17 1.15 r Injury 21361181 <i>ATP1A1</i> 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.73 0.75 0.74 0.70 44680145 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 6.48 2.46 2.48 2.48 2.48 2.48 2.48 1.72 1.64 1.20 1.12	0.44 0.42 0.39 0.37 0.37 0.34 4507033 SLC5A2 2.98 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.12 0.19 0.17 0.15 0.12 0.12 0.12 0.12 0.12 0.12 0.12 0.05 1.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 -0.30 -0.30 -0.26 -0.30 -0.22 -0.26 -0.30 -0.22 -0.26 -0.30 -0.22 -0.26
C	ted Rejection	4502337 41330614 405379062 7705885 4557417 56682265 189163485 189163485 CMR GI No. 22538440 26024195 34485711 54607120 29788785 4502101 5174735 5902145 4502337 59032155 5902142 4507953 10835049 5902148 12667788	ARF1 ARF1 VPS28 CD14 FTH1 CTSA Vs. TI Gene CTSC CTSC CNFN RAB27A LTF TUBBS ANXA1 UPK3 CFL1 UPK32 CFL1 UPK32 RHOA UPK14 RHOA UPK149	8.15 3.03 4.42 5.65 4.65 GI No. Gene SC 22.64 19.92 3.56 8.54 3.21 16.17 2.42 39.10 20.54 13.57 2.77 5.75 9.12 30.33 2.09	2,81 2,75 2,74 2,70 225637552 <i>SLC132</i> 11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.54 2.49 109659836 SLC5A10 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.40 2.38 2.38 2.32 32 32 32 32 802 802 802 802 802 802 802 802 802 80	2.00 1.98 1.96 1.92 186910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.02 1.99 1.97 1.97 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.34 1.39 1.36 1.34 1.34 1.34 1.34 1.34 245459 2.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 <i>ATP1A1</i> 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.73 0.75 0.74 0.70 0.70 0.70 0.70 0.70 0.70 0.70	0.54 0.51 0.49 0.47 0.47 0.47 10.47 10.47 10.47 10.47 10.44 1.02 10.2 10.2 10.2 10.2 10.2 10.2 10.2	0.44 0.42 0.39 0.37 0.37 4507033 <i>SLC5A2</i> 2.98 8.02 8.02 8.02 8.02 8.02 1.58 1.37 1.26 1.18 1.00 8.03 0.63 0.74 0.65	0.12 0.19 0.17 0.15 0.12 4507031 <i>SLC5A1</i> 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 \$LC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
C	liated Rejection	4502337 41333614 68579662 7705885 4557417 566822959 189163485 CMR GI NO. 22538440 26024195 34485711 54607120 29788785 44502101 5174735 44502315 5031635 59302152 5032155 5031635 59302148 128677788 194394237	ARF1 ARF1 VP528 CD14 FTH1 CTSA Vs. TI Gene CTSC CNFN RAE27 LTF TUBB ANXA1 TUBBB2C AZGP1 UPK2 CFL1 UPK2 CFL1 UPK2 RH02 RH02 RH02 VH42 RH04 VH42 RH04 VH49 VH49 VH49 VH49 VH49 VH49	8.15 3.03 4.42 5.65 4.65 GI No. Gen SC 22.64 19.92 3.56 8.54 3.21 16.17 2.42 39.10 20.54 13.57 2.77 5.75 9.12 30.33 2.09 2.06	2.87 2.78 2.75 2.74 2.70 2256037552 3.11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.54 3.249 109659836 5LC5A10 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.40 2.38 2.36 2.32 32 32 3.32 8.02 8.02 8.02 8.02 8.02 8.02 7.83 3.80 3.53 3.81 3.53 3.81 3.53 3.81 3.53 3.81 2.64 2.64 2.64 2.47 2.45	2.00 1.98 1.96 1.92 186910319 5.LC12A3 6.06 8.02 8.02 8.02 8.02 7.77 3.75 3.47 3.37 3.47 3.312 3.01 2.93 3.47 3.01 2.93 2.75 2.58 2.49 2.41 2.40	2.02 1.99 1.97 1.97 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 7.61 3.58 3.31 3.17 2.96 2.85 2.77 2.58 2.42 2.25 2.23 2.17	1.34 1.39 1.36 1.34 1.34 1.34 1.34 1.34 2.54459 2.25 2.39 2.26 2.39 2.26 2.39 2.25 2.39 1.83 1.83 1.66 1.49 1.66 1.49 1.33 1.33 1.33	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 <i>ATP1A1</i> 100 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.	0.81 0.75 0.75 0.74 0.70 44680145 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 6.48 2.46 2.48 2.48 2.48 2.48 2.48 1.72 1.64 1.20 1.12 1.10 1.04	0.44 0.42 0.39 0.37 0.34 4507033 SLC542 2.98 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.12 0.19 0.17 0.15 0.12 4507031 54.C5A1 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
C	ediated Rejection	4502337 413303614 66879662 7705885 4557417 56682265 189163485 189163485 CMR GI No. 22538440 26024195 34485711 54607120 29788785 4502101 5174735 5902148 4502337 5902152 4502152 1450336 5902152 14507953 10835049 5902148 12667788	ARE1 ARE1 VPS28 CD14 FTH1 CTSA Vs. TI Gene CTSC CTSC CTSC CTSC CTSC CTSC CTSC CTS	8.15 3.03 4.42 5.65 4.65 GI No. Gene I SC 22.64 19.92 3.56 8.54 3.21 16.17 2.42 39.10 20.54 13.57 2.75 9.12 .75 9.12 3.03 3.2.09 2.06 2.76	2,81 2,75 2,74 2,70 225637552 3,1153 8,02 8,02 8,02 8,02 8,02 8,02 8,02 8,02	2.57 2.54 2.54 2.49 109659836 3LC5A10 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.03 8.03 8.03 8.03 8.03 8.03 8.03 8.03	2.40 2.38 2.36 2.32 32 32 5.32 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	2.00 1.98 1.96 1.92 186910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02 8.02 7.77 3.75 3.47 3.33 3.12 2.93 2.75 2.58 2.49 2.41 2.40 2.40 2.43 2.47	2.002 1.99 1.97 1.97 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 7.61 3.58 3.31 3.58 3.31 2.96 2.85 2.277 2.58 2.42 2.23 2.42 2.23 2.17	1.34 1.39 1.36 1.34 1.34 1.31 13425459 <i>SLC12A1</i> 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 1.19 1.17 1.15 1.12 1.12 1.11 1.12 1.12 1.12 1.12	0.81 0.75 0.77 0.70 44680145 5.21 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5472 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.37 0.37 0.34 4507033 SLC562 2.98 8.02 2.98 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.12 0.19 0.17 0.15 0.12 4507031 <i>SLC5A1</i> 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 \$LC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
C	Mediated Rejection	4502337 41393614 66879662 7705885 4557417 56682959 18916385 18916385 28024195 24024195 24024195 24024195 246207120 29788785 4450710 29788785 45002102 29788785 45002102 29788785 45002122 450024155 5031635 5502163 5502163 55022145 10835049 55022145 10835049 55022145 1943842377 1890683772 29065557	ARF1 ARF1 VP528 CD14 FTH1 CTSA Vs. TI Gene CTSC CNFN RAE25 CNFN RAE25 AD26 AD26 AD26 AD26 AD26 AD26 AD26 AD26	8.15 3.03 4.42 5.65 4.65 GI No. Gene (SC 22.64 19.92 (SC 326 3.21 19.32 3.26 3.21 19.32 3.21 10.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 11.32 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.21 3.213.213.213.213.213.213.213.213.213.213.213.213.21	2,87 2,77 2,77 2,77 2,70 225637552 3,17 5,00 8,02 8,02 8,02 8,02 8,02 8,02 8,02 8	2.57 2.54 2.54 2.54 3.2.49 1009659836 5.LC5A10 10.27 8.02 8.02 8.02 7.83 3.81 3.53 3.39 3.18 3.07 2.99 2.81 2.64 2.64 2.64 2.64 2.47 2.45 2.47 2.45 2.49	2.40 2.38 2.36 2.32 32 32 32 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	2.00 1.98 1.96 1.92 1.92 1.92 1.92 1.92 1.92 1.92 1.92	2.02 1.99 1.97 1.97 1.91 4502277 ATP161 3.23 8.02 8.02 8.02 8.02 7.61 3.58 3.31 3.17 2.96 2.85 2.77 2.58 2.42 2.25 2.23 2.25 2.217 2.00 1.96	1.32 1.39 1.36 1.34 1.31 Tubula 13425459 SLC12A1 23.26 8.02 8.03 8.184	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 ATP1A1 10.60 6.02 8	0.81 0.75 0.77 0.70 44680145 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 <i>SLCSA12</i> 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.37 4507033 SLC542 2.98 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.12 0.19 0.17 0.15 0.12 4507031 5.LC5A1 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 4506979 SLC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
C	II-Mediated Rejection	4502337 41393614 66879662 7705885 4557417 56682959 169163485 169163485 22530440 22530440 226024195 34485711 54607120 29788785 44607120 29788785 44607120 29788785 5031635 5031635 5031635 5031635 5031635 5031635 5031635 5031635 5031635 5031635 5031635 5031635 5031635 5031635 5031635 5031635 5031635 503165 503005 503165 5055 503165 5055 5055 50555 505555 505555 5055555 50555555	ARF1 ARF1 VP528 CD14 FTH1 CTSA Vs. TI Gene CTSC CTSC CTSC CTSC CTSC CTSC CTSC CTS	8.15 3.03 4.42 5.65 4.65 Gi No [BC 22.64 H No. [BC 22.64 19.92 3.56 8.54 3.56 8.54 3.56 8.54 13.57 5.75 9.12 2.03 2.09 2.06 2.03 2.09 2.06 4.57 4.57 5.75 5.75 5.75 5.75 5.75 5.75	2,81 2,75 2,74 2,70 225637552 25,07552 2,74 2,70 2,256 8,02 8,02 8,02 8,02 8,02 8,02 8,02 8,02	2.57 2.54 2.54 2.49 109659836 3LC5A10 10.27 8.02 8.02 8.02 8.02 7.83 3.81 3.53 3.38 3.18 3.07 8.33 3.18 3.07 2.99 2.81 2.54 2.54 2.54 2.54 2.54 2.54 2.54 2.54	2.40 2.38 2.36 2.32 32 32 5.32 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	2.00 1.98 1.96 1.92 186910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02 8.02 7.77 3.75 3.47 3.33 3.12 2.93 2.75 2.49 2.41 2.40 2.43 2.49 2.41 2.40 2.43 2.41 2.40 2.43 2.41 2.40 2.43 2.41 2.41 2.41 2.41 2.41 2.41 2.41 2.41	2.002 1.99 1.97 1.97 1.91 4502277 ATP181 3.23 8.02 8.22	1.34 1.39 1.36 1.34 1.31 13425459 <i>SLC12A1</i> 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 1.19 1.17 1.15 1.12 1.12 1.12 1.12 1.12 1.12 1.12	0.81 0.75 0.77 0.70 44680145 5.21 5.21 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.37 0.37 0.37 0.37 0.37 0.37 0.37	0.12 0.19 0.17 0.15 0.12 4507031 3LC5A1 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	-0.19 -0.22 -0.25 -0.26 -0.30 SLC13A2 2.34 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02
C	Cell-Mediated Rejection	4502337 41393614 66879662 7705885 4557417 56682250 189163485 189163485 189163485 22538440 26024195 2485740 26024195 24485711 54607120 29788785 44502101 5174735 44502115 5031635 5502148 12607788 1943842371 189083772 23085552 32455265	ARF1 ARF1 VP328 CD14 FTH1 CTSA Vs. TI Gene CTSC CNFN RAB27A LTF TUBB2CA CNFN RAB27A LTF TUBB2CA CPL1 UPK2 CFL1 UPK3A CFL1 UPK1 SSN GSTM3 PRDX1 CSSN	8.15 3.03 4.42 5.65 4.65 GI NO. Gene SC 22.64 3.56 8.54 3.21 16.17 2.054 3.21 16.17 2.054 3.910 2.054 2.07 2.07 5.75 5.75 2.033 2.06 2.07 2.07 2.034 2.06 4.65	2,87 2,77 2,77 2,77 2,70 225637552 3,17 8,02 8,02 8,02 8,02 8,02 8,02 8,02 8,02	2.57 2.54 2.54 2.54 3.2.49 109659836 5.LC5A10 10.27 8.02 8.02 8.02 7.83 3.81 3.53 3.39 3.18 3.53 3.39 3.18 2.64 2.64 2.64 2.64 2.64 2.64 2.47 2.45 2.47 2.45 2.49 9 2.81 2.49 2.41 2.45 2.49 3.10 2.41 2.45 3.25 3.39 3.10 2.41 2.45 3.39 3.45 3.39 3.45 3.45 3.45 3.45 3.45 3.45 3.45 3.45	2.40 2.38 2.36 2.32 32 32 32 8.02 8.02 8.02 7.83 3.81 3.53 3.39 3.81 2.64 2.54 2.64 2.64 2.64 2.64 2.47 2.45 2.219 2.219	2.00 1.98 1.96 1.92 1.92 1.92 1.92 1.92 1.92 1.92 1.92	2.02 1.99 1.97 1.95 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.34 1.39 1.36 1.34 1.34 1.31 134254459 5.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 ATP1A1 10.60 6.02 6.02 8.05 8	0.81 0.75 0.77 0.77 0.70 44680145 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 <i>SLCSA12</i> 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.34 4507033 <i>SLC532</i> 2.98 8.92 8.92 8.92 8.92 8.92 2.00 1.75 8.92 8.92 8.92 8.92 8.92 8.92 8.92 8.92	0.12 0.19 0.17 0.15 0.12 4507031 3.0.72 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	-0.19 -0.22 -0.25 -0.26 -0.30 -0.26 -0.30 -0.26 -0.30 -0.25 -0.26 -0.30 -0.25 -0.26 -0.30 -0.30 -0.44 -0.26 -0.39 -0.44 -0.26 -0.32 -0.37 -0.37 -0.37
C	Cell-Mediated Rejection	4502337 41393614 66879662 7705885 4557417 56682959 189163485 189163485 22538440 22024195 24024195 24024195 24024195 24627120 29788785 4402101 5174735 4402101 5174735 4502125 5031635 5502152 5032155 5032152 12667788 194394237 23065552 232455266 4557417	ARF1 ARF1 ARF1 VP528 CD14 FTH1 CTSA Gene CTSC CNSA CTSC CNSA LTF TUBB ANDA1 TUBEC CFL1 UPK2 CFL1 UPK3A YWHAZ WHAA UPK1A MYH9 VL1 GSTM3 PRDX14	8,15 3,03 4,42 5,65 4,65 GI No. Gene SC 4,65 3 ,25 4,65 3 ,25 4,65 3 ,21 10,92 3,56 4,22 39,10 20,54 11,57 2,27 5,22 4,65	2,81 2,78 2,75 2,74 2,70 225637552 3,07 8,02 8,02 8,02 8,02 8,02 8,02 8,02 8,02	2.57 2.54 2.53 2.49 109659836 5.LC5A10 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.40 2.38 2.36 2.32 32 32 32 30 30 3.07 2.81 2.64 2.54 2.54 2.45 2.45 2.45 2.45 2.45 2.4	2.00 1.98 1.96 1.92 186910319 5.C72A3 6.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.02 1.99 1.97 1.95 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.34 1.39 1.36 1.34 1.34 1.31 13425459 3.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8	1.22 1.19 1.17 1.15 1.12 1.16 1.17 1.15 1.12 21361181 ATP1A1 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.75 0.75 0.74 0.70 44680145 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 4507033 851C5A2 2.98 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.12 0.19 0.17 0.15 0.12 4507031 3LC5A1 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	4.1.19 4.0.22 4.0.22 4.0.25 4.0.26 5.0.20 5.1.2132 5.23 4.506079 5.2.2 5.20 6.63 5.20 6.63 5.20 6.63 5.20 6.63 5.20 6.63 6.63 6.63 6.63 6.63 6.63 6.63 6.6
C	Cell-Mediated Rejection	4502337 41393614 66879662 7705885 4557417 56682259 189163485 189163485 189163485 24857417 2558440 26024195 34455711 5174735 4502162 5031635 5902148 12667788 194394237 194394237 194394237 194394237 194394237	ARF1 ARF1 CD14 FTH1 CTSA Vs. TI Gene CTSC CNFN RAB27A LTB TUBB2C ACP1 UPK2 ARAD1 UPK2 RH0A UPK4 CFL1 UPKA RH0A UPK4 CFL1 UPKA SRN GSTM3 GSTM3 GSTM3 GSTM3 CD14 CE2 R	8.15 3.03 4.42 5.65 4.65 GI NO. Gene I SC 22.84 3.56 8.54 3.51 16.17 2.054 3.51 16.17 2.054 3.51 16.17 2.054 3.010 2.06 2.06 2.06 4.65 4.45 5.27 7.77 5.75 5.75 2.177 2.033 2.06 2.06 4.65	2.81 2.78 2.75 2.74 2.70 2256037552 3.07 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 100859836 SLC5A10 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.40 2.38 2.36 2.32 32 32 32 8.02 8.02 8.02 7.83 3.81 3.53 3.39 3.18 3.07 2.99 2.81 2.64 2.54 2.64 2.54 2.64 2.54 2.64 2.54 2.24 2.24 2.24 2.21 2.32 3.39 2.81 2.25 2.22 2.32 3.39 2.81 2.64 2.64 2.64 2.64 2.64 2.64 2.64 2.64	2.00 1.98 1.96 1.92 186910319 <i>SLC12A</i> 3 6.06 6.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8	2.02 1.99 1.97 1.95 1.91 4502277 ATP161 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.32 1.36 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.425 1.32 1.32 1.32 1.32 1.32 1.32 1.32 1.32 1.32 1.32 1.32 1.32 1.32 1.33 1.34 1.425 1.425 1.34 1.425 1.34 1.425 1.34 1.425 1.425 1.34 1.425 1.54 1.45 1.54 1.45 1.54 1.45 1.54 1.66 1.33 1.33 1.33 1.35 1.35 1.35 1.35 1.35 1.35 1.40 1.40 1.33 1.35 1.08 1.03	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 ATP141 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.75 0.75 0.74 0.70 44680145 5.22 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 6.48 2.46 2.18 2.46 2.18 1.29 1.20 1.12 1.12 1.104 1.64 1.46 1.29 1.20 1.12 1.104 1.64 1.64 1.64 1.64 1.64 1.64 1.64 1.6	0.44 0.42 0.39 0.37 0.34 4507033 5LC342 2.96 8.92 8.92 8.92 8.92 8.92 8.92 8.92 8.92	0.12 0.19 0.17 0.15 0.12 4507031 3 <i>LC5A1</i> 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	4.1.19 4.0.22 4.0.22 4.0.26 4.30 5.1.01 5.1.
С	Cell-Mediated Rejection	4502337 41333614 66879662 7705885 4557417 56682259 189163485 189163485 250224195 34485711 54607120 29788785 4502101 5174735 4502215 5031635 5002182 5002180 5002180 5002180 5002180 5002180 5002180 5002180 5002180 50	ARF1 ARF1 ARF1 ARF1 ARF1 CD14 FTH1 CT5A VS. TI Gene CTSA CNFN RAB27A LTF TUBB2 ANXA1 ANXA1 UPK2 CFL1 UPK2 CFL1 UPK3 UPK1A WH1A2 RH0A WP(1) GSTM3 PR0X1 CD14 EZT ACTM ACTM	8,15 3,03 4,42 5,65 4,65 GI No. Gene SC 4,65 3,56 4,65 3,21 1,22,42 3,56 3,21 1,22,42 3,21 1,22,42 3,210 1,22,42 3,210 2,05 4,15 5,77 5,912 2,07 4,02 2,06 4,05 5,77 5,77 5,12 2,12 4,12 2,12 4,12 5,12 5,12 5,12 5,12 5,12 5,12 5,12 5	2.88 2.75 2.74 2.70 2256037552 3.002 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 109659836 <i>SLC5A10</i> 10.27 8.62 8.62 8.62 8.62 8.62 8.62 8.62 8.62	2.40 2.38 2.36 2.32 32 32 32 30 30 30 3.07 2.81 2.64 2.51 2.51 3.30 3.07 2.81 2.64 2.54 2.45 2.45 2.39 2.22 2.19 2.13 2.11 2.10	2.00 1.98 1.96 1.92 186910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02 8.02 8.02 7.77 3.75 3.47 3.33 3.12 3.01 2.93 2.75 2.58 2.49 2.41 2.40 2.33 2.17 2.13 2.11 2.11 2.11 2.11 2.11 2.11 2.11	2.02 1.99 1.97 1.95 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.30 1.36 1.34 1.34 1.34 1.34 1.34 1.34 1.34 23.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.12 1.16 1.17 1.15 1.12 21361181 ATP1A1 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.75 0.75 0.74 0.70 44680145 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 5LC5A12 11.11 8.02 8.02 6.43 2.46 2.46 2.46 2.46 2.46 1.20 4.172 1.64 1.20 1.12 1.10 1.04 0.84 0.84 0.84 0.84 0.65 0.75	0.44 0.42 0.39 0.37 0.34 4507033 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.12 0.19 0.17 0.15 0.12 4507031 5.05 0.12 0.12 0.12 0.05 1.05 1.35 1.35 1.35 1.35 1.35 1.35 1.35 0.61 0.61 0.61 0.61 0.61 0.61 0.61 0.61	4.1.9 4.1.9 4.2.9 4.506979 4.506979 2.3.4 4.506979 2.5069 2.50
C	Cell-Mediated Rejection	4502337 41333614 66879662 7705885 4557417 56862295 189163485 189163485 189163485 189163485 189163485 28024195 34485711 54607120 29788785 4502155 5031635 5502152 29788785 10435549 5502148 156972185 19439531 19639542 12667788 194394237 189083772 23065552 23455266 4557417 161702986 12025678	ARFI ARFI CD14 FTH1 CTSA V9528 CD14 FTH1 CTSA V9528 CD14 FTH1 CTSA CONFN RAB27A LTF TUBB ANXA1 UPK2 CFL1 CFL1 CFL1 CFL1 CFL1 CFL1 CFL1 CFL1	8,15 3,03 4,42 5,65 4,65 Gi No. Gi N	2.81 2.75 2.74 2.70 2.26637552 3.12 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	2.57 2.54 2.53 2.49 100855836 SLC5A10 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.40 2.38 2.36 2.32 32 5.32 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	2.00 1.98 1.96 1.92 185910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.02 1.99 1.97 1.97 1.97 1.97 1.97 1.91 4502277 ATP181 3.23 8.02 8.02 8.02 8.02 7.61 3.58 3.31 3.17 2.96 2.87 2.42 2.32 2.47 2.42 2.32 2.47 2.42 2.42 2.42 2.42 2.42 2.42 2.4	1.34 1.36 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.42 8.03 1.84 1.84 1.84 1.84 1.84 1.84 1.84 1.84 1.84 1.84 1.84 1.84 1.83 1.84 1.85 1.84 1.84 1.85 1.84 1.85 1.84 1.85 1.84 1.85 1.88 1.09 1.83 1.84 1.66 1.03 1.03 1.03 0.03 0.97 0.97 0.98 0.97 0.98 0.97 0.98 0.97 0.98 0.97 0.98 0.97 0.98 0.97 0.98 0.97 0.98 0.97 0.98 0.97 0.98 0.97 0.98 0.97 0.98 0.97 0.98 0.98 0.97 0.98 0.81	1.22 1.19 1.17 1.15 1.12 r Injury 21361181 ATP141 10.60 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.75 0.75 0.74 0.70 44680145 5.223A7 5.21 5.21 5.22 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8	0.54 0.51 0.49 0.47 0.44 157671931 SLC5A12 11.11 8.02 8.02 8.02 6.48 2.46 2.48 2.48 2.48 2.48 1.23 1.72 1.64 1.48 1.29 1.20 1.12 1.10 1.04 0.67 0.67 0.64 0.67 0.64 0.67 0.64 0.67 0.64 0.67 0.64 0.67 0.64 0.67 0.67 0.64 0.67 0.67 0.67 0.64 0.67 0.67 0.67 0.67 0.64 0.67 0.64 0.67 0.67 0.64 0.64 0.64 0.64 0.64 0.64 0.64 0.64	0.44 0.42 0.39 0.37 0.34 4507033 58,C5A2 2.98 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.12 0.19 0.17 0.17 0.12 4507031 5LC5A1 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	4.1.9 4.1.92 4.506770 4.506770 2.34 4.50 2.34 4.50 2.34 4.50 2.34 4.50 2.34 4.50 2.34 4.50 2.34 4.50 2.50 2.50 4.50 2.50 2.50 4.50 2.50 4.50 2.50 4.50 2.50 4.50 2.50 4
C	Cell-Mediated Rejection	490337 4903614 4935414 4935414 4957417 896259 189163485 4957417 490215 490216 4	AGEOU VPS289 CD14 FTH1 CTSA Vs. TI Gene CTSC CTSC CTSC CTSC CTSC CTSC CTSC CTS	8,15 3,03 4,42 5,65 4,65 6 19,92 22,84 19,92 22,84 19,92 22,84 19,92 22,84 19,92 22,84 19,92 22,84 19,92 22,84 19,92 22,84 19,92 22,84 19,92 22,84 19,92 22,84 19,92 22,84 10,92 20,94 20,92 20,	2.88 2.78 2.75 2.74 2.70 225637652 SLC13A2 11.53 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.54 2.53 2.49 100659836 <i>SLC5A10</i> 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.40 2.38 2.36 2.32 8.02 8.02 8.02 7.83 3.60 2.81 3.53 3.18 3.07 2.99 2.81 2.64 2.54 2.64 2.54 2.47 2.45 2.47 2.45 2.219 2.219 2.11 2.11 2.11 2.11 2.11 2.	2.00 1.98 1.96 1.92 186910319 <i>SLC12A3</i> 6.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.02 1.99 1.97 1.95 1.91 4502277 ATP181 3.23 8.02 6.02 6.02 6.02 7.61 8.02 6.02 7.61 3.31 7.296 2.85 3.31 7.296 2.85 2.42 2.25 2.23 3.17 2.96 1.95 1.95 1.95 1.95 1.95 1.88 1.74 5.88 1.74	1.32 1.36 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.42 1.32 1.02 0.03 1.93 1.84 1.49 1.49 1.49 1.49 1.49 1.49 1.04 0.03 0.08 0.09 0.00 0.09	1.22 1.19 1.17 1.15 1.12 21361181 1.12 21361181 1.12 21361181 1.060 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.81 0.75 0.75 0.74 0.70 44680145 <i>SLC23A1</i> 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5412 11.11 SLC5412 1.02 6.02 6.42 6.02 6.42 1.23 1.64 1.29 1.20 1.20 1.22 1.64 1.29 1.20 1.20 1.20 1.20 1.20 1.20 1.20 1.20	0.44 0.42 0.30 0.37 0.34 45070033 5LC5A2 2.88 8.02 8.02 8.02 8.02 8.02 8.02 8.0	0.19 0.19 0.17 0.15 0.12 4507031 <i>SLC5A</i> 1 2.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	4.1.9 4.1.9 4.2.9 4.2.6 4.3.0 4.5.0677 2.3.4 4.5.0677 2.3.4 4.5.0677 8.02 8.03 8.02 8.03 8.04 8.02 8.03 8.03 8.04 8.02 8.03 8.04 8.02 8.03 8.044 8.04 8.04 8.044
2	Cell-Mediated Rejection	490337 41393614 41393614 41393614 41557417 80687682 41557417 415927 4159	Ансси VP5209 CD14 FTH1 CTSA CD14 FTH1 CTSA CD14 FTH1 CTSA CD14 FTH1 CTSA CD14 FTH1 CTSA CD14 FTH1 CTSA CD14 FTH1 CTSA CD14 CD14 CTSA CD14 CD	8,15 3,03 4,42 5,65 4,65 Gi No. Gi N	2.88 2.78 2.75 2.74 2.70 225637552 3.07 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.57 2.57 2.54 2.53 2.49 109659836 5.125A10 10.27 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.40 2.38 2.36 2.32 35 35 3.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8	2.00 1.96 1.96 1.96 1.92 186910319 SLC12A3 6.06 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.02 2.03 1.39 1.39 1.39 1.37 1.37 1.37 1.37 1.37 1.37 1.37 1.33 8.02 8.02 8.02 8.02 7.61 3.37 7.61 3.35 8.02 7.61 3.35 8.02 7.61 3.35 8.02 7.61 3.35 8.02 7.61 1.35 1.35 1.35 1.35 1.35 1.35 1.35 1.3	1.30 1.30 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34	1.22 1.19 1.17 1.15 1.12 21361181 ATP1A1 10.60 6.02 6.02 6.02 6.02 6.02 2.24 2.36 2.24 2.36 2.24 2.36 2.24 1.47 1.37 1.30 1.28 1.22 1.64 1.47 1.37 1.30 1.28 1.28 1.28 1.28 1.28 1.28 1.28 1.28	0.8 0.75 0.75 0.74 0.70 44680145 5.21 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.64 0.67 0.47 0.44 157671931 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.39 0.37 0.34 4507033 5LC542 2.99 5.02 6.02 6.02 6.02 6.02 7.52 6.02 7.52 1.37 1.26 1.18 1.37 1.26 1.18 1.37 1.26 1.18 1.37 1.26 1.18 1.37 1.26 1.18 1.37 1.26 1.33 1.35 1.35 1.35 1.35 1.35 1.35 1.35	0.22 0.19 0.17 0.15 0.15 0.15 0.15 0.15 0.15 0.15 0.15	4.1.9 4.1.9 4.506770 4.506770 2.34 4.50 2.34 4.50 2.34 4.50 2.34 4.50 2.34 4.50 2.50 4.
	Cell-Mediated Rejection	4002377 41303614 40873902 41530414 40873902 41537417 8080216 4153747 405720 41557377 416622211	AREFI AREFI VP3289 CD14 FTH1 CTTSA CD14 FTH1 CTTSA CTSC CTSC CTSC CTSC CTSC CTSC CTS	8.15 3.03 4.42 5.65 4.65 8.54 19.92 22.84 19.92 22.84 19.92 23.85 8.54 13.57 2.77 5.9.12 30.33 9.12 30.30 2.06 4.65 4.65 5.22 14.07 2.28 4.65 5.22 14.07 2.37 3.73 3.73 3.73	2.87 2.77 2.75 2.74 2.70 2.25637552 3.07 3.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8	2,57 2,57 2,54 2,53 2,49 100859836 5LC5A10 10,27 8,02 8,02 8,02 8,02 8,02 8,02 8,02 8,02	2.40 2.33 2.32 2.32 107/486278 2.52 2.52 2.52 2.52 2.52 2.52 2.52 2.5	2.00 1.98 1.96 1.96 1.96 1.96 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.02 2.03 2.05 1.39 1.39 1.39 1.37 1.37 1.37 1.37 1.37 1.37 1.37 1.37	1.36 1.36 1.34 1.34 1.34 1.34 1.34 1.34254459 5.LC12A1 2.3.26 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	1.22 1.19 1.17 1.15 1.15 1.15 1.15 1.15 1.15 1.15	0.88 0.75 0.75 0.74 0.70 44680145 5.21 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.54 0.51 0.49 0.47 0.44 157671931 SLC5472 11.11 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	0.44 0.42 0.42 0.37 0.37 0.34 8 8 0.37 0.34 8 0.37 0.34 8 0.2 0.38 0.38 0.38 0.32 0.35 0.35 0.35 0.35 0.35 0.35 0.35 0.35	0.22 0.19 0.17 0.15 0.15 0.15 0.15 0.15 0.15 0.15 0.15	4.1.9 4.1.9 4.506079 5.L.01342 2.34 5.L.01342 2.34 5.2.9 5.2
0	Cell-Mediated Rejection	400337 41393614 41393614 41393614 41393614 41393614 41393614 80627088 806289 806218 4052701 40507180718 4000718 40070718 40070718 40070718 400	новен чреза че	8.15 3.03 4.65 5.65 4.65 5.05 7.22,64 18.01 18.01 18.01 18.01 22,64 18.01 18.01 22,64 18.01 18.01 20.04 2.05 2.05 2.05 2.05 2.05 2.05 2.05 2.05	241 275 275 274 275 274 270 225637552 340752 340752 802 802 802 802 802 802 802 802 802 80	2.57 2.54 2.54 2.53 2.49 109059836 8.025 8.025 7.83 8.02 8.02 8.02 8.02 8.02 8.02 8.02 8.02	2.40 2.33 2.32 2.32 107/462778 2.32 2.32 8.52 8.52 8.62 8.62 8.62 8.62 8.62 8.62 8.62 8.6	200 1.98 1.32 1.92 1.92 1.92 1.92 1.92 1.92 1.92 1.9	2.02 2.03 1.39 1.39 1.39 1.39 1.37 1.37 1.37 1.37 1.37 1.37 1.37 2.65 2.65 2.65 2.65 2.65 2.65 2.65 2.65	1.30 1.30 1.30 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34	1.22 1.19 1.17 1.15 1.15 1.15 1.15 1.15 1.15 1.15	0.03 0.78 0.78 0.77 44680145 5.21 5.21 5.22 5.21 5.22 5.21 5.22 5.21 5.22 5.21 5.22 5.24 5.22 5.24 5.24 5.24 5.24 5.24	0.54 0.51 0.61 0.64 0.64 0.64 0.64 0.65 0.65 0.65 0.65 0.65 0.65 0.65 0.65	0.44 0.42 0.30 0.47 0.37 0.34 4507033 51.0542 2.86 0.22 0.22 0.22 0.22 0.22 0.22 0.22 0.2	0.2 0.19 0.19 0.17 0.15 0.15 0.15 0.15 0.15 0.15 0.15 0.15	4.1.19 4.0.22 0.25 0.22 0.26 0.20 0.26 0.20 0.20 0.20 0.20
C	Cell-Mediated Rejection	400237 41303014 4037070885 4557417 700885 4557417 455745 455745 450710 45070000000000000000000000000000000000	Анбегі ЧРБ29	8.15 3.03 4.42 5.65 4.65 GI No. Gi No. Gi No. Gi No. Gi No. Gi No. Gi No. 7 22.64 3.02 3.56 4.52 2.77 5.75 5.75 2.00 4.65 4.15 2.20 4.65 4.65 4.65 3.20 5.20 5.20 5.20 5.20 5.20 5.20 5.20 5	238 278 278 278 278 275 275 275 275 275 275 8 275 8 275 3 28 3 28 3 28 272 327 328 327 328 327 327 328 327 327 327 327 327 327 327 327 327 327	2.557 2.548 2.53 2.49 100856936 SLCSA107 8.002 8.000 8.002 8	2.40 2.33 2.35 2.32 107/466278 2.532 8.05 8.05 8.05 8.05 8.05 8.05 8.05 8.05	2000 1.98 1.98 1.92 186910319 1822 186910319 1.92 1.92 1.92 1.92 1.92 1.92 1.92 1.	2.02 2.03 1.39 1.39 1.35 1.35 1.35 1.35 1.35 1.35 1.35 3.60 2.65 2.65 2.65 2.65 2.65 2.65 2.65 2.65	1.30 1.30 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34	1.22 1.19 1.17 1.15 1.15 1.15 1.15 1.15 1.15 1.15	0.03 0.78 0.78 0.78 0.78 0.78 0.78 0.78 0.74 0.74 0.74 0.74 0.74 0.74 0.74 0.74	0.34 0.35 0.47 0.47 0.44 157671031 157671031 157671031 157671031 11.11 11.11 1.20 1.20 1.20 1.20 1.20 1	0.44 0.42 0.30 0.37 0.37 0.34 4507033 51C542 2.86 0.22 0.22 0.22 0.22 0.22 0.22 0.22 0.2	0.22 0.19 0.19 0.15 0.15 0.15 0.15 0.15 0.15 0.15 0.15	4.1.19 4.1.20 4.200979 4.500979 5.LC13A2 2.34 8.02 8.03 8.03 8.03 8.03 8.03 8.04 8.04 8.05 8.
C	Cell-Mediated Rejection	400237 41390314 403747 41390314 4057417 506882 5062299 189105485 4057417 510755 30465714 510755 30465714 510755 30465714 5107555 5002152 5002155 5002152 5002155 50020000000000	новен VPS28 V	8.15 3.03 4.65 5.65 4.65 5.22,64 118,07 18,07 19	2.83 2.75 2.75 2.74 2.74 2.74 2.74 2.74 2.74 2.74 2.74	2.57 2.54 2.54 3.25 3.249 100659936 5.125A107 7.825 2.855 2.8555 2.855 2.855 2.855 2.855 2.855 2.855 2.8555 2.855 2.855	2.40 2.38 2.38 2.38 2.38 2.38 2.32 2.32 2.32	2000 199 199 199 199 199 199 199 199 199	2.02 2.03 2.05 2.05 2.05 2.05 2.05 2.05 2.05 2.05	1.30 1.36 1.36 1.37 1.34 1.31 1.34 1.34 1.34 1.34 1.34 1.34	1.22 1.19 1.17 1.15 1.15 1.12 2.1361181 4.77/41 2.1361181 4.77/41 2.1361181 4.77/41 4.77/41 4.77/41 4.77/41 4.77/41 1.60 6.62 0.64 0.64	0.03 0.78 0.78 0.78 0.74 0.74 0.74 0.74 0.74 0.74 0.74 0.74	0.54 0.51 0.61 0.61 0.67 0.64 0.67 0.67 0.67 0.67 0.67 0.67 0.67 0.67	0.44 0.42 0.42 0.37 0.37 0.34 4507033 51.C542 2.86 0.22 0.22 0.22 0.22 0.22 0.22 0.22 0.2	0.22 0.19 0.19 0.17 0.15 0.15 0.15 0.15 0.15 0.15 0.15 0.15	4.1.19 4.1.22 4.22 4.2.22 4.2.25 4.2.244 4.2.244 4.2.244 4.2.244 4.2.244 4.2.2444 4.2.244444444
С	Cell-Mediated Rejection	400237 41303014 4037070885 4557417 2058652299 189163485 455747 2802165 450716 450715 4	ABFF1 YP529 YP529 YP520 GENE CTSA TT Gene CTSC CRLT TUBB CPLY VULT VULT VULT VERK2 CFLT VULT VULT VULT VULT VULT VULT VULT GSTM3	8.15 3.03 4.42 5.65 4.65 7.22,64 19,92 3.56 8.54 3.21 19,92 3.56 8.54 3.21 19,92 3.20 5.77 5.75 2.00 4.277 5.75 2.00 4.65 4.15 2.20,64 4.52 2.06 4.52 2.06 4.52 3.03 3.20 6.277 5.75 5.20 5.20 5.20 5.20 5.20 5.20 5.20 5.2	235 278 278 278 277 277 270 225637652 802 802 802 802 802 802 802 802 802 80		2.40 2.33 2.35 2.35 2.35 2.35 2.35 2.35 8.05 8.05 8.05 8.05 8.05 8.05 8.05 8.0	2000 1.98 1.99 1.99 1.92 1.92 1.92 1.92 1.92 1.92	2.02 2.03 1.39 1.39 1.37 1.35 1.31 4502277 4.19 4.502277 4.19 4.502277 4.19 4.502 4.	1.30 1.30 1.34 1.34 1.34 1.34 1.34 1.34 1.34 1.34	1.22 1.19 1.17 1.15 1.15 1.15 1.15 1.15 2.1361181 4.7744 4.7744 8.62 8.62 8.62 8.63 8.63 8.63 8.64 8.64 8.64 1.00 1.12 1.00 1.128 1.120 1.	0.03 0.78 0.78 0.78 0.74 0.74 0.74 0.74 0.74 0.74 0.74 0.74	0.34 0.35 0.47 0.44 157671031 157671031 11.11 11.11 1.11 1.20 1.22 0.40 1.22 0.40 1.22 1.44 1.20 1.12 1.20 1.12 1.20 1.12 1.20 1.12 0.46 0.46 0.46 0.46	0.44 0.42 0.39 0.37 0.34 4507033 SLC542 2.86 0.22 0.22 0.22 0.22 0.22 0.22 0.22 0.2	0.22 0.19 0.19 0.17 0.15 0.15 0.15 0.15 0.15 0.15 0.15 0.15	4.1.0 4.

Figure 1. Heat map representation of discrimination factors for candidate protein biomarker pairs in discrimination of (A) All Rejection versus Tubular Injury; (B) Antibody-Mediated Rejection versus Tubular Injury; and (C) Cell-Mediated Rejection versus Tubular Injury Proteins for All Rejection were selected from the "immune response" list (supporting Information Table S3) and common proteins enriched in both Antibody-Mediated Rejection and Cell-Mediated Rejection. Proteins for Antibody-Mediated Rejection were selected from the "acute inflammatory response" list (Table 4), the "protein localization" list (supporting Information Table S5), and the "response to unfolded proteina list (supporting Information Table S6). Proteins for Cell-Mediated Rejection were selected from the "epithelial cell differentiation" list (Table 3) and the "actin filament based process" list (supporting

Information Table S4). Proteins for *Tubular Injury* were selected from the "sodium ion transport" list (Table 2). Discrimination factors (colored boxes) are $log_2(R_X/R_{TI})$, where R_X is the median-normalized spectral count ratio of the two proteins for indicated Rejection group and R_{TI} is the ratio of the two proteins in *Tubular Injury*. Colors stratify discrimination factors from high (red) to low (green). The spectral counts shown for specific proteins represent the median-normalized spectral count values (|SC|) obtained in tubular injury (across top) or in appropriate rejection state (left); values for 'all rejection' represent average of cell-mediated and antibody-mediated values. Proteins are listed by both the GI accession number and the official gene symbol. Full annotation of the candidate biomarkers listed can be obtained using the GI accession number at the *Entrez Protein* online site (http://www.ncbi.nlm.nih.gov/protein).

											OCII-MIC		ejection							
			GI No.	26024195	4506773	4502101	5902148	4504165	5803215	7706683	5031635	4826898	23065552	10835049	4757952	161702986	4885049	55749523	89903012	5624352
			Gene	CNFN	S100A9	ANXA1	UPK1A	GSN	UPK2	RHCG	CFL1	PFN1	GSTM3	RHOA	CDC42	EZR	ACTC1	SDCBP	CDC42	SDCBP
	GI No.	Gene	SC	19.92	16.78	16.17	30.33	12.78	20.54	5.06	13.57	12.71	4.65	9.12	4.68	14.07	26.13	8.62	9.94	4.08
	166235903	C1QC	10.04	8.16	7.95	6.63	5.95	5.30	5.12	5.02	4.70	4.62	4.59	4.56	4.38	4.33	4.01	3.95	3.70	3.06
	166197660	C8G	9.39	8.16	7.95	6.63	5.95	5.30	5.12	5.02	4.70	4.62	4.59	4.56	4.38	4.33	4.01	3.95	3.70	3.06
	19923483	RAB14	5.96	8.16	5.51	4.19	3.51	2.87	2.68	2.58	2.26	2.18	2.16	2.13	1.94	1.89	1.57	1.51	1.26	0.63
	34147513	RAB7A	11.14	8.16	5.20	3.87	3.20	2.55	2.36	2.27	1.95	1.87	1.84	1.81	1.63	1.58	1.25	1.20	0.95	0.31
	50234889	RAB43	4.20	8.16	5.10	3.77	3.10	2.45	2.26	2.17	1.85	1.77	1.74	1.71	1.53	1.48	1.15	1.10	0.85	0.21
	7706563	RAB8B	5.28	8.16	5.01	3.69	3.01	2.37	2.18	2.09	1.77	1.68	1.66	1.63	1.44	1.40	1.07	1.01	0.77	0.13
	56243522	SDCBP	5.97	8.16	4.89	3.56	2.89	2.24	2.05	1.96	1.64	1.55	1.53	1.50	1.32	1.27	0.94	0.89	0.64	0.00
	13569962	RAB1B	6.07	8.16	4.89	3.56	2.89	2.24	2.05	1.96	1.64	1.55	1.53	1.50	1.32	1.27	0.94	0.89	0.64	0.00
	16933567	RAB8A	6.60	8.16	4.83	3.51	2.83	2.19	2.00	1.91	1.58	1.50	1.48	1.45	1.26	1.22	0.89	0.83	0.58	-0.05
	5803135	RAB35	6.00	8.16	4.73	3.41	2.73	2.09	1.90	1.81	1.49	1.40	1.38	1.35	1.16	1.12	0.79	0.73	0.49	-0.15
	4759000	RAB3D	6.91	8.16	4.73	3.41	2.73	2.09	1.90	1.81	1.49	1.40	1.38	1.35	1.16	1.12	0.79	0.73	0.49	-0.15
-	256222019	RAB10	5.37	8.16	4.70	3.37	2.70	2.05	1.86	1.77	1.45	1.36	1.34	1.31	1.13	1.08	0.75	0.70	0.45	-0.19
3	21464101	YWHAG	4.35	8.16	4.66	3.34	2.66	2.02	1.83	1.74	1.42	1.33	1.31	1.28	1.09	1.05	0.72	0.66	0.42	-0.22
נ	4758988	RAB1A	6.10	8.16	4.60	3.27	2.60	1.95	1.76	1.67	1.35	1.27	1.24	1.21	1.03	0.98	0.65	0.60	0.35	-0.29
5	21264361	MASP2	54.86	8.16	4.55	3.23	2.55	1.90	1.71	1.62	1.30	1.22	1.19	1.16	0.98	0.93	0.61	0.55	0.30	-0.34
3	189163485	CTSA	4.65	8.16	4.49	3.17	2.49	1.84	1.66	1.56	1.24	1.16	1.13	1.10	0.92	0.87	0.55	0.49	0.24	-0.40
5	19923750	RAB3B	7.31	8.16	4.35	3.03	2.35	1.70	1.51	1.42	1.10	1.02	0.99	0.96	0.78	0.73	0.41	0.35	0.10	-0.54
n	24234686	HSPA8	8.13	8.16	4.33	3.01	2.33	1.68	1.50	1.40	1.08	1.00	0.97	0.94	0.76	0.71	0.39	0.33	0.08	-0.56
D.	194248072	HSPA1A	4.18	8.16	4.30	2.98	2.30	1.66	1.47	1.37	1.05	0.97	0.95	0.91	0.73	0.68	0.36	0.30	0.05	-0.58
5	89903012	CDC42	9.34	8.16	4.25	2.93	2.25	1.60	1.42	1.32	1.00	0.92	0.89	0.86	0.68	0.63	0.31	0.25	0.00	-0.64
ŝ.	41393614	RAB5C	10.13	8.16	4.18	2.86	2.18	1.53	1.34	1.25	0.93	0.85	0.82	0.79	0.61	0.56	0.24	0.18	-0.07	-0.71
ž	208973244	YWHAZ	5.40	8.16	4.16	2.84	2.16	1.52	1.33	1.23	0.91	0.83	0.81	0.78	0.59	0.54	0.22	0.16	-0.09	-0.72
Ĭ	126012573	LRP2	9.42	8.16	4.15	2.83	2.15	1.50	1.32	1.22	0.90	0.82	0.79	0.76	0.58	0.53	0.21	0.15	-0.10	-0.74
L	4557871	TF	97.27	8.16	4.10	2.78	2.10	1.45	1.26	1.17	0.85	0.77	0.74	0.71	0.53	0.48	0.16	0.10	-0.15	-0.79
	55749523	SDCBP	6.82	8.16	4.00	2.68	2.00	1.36	1.17	1.07	0.75	0.67	0.65	0.61	0.43	0.38	0.06	0.00	-0.25	-0.89
	66879662	ARF1	8.15	8.16	3.97	2.65	1.97	1.32	1.13	1.04	0.72	0.64	0.61	0.58	0.40	0.35	0.03	-0.03	-0.28	-0.92
	22027538	PDCD6IP	8.92	8.16	3.80	2.48	1.80	1.16	0.97	0.87	0.55	0.47	0.45	0.42	0.23	0.18	-0.14	-0.20	-0.45	-1.08
	5803225	YWHAE	5.04	8.16	3.76	2.44	1.76	1.12	0.93	0.84	0.51	0.43	0.41	0.38	0.19	0.15	-0.18	-0.24	-0.49	-1.12
	161702986	EZR	8.54	8.16	3.62	2.29	1.62	0.97	0.78	0.69	0.37	0.29	0.26	0.23	0.05	0.00	-0.33	-0.38	-0.63	-1.27
	262050538	ITIH4	9.66	8.16	3.42	2.10	1.42	0.77	0.59	0.49	0.17	0.09	0.06	0.03	-0.15	-0.20	-0.52	-0.58	-0.83	-1.47
	14251209	CLIC1	6.88	8.16	3.40	2.08	1.40	0.76	0.57	0.47	0.15	0.07	0.05	0.01	-0.17	-0.22	-0.54	-0.60	-0.85	-1.49
	4502205	ARF4	5.03	8.16	3.34	2.02	1.34	0.70	0.51	0.42	0.09	0.01	-0.01	-0.04	-0.23	-0.28	-0.60	-0.66	-0.91	-1.54
	4757944	CD81	6.37	8.16	3.08	1.76	1.08	0.43	0.25	0.15	-0.17	-0.25	-0.28	-0.31	-0.49	-0.54	-0.86	-0.92	-1.17	-1.81
	126091152	CUBN	10.37	8.16	2.76	1.44	0.76	0.12	-0.07	-0.16	-0.48	-0.57	-0.59	-0.62	-0.81	-0.85	-1.18	-1.24	-1.48	-2.12
	73858570	SERPING	1 4.93	8.16	2.76	1.43	0.76	0.11	-0.08	-0.17	-0.49	-0.57	-0.60	-0.63	-0.81	-0.86	-1.19	-1.24	-1.49	-2.13

Cell-Mediated Rejection

Figure 2. Heat map representation of discrimination factors for candidate protein biomarker pairs in discrimination of *Antibody-Mediated Rejection* versus *Cell-Mediated Rejection*

Proteins for *Antibody-Mediated Rejection* were selected from the "acute inflammatory response" list (Table 4), the "protein localization" list (supporting Information Table S5), and the "response to unfolded protein" list (supporting Information Table S6). Proteins for *Cell-Mediated Rejection* were selected from the "epithelial cell differentiation" list (Table 3) and the "actin filament based process" list (supporting Information Table S4). Discrimination factors (colored boxes) are log₂(R_{AMR}/R_{CMR}), where R_{AMR} is the mediannormalized spectral count ratio of the two proteins for the *Antibody-Mediated Rejection* group. Colors stratify discrimination factors from high (yellow) to low (blue). The spectral counts shown for specific proteins represent the mediannormalized spectral count values (|SC|) obtained in the appropriate rejection states. Proteins are listed by both the GI accession number and the official gene symbol. Full annotation of the candidate biomarkers listed can be obtained using the GI accession number at the *Entrez Protein* online site (http://www.ncbi.nlm.nih.gov/protein).

Gene Ontology Biological Process terms over-represented in lists of exosomal proteins associated with different biopsy findings. Categories unique to a given group are shown in **Bold**.

	<u>No.</u> Proteins	p-value	<u>FDR</u> (%)
A. <u>Tubular Injury</u>			
GO:0007264 Small GTPase mediated signal transduction	64	0.0036	6.2
G0:0006814 Sodium ion transport	26	0.0050	8.6
GO:0010033 Response to organic substance	73	0.0073	12.4
B. Cell-Mediated Rejection			
GO:0030029 Actin filament-based process	47	0.0005	0.8
GO:0030855 Epithelial cell differentiation	21	0.0018	3.2
GO:0007264 Small GTPase mediated signal transduction	62	0.0021	3.7
GO:0030036 Actin cytoskeleton organization	41	0.0026	4.5
GO:0007010 Cytoskeleton organization	63	0.0031	5.5
GO:0006955 Immune response	49	0.0118	19.1
GO:0043603 Cellular amide metabolic process	16	0.0118	19.2
C. Antibody-Mediated Rejection			
GO:0007264 Small GTPase mediated signal transduction	64	< 0.0000	0.0
GO:0015031 Protein transport	97	< 0.0000	0.1
GO:0045184 Establishment of protein localization	97	0.0001	0.1
GO:0008104 Protein localization	103	0.0003	0.5
GO:0010033 Response to organic substance	64	0.0018	3.1
GO:0007242 Intracellular signaling cascade	105	0.0034	6.0
GO:0044057 Regulation of system process	26	0.0039	6.7
GO:0006986 Response to unfolded protein	13	0.0063	10.6
GO:0002526 Acute inflammatory response	18	0.0066	11.1
GO:0010035 Response to inorganic substance	28	0.0083	13.7
GO:0051605 Protein maturation by peptide bond cleavage	15	0.0086	14.2
GO:0006955 Immune response	44	0.0094	15.5

Protein list for Gene Ontology Biological Process "sodium ion transport" enriched in urinary exosomes from transplants with Tubular Injury compared with all transplants. Asterisks indicate proteins that were expressed with relatively high signal values in proximal tubule based on the transcriptomic databases of proximal tubule, medullary thick ascending limb, and inner medullary collecting duct [14], [15].

Protein Name	GI Accession	Gene Symbol
sodium/potassium-transporting ATPase subunit alpha-1 isoform a *	21361181	ATP1A1
sodium/potassium-transporting ATPase subunit beta-1 *	4502277	ATP1B1
sodium/potassium-transporting ATPase subunit gamma isoform 2 *	11125764	FXYD2
solute carrier family 12 member 3 isoform 1	186910315	SLC12A3
solute carrier family 12 member 3 isoform 3	186910319	SLC12A3
solute carrier family 12 member 1 isoform A	134254459	SLC12A1
solute carrier family 12 member 2 *	4506975	SLC12A2
solute carrier family 13 member 1 *	19923838	SLC13A1
solute carrier family 13 member 2 isoform b *	4506979	SLC13A2
solute carrier family 13 member 2 isoform c *	225637552	SLC13A2
solute carrier family 13 member 3 isoform a *	31377715	SLC13A3
solute carrier family 13 member 3 isoform b *	58761541	SLC13A3
sodium-dependent phosphate transport protein 1 *	154800443	SLC17A1
sodium-dependent phosphate transport protein 4 isoform a *	148743791	SLC17A3
solute carrier family 22 member 5 *	4507005	SLC22A5
solute carrier family 22 member 4 *	24497490	SLC22A4
solute carrier family 23 member 1 isoform a *	44680145	SLC23A1
sodium-dependent phosphate transport protein 2B isoform a	110611906	SLC34A2
sodium-coupled neutral amino acid transporter 2 *	21361602	SLC38A2
electrogenic sodium bicarbonate cotransporter 1 isoform 2 *	4507025	SLC4A4
sodium-coupled monocarboxylate transporter 1 *	167466278	SLC5A8
sodium/glucose cotransporter 1 *	4507031	SLC5A1
sodium/glucose cotransporter 5 isoform 2 *	109659836	SLC5A10
sodium/myo-inositol cotransporter 2 *	17941285	SLC5A11
sodium-coupled monocarboxylate transporter 2 *	157671931	SLC5A12
sodium/glucose cotransporter 2 *	4507033	SLC5A2
sodium/glucose cotransporter 4 isoform 2 *	206597483	SLC5A9
sodium- and chloride-dependent creatine transporter 1 isoform 3 *	218563758	SLC6A8
sodium/hydrogen exchanger 3 *	194239733	SLC9A3

Protein list for Gene Ontology Biological Process *"epithelial cell differentiation"* enriched in urinary exosomes from transplants with Cell-Mediated Rejection compared with all transplants.

Protein Name	GI Accession	Gene Symbol
ammonium transporter Rh type C	7706683	RHCG
annexin A1	4502101	ANXA1
cornifelin	26024195	CNFN
desmoplakin isoform I	58530840	DSP
envoplakin	156104874	EVPL
ezrin	161702986	EZR
filaggrin	60097902	FLG
glutathione S-transferase Mu 3	23065552	GSTM3
hornerin	57864582	HRNR
periplakin	45439327	PPL
protein-glutamine gamma-glutamyltransferase K	4507475	TGM1
tumor susceptibility gene 101 protein	5454140	TSG101
uroplakin-1a	5902148	UPK1A
uroplakin-1b	49619237	UPK1B
uroplakin-2 precursor	5803215	UPK2
uroplakin-3a isoform 1	5902152	UPK3A

Protein list for Gene Ontology Biological Process *"acute inflammatory response"* enriched in urinary exosomes from transplanted kidneys with Antibody-Mediated Rejection compared with all transplants.

Protein Name	GI Accession	Gene Symbol
14-3-3 protein zeta/delta	208973244	YWHAZ
alpha-1-antichymotrypsin precursor	50659080	SERPINA3
C4b-binding protein alpha chain precursor	4502503	C4BPA
complement C1q subcomponent subunit B precursor	87298828	CIQB
complement C1q subcomponent subunit C precursor	166235903	CIQC
complement component C7 precursor	45580688	С7
complement component C8 gamma chain precursor	166197660	C8G
complement component C9 precursor	4502511	С9
complement factor B preproprotein	67782358	CFB
complement receptor type 1 isoform F precursor	86793036	CR1
complement receptor type 1 isoform S precursor	86793109	CR1
inter-alpha-trypsin inhibitor heavy chain H4 isoform 1 precursor	31542984	ITIH4
inter-alpha-trypsin inhibitor heavy chain H4 isoform 2 precursor	262050538	ITIH4
mannan-binding lectin serine protease 2 isoform 1 precursor	21264363	MASP2
mannan-binding lectin serine protease 2 isoform 2 precursor	21264361	MASP2
peroxiredoxin-2 isoform a	32189392	PRDX2
plasma protease C1 inhibitor precursor	73858570	SERPING1
PREDICTED: complement C3-like, partial	169218213	LOC100133511
serotransferrin precursor	4557871	TF
tuberin isoform 4	116256350	TSC2

KEGG pathways over-represented in lists of urinary exosomal proteins associated with different biopsy findings. Pathways unique to a histological category are indicated in Bold.

	No. Proteins	p-value	<u>FDR (%)</u>
A. <u>Tubular Injury</u>			
none			
B. Cell-Mediated Rejection			
hsa04530:Tight junction	28	0.01	16.62
hsa04144:Endocytosis	40	0.02	19.59
hsa00480:Glutathione metabolism	16	0.06	53.13
C. Antibody-Mediated Rejection			
hsa04612:Antigen processing and presentation	15	< 0.01	4.20
hsa04722:Neurotrophin signaling pathway	22	0.01	6.73
hsa05200:Pathways in cancer	25	0.01	11.71
hsa05130:Pathogenic Escherichia coli infection	20	0.01	14.04
hsa04144:Endocytosis	36	0.01	16.30

List of proteins identified in urinary exosomes of patients in Antibody-Mediated Rejection group that are present in KEGG pathway *"antigen processing and presentation"*.

Protein Name	GI Accession	Gene Symbol
calreticulin precursor	4757900	CALR
cathepsin S isoform 1 preproprotein	23110962	CTSS
HLA class I histocompatibility antigen, A-1 alpha chain precursor	24797067	HLA-A
major histocompatibility complex, class I, B precursor	17986001	HLA-B
major histocompatibility complex, class I, B precursor	17986001	HLA-B
HLA class II histocompatibility antigen, DM alpha chain precursor	18765715	HLA-DMA
HLA class II histocompatibility antigen, DM beta chain precursor	4504399	HLA-DMB
HLA class II histocompatibility antigen, DR alpha chain precursor	52426774	HLA-DRA
heat shock protein HSP 90-alpha isoform 2	154146191	HSP90AA1
heat shock protein HSP 90-alpha isoform 2	154146191	HSP90AA1
heat shock protein HSP 90-beta	20149594	HSP90AB1
heat shock 70 kDa protein 1A/1B	194248072	HSPA1A
heat shock 70 kDa protein 1A/1B	194248072	HSPA1A
heat shock 70 kDa protein 1-like	124256496	HSPA1L
heat shock-related 70 kDa protein 2	13676857	HSPA2
heat shock 70 kDa protein 6	34419635	HSPA6
heat shock 70 kDa protein 6	34419635	HSPA6
heat shock cognate 71 kDa protein isoform 2	24234686	HSPA8
proteasome activator complex subunit 1 isoform 1	5453990	PSME1