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(54) **Title**: METHODS AND COMPOSITIONS FOR DIAGNOSIS AND PROGNOSIS OF RENAL INJURY AND RENAL FAILURE

(57) **Abstract**: The present invention relates to methods and compositions for monitoring, diagnosis, prognosis, and determination of treatment regimens in subjects suffering from or suspected of having a renal injury. In particular, the invention relates to using assays that detect one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 1OB, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, Carcinoembryonic antigen-related cell adhesion molecule 5, and Cellular tumor antigen p53 as diagnostic and prognostic biomarker assays in renal injuries.

METHODS AND COMPOSITIONS FOR DIAGNOSIS AND PROGNOSIS OF RENAL INJURY AND RENAL FAILURE

[0001] The present invention claims priority to U.S. provisional patent applications 61/238,115 filed 8/28/2009, 61/238,118 filed 8/28/2009, 61/238,120 filed 8/28/2009, 61/238,121 filed 8/28/2009, 61/238,123 filed 8/28/2009, 61/238,125 filed 8/28/2009, 61/238,127 filed 8/28/2009, 61/238,129 filed 8/28/2009, 61/238,134 filed 8/28/2009, 61/243,991 filed 9/18/2009, 61/243,997 filed 9/18/2009, 61/244,002 filed 9/18/2009, 61/243,993 filed 9/18/2009, and 61/238,128 filed 8/28/2009, each of which is hereby incorporated in its entirety including all tables, figures and claims.

BACKGROUND OF THE INVENTION

[0002] The following discussion of the background of the invention is merely provided to aid the reader in understanding the invention and is not admitted to describe or constitute prior art to the present invention.

[0003] The kidney is responsible for water and solute excretion from the body. Its functions include maintenance of acid-base balance, regulation of electrolyte concentrations, control of blood volume, and regulation of blood pressure. As such, loss of kidney function through injury and/or disease results in substantial morbidity and mortality. A detailed discussion of renal injuries is provided in Harrison's Principles of Internal Medicine, 17th Ed., McGraw Hill, New York, pages 1741-1830, which are hereby incorporated by reference in their entirety. Renal disease and/or injury may be acute or chronic. Acute and chronic kidney disease are described as follows (from Current Medical Diagnosis & Treatment 2008, 47th Ed, McGraw Hill, New York, pages 785-815, which are hereby incorporated by reference in their entirety): "Acute renal failure is worsening of renal function over hours to days, resulting in the retention of nitrogenous wastes (such as urea nitrogen) and creatinine in the blood. Retention of these substances is called azotemia. Chronic renal failure (chronic kidney disease) results from an abnormal loss of renal function over months to years".

[0004] Acute renal failure (ARF, also known as acute kidney injury, or AKI) is an abrupt (typically detected within about 48 hours to 1 week)reduction in glomerular filtration. This loss of filtration capacity results in retention of nitrogenous (urea and creatinine) and non-nitrogenous waste products that are normally excreted by the kidney,

a reduction in urine output, or both. It is reported that ARF complicates about 5% of hospital admissions, 4-15% of cardiopulmonary bypass surgeries, and up to 30% of intensive care admissions. ARF may be categorized as prerenal, intrinsic renal, or postrenal in causation. Intrinsic renal disease can be further divided into glomerular, tubular, interstitial, and vascular abnormalities. Major causes of ARF are described in the following table, which is adapted from the Merck Manual, 17th ed., Chapter 222, and which is hereby incorporated by reference in their entirety:

Type	**Risk Factors**
Prerenal	
ECF volume depletion	Excessive diuresis, hemorrhage, GI losses, loss of intravascular fluid into the extravascular space (due to ascites, peritonitis, pancreatitis, or burns), loss of skin and mucus membranes, renal salt- and water-wasting states
Low cardiac output	Cardiomyopathy, MI, cardiac tamponade, pulmonary embolism, pulmonary hypertension, positive-pressure mechanical ventilation
Low systemic vascular resistance	Septic shock, liver failure, antihypertensive drugs
Increased renal vascular resistance	NSAIDs, cyclosporines, tacrolimus, hypercalcemia, anaphylaxis, anesthetics, renal artery obstruction, renal vein thrombosis, sepsis, hepatorenal syndrome
Decreased efferent arteriolar tone (leading to decreased GFR from reduced glomerular transcapillary pressure, especially in patients with bilateral renal artery stenosis)	ACE inhibitors or angiotensin II receptor blockers
Intrinsic Renal	
Acute tubular injury	Ischemia (prolonged or severe prerenal state): surgery, hemorrhage, arterial or venous obstruction; Toxins: NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, streptozotocin
Acute glomerulonephritis	ANCA-associated: Crescentic glomerulonephritis, polyarteritis nodosa, Wegener's granulomatosis; Anti-GBM glomerulonephritis: Goodpasture's syndrome; Immune-complex: Lupus glomerulonephritis, postinfectious glomerulonephritis, cryoglobulinemic glomerulonephritis
Acute tubulointerstitial nephritis	Drug reaction (eg, β-lactams, NSAIDs, sulfonamides, ciprofloxacin, thiazide diuretics, furosemide, phenytoin, allopurinol, pyelonephritis, papillary necrosis

Acute vascular nephropathy	Vasculitis, malignant hypertension, thrombotic microangiopathies, scleroderma, atheroembolism
Infiltrative diseases	Lymphoma, sarcoidosis, leukemia
Postrenal	
Tubular precipitation	Uric acid (tumor lysis), sulfonamides, triamterene, acyclovir, indinavir, methotrexate, ethylene glycol ingestion, myeloma protein, myoglobin
Ureteral obstruction	Intrinsic: Calculi, clots, sloughed renal tissue, fungus ball, edema, malignancy, congenital defects; Extrinsic: Malignancy, retroperitoneal fibrosis, ureteral trauma during surgery or high impact injury
Bladder obstruction	Mechanical: Benign prostatic hyperplasia, prostate cancer, bladder cancer, urethral strictures, phimosis, paraphimosis, urethral valves, obstructed indwelling urinary catheter; Neurogenic: Anticholinergic drugs, upper or lower motor neuron lesion

[0005] In the case of ischemic ARF, the course of the disease may be divided into four phases. During an initiation phase, which lasts hours to days, reduced perfusion of the kidney is evolving into injury. Glomerular ultrafiltration reduces, the flow of filtrate is reduced due to debris within the tubules, and back leakage of filtrate through injured epithelium occurs. Renal injury can be mediated during this phase by reperfusion of the kidney. Initiation is followed by an extension phase which is characterized by continued ischemic injury and inflammation and may involve endothelial damage and vascular congestion. During the maintenance phase, lasting from 1 to 2 weeks, renal cell injury occurs, and glomerular filtration and urine output reaches a minimum. A recovery phase can follow in which the renal epithelium is repaired and GFR gradually recovers. Despite this, the survival rate of subjects with ARF may be as low as about 60%.

[0006] Acute kidney injury caused by radiocontrast agents (also called contrast media) and other nephrotoxins such as cyclosporine, antibiotics including aminoglycosides and anticancer drugs such as cisplatin manifests over a period of days to about a week. Contrast induced nephropathy (CIN, which is AKI caused by radiocontrast agents) is thought to be caused by intrarenal vasoconstriction (leading to ischemic injury) and from the generation of reactive oxygen species that are directly toxic to renal tubular epithelial cells. CIN classically presents as an acute (onset within 24-48h) but reversible (peak 3-5 days, resolution within 1 week) rise in blood urea nitrogen and serum creatinine.

[0007] A commonly reported criteria for defining and detecting AKI is an abrupt (typically within about 2-7 days or within a period of hospitalization) elevation of serum creatinine. Although the use of serum creatinine elevation to define and detect AKI is well established, the magnitude of the serum creatinine elevation and the time over which it is measured to define AKI varies considerably among publications. Traditionally, relatively large increases in serum creatinine such as 100%, 200%, an increase of at least 100% to a value over 2 mg/dL and other definitions were used to define AKI. However, the recent trend has been towards using smaller serum creatinine rises to define AKI. The relationship between serum creatinine rise, AKI and the associated health risks are reviewed in Praught and Shlipak, *Curr Opin Nephrol Hypertens* 14:265-270, 2005 and Chertow et al, *J Am Soc Nephrol* 16: 3365-3370, 2005, which, with the references listed therein, are hereby incorporated by reference in their entirety. As described in these publications, acute worsening renal function (AKI) and increased risk of death and other detrimental outcomes are now known to be associated with very small increases in serum creatinine. These increases may be determined as a relative (percent) value or a nominal value. Relative increases in serum creatinine as small as 20% from the pre-injury value have been reported to indicate acutely worsening renal function (AKI) and increased health risk, but the more commonly reported value to define AKI and increased health risk is a relative increase of at least 25%. Nominal increases as small as 0.3 mg/dL, 0.2 mg/dL or even 0.1 mg/dL have been reported to indicate worsening renal function and increased risk of death. Various time periods for the serum creatinine to rise to these threshold values have been used to define AKI, for example, ranging from 2 days, 3 days, 7 days, or a variable period defined as the time the patient is in the hospital or intensive care unit. These studies indicate there is not a particular threshold serum creatinine rise (or time period for the rise) for worsening renal function or AKI, but rather a continuous increase in risk with increasing magnitude of serum creatinine rise.

[0008] One study (Lassnigg et all, J Am Soc Nephrol 15:1597-1605, 2004, hereby incorporated by reference in its entirety) investigated both increases and decreases in serum creatinine. Patients with a mild fall in serum creatinine of -0.1 to -0.3 mg/dL following heart surgery had the lowest mortality rate. Patients with a larger fall in serum creatinine (more than or equal to -0.4 mg/dL) or any increase in serum creatinine had a larger mortality rate. These findings caused the authors to conclude that even very subtle changes in renal function (as detected by small creatinine changes within 48 hours of

surgery) seriously effect patient's outcomes. In an effort to reach consensus on a unified classification system for using serum creatinine to define AKI in clinical trials and in clinical practice, Bellomo *et al., Crit Care*. 8(4):R204-12, 2004, which is hereby incorporated by reference in its entirety, proposes the following classifications for stratifying AKI patients:

"Risk": serum creatinine increased 1.5 fold from baseline OR urine production of <0.5 ml/kg body weight/hr for 6 hours;

"Injury": serum creatinine increased 2.0 fold from baseline OR urine production <0.5 ml/kg/hr for 12 h;

"Failure": serum creatinine increased 3.0 fold from baseline OR creatinine >355 μmol/l (with a rise of >44) or urine output below 0.3 ml/kg/hr for 24 h or anuria for at least 12 hours;

And included two clinical outcomes:

"Loss": persistent need for renal replacement therapy for more than four weeks.

"ESRD": end stage renal disease—the need for dialysis for more than 3 months.

[0009] These criteria are called the RIFLE criteria, which provide a useful clinical tool to classify renal status. As discussed in Kellum, *Crit. Care Med.* 36: S141-45, 2008 and Ricci *et al., Kidney Int.* 73, 538-546, 2008, each hereby incorporated by reference in its entirety, the RIFLE criteria provide a uniform definition of AKI which has been validated in numerous studies.

[0010] More recently, Mehta *et al., Crit. Care* 11:R31 (doi:10.1186.cc5713), 2007, hereby incorporated by reference in its entirety, proposes the following similar classifications for stratifying AKI patients, which have been modified from RIFLE:

"Stage I": increase in serum creatinine of more than or equal to 0.3 mg/dL (≥ 26.4 μmol/L) or increase to more than or equal to 150% (1.5-fold) from baseline OR urine output less than 0.5 mL/kg per hour for more than 6 hours;

"Stage II": increase in serum creatinine to more than 200% (> 2-fold) from baseline OR urine output less than 0.5 mL/kg per hour for more than 12 hours;

"Stage III": increase in serum creatinine to more than 300% (> 3-fold) from baseline OR serum creatinine ≥ 354 μmol/L accompanied by an acute increase of at least 44 μmol/L OR urine output less than 0.3 mL/kg per hour for 24 hours or anuria for 12 hours.

[0011] The CIN Consensus Working Panel (McCollough et al, Rev Cardiovasc Med. *2006;7(4):177-197,* hereby incorporated by reference in its entirety*)* uses a serum creatinine rise of 25% to define Contrast induced nephropathy (which is a type of AKI).Although various groups propose slightly different criteria for using serum creatinine to detect AKI, the consensus is that small changes in serum creatinine, such as 0.3 mg/dL or 25%, are sufficient to detect AKI (worsening renal function) and that the magnitude of the serum creatinine change is an indicator of the severity of the AKI and mortality risk.

[0012] Although serial measurement of serum creatinine over a period of days is an accepted method of detecting and diagnosing AKI and is considered one of the most important tools to evaluate AKI patients, serum creatinine is generally regarded to have several limitations in the diagnosis, assessment and monitoring of AKI patients. The time period for serum creatinine to rise to values (e.g., a 0.3 mg/dL or 25% rise) considered diagnostic for AKI can be 48 hours or longer depending on the definition used. Since cellular injury in AKI can occur over a period of hours, serum creatinine elevations detected at 48 hours or longer can be a late indicator of injury, and relying on serum creatinine can thus delay diagnosis of AKI. Furthermore, serum creatinine is not a good indicator of the exact kidney status and treatment needs during the most acute phases of AKI when kidney function is changing rapidly. Some patients with AKI will recover fully, some will need dialysis (either short term or long term) and some will have other detrimental outcomes including death, major adverse cardiac events and chronic kidney disease. Because serum creatinine is a marker of filtration rate, it does not differentiate between the causes of AKI (pre-renal, intrinsic renal, post-renal obstruction, atheroembolic, etc) or the category or location of injury in intrinsic renal disease (for example, tubular, glomerular or interstitial in origin). Urine output is similarly limited, Knowing these things can be of vital importance in managing and treating patients with AKI.

[0013] These limitations underscore the need for better methods to detect and assess AKI, particularly in the early and subclinical stages, but also in later stages when

recovery and repair of the kidney can occur. Furthermore, there is a need to better identify patients who are at risk of having an AKI.

BRIEF SUMMARY OF THE INVENTION

[0014] It is an object of the invention to provide methods and compositions for evaluating renal function in a subject. As described herein, measurement of one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, Carcinoembryonic antigen-related cell adhesion molecule 5, and Cellular tumor antigen p53 (referred to herein as a "kidney injury marker") can be used for diagnosis, prognosis, risk stratification, staging, monitoring, categorizing and determination of further diagnosis and treatment regimens in subjects suffering or at risk of suffering from an injury to renal function, reduced renal function, and/or acute renal failure (also called acute kidney injury).

[0015] The kidney injury markers of the present invention may be used, individually or in panels comprising a plurality of kidney injury markers, for risk stratification (that is, to identify subjects at risk for a future injury to renal function, for future progression to reduced renal function, for future progression to ARF, for future improvement in renal function, *etc.*); for diagnosis of existing disease (that is, to identify subjects who have suffered an injury to renal function, who have progressed to reduced renal function, who have progressed to ARF, *etc.*); for monitoring for deterioration or improvement of renal function; and for predicting a future medical outcome, such as improved or worsening renal function, a decreased or increased mortality risk, a decreased or increased risk that a subject will require renal replacement therapy (*i.e.*, hemodialysis, peritoneal dialysis, hemofiltration, and/or renal transplantation, a decreased or increased risk that a subject will recover from an injury to renal function, a decreased or increased risk that a subject will recover from ARF, a decreased or increased risk that a subject will progress to end stage renal disease, a decreased or increased risk that a subject will progress to chronic renal failure, a decreased or increased risk that a subject will suffer rejection of a transplanted kidney, *etc.*

[0016] In a first aspect, the present invention relates to methods for evaluating renal status in a subject. These methods comprise performing an assay method that is configured to detect one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, Carcinoembryonic antigen-related cell adhesion molecule 5, and Cellular tumor antigen p53 in a body fluid sample obtained from the subject. The assay result(s), for example measured concentration(s) of one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, is/are then correlated to the renal status of the subject. This correlation to renal status may include correlating the assay result(s) to one or more of risk stratification, diagnosis, prognosis, staging, classifying and monitoring of the subject as described herein. Thus, the present invention utilizes one or more kidney injury markers of the present invention for the evaluation of renal injury.

[0017] In certain embodiments, the methods for evaluating renal status described herein are methods for risk stratification of the subject; that is, assigning a likelihood of one or more future changes in renal status to the subject. In these embodiments, the assay result(s) is/are correlated to one or more such future changes. The following are preferred risk stratification embodiments.

[0018] In preferred risk stratification embodiments, these methods comprise determining a subject's risk for a future injury to renal function, and the assay result(s) is/are correlated to a likelihood of such a future injury to renal function. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of suffering a future injury to renal function is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of suffering a future injury to renal function is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

[0019] In other preferred risk stratification embodiments, these methods comprise determining a subject's risk for future reduced renal function, and the assay result(s) is/are correlated to a likelihood of such reduced renal function. For example, the measured concentrations may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of suffering a future reduced renal function is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of future reduced renal function is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

[0020] In still other preferred risk stratification embodiments, these methods comprise determining a subject's likelihood for a future improvement in renal function, and the assay result(s) is/are correlated to a likelihood of such a future improvement in renal function. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of a future improvement in renal function is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold. For a "negative going" kidney injury marker, an increased likelihood of a future improvement in renal function is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold.

[0021] In yet other preferred risk stratification embodiments, these methods comprise determining a subject's risk for progression to ARF, and the result(s) is/are correlated to a likelihood of such progression to ARF. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of progression to ARF is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of progression to ARF is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

[0022] And in other preferred risk stratification embodiments, these methods comprise determining a subject's outcome risk, and the assay result(s) is/are correlated to a likelihood of the occurrence of a clinical outcome related to a renal injury suffered by the subject. For example, the measured concentration(s) may each be compared to a threshold value. For a "positive going" kidney injury marker, an increased likelihood of one or more of: acute kidney injury, progression to a worsening stage of AKI, mortality, a requirement for renal replacement therapy, a requirement for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, progression to chronic kidney disease, *etc.*, is assigned to the subject when the measured concentration is above the threshold, relative to a likelihood assigned when the measured concentration is below the threshold. For a "negative going" kidney injury marker, an increased likelihood of one or more of: acute kidney injury, progression to a worsening stage of AKI, mortality, a requirement for renal replacement therapy, a requirement for withdrawal of renal toxins, end stage renal disease, heart failure, stroke, myocardial infarction, progression to chronic kidney disease, *etc.*, is assigned to the subject when the measured concentration is below the threshold, relative to a likelihood assigned when the measured concentration is above the threshold.

[0023] In such risk stratification embodiments, preferably the likelihood or risk assigned is that an event of interest is more or less likely to occur within 180 days of the time at which the body fluid sample is obtained from the subject. In particularly preferred embodiments, the likelihood or risk assigned relates to an event of interest occurring within a shorter time period such as 18 months, 120 days, 90 days, 60 days, 45 days, 30 days, 21 days, 14 days, 7 days, 5 days, 96 hours, 72 hours, 48 hours, 36 hours, 24 hours, 12 hours, or less. A risk at 0 hours of the time at which the body fluid sample is obtained from the subject is equivalent to diagnosis of a current condition.

[0024] In preferred risk stratification embodiments, the subject is selected for risk stratification based on the pre-existence in the subject of one or more known risk factors for prerenal, intrinsic renal, or postrenal ARF. For example, a subject undergoing or having undergone major vascular surgery, coronary artery bypass, or other cardiac surgery; a subject having pre-existing congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, glomerular filtration below the normal range, cirrhosis, serum creatinine above the normal range, or sepsis; or a subject exposed to NSAIDs, cyclosporines, tacrolimus,

aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin are all preferred subjects for monitoring risks according to the methods described herein. This list is not meant to be limiting. By "pre-existence" in this context is meant that the risk factor exists at the time the body fluid sample is obtained from the subject. In particularly preferred embodiments, a subject is chosen for risk stratification based on an existing diagnosis of injury to renal function, reduced renal function, or ARF.

[0025] In other embodiments, the methods for evaluating renal status described herein are methods for diagnosing a renal injury in the subject; that is, assessing whether or not a subject has suffered from an injury to renal function, reduced renal function, or ARF. In these embodiments, the assay result(s), for example measured concentration(s) of one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, is/are correlated to the occurrence or nonoccurrence of a change in renal status. The following are preferred diagnostic embodiments.

[0026] In preferred diagnostic embodiments, these methods comprise diagnosing the occurrence or nonoccurrence of an injury to renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of such an injury. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury to renal function is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury to renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury to renal function is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury to renal function may

be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

[0027] In other preferred diagnostic embodiments, these methods comprise diagnosing the occurrence or nonoccurrence of reduced renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of an injury causing reduced renal function. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury causing reduced renal function is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury causing reduced renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury causing reduced renal function is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury causing reduced renal function may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

[0028] In yet other preferred diagnostic embodiments, these methods comprise diagnosing the occurrence or nonoccurrence of ARF, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of an injury causing ARF. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of ARF is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of ARF may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of ARF is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold);

alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of ARF may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

[0029] In still other preferred diagnostic embodiments, these methods comprise diagnosing a subject as being in need of renal replacement therapy, and the assay result(s) is/are correlated to a need for renal replacement therapy. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury creating a need for renal replacement therapy is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal replacement therapy may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury creating a need for renal replacement therapy is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal replacement therapy may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

[0030] In still other preferred diagnostic embodiments, these methods comprise diagnosing a subject as being in need of renal transplantation, and the assay result(s0 is/are correlated to a need for renal transplantation. For example, each of the measured concentration(s) may be compared to a threshold value. For a positive going marker, an increased likelihood of the occurrence of an injury creating a need for renal transplantation is assigned to the subject when the measured concentration is above the threshold (relative to the likelihood assigned when the measured concentration is below the threshold); alternatively, when the measured concentration is below the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal transplantation may be assigned to the subject (relative to the likelihood assigned when the measured concentration is above the threshold). For a negative going marker, an increased likelihood of the occurrence of an injury creating a need for renal

transplantation is assigned to the subject when the measured concentration is below the threshold (relative to the likelihood assigned when the measured concentration is above the threshold); alternatively, when the measured concentration is above the threshold, an increased likelihood of the nonoccurrence of an injury creating a need for renal transplantation may be assigned to the subject (relative to the likelihood assigned when the measured concentration is below the threshold).

[0031] In still other embodiments, the methods for evaluating renal status described herein are methods for monitoring a renal injury in the subject; that is, assessing whether or not renal function is improving or worsening in a subject who has suffered from an injury to renal function, reduced renal function, or ARF. In these embodiments, the assay result(s), for example measured concentration(s) of one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, is/are correlated to the occurrence or nonoccurrence of a change in renal status. The following are preferred monitoring embodiments.

[0032] In preferred monitoring embodiments, these methods comprise monitoring renal status in a subject suffering from an injury to renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

[0033] In other preferred monitoring embodiments, these methods comprise monitoring renal status in a subject suffering from reduced renal function, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively,

when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

[0034] In yet other preferred monitoring embodiments, these methods comprise monitoring renal status in a subject suffering from acute renal failure, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

[0035] In other additional preferred monitoring embodiments, these methods comprise monitoring renal status in a subject at risk of an injury to renal function due to the pre-existence of one or more known risk factors for prerenal, intrinsic renal, or postrenal ARF, and the assay result(s) is/are correlated to the occurrence or nonoccurrence of a change in renal status in the subject. For example, the measured concentration(s) may be compared to a threshold value. For a positive going marker, when the measured concentration is above the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is below the threshold, an improvement of renal function may be assigned to the subject. For a negative going marker, when the measured concentration is below the threshold, a worsening of renal function may be assigned to the subject; alternatively, when the measured concentration is above the threshold, an improvement of renal function may be assigned to the subject.

[0036] In still other embodiments, the methods for evaluating renal status described herein are methods for classifying a renal injury in the subject; that is, determining whether a renal injury in a subject is prerenal, intrinsic renal, or postrenal; and/or further subdividing these classes into subclasses such as acute tubular injury, acute

glomerulonephritis acute tubulointerstitial nephritis, acute vascular nephropathy, or infiltrative disease; and/or assigning a likelihood that a subject will progress to a particular RIFLE stage. In these embodiments, the assay result(s), for example measured concentration(s) of one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, is/are correlated to a particular class and/or subclass. The following are preferred classification embodiments.

[0037] In preferred classification embodiments, these methods comprise determining whether a renal injury in a subject is prerenal, intrinsic renal, or postrenal; and/or further subdividing these classes into subclasses such as acute tubular injury, acute glomerulonephritis acute tubulointerstitial nephritis, acute vascular nephropathy, or infiltrative disease; and/or assigning a likelihood that a subject will progress to a particular RIFLE stage, and the assay result(s) is/are correlated to the injury classification for the subject. For example, the measured concentration may be compared to a threshold value, and when the measured concentration is above the threshold, a particular classification is assigned; alternatively, when the measured concentration is below the threshold, a different classification may be assigned to the subject.

[0038] A variety of methods may be used by the skilled artisan to arrive at a desired threshold value for use in these methods. For example, the threshold value may be determined from a population of normal subjects by selecting a concentration representing the 75^{th}, 85^{th}, 90^{th}, 95^{th}, or 99^{th} percentile of a kidney injury marker measured in such normal subjects. Alternatively, the threshold value may be determined from a "diseased" population of subjects, e.g., those suffering from an injury or having a predisposition for an injury (e.g., progression to ARF or some other clinical outcome such as death, dialysis, renal transplantation, *etc.*), by selecting a concentration representing the 75^{th}, 85^{th}, 90^{th}, 95^{th}, or 99^{th} percentile of a kidney injury marker measured in such subjects. In another alternative, the threshold value may be determined from a prior measurement of a kidney injury marker in the same subject; that is, a temporal change in the level of a kidney injury marker in the subject may be used to assign risk to the subject.

[0039] The foregoing discussion is not meant to imply, however, that the kidney injury markers of the present invention must be compared to corresponding individual

thresholds. Methods for combining assay results can comprise the use of multivariate logistical regression, loglinear modeling, neural network analysis, n-of-m analysis, decision tree analysis, calculating ratios of markers, *etc*. This list is not meant to be limiting. In these methods, a composite result which is determined by combining individual markers may be treated as if it is itself a marker; that is, a threshold may be determined for the composite result as described herein for individual markers, and the composite result for an individual patient compared to this threshold.

[0040] The ability of a particular test to distinguish two populations can be established using ROC analysis. For example, ROC curves established from a "first" subpopulation which is predisposed to one or more future changes in renal status, and a "second" subpopulation which is not so predisposed can be used to calculate a ROC curve, and the area under the curve provides a measure of the quality of the test. Preferably, the tests described herein provide a ROC curve area greater than 0.5, preferably at least 0.6, more preferably 0.7, still more preferably at least 0.8, even more preferably at least 0.9, and most preferably at least 0.95.

[0041] In certain aspects, the measured concentration of one or more kidney injury markers, or a composite of such markers, may be treated as continuous variables. For example, any particular concentration can be converted into a corresponding probability of a future reduction in renal function for the subject, the occurrence of an injury, a classification, etc. In yet another alternative, a threshold that can provide an acceptable level of specificity and sensitivity in separating a population of subjects into "bins" such as a "first" subpopulation (e.g., which is predisposed to one or more future changes in renal status, the occurrence of an injury, a classification, etc.) and a "second" subpopulation which is not so predisposed. A threshold value is selected to separate this first and second population by one or more of the following measures of test accuracy:

an odds ratio greater than 1, preferably at least about 2 or more or about 0.5 or less, more preferably at least about 3 or more or about 0.33 or less, still more preferably at least about 4 or more or about 0.25 or less, even more preferably at least about 5 or more or about 0.2 or less, and most preferably at least about 10 or more or about 0.1 or less;

a specificity of greater than 0.5, preferably at least about 0.6, more preferably at least about 0.7, still more preferably at least about 0.8, even more preferably at least about 0.9 and most preferably at least about 0.95, with a corresponding sensitivity greater than 0.2,

preferably greater than about 0.3, more preferably greater than about 0.4, still more preferably at least about 0.5, even more preferably about 0.6, yet more preferably greater than about 0.7, still more preferably greater than about 0.8, more preferably greater than about 0.9, and most preferably greater than about 0.95;

a sensitivity of greater than 0.5, preferably at least about 0.6, more preferably at least about 0.7, still more preferably at least about 0.8, even more preferably at least about 0.9 and most preferably at least about 0.95, with a corresponding specificity greater than 0.2, preferably greater than about 0.3, more preferably greater than about 0.4, still more preferably at least about 0.5, even more preferably about 0.6, yet more preferably greater than about 0.7, still more preferably greater than about 0.8, more preferably greater than about 0.9, and most preferably greater than about 0.95;

at least about 75% sensitivity, combined with at least about 75% specificity;

a positive likelihood ratio (calculated as sensitivity/(1-specificity)) of greater than 1, at least about 2, more preferably at least about 3, still more preferably at least about 5, and most preferably at least about 10; or

a negative likelihood ratio (calculated as (1-sensitivity)/specificity) of less than 1, less than or equal to about 0.5, more preferably less than or equal to about 0.3, and most preferably less than or equal to about 0.1.

[0042] The term "about" in the context of any of the above measurements refers to +/- 5% of a given measurement.

[0043] Multiple thresholds may also be used to assess renal status in a subject. For example, a "first" subpopulation which is predisposed to one or more future changes in renal status, the occurrence of an injury, a classification, etc., and a "second" subpopulation which is not so predisposed can be combined into a single group. This group is then subdivided into three or more equal parts (known as tertiles, quartiles, quintiles, etc., depending on the number of subdivisions). An odds ratio is assigned to subjects based on which subdivision they fall into. If one considers a tertile, the lowest or highest tertile can be used as a reference for comparison of the other subdivisions. This reference subdivision is assigned an odds ratio of 1. The second tertile is assigned an odds ratio that is relative to that first tertile. That is, someone in the second tertile might be 3 times more likely to suffer one or more future changes in renal status in comparison to

someone in the first tertile. The third tertile is also assigned an odds ratio that is relative to that first tertile.

[0044] In certain embodiments, the assay method is an immunoassay. Antibodies for use in such assays will specifically bind a full length kidney injury marker of interest, and may also bind one or more polypeptides that are "related" thereto, as that term is defined hereinafter. Numerous immunoassay formats are known to those of skill in the art. Preferred body fluid samples are selected from the group consisting of urine, blood, serum, saliva, tears, and plasma.

[0045] The foregoing method steps should not be interpreted to mean that the kidney injury marker assay result(s) is/are used in isolation in the methods described herein. Rather, additional variables or other clinical indicia may be included in the methods described herein. For example, a risk stratification, diagnostic, classification, monitoring, etc. method may combine the assay result(s) with one or more variables measured for the subject selected from the group consisting of demographic information (e.g., weight, sex, age, race), medical history (e.g., family history, type of surgery, pre-existing disease such as aneurism, congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, or sepsis, type of toxin exposure such as NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin), clinical variables (e.g., blood pressure, temperature, respiration rate), risk scores (APACHE score, PREDICT score, TIMI Risk Score for UA/NSTEMI, Framingham Risk Score), a glomerular filtration rate, an estimated glomerular filtration rate, a urine production rate, a serum or plasma creatinine concentration, a urine creatinine concentration, a fractional excretion of sodium, a urine sodium concentration, a urine creatinine to serum or plasma creatinine ratio, a urine specific gravity, a urine osmolality, a urine urea nitrogen to plasma urea nitrogen ratio, a plasma BUN to creatnine ratio, a renal failure index calculated as urine sodium / (urine creatinine / plasma creatinine), a serum or plasma neutrophil gelatinase (NGAL) concentration, a urine NGAL concentration, a serum or plasma cystatin C concentration, a serum or plasma cardiac troponin concentration, a serum or plasma BNP concentration, a serum or plasma NTproBNP concentration, and a serum or plasma proBNP concentration. Other measures of renal function which may be combined with one or more kidney injury marker assay result(s) are described hereinafter and in Harrison's

Principles of Internal Medicine, 17th Ed., McGraw Hill, New York, pages 1741-1830, and Current Medical Diagnosis & Treatment 2008, 47th Ed, McGraw Hill, New York, pages 785-815, each of which are hereby incorporated by reference in their entirety.

[0046] When more than one marker is measured, the individual markers may be measured in samples obtained at the same time, or may be determined from samples obtained at different (e.g., an earlier or later) times. The individual markers may also be measured on the same or different body fluid samples. For example, one kidney injury marker may be measured in a serum or plasma sample and another kidney injury marker may be measured in a urine sample. In addition, assignment of a likelihood may combine an individual kidney injury marker assay result with temporal changes in one or more additional variables.

[0047] In various related aspects, the present invention also relates to devices and kits for performing the methods described herein. Suitable kits comprise reagents sufficient for performing an assay for at least one of the described kidney injury markers, together with instructions for performing the described threshold comparisons.

[0048] In certain embodiments, reagents for performing such assays are provided in an assay device, and such assay devices may be included in such a kit. Preferred reagents can comprise one or more solid phase antibodies, the solid phase antibody comprising antibody that detects the intended biomarker target(s) bound to a solid support. In the case of sandwich immunoassays, such reagents can also include one or more detectably labeled antibodies, the detectably labeled antibody comprising antibody that detects the intended biomarker target(s) bound to a detectable label. Additional optional elements that may be provided as part of an assay device are described hereinafter.

[0049] Detectable labels may include molecules that are themselves detectable (e.g., fluorescent moieties, electrochemical labels, ecl (electrochemical luminescence) labels, metal chelates, colloidal metal particles, *etc.*) as well as molecules that may be indirectly detected by production of a detectable reaction product (*e.g.*, enzymes such as horseradish peroxidase, alkaline phosphatase, *etc.*) or through the use of a specific binding molecule which itself may be detectable (*e.g.*, a labeled antibody that binds to the second antibody, biotin, digoxigenin, maltose, oligohistidine, 2,4-dintrobenzene, phenylarsenate, ssDNA, dsDNA, etc.).

[0050] Generation of a signal from the signal development element can be performed using various optical, acoustical, and electrochemical methods well known in the art. Examples of detection modes include fluorescence, radiochemical detection, reflectance, absorbance, amperometry, conductance, impedance, interferometry, ellipsometry, *etc*. In certain of these methods, the solid phase antibody is coupled to a transducer (*e.g*., a diffraction grating, electrochemical sensor, etc) for generation of a signal, while in others, a signal is generated by a transducer that is spatially separate from the solid phase antibody (*e.g*., a fluorometer that employs an excitation light source and an optical detector). This list is not meant to be limiting. Antibody-based biosensors may also be employed to determine the presence or amount of analytes that optionally eliminate the need for a labeled molecule.

DETAILED DESCRIPTION OF THE INVENTION

[0051] The present invention relates to methods and compositions for diagnosis, differential diagnosis, risk stratification, monitoring, classifying and determination of treatment regimens in subjects suffering or at risk of suffering from injury to renal function, reduced renal function and/or acute renal failure through measurement of one or more kidney injury markers. In various embodiments, a measured concentration of one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, or one or more markers related thereto, are correlated to the renal status of the subject.

[0052] For purposes of this document, the following definitions apply:

[0053] As used herein, an "injury to renal function" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) measurable reduction in a measure of renal function. Such an injury may be identified, for example, by a decrease in glomerular filtration rate or estimated GFR, a reduction in urine output, an increase in serum creatinine, an increase in serum cystatin C, a requirement for renal replacement therapy, *etc*. "Improvement in Renal Function" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) measurable increase in a measure of renal function. Preferred methods for measuring and/or estimating GFR are described hereinafter.

[0054] As used herein, "reduced renal function" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) reduction in kidney function identified by an absolute increase in serum creatinine of greater than or equal to 0.1 mg/dL (≥ 8.8 μmol/L), a percentage increase in serum creatinine of greater than or equal to 20% (1.2-fold from baseline), or a reduction in urine output (documented oliguria of less than 0. 5 ml/kg per hour).

[0055] As used herein, "acute renal failure" or "ARF" is an abrupt (within 14 days, preferably within 7 days, more preferably within 72 hours, and still more preferably within 48 hours) reduction in kidney function identified by an absolute increase in serum creatinine of greater than or equal to 0.3 mg/dl (≥ 26.4 μmol/l), a percentage increase in serum creatinine of greater than or equal to 50% (1. 5-fold from baseline), or a reduction in urine output (documented oliguria of less than 0.5 ml/kg per hour for at least 6 hours). This term is synonymous with "acute kidney injury" or "AKI."

[0056] As used herein, the term "tumor necrosis factor receptor superfamily member 10B" refers to one or more polypeptides present in a biological sample that are derived from the tumor necrosis factor receptor superfamily member 10B precursor (Swiss-Prot O14763 (SEQ ID NO: 1)).

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        10         20         30         40         50         60
MEQRGQNAPA ASGARKRHGP GPREARGARP GPRVPKTLVL VVAAVLLLVS AESALITQQD
        70         80         90        100        110        120
LAPQQRAAPQ QKRSSPSEGL CPPGHHISED GRDCISCKYG QDYSTHWNDL LFCLRCTRCD
       130        140        150        160        170        180
SGEVELSPCT TTRNTVCQCE EGTFREEDSP EMCRKCRTGC PRGMVKVGDC TPWSDIECVH
       190        200        210        220        230        240
KESGTKHSGE APAVEETVTS SPGTPASPCS LSGIIIGVTV AAVVLIVAVF VCKSLLWKKV
       250        260        270        280        290        300
LPYLKGICSG GGGDPERVDR SSQRPGAEDN VLNEIVSILQ PTQVPEQEME VQEPAEPTGV
       310        320        330        340        350        360
NMLSPGESEH LLEPAEAERS QRRRLLVPAN EGDPTETLRQ CFDDFADLVP FDSWEPLMRK
       370        380        390        400        410        420
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LGLMDNEIKV AKAEAAGHRD TLYTMLIKWV NKTGRDASVH TLLDALETLG ERLAKQKIED
       430        440
HLLSSGKFMY LEGNADSAMS
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[0057] Most preferably, the tumor necrosis factor receptor superfamily member 10B assay detects one or more soluble forms of tumor necrosis factor receptor superfamily member 10B. Tumor necrosis factor receptor superfamily member 10B is a single-pass type I membrane protein having a large extracellular domain, most or all of which is present in soluble forms of tumor necrosis factor receptor superfamily member 10B generated either through alternative splicing event which deletes all or a portion of the transmembrane domain, or by proteolysis of the membrane-bound form. In the case of an immunoassay, one or more antibodies that bind to epitopes within this extracellular domain may be used to detect these soluble form(s). The following domains have been identified in tumor necrosis factor receptor superfamily member 10B:

Residues	Length	Domain ID
1-55	55	signal sequence
56-440	385	tumor necrosis factor receptor superfamily member 10B
56-210	155	extracellular
211-231	21	transmembrane
232-440	209	cytoplasmic

[0058] As used herein, the term “cadherin-16” refers to one or more polypeptides present in a biological sample that are derived from the cadherin-16 precursor (Swiss-Prot O75309 (SEQ ID NO: 2)).

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        10         20         30         40         50         60
MVPAWLWLLC VSVPQALPKA QPAELSVEVP ENYGGNFPLY LTKLPLPREG AEGQIVLSGD
        70         80         90        100        110        120
SGKATEGPFA MDPDSGFLLV TRALDREEQA EYQLQVTLEM QDGHVLWGPQ PVLVHVKDEN
       130        140        150        160        170        180
DQVPHFSQAI YRARLSRGTR PGIPFLFLEA SDRDEPGTAN SDLRFHILSQ APAQPSPDMF
       190        200        210        220        230        240
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QLEPRLGALA LSPKGSTSLD HALERTYQLL VQVKDMGDQA SGHQATATVE VSIIESTWVS
       250        260        270        280        290        300
LEPIHLAENL KVLYPHHMAQ VHWSGGDVHY HLESHPPGPF EVNAEGNLYV TRELDREAQA
       310        320        330        340        350        360
EYLLQVRAQN SHGEDYAAPL ELHVLVMDEN DNVPICPPRD PTVSIPELSP PGTEVTRLSA
       370        380        390        400        410        420
EDADAPGSPN SHVVYQLLSP EPEDGVEGRA FQVDPTSGSV TLGVLPLRAG QNILLLVLAM
       430        440        450        460        470        480
DLAGAEGGFS STCEVEVAVT DINDHAPEFI TSQIGPISLP EDVEPGTLVA MLTAIDADLE
       490        500        510        520        530        540
PAFRLMDFAI ERGDTEGTFG LDWEPDSGHV RLRLCKNLSY EAAPSHEVVV VVQSVAKLVG
       550        560        570        580        590        600
PGPGPGATAT VTVLVERVMP PPKLDQESYE ASVPISAPAG SFLLTIQPSD PISRTLRFSL
       610        620        630        640        650        660
VNDSEGWLCI EKFSGEVHTA QSLQGAQPGD TYTVLVEAQD TDEPRLSASA PLVIHFLKAP
       670        680        690        700        710        720
PAPALTLAPV PSQYLCTPRQ DHGLIVSGPS KDPDLASGHG PYSFTLGPNP TVQRDWRLQT
       730        740        750        760        770        780
LNGSHAYLTL ALHWVEPREH IIPVVVSHNA QMWQLLVRVI VCRCNVEGQC MRKVGRMKGM
       790        800        810        820
PTKLSAVGIL VGTLVAIGIF LILIFTHWTM SRKKDPDQPA DSVPLKATV
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[0059] Most preferably, the cadherin-16 assay detects one or more soluble forms of cadherin-16. Cadherin-16 is a single-pass type I membrane protein having a large extracellular domain, most or all of which is present in soluble forms of cadherin-16 generated either through alternative splicing event which deletes all or a portion of the transmembrane domain, or by proteolysis of the membrane-bound form. In the case of an immunoassay, one or more antibodies that bind to epitopes within this extracellular domain may be used to detect these soluble form(s). The following domains have been identified in cadherin-16:

Residues	Length	Domain ID
1-18	18	signal sequence
19	829	cadherin-16
19-786	768	extracellular
787-807	22	transmembrane
808-829	22	cytoplasmic

[0060] As used herein, the term "caspase-9" refers to one or more polypeptides present in a biological sample that are derived from the caspase-9 precursor (Swiss-Prot P55211 (SEQ ID NO: 3)).

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        10         20         30         40         50         60
MDEADRRLLR RCRLRLVEEL QVDQLWDALL SRELFRPHMI EDIQRAGSGS RRDQARQLII
        70         80         90        100        110        120
DLETRGSQAL PLFISCLEDT GQDMLASFLR TNRQAAKLSK PTLENLTPVV LRPEIRKPEV
       130        140        150        160        170        180
LRPETPRPVD IGSGGFGDVG ALESLRGNAD LAYILSMEPC GHCLIINNVN FCRESGLRTR
       190        200        210        220        230        240
TGSNIDCEKL RRRFSSLHFM VEVKGDLTAK KMVLALLELA QQDHGALDCC VVVILSHGCQ
       250        260        270        280        290        300
ASHLQFPGAV YGTDGCPVSV EKIVNIFNGT SCPSLGGKPK LFFIQACGGE QKDHGFEVAS
       310        320        330        340        350        360
TSPEDESPGS NPEPDATPFQ EGLRTFDQLD AISSLPTPSD IFVSYSTFPG FVSWRDPKSG
       370        380        390        400        410
SWYVETLDDI FEQWAHSEDL QSLLLRVANA VSVKGIYKQM PGCFNFLRKK LFFKTS
```

[0061] The following domains have been identified in caspase-9:

Residues	Length	Domain ID
1-315	315	caspase-9 p35 subunit
316-330	15	pro-peptide
331-416	86	caspase-9 subunit p10

[0062] As used herein, the term "Bcl2 antagonist of cell death" refers to one or more polypeptides present in a biological sample that are derived from the Bcl2 antagonist of cell death precursor (Swiss-Prot Q92934 (SEQ ID NO: 4)).

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        10         20         30         40         50         60
MFQIPEFEPS EQEDSSSAER GLGPSPAGDG PSGSGKHHRQ APGLLWDASH QQEQPTSSSH
        70         80         90        100        110        120
HGGAGAVEIR SRHSSYPAGT EDDEGMGEEP SPFRGRSRSA PPNLWAAQRY GRELRRMSDE
       130        140        150        160
FVDSFKKGLP RPKSAGTATQ MRQSSSWTRV FQSWWDRNLG RGSSAPSQ
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[0063] As used herein, the term "caspase-1" refers to one or more polypeptides present in a biological sample that are derived from the caspase-1 precursor (Swiss-Prot P29466 (SEQ ID NO: 5)).

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        10         20         30         40         50         60
MADKVLKEKR KLFIRSMGEG TINGLLDELL QTRVLNKEEM EKVKRENATV MDKTRALIDS
        70         80         90        100        110        120
VIPKGAQACQ ICITYICEED SYLAGTLGLS ADQTSGNYLN MQDSQGVLSS FPAPQAVQDN
       130        140        150        160        170        180
PAMPTSSGSE GNVKLCSLEE AQRIWKQKSA EIYPIMDKSS RTRLALIICN EEFDSIPRRT
       190        200        210        220        230        240
GAEVDITGMT MLLQNLGYSV DVKKNLTASD MTTELEAFAH RPEHKTSDST FLVFMSHGIR
       250        260        270        280        290        300
EGICGKKHSE QVPDILQLNA IFNMLNTKNC PSLKDKPKVI IIQACRGDSP GVVWFKDSVG
       310        320        330        340        350        360
VSGNLSLPTT EEFEDDAIKK AHIEKDFIAF CSSTPDNVSW RHPTMGSVFI GRLIEHMQEY
       370        380        390        400
ACSCDVEEIF RKVRFSFEQP DGRAQMPTTE RVTLTRCFYL FPGH
```

[0064] The following domains have been identified in caspase-1:

Residues	Length	Domain ID
1-119	119	pro-peptide

120-297	178	caspase-1 p20 subunit
298-316	19	pro-peptide
317-404	88	caspase-1 p10 subunit

[0065] As used herein, the terms "epithelial cadherin" or "Cadherin-1" refers to one or more polypeptides present in a biological sample that are derived from the epithelial cadherin precursor (Swiss-Prot P12830 (SEQ ID NO: 6)).

```
        10         20         30         40         50         60
MGPWSRSLSA LLLLLQVSSW LCQEPEPCHP GFDAESYTFT VPRRHLERGR VLGRVNFEDC
        70         80         90        100        110        120
TGRQRTAYFS LDTRFKVGTD GVITVKRPLR FHNPQIHFLV YAWDSTYRKF STKVTLNTVG
       130        140        150        160        170        180
HHHRPPPHQA SVSGIQAELL TFPNSSPGLR RQKRDWVIPP ISCPENEKGP FPKNLVQIKS
       190        200        210        220        230        240
NKDKEGKVFY SITGQGADTP PVGVFIIERE TGWLKVTEPL DRERIATYTL FSHAVSSNGN
       250        260        270        280        290        300
AVEDPMEILI TVTDQNDNKP EFTQEVFKGS VMEGALPGTS VMEVTATDAD DDVNTYNAAI
       310        320        330        340        350        360
AYTILSQDPE LPDKNMFTIN RNTGVISVVT TGLDRESFPT YTLVVQAADL QGEGLSTTAT
       370        380        390        400        410        420
AVITVTDTND NPPIFNPTTY KGQVPENEAN VVITTLKVTD ADAPNTPAWE AVYTILNDDG
       430        440        450        460        470        480
GQFVVTTNPV NNDGILKTAK GLDFEAKQQY ILHVAVTNVV PFEVSLTTST ATVTVDVLDV
       490        500        510        520        530        540
NEAPIFVPPE KRVEVSEDFG VGQEITSYTA QEPDTFMEQK ITYRIWRDTA NWLEINPDTG
       550        560        570        580        590        600
AISTRAELDR EDFEHVKNST YTALIIATDN GSPVATGTGT LLLILSDVND NAPIPEPRTI
       610        620        630        640        650        660
FFCERNPKPQ VINIIDADLP PNTSPFTAEL THGASANWTI QYNDPTQESI ILKPKMALEV
```

```
       670         680         690         700         710         720
GDYKINLKLM DNQNKDQVTT LEVSVCDCEG AAGVCRKAQP VEAGLQIPAI LGILGGILAL
       730         740         750         760         770         780
LILILLLLLF LRRRAVVKEP LLPPEDDTRD NVYYYDEEGG GEEDQDFDLS QLHRGLDARP
       790         800         810         820         830         840
EVTRNDVAPT LMSVPRYLPR PANPDEIGNF IDENLKAADT DPTAPPYDSL LVFDYEGSGS
       850         860         870         880
EAASLSSLNS SESDKDQDYD YLNEWGNRFK KLADMYGGGE DD
```

[0066] Most preferably, the epithelial cadherin assay detects one or more soluble forms of epithelial cadherin. Epithelial cadherin is a single-pass type I membrane protein having a large extracellular domain, most or all of which is present in soluble forms of epithelial cadherin generated either through alternative splicing event which deletes all or a portion of the transmembrane domain, or by proteolysis of the membrane-bound form. In the case of an immunoassay, one or more antibodies that bind to epitopes within this extracellular domain may be used to detect these soluble form(s). The following domains have been identified in epithelial cadherin:

Residues	Length	Domain ID
1-22	22	signal sequence
23-154	132	pro-peptide
155-882	728	epithelial cadherin
155-709	555	extracellular
710-730	21	transmembrane
731-882	152	cytoplasmic

[0067] As used herein, the term “poly [ADP-ribose] polymerase 1” refers to one or more polypeptides present in a biological sample that are derived from the poly [ADP-ribose] polymerase 1 precursor (Swiss-Prot 09874 (SEQ ID NO: 7)).

```
        10          20          30          40          50          60
MAESSDKLYR VEYAKSGRAS CKKCSESIPK DSLRMAIMVQ SPMFDGKVPH WYHFSCFWKV
        70          80          90         100         110         120
```

GHSIRHPDVE VDGFSELRWD DQQKVKKTAE AGGVTGKGQD GIGSKAEKTL GDFAAEYAKS

130 140 150 160 170 180

NRSTCKGCME KIEKGQVRLS KKMVDPEKPQ LGMIDRWYHP GCFVKNREEL GFRPEYSASQ

190 200 210 220 230 240

LKGFSLLATE DKEALKKQLP GVKSEGKRKG DEVDGVDEVA KKKSKKEKDK DSKLEKALKA

250 260 270 280 290 300

QNDLIWNIKD ELKKVCSTND LKELLIFNKQ QVPSGESAIL DRVADGMVFG ALLPCEECSG

310 320 330 340 350 360

QLVFKSDAYY CTGDVTAWTK CMVKTQTPNR KEWVTPKEFR EISYLKKLKV KKQDRIFPPE

370 380 390 400 410 420

TSASVAATPP PSTASAPAAV NSSASADKPL SNMKILTLGK LSRNKDEVKA MIEKLGGKLT

430 440 450 460 470 480

GTANKASLCI STKKEVEKMN KKMEEVKEAN IRVVSEDFLQ DVSASTKSLQ ELFLAHILSP

490 500 510 520 530 540

WGAEVKAEPV EVVAPRGKSG AALSKKSKGQ VKEEGINKSE KRMKLTLKGG AAVDPDSGLE

550 560 570 580 590 600

HSAHVLEKGG KVFSATLGLV DIVKGTNSYY KLQLLEDDKE NRYWIFRSWG RVGTVIGSNK

610 620 630 640 650 660

LEQMPSKEDA IEHFMKLYEE KTGNAWHSKN FTKYPKKFYP LEIDYGQDEE AVKKLTVNPG

670 680 690 700 710 720

TKSKLPKPVQ DLIKMIFDVE SMKKAMVEYE IDLQKMPLGK LSKRQIQAAY SILSEVQQAV

730 740 750 760 770 780

SQGSSDSQIL DLSNRFYTLI PHDFGMKKPP LLNNADSVQA KVEMLDNLLD IEVAYSLLRG

790 800 810 820 830 840

GSDDSSKDPI DVNYEKLKTD IKVVDRDSEE AEIIRKYVKN THATTHNAYD LEVIDIFKIE

850 860 870 880 890 900

REGECQRYKP FKQLHNRRLL WHGSRTTNFA GILSQGLRIA PPEAPVTGYM FGKGIYFADM

910 920 930 940 950 960

```
VSKSANYCHT SQGDPIGLIL LGEVALGNMY ELKHASHISK LPKGKHSVKG LGKTTPDPSA
       970        980        990       1000       1010
NISLDGVDVP LGTGISSGVN DTSLLYNEYI VYDIAQVNLK YLLKLKFNFK TSLW
```

[0068] The following domains have been identified in poly [ADP-ribose] polymerase 1:

Residues	Length	Domain ID
1	1	initiator methionine
2-1014	1013	poly [ADP-ribose] polymerase 1

[0069] Poly [ADP-ribose] polymerase 1can be cleaved by many caspases in vitro and is one of the main cleavage targets of caspase-3 in vivo. The cleavage occurs between Asp(214) and Gly(215), which separates PARP's N-terminal DNA binding domain (24 kDa) from its C-terminal catalytic domain (89 kDa). Suitable assays may recognize only the large fragment of poly [ADP-ribose] polymerase 1 (89 kDa) but not the full length poly [ADP-ribose] polymerase 1, may recognize only the small fragment of poly [ADP-ribose] polymerase 1 (24 kDa) but not the full length poly [ADP-ribose] polymerase 1, may recognize only full length poly [ADP-ribose] polymerase 1, or may recognize one fragment and the full length full length poly [ADP-ribose] polymerase 1.

[0070] As used herein, the term "cyclin-dependent kinase inhibitor 1" refers to one or more polypeptides present in a biological sample that are derived from the cyclin-dependent kinase inhibitor 1 precursor (Swiss-Prot P38936 (SEQ ID NO: 8)).

```
        10         20         30         40         50         60
MSEPAGDVRQ NPCGSKACRR LFGPVDSEQL SRDCDALMAG CIQEARERWN FDFVTETPLE
        70         80         90        100        110        120
GDFAWERVRG LGLPKLYLPT GPRRGRDELG GGRRPGTSPA LLQGTAEEDH VDLSLSCTLV
       130        140        150        160
PRSGEQAEGS PGGPGDSQGR KRRQTSMTDF YHSKRRLIFS KRKP
```

[0071] The following domains have been identified in cyclin-dependent kinase inhibitor 1:

Residues	Length	Domain

1	1	initiator methionine
2-164	163	cyclin-dependent kinase inhibitor 1

[0072] As used herein, the term "cadherin-5" refers to one or more polypeptides present in a biological sample that are derived from the cadherin-5 precursor (Swiss-Prot P33151 (SEQ ID NO: 9)).

```
        10         20         30         40         50         60
MQRLMMLLAT SGACLGLLAV AAVAAAGANP AQRDTHSLLP THRRQKRDWI WNQMHIDEEK
        70         80         90        100        110        120
NTSLPHHVGK IKSSVSRKNA KYLLKGEYVG KVFRVDAETG DVFAIERLDR ENISEYHLTA
       130        140        150        160        170        180
VIVDKDTGEN LETPSSFTIK VHDVNDNWPV FTHRLFNASV PESSAVGTSV ISVTAVDADD
       190        200        210        220        230        240
PTVGDHASVM YQILKGKEYF AIDNSGRIIT ITKSLDREKQ ARYEIVVEAR DAQGLRGDSG
       250        260        270        280        290        300
TATVLVTLQD INDNFPFFTQ TKYTFVVPED TRVGTSVGSL FVEDPDEPQN RMTKYSILRG
       310        320        330        340        350        360
DYQDAFTIET NPAHNEGIIK PMKPLDYEYI QQYSFIVEAT DPTIDLRYMS PPAGNRAQVI
       370        380        390        400        410        420
INITDVDEPP IFQQPFYHFQ LKENQKKPLI GTVLAMDPDA ARHSIGYSIR RTSDKGQFFR
       430        440        450        460        470        480
VTKKGDIYNE KELDREVYPW YNLTVEAKEL DSTGTPTGKE SIVQVHIEVL DENDNAPEFA
       490        500        510        520        530        540
KPYQPKVCEN AVHGQLVLQI SAIDKDITPR NVKFKFTLNT ENNFTLTDNH DNTANITVKY
       550        560        570        580        590        600
GQFDREHTKV HFLPVVISDN GMPSRTGTST LTVAVCKCNE QGEFTFCEDM AAQVGVSIQA
       610        620        630        640        650        660
VVAILLCILT ITVITLLIFL RRRLRKQARA HGKSVPEIHE QLVTYDEEGG GEMDTTSYDV
       670        680        690        700        710        720
```

```
SVLNSVRRGG AKPPRPALDA RPSLYAQVQK PPRHAPGAHG GPGEMAAMIE VKKDEADHDG
       730        740        750        760        770        780
DGPPYDTLHI YGYEGSESIA ESLSSLGTDS SDSDVDYDFL NDWGPRFKML AELYGSDPRE

ELLY
```

[0073] Most preferably, the cadherin-5 assay detects one or more soluble forms of cadherin-5. Cadherin-5 is a single-pass type I membrane protein having a large extracellular domain, most or all of which is present in soluble forms of cadherin-5 generated either through alternative splicing event which deletes all or a portion of the transmembrane domain, or by proteolysis of the membrane-bound form. In the case of an immunoassay, one or more antibodies that bind to epitopes within this extracellular domain may be used to detect these soluble form(s). The following domains have been identified in cadherin-5:

Residues	Length	Domain ID
1-25	251	signal sequence
26-47	22	pro-peptide
48-784	737	cadherin-5
48-599	522	extracellular
600-620	21	transmembrane
621-784	164	cytoplasmic

[0074] As used herein, the term “Myoglobin” refers to one or polypeptides present in a biological sample that are derived from the Myoglobin precursor (Swiss-Prot P02144 (SEQ ID NO: 10)).

```
        10         20         30         40         50         60
MGLSDGEWQL VLNVWGKVEA DIPGHGQEVL IRLFKGHPET LEKFDKFKHL KSEDEMKASE
        70         80         90        100        110        120
DLKKHGATVL TALGGILKKK GHHEAEIKPL AQSHATKHKI PVKYLEFISE CIIQVLQSKH
       130        140        150
PGDFGADAQG AMNKALELFR KDMASNYKEL GFQG
```

[0075] The following domains have been identified in Myoglobin:

Residues	Length	Domain ID
1	1	Initiator Methionine
2-154	153	Myoglobin

[0076] As used herein, the term "Apolipoprotein A-II" refers to one or polypeptides present in a biological sample that are derived from the Apolipoprotein A-II precursor (Swiss-Prot P02652 (SEQ ID NO: 11)).

```
        10          20          30          40          50          60
MKLLAATVLL LTICSLEGAL VRRQAKEPCV ESLVSQYFQT VTDYGKDLME KVKSPELQAE
        70          80          90         100
AKSYFEKSKE QLTPLIKKAG TELVNFLSYF VELGTQPATQ
```

[0077] The following domains have been identified in Apolipoprotein A-II:

Residues	Length	Domain ID
1-18	18	Signal sequence
19-23	5	Propeptide
24-100	77	Apolipoprotein A-II
24-99	76	Apolipoprotein A-II(1-76)

[0078] As used herein, the term "Mucin-16" refers to one or polypeptides present in a biological sample that are derived from the Mucin-16 precursor (Swiss-Prot Q8WXI7 (SEQ ID NO: 12)).

```
        10          20          30          40          50          60
MLKPSGLPGS SSPTRSLMTG SRSTKATPEM DSGLTGATLS PKTSTGAIVV TEHTLPFTSP
        70          80          90         100         110         120
DKTLASPTSS VVGRTTQSLG VMSSALPEST SRGMTHSEQR TSPSLSPQVN GTPSRNYPAT
       130         140         150         160         170         180
SMVSGLSSPR TRTSSTEGNF TKEASTYTLT VETTSGPVTE KYTVPTETST TEGDSTETPW
```

```
       190        200        210        220        230        240
DTRYIPVKIT SPMKTFADST ASKENAPVSM TPAETTVTDS HTPGRTNPSF GTLYSSFLDL
       250        260        270        280        290        300
SPKGTPNSRG ETSLELILST TGYPFSSPEP GSAGHSRIST SAPLSSSASV LDNKISETSI
       310        320        330        340        350        360
FSGQSLTSPL SPGVPEARAS TMPNSAIPFS MTLSNAETSA ERVRSTISSL GTPSISTKQT
       370        380        390        400        410        420
AETILTFHAF AETMDIPSTH IAKTLASEWL GSPGTLGGTS TSALTTTSPS TTLVSEETNT
       430        440        450        460        470        480
HHSTSGKETE GTLNTSMTPL ETSAPGEESE MTATLVPTLG FTTLDSKIRS PSQVSSSHPT
       490        500        510        520        530        540
RELRTTGSTS GRQSSSTAAH GSSDILRATT SSTSKASSWT SESTAQQFSE PQHTQWVETS
       550        560        570        580        590        600
PSMKTERPPA STSVAAPITT SVPSVVSGFT TLKTSSTKGI WLEETSADTL IGESTAGPTT
       610        620        630        640        650        660
HQFAVPTGIS MTGGSSTRGS QGTTHLLTRA TASSETSADL TLATNGVPVS VSPAVSKTAA
       670        680        690        700        710        720
GSSPPGGTKP SYTMVSSVIP ETSSLQSSAF REGTSLGLTP LNTRHPFSSP EPDSAGHTKI
       730        740        750        760        770        780
STSIPLLSSA SVLEDKVSAT STFSHHKATS SITTGTPEIS TKTKPSSAVL SSMTLSNAAT
       790        800        810        820        830        840
SPERVRNATS PLTHPSPSGE ETAGSVLTLS TSAETTDSPN IHPTGTLTSE SSESPSTLSL
       850        860        870        880        890        900
PSVSGVKTTF SSSTPSTHLF TSGEETEETS NPSVSQPETS VSRVRTTLAS TSVPTPVFPT
       910        920        930        940        950        960
MDTWPTRSAQ FSSSHLVSEL RATSSTSVTN STGSALPKIS HLTGTATMSQ TNRDTFNDSA
       970        980        990       1000       1010       1020
APQSTTWPET SPRFKTGLPS ATTTVSTSAT SLSATVMVSK FTSPATSSME ATSIREPSTT
```

```
      1030       1040       1050       1060       1070       1080
ILTTETTNGP GSMAVASTNI PIGKGYITEG RLDTSHLPIG TTASSETSMD FTMAKESVSM
      1090       1100       1110       1120       1130       1140
SVSPSQSMDA AGSSTPGRTS QFVDTFSDDV YHLTSREITI PRDGTSSALT PQMTATHPPS
      1150       1160       1170       1180       1190       1200
PDPGSARSTW LGILSSSPSS PTPKVTMSST FSTQRVTTSM IMDTVETSRW NMPNLPSTTS
      1210       1220       1230       1240       1250       1260
LTPSNIPTSG AIGKSTLVPL DTPSPATSLE ASEGGLPTLS TYPESTNTPS IHLGAHASSE
      1270       1280       1290       1300       1310       1320
SPSTIKLTMA SVVKPGSYTP LTFPSIETHI HVSTARMAYS SGSSPEMTAP GETNTGSTWD
      1330       1340       1350       1360       1370       1380
PTTYITTTDP KDTSSAQVST PHSVRTLRTT ENHPKTESAT PAAYSGSPKI SSSPNLTSPA
      1390       1400       1410       1420       1430       1440
TKAWTITDTT EHSTQLHYTK LAEKSSGFET QSAPGPVSVV IPTSPTIGSS TLELTSDVPG
      1450       1460       1470       1480       1490       1500
EPLVLAPSEQ TTITLPMATW LSTSLTEEMA STDLDISSPS SPMSTFAIFP PMSTPSHELS
      1510       1520       1530       1540       1550       1560
KSEADTSAIR NTDSTTLDQH LGIRSLGRTG DLTTVPITPL TTTWTSVIEH STQAQDTLSA
      1570       1580       1590       1600       1610       1620
TMSPTHVTQS LKDQTSIPAS ASPSHLTEVY PELGTQGRSS SEATTFWKPS TDTLSREIET
      1630       1640       1650       1660       1670       1680
GPTNIQSTPP MDNTTTGSSS SGVTLGIAHL PIGTSSPAET STNMALERRS STATVSMAGT
      1690       1700       1710       1720       1730       1740
MGLLVTSAPG RSISQSLGRV SSVLSESTTE GVTDSSKGSS PRLNTQGNTA LSSSLEPSYA
      1750       1760       1770       1780       1790       1800
EGSQMSTSIP LTSSPTTPDV EFIGGSTFWT KEVTTVMTSD ISKSSARTES SSATLMSTAL
      1810       1820       1830       1840       1850       1860
GSTENTGKEK LRTASMDLPS PTPSMEVTPW ISLTLSNAPN TTDSLDLSHG VHTSSAGTLA
```

1870 1880 1890 1900 1910 1920

TDRSLNTGVT RASRLENGSD TSSKSLSMGN STHTSMTDTE KSEVSSSIHP RPETSAPGAE

1930 1940 1950 1960 1970 1980

TTLTSTPGNR AISLTLPFSS IPVEEVISTG ITSGPDINSA PMTHSPITPP TIVWTSTGTI

1990 2000 2010 2020 2030 2040

EQSTQPLHAV SSEKVSVQTQ STPYVNSVAV SASPTHENSV SSGSSTSSPY SSASLESLDS

2050 2060 2070 2080 2090 2100

TISRRNAITS WLWDLTTSLP TTTWPSTSLS EALSSGHSGV SNPSSTTTEF PLFSAASTSA

2110 2120 2130 2140 2150 2160

AKQRNPETET HGPQNTAAST LNTDASSVTG LSETPVGASI SSEVPLPMAI TSRSDVSGLT

2170 2180 2190 2200 2210 2220

SESTANPSLG TASSAGTKLT RTISLPTSES LVSFRMNKDP WTVSIPLGSH PTTNTETSIP

2230 2240 2250 2260 2270 2280

VNSAGPPGLS TVASDVIDTP SDGAESIPTV SFSPSPDTEV TTISHFPEKT THSFRTISSL

2290 2300 2310 2320 2330 2340

THELTSRVTP IPGDWMSSAM STKPTGASPS ITLGERRTIT SAAPTTSPIV LTASFTETST

2350 2360 2370 2380 2390 2400

VSLDNETTVK TSDILDARKT NELPSDSSSS SDLINTSIAS STMDVTKTAS ISPTSISGMT

2410 2420 2430 2440 2450 2460

ASSSPSLFSS DRPQVPTSTT ETNTATSPSV SSNTYSLDGG SNVGGTPSTL PPFTITHPVE

2470 2480 2490 2500 2510 2520

TSSALLAWSR PVRTFSTMVS TDTASGENPT SSNSVVTSVP APGTWASVGS TTDLPAMGFL

2530 2540 2550 2560 2570 2580

KTSPAGEAHS LLASTIEPAT AFTPHLSAAV VTGSSATSEA SLLTTSESKA IHSSPQTPTT

2590 2600 2610 2620 2630 2640

PTSGANWETS ATPESLLVVT ETSDTTLTSK ILVTDTILFS TVSTPPSKFP STGTLSGASF

2650 2660 2670 2680 2690 2700

PTLLPDTPAI PLTATEPTSS LATSFDSTPL VTIASDSLGT VPETTLTMSE TSNGDALVLK

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      2710       2720       2730       2740       2750       2760
TVSNPDRSIP GITIQGVTES PLHPSSTSPS KIVAPRNTTY EGSITVALST LPAGTTGSLV
      2770       2780       2790       2800       2810       2820
FSQSSENSET TALVDSSAGL ERASVMPLTT GSQGMASSGG IRSGSTHSTG TKTFSSLPLT
      2830       2840       2850       2860       2870       2880
MNPGEVTAMS EITTNRLTAT QSTAPKGIPV KPTSAESGLL TPVSASSSPS KAFASLTTAP
      2890       2900       2910       2920       2930       2940
PSTWGIPQST LTFEFSEVPS LDTKSASLPT PGQSLNTIPD SDASTASSSL SKSPEKNPRA
      2950       2960       2970       2980       2990       3000
RMMTSTKAIS ASSFQSTGFT ETPEGSASPS MAGHEPRVPT SGTGDPRYAS ESMSYPDPSK
      3010       3020       3030       3040       3050       3060
ASSAMTSTSL ASKLTTLFST GQAARSGSSS SPISLSTEKE TSFLSPTAST SRKTSLFLGP
      3070       3080       3090       3100       3110       3120
SMARQPNILV HLQTSALTLS PTSTLNMSQE EPPELTSSQT IAEEEGTTAE TQTLTFTPSE
      3130       3140       3150       3160       3170       3180
TPTSLLPVSS PTEPTARRKS SPETWASSIS VPAKTSLVET TDGTLVTTIK MSSQAAQGNS
      3190       3200       3210       3220       3230       3240
TWPAPAEETG TSPAGTSPGS PEVSTTLKIM SSKEPSISPE IRSTVRNSPW KTPETTVPME
      3250       3260       3270       3280       3290       3300
TTVEPVTLQS TALGSGSTSI SHLPTGTTSP TKSPTENMLA TERVSLSPSP PEAWTNLYSG
      3310       3320       3330       3340       3350       3360
TPGGTRQSLA TMSSVSLESP TARSITGTGQ QSSPELVSKT TGMEFSMWHG STGGTTGDTH
      3370       3380       3390       3400       3410       3420
VSLSTSSNIL EDPVTSPNSV SSLTDKSKHK TETWVSTTAI PSTVLNNKIM AAEQQTSRSV
      3430       3440       3450       3460       3470       3480
DEAYSSTSSW SDQTSGSDIT LGASPDVTNT LYITSTAQTT SLVSLPSGDQ GITSLTNPSG
      3490       3500       3510       3520       3530       3540
GKTSSASSVT SPSIGLETLR ANVSAVKSDI APTAGHLSQT SSPAEVSILD VTTAPTPGIS
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      3550       3560       3570       3580       3590       3600
TTITTMGTNS ISTTTPNPEV GMSTMDSTPA TERRTTSTEH PSTWSSTAAS DSWTVTDMTS
      3610       3620       3630       3640       3650       3660
NLKVARSPGT ISTMHTTSFL ASSTELDSMS TPHGRITVIG TSLVTPSSDA SAVKTETSTS
      3670       3680       3690       3700       3710       3720
ERTLSPSDTT ASTPISTFSR VQRMSISVPD ILSTSWTPSS TEAEDVPVSM VSTDHASTKT
      3730       3740       3750       3760       3770       3780
DPNTPLSTFL FDSLSTLDWD TGRSLSSATA TTSAPQGATT PQELTLETMI SPATSQLPFS
      3790       3800       3810       3820       3830       3840
IGHITSAVTP AAMARSSGVT FSRPDPTSKK AEQTSTQLPT TTSAHPGQVP RSAATTLDVI
      3850       3860       3870       3880       3890       3900
PHTAKTPDAT FQRQGQTALT TEARATSDSW NEKEKSTPSA PWITEMMNSV SEDTIKEVTS
      3910       3920       3930       3940       3950       3960
SSSVLKDPEY AGHKLGIWDD FIPKFGKAAH MRELPLLSPP QDKEAIHPST NTVETTGWVT
      3970       3980       3990       4000       4010       4020
SSEHASHSTI PAHSASSKLT SPVVTTSTRE QAIVSMSTTT WPESTRARTE PNSFLTIELR
      4030       4040       4050       4060       4070       4080
DVSPYMDTSS TTQTSIISSP GSTAITKGPR TEITSSKRIS SSFLAQSMRS SDSPSEAITR
      4090       4100       4110       4120       4130       4140
LSNFPAMTES GGMILAMQTS PPGATSLSAP TLDTSATASW TGTPLATTQR FTYSEKTTLF
      4150       4160       4170       4180       4190       4200
SKGPEDTSQP SPPSVEETSS SSSLVPIHAT TSPSNILLTS QGHSPSSTPP VTSVFLSETS
      4210       4220       4230       4240       4250       4260
GLGKTTDMSR ISLEPGTSLP PNLSSTAGEA LSTYEASRDT KAIHHSADTA VTNMEATSSE
      4270       4280       4290       4300       4310       4320
YSPIPGHTKP SKATSPLVTS HIMGDITSST SVFGSSETTE IETVSSVNQG LQERSTSQVA
      4330       4340       4350       4360       4370       4380
SSATETSTVI THVSSGDATT HVTKTQATFS SGTSISSPHQ FITSTNTFTD VSTNPSTSLI
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      4390       4400       4410       4420       4430       4440
MTESSGVTIT TQTGPTGAAT QGPYLLDTST MPYLTETPLA VTPDFMQSEK TTLISKGPKD
      4450       4460       4470       4480       4490       4500
VTWTSPPSVA ETSYPSSLTP FLVTTIPPAT STLQGQHTSS PVSATSVLTS GLVKTTDMLN
      4510       4520       4530       4540       4550       4560
TSMEPVTNSP QNLNNPSNEI LATLAATTDI ETIHPSINKA VTNMGTASSA HVLHSTLPVS
      4570       4580       4590       4600       4610       4620
SEPSTATSPM VPASSMGDAL ASISIPGSET TDIEGEPTSS LTAGRKENST LQEMNSTTES
      4630       4640       4650       4660       4670       4680
NIILSNVSVG AITEATKMEV PSFDATFIPT PAQSTKFPDI FSVASSRLSN SPPMTISTHM
      4690       4700       4710       4720       4730       4740
TTTQTGSSGA TSKIPLALDT STLETSAGTP SVVTEGFAHS KITTAMNNDV KDVSQTNPPF
      4750       4760       4770       4780       4790       4800
QDEASSPSSQ APVLVTTLPS SVAFTPQWHS TSSPVSMSSV LTSSLVKTAG KVDTSLETVT
      4810       4820       4830       4840       4850       4860
SSPQSMSNTL DDISVTSAAT TDIETTHPSI NTVVTNVGTT GSAFESHSTV SAYPEPSKVT
      4870       4880       4890       4900       4910       4920
SPNVTTSTME DTTISRSIPK SSKTTRTETE TTSSLTPKLR ETSISQEITS STETSTVPYK
      4930       4940       4950       4960       4970       4980
ELTGATTEVS RTDVTSSSST SFPGPDQSTV SLDISTETNT RLSTSPIMTE SAEITITTQT
      4990       5000       5010       5020       5030       5040
GPHGATSQDT FTMDPSNTTP QAGIHSAMTH GFSQLDVTTL MSRIPQDVSW TSPPSVDKTS
      5050       5060       5070       5080       5090       5100
SPSSFLSSPA MTTPSLISST LPEDKLSSPM TSLLTSGLVK ITDILRTRLE PVTSSLPNFS
      5110       5120       5130       5140       5150       5160
STSDKILATS KDSKDTKEIF PSINTEETNV KANNSGHESH SPALADSETP KATTQMVITT
      5170       5180       5190       5200       5210       5220
TVGDPAPSTS MPVHGSSETT NIKREPTYFL TPRLRETSTS QESSFPTDTS FLLSKVPTGT
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5230 5240 5250 5260 5270 5280

ITEVSSTGVN SSSKISTPDH DKSTVPPDTF TGEIPRVFTS SIKTKSAEMT ITTQASPPES

5290 5300 5310 5320 5330 5340

ASHSTLPLDT STTLSQGGTH STVTQGFPYS EVTTLMGMGP GNVSWMTTPP VEETSSVSSL

5350 5360 5370 5380 5390 5400

MSSPAMTSPS PVSSTSPQSI PSSPLPVTAL PTSVLVTTTD VLGTTSPESV TSSPPNLSSI

5410 5420 5430 5440 5450 5460

THERPATYKD TAHTEAAMHH STNTAVTNVG TSGSGHKSQS SVLADSETSK ATPLMSTTST

5470 5480 5490 5500 5510 5520

LGDTSVSTST PNISQTNQIQ TEPTASLSPR LRESSTSEKT SSTTETNTAF SYVPTGAITQ

5530 5540 5550 5560 5570 5580

ASRTEISSSR TSISDLDRPT IAPDISTGMI TRLFTSPIMT KSAEMTVTTQ TTTPGATSQG

5590 5600 5610 5620 5630 5640

ILPWDTSTTL FQGGTHSTVS QGFPHSEITT LRSRTPGDVS WMTTPPVEET SSGFSLMSPS

5650 5660 5670 5680 5690 5700

MTSPSPVSST SPESIPSSPL PVTALLTSVL VTTTNVLGTT SPETVTSSPP NLSSPTQERL

5710 5720 5730 5740 5750 5760

TTYKDTAHTE AMHASMHTNT AVANVGTSIS GHESQSSVPA DSHTSKATSP MGITFAMGDT

5770 5780 5790 5800 5810 5820

SVSTSTPAFF ETRIQTESTS SLIPGLRDTR TSEEINTVTE TSTVLSEVPT TTTTEVSRTE

5830 5840 5850 5860 5870 5880

VITSSRTTIS GPDHSKMSPY ISTETITRLS TFPFVTGSTE MAITNQTGPI GTISQATLTL

5890 5900 5910 5920 5930 5940

DTSSTASWEG THSPVTQRFP HSEETTTMSR STKGVSWQSP PSVEETSSPS SPVPLPAITS

5950 5960 5970 5980 5990 6000

HSSLYSAVSG SSPTSALPVT SLLTSGRRKT IDMLDTHSEL VTSSLPSASS FSGEILTSEA

6010 6020 6030 6040 6050 6060

STNTETIHFS ENTAETNMGT TNSMHKLHSS VSIHSQPSGH TPPKVTGSMM EDAIVSTSTP

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      6070       6080       6090       6100       6110       6120
GSPETKNVDR DSTSPLTPEL KEDSTALVMN STTESNTVFS SVSLDAATEV SRAEVTYYDP
      6130       6140       6150       6160       6170       6180
TFMPASAQST KSPDISPEAS SSHSNSPPLT ISTHKTIATQ TGPSGVTSLG QLTLDTSTIA
      6190       6200       6210       6220       6230       6240
TSAGTPSART QDFVDSETTS VMNNDLNDVL KTSPFSAEEA NSLSSQAPLL VTTSPSPVTS
      6250       6260       6270       6280       6290       6300
TLQEHSTSSL VSVTSVPTPT LAKITDMDTN LEPVTRSPQN LRNTLATSEA TTDTHTMHPS
      6310       6320       6330       6340       6350       6360
INTAMANVGT TSSPNEFYFT VSPDSDPYKA TSAVVITSTS GDSIVSTSMP RSSAMKKIES
      6370       6380       6390       6400       6410       6420
ETTFSLIFRL RETSTSQKIG SSSDTSTVFD KAFTAATTEV SRTELTSSSR TSIQGTEKPT
      6430       6440       6450       6460       6470       6480
MSPDTSTRSV TMLSTFAGLT KSEERTIATQ TGPHRATSQG TLTWDTSITT SQAGTHSAMT
      6490       6500       6510       6520       6530       6540
HGFSQLDLST LTSRVPEYIS GTSPPSVEKT SSSSSLLSLP AITSPSPVPT TLPESRPSSP
      6550       6560       6570       6580       6590       6600
VHLTSLPTSG LVKTTDMLAS VASLPPNLGS TSHKIPTTSE DIKDTEKMYP STNIAVTNVG
      6610       6620       6630       6640       6650       6660
TTTSEKESYS SVPAYSEPPK VTSPMVTSFN IRDTIVSTSM PGSSEITRIE MESTFSVAHG
      6670       6680       6690       6700       6710       6720
LKGTSTSQDP IVSTEKSAVL HKLTTGATET SRTEVASSRR TSIPGPDHST ESPDISTEVI
      6730       6740       6750       6760       6770       6780
PSLPISLGIT ESSNMTIITR TGPPLGSTSQ GTFTLDTPTT SSRAGTHSMA TQEFPHSEMT
      6790       6800       6810       6820       6830       6840
TVMNKDPEIL SWTIPPSIEK TSFSSSLMPS PAMTSPPVSS TLPKTIHTTP SPMTSLLTPS
      6850       6860       6870       6880       6890       6900
LVMTTDTLGT SPEPTTSSPP NLSSTSHVIL TTDEDTTAIE AMHPSTSTAA TNVETTCSGH
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      6910       6920       6930       6940       6950       6960
GSQSSVLTDS EKTKATAPMD TTSTMGHTTV STSMSVSSET TKIKRESTYS LTPGLRETSI
      6970       6980       6990       7000       7010       7020
SQNASFSTDT SIVLSEVPTG TTAEVSRTEV TSSGRTSIPG PSQSTVLPEI STRTMTRLFA
      7030       7040       7050       7060       7070       7080
SPTMTESAEM TIPTQTGPSG STSQDTLTLD TSTTKSQAKT HSTLTQRFPH SEMTTLMSRG
      7090       7100       7110       7120       7130       7140
PGDMSWQSSP SLENPSSLPS LLSLPATTSP PPISSTLPVT ISSSPLPVTS LLTSSPVTTT
      7150       7160       7170       7180       7190       7200
DMLHTSPELV TSSPPKLSHT SDERLTTGKD TTNTEAVHPS TNTAASNVEI PSFGHESPSS
      7210       7220       7230       7240       7250       7260
ALADSETSKA TSPMFITSTQ EDTTVAISTP HFLETSRIQK ESISSLSPKL RETGSSVETS
      7270       7280       7290       7300       7310       7320
SAIETSAVLS EVSIGATTEI SRTEVTSSSR TSISGSAEST MLPEISTTRK IIKFPTSPIL
      7330       7340       7350       7360       7370       7380
AESSEMTIKT QTSPPGSTSE STFTLDTSTT PSLVITHSTM TQRLPHSEIT TLVSRGAGDV
      7390       7400       7410       7420       7430       7440
PRPSSLPVEE TSPPSSQLSL SAMISPSPVS STLPASSHSS SASVTSPLTP GQVKTTEVLD
      7450       7460       7470       7480       7490       7500
ASAEPETSSP PSLSSTSVEI LATSEVTTDT EKIHPFPNTA VTKVGTSSSG HESPSSVLPD
      7510       7520       7530       7540       7550       7560
SETTKATSAM GTISIMGDTS VSTLTPALSN TRKIQSEPAS SLTTRLRETS TSEETSLATE
      7570       7580       7590       7600       7610       7620
ANTVLSKVST GATTEVSRTE AISFSRTSMS GPEQSTMSQD ISIGTIPRIS ASSVLTESAK
      7630       7640       7650       7660       7670       7680
MTITTQTGPS ESTLESTLNL NTATTPSWVE THSIVIQGFP HPEMTTSMGR GPGGVSWPSP
      7690       7700       7710       7720       7730       7740
PFVKETSPPS SPLSLPAVTS PHPVSTTFLA HIPPSPLPVT SLLTSGPATT TDILGTSTEP
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      7750       7760       7770       7780       7790       7800
GTSSSSSLST TSHERLTTYK DTAHTEAVHP STNTGGTNVA TTSSGYKSQS SVLADSSPMC
      7810       7820       7830       7840       7850       7860
TTSTMGDTSV LTSTPAFLET RRIQTELASS LTPGLRESSG SEGTSSGTKM STVLSKVPTG
      7870       7880       7890       7900       7910       7920
ATTEISKEDV TSIPGPAQST ISPDISTRTV SWFSTSPVMT ESAEITMNTH TSPLGATTQG
      7930       7940       7950       7960       7970       7980
TSTLATSSTT SLTMTHSTIS QGFSHSQMST LMRRGPEDVS WMSPPLLEKT RPSFSLMSSP
      7990       8000       8010       8020       8030       8040
ATTSPSPVSS TLPESISSSP LPVTSLLTSG LAKTTDMLHK SSEPVTNSPA NLSSTSVEIL
      8050       8060       8070       8080       8090       8100
ATSEVTTDTE KTHPSSNRTV TDVGTSSSGH ESTSFVLADS QTSKVTSPMV ITSTMEDTSV
      8110       8120       8130       8140       8150       8160
STSTPGFFET SRIQTEPTSS LTLGLRKTSS SEGTSLATEM STVLSGVPTG ATAEVSRTEV
      8170       8180       8190       8200       8210       8220
TSSSRTSISG FAQLTVSPET STETITRLPT SSIMTESAEM MIKTQTDPPG STPESTHTVD
      8230       8240       8250       8260       8270       8280
ISTTPNWVET HSTVTQRFSH SEMTTLVSRS PGDMLWPSQS SVEETSSASS LLSLPATTSP
      8290       8300       8310       8320       8330       8340
SPVSSTLVED FPSASLPVTS LLTPGLVITT DRMGISREPG TSSTSNLSST SHERLTTLED
      8350       8360       8370       8380       8390       8400
TVDTEDMQPS THTAVTNVRT SISGHESQSS VLSDSETPKA TSPMGTTYTM GETSVSISTS
      8410       8420       8430       8440       8450       8460
DFFETSRIQI EPTSSLTSGL RETSSSERIS SATEGSTVLS EVPSGATTEV SRTEVISSRG
      8470       8480       8490       8500       8510       8520
TSMSGPDQFT ISPDISTEAI TRLSTSPIMT ESAESAITIE TGSPGATSEG TLTLDTSTTT
      8530       8540       8550       8560       8570       8580
FWSGTHSTAS PGFSHSEMTT LMSRTPGDVP WPSLPSVEEA SSVSSSLSSP AMTSTSFFSA
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8590 8600 8610 8620 8630 8640

LPESISSSPH PVTALLTLGP VKTTDMLRTS SEPETSSPPN LSSTSAEILA TSEVTKDREK

8650 8660 8670 8680 8690 8700

IHPSSNTPVV NVGTVIYKHL SPSSVLADLV TTKPTSPMAT TSTLGNTSVS TSTPAFPETM

8710 8720 8730 8740 8750 8760

MTQPTSSLTS GLREISTSQE TSSATERSAS LSGMPTGATT KVSRTEALSL GRTSTPGPAQ

8770 8780 8790 8800 8810 8820

STISPEISTE TITRISTPLT TTGSAEMTIT PKTGHSGASS QGTFTLDTSS RASWPGTHSA

8830 8840 8850 8860 8870 8880

ATHRSPHSGM TTPMSRGPED VSWPSRPSVE KTSPPSSLVS LSAVTSPSPL YSTPSESSHS

8890 8900 8910 8920 8930 8940

SPLRVTSLFT PVMMKTTDML DTSLEPVTTS PPSMNITSDE SLATSKATME TEAIQLSENT

8950 8960 8970 8980 8990 9000

AVTQMGTISA RQEFYSSYPG LPEPSKVTSP VVTSSTIKDI VSTTIPASSE ITRIEMESTS

9010 9020 9030 9040 9050 9060

TLTPTPRETS TSQEIHSATK PSTVPYKALT SATIEDSMTQ VMSSSRGPSP DQSTMSQDIS

9070 9080 9090 9100 9110 9120

SEVITRLSTS PIKAESTEMT ITTQTGSPGA TSRGTLTLDT STTFMSGTHS TASQGFSHSQ

9130 9140 9150 9160 9170 9180

MTALMSRTPG DVPWLSHPSV EEASSASFSL SSPVMTSSSP VSSTLPDSIH SSSLPVTSLL

9190 9200 9210 9220 9230 9240

TSGLVKTTEL LGTSSEPETS SPPNLSSTSA EILATTEVTT DTEKLEMTNV VTSGYTHESP

9250 9260 9270 9280 9290 9300

SSVLADSVTT KATSSMGITY PTGDTNVLTS TPAFSDTSRI QTKSKLSLTP GLMETSISEE

9310 9320 9330 9340 9350 9360

TSSATEKSTV LSSVPTGATT EVSRTEAISS SRTSIPGPAQ STMSSDTSME TITRISTPLT

9370 9380 9390 9400 9410 9420

RKESTDMAIT PKTGPSGATS QGTFTLDSSS TASWPGTHSA TTQRFPQSVV TTPMSRGPED

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      9430       9440       9450       9460       9470       9480
VSWPSPLSVE KNSPPSSLVS SSSVTSPSPL YSTPSGSSHS SPVPVTSLFT SIMMKATDML
      9490       9500       9510       9520       9530       9540
DASLEPETTS APNMNITSDE SLATSKATTE TEAIHVFENT AASHVETTSA TEELYSSSPG
      9550       9560       9570       9580       9590       9600
FSEPTKVISP VVTSSSIRDN MVSTTMPGSS GITRIEIESM SSLTPGLRET RTSQDITSST
      9610       9620       9630       9640       9650       9660
ETSTVLYKMS SGATPEVSRT EVMPSSRTSI PGPAQSTMSL DISDEVVTRL STSPIMTESA
      9670       9680       9690       9700       9710       9720
EITITTQTGY SLATSQVTLP LGTSMTFLSG THSTMSQGLS HSEMTNLMSR GPESLSWTSP
      9730       9740       9750       9760       9770       9780
RFVETTRSSS SLTSLPLTTS LSPVSSTLLD SSPSSPLPVT SLILPGLVKT TEVLDTSSEP
      9790       9800       9810       9820       9830       9840
KTSSSPNLSS TSVEIPATSE IMTDTEKIHP SSNTAVAKVR TSSSVHESHS SVLADSETTI
      9850       9860       9870       9880       9890       9900
TIPSMGITSA VDDTTVFTSN PAFSETRRIP TEPTFSLTPG FRETSTSEET TSITETSAVL
      9910       9920       9930       9940       9950       9960
YGVPTSATTE VSMTEIMSSN RTHIPDSDQS TMSPDIITEV ITRLSSSSMM SESTQMTITT
      9970       9980       9990      10000      10010      10020
QKSSPGATAQ STLTLATTTA PLARTHSTVP PRFLHSEMTT LMSRSPENPS WKSSPFVEKT
     10030      10040      10050      10060      10070      10080
SSSSSLLSLP VTTSPSVSST LPQSIPSSSF SVTSLLTPGM VKTTDTSTEP GTSLSPNLSG
     10090      10100      10110      10120      10130      10140
TSVEILAASE VTTDTEKIHP SSSMAVTNVG TTSSGHELYS SVSIHSEPSK ATYPVGTPSS
     10150      10160      10170      10180      10190      10200
MAETSISTSM PANFETTGFE AEPFSHLTSG FRKTNMSLDT SSVTPTNTPS SPGSTHLLQS
     10210      10220      10230      10240      10250      10260
SKTDFTSSAK TSSPDWPPAS QYTEIPVDII TPFNASPSIT ESTGITSFPE SRFTMSVTES
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10270 10280 10290 10300 10310 10320

THHLSTDLLP SAETISTGTV MPSLSEAMTS FATTGVPRAI SGSGSPFSRT ESGPGDATLS

10330 10340 10350 10360 10370 10380

TIAESLPSST PVPFSSSTFT TTDSSTIPAL HEITSSSATP YRVDTSLGTE SSTTEGRLVM

10390 10400 10410 10420 10430 10440

VSTLDTSSQP GRTSSTPILD TRMTESVELG TVTSAYQVPS LSTRLTRTDG IMEHITKIPN

10450 10460 10470 10480 10490 10500

EAAHRGTIRP VKGPQTSTSP ASPKGLHTGG TKRMETTTTA LKTTTTALKT TSRATLTTSV

10510 10520 10530 10540 10550 10560

YTPTLGTLTP LNASRQMAST ILTEMMITTP YVFPDVPETT SSLATSLGAE TSTALPRTTP

10570 10580 10590 10600 10610 10620

SVLNRESETT ASLVSRSGAE RSPVIQTLDV SSSEPDTTAS WVIHPAETIP TVSKTTPNFF

10630 10640 10650 10660 10670 10680

HSELDTVSST ATSHGADVSS AIPTNISPSE LDALTPLVTI SGTDTSTTFP TLTKSPHETE

10690 10700 10710 10720 10730 10740

TRTTWLTHPA ETSSTIPRTI PNFSHHESDA TPSIATSPGA ETSSAIPIMT VSPGAEDLVT

10750 10760 10770 10780 10790 10800

SQVTSSGTDR NMTIPTLTLS PGEPKTIASL VTHPEAQTSS AIPTSTISPA VSRLVTSMVT

10810 10820 10830 10840 10850 10860

SLAAKTSTTN RALTNSPGEP ATTVSLVTHP AQTSPTVPWT TSIFFHSKSD TTPSMTTSHG

10870 10880 10890 10900 10910 10920

AESSSAVPTP TVSTEVPGVV TPLVTSSRAV ISTTIPILTL SPGEPETTPS MATSHGEEAS

10930 10940 10950 10960 10970 10980

SAIPTPTVSP GVPGVVTSLV TSSRAVTSTT IPILTFSLGE PETTPSMATS HGTEAGSAVP

10990 11000 11010 11020 11030 11040

TVLPEVPGMV TSLVASSRAV TSTTLPTLTL SPGEPETTPS MATSHGAEAS STVPTVSPEV

11050 11060 11070 11080 11090 11100

PGVVTSLVTS SSGVNSTSIP TLILSPGELE TTPSMATSHG AEASSAVPTP TVSPGVSGVV

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     11110      11120      11130      11140      11150      11160
TPLVTSSRAV TSTTIPILTL SSSEPETTPS MATSHGVEAS SAVLTVSPEV PGMVTSLVTS
     11170      11180      11190      11200      11210      11220
SRAVTSTTIP TLTISSDEPE TTTSLVTHSE AKMISAIPTL AVSPTVQGLV TSLVTSSGSE
     11230      11240      11250      11260      11270      11280
TSAFSNLTVA SSQPETIDSW VAHPGTEASS VVPTLTVSTG EPFTNISLVT HPAESSSTLP
     11290      11300      11310      11320      11330      11340
RTTSRFSHSE LDTMPSTVTS PEAESSSAIS TTISPGIPGV LTSLVTSSGR DISATFPTVP
     11350      11360      11370      11380      11390      11400
ESPHESEATA SWVTHPAVTS TTVPRTTPNY SHSEPDTTPS IATSPGAEAT SDFPTITVSP
     11410      11420      11430      11440      11450      11460
DVPDMVTSQV TSSGTDTSIT IPTLTLSSGE PETTTSFITY SETHTSSAIP TLPVSPGASK
     11470      11480      11490      11500      11510      11520
MLTSLVISSG TDSTTTFPTL TETPYEPETT AIQLIHPAET NTMVPKTTPK FSHSKSDTTL
     11530      11540      11550      11560      11570      11580
PVAITSPGPE ASSAVSTTTI SPDMSDLVTS LVPSSGTDTS TTFPTLSETP YEPETTVTWL
     11590      11600      11610      11620      11630      11640
THPAETSTTV SGTIPNFSHR GSDTAPSMVT SPGVDTRSGV PTTTIPPSIP GVVTSQVTSS
     11650      11660      11670      11680      11690      11700
ATDTSTAIPT LTPSPGEPET TASSATHPGT QTGFTVPIRT VPSSEPDTMA SWVTHPPQTS
     11710      11720      11730      11740      11750      11760
TPVSRTTSSF SHSSPDATPV MATSPRTEAS SAVLTTISPG APEMVTSQIT SSGAATSTTV
     11770      11780      11790      11800      11810      11820
PTLTHSPGMP ETTALLSTHP RTGTSKTFPA STVFPQVSET TASLTIRPGA ETSTALPTQT
     11830      11840      11850      11860      11870      11880
TSSLFTLLVT GTSRVDLSPT ASPGVSAKTA PLSTHPGTET STMIPTSTLS LGLLETTGLL
     11890      11900      11910      11920      11930      11940
ATSSSAETST STLTLTVSPA VSGLSSASIT TDKPQTVTSW NTETSPSVTS VGPPEFSRTV
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     11950      11960      11970      11980      11990      12000
TGTTMTLIPS EMPTPPKTSH GEGVSPTTIL RTTMVEATNL ATTGSSPTVA KTTTTFNTLA
     12010      12020      12030      12040      12050      12060
GSLFTPLTTP GMSTLASESV TSRTSYNHRS WISTTSSYNR RYWTPATSTP VTSTFSPGIS
     12070      12080      12090      12100      12110      12120
TSSIPSSTAA TVPFMVPFTL NFTITNLQYE EDMRHPGSRK FNATERELQG LLKPLFRNSS
     12130      12140      12150      12160      12170      12180
LEYLYSGCRL ASLRPEKDSS AMAVDAICTH RPDPEDLGLD RERLYWELSN LTNGIQELGP
     12190      12200      12210      12220      12230      12240
YTLDRNSLYV NGFTHRSSMP TTSTPGTSTV DVGTSGTPSS SPSPTAAGPL LMPFTLNFTI
     12250      12260      12270      12280      12290      12300
TNLQYEEDMR RTGSRKFNTM ESVLQGLLKP LFKNTSVGPL YSGCRLTLLR PEKDGAATGV
     12310      12320      12330      12340      12350      12360
DAICTHRLDP KSPGLNREQL YWELSKLTND IEELGPYTLD RNSLYVNGFT HQSSVSTTST
     12370      12380      12390      12400      12410      12420
PGTSTVDLRT SGTPSSLSSP TIMAAGPLLV PFTLNFTITN LQYGEDMGHP GSRKFNTTER
     12430      12440      12450      12460      12470      12480
VLQGLLGPIF KNTSVGPLYS GCRLTSLRSE KDGAATGVDA ICIHHLDPKS PGLNRERLYW
     12490      12500      12510      12520      12530      12540
ELSQLTNGIK ELGPYTLDRN SLYVNGFTHR TSVPTTSTPG TSTVDLGTSG TPFSLPSPAT
     12550      12560      12570      12580      12590      12600
AGPLLVLFTL NFTITNLKYE EDMHRPGSRK FNTTERVLQT LLGPMFKNTS VGLLYSGCRL
     12610      12620      12630      12640      12650      12660
TLLRSEKDGA ATGVDAICTH RLDPKSPGLD REQLYWELSQ LTNGIKELGP YTLDRNSLYV
     12670      12680      12690      12700      12710      12720
NGFTHWIPVP TSSTPGTSTV DLGSGTPSSL PSPTAAGPLL VPFTLNFTIT NLQYEEDMHH
     12730      12740      12750      12760      12770      12780
PGSRKFNTTE RVLQGLLGPM FKNTSVGLLY SGCRLTLLRS EKDGAATGVD AICTHRLDPK
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12790 12800 12810 12820 12830 12840

SPGVDREQLY WELSQLTNGI KELGPYTLDR NSLYVNGFTH QTSAPNTSTP GTSTVDLGTS

12850 12860 12870 12880 12890 12900

GTPSSLPSPT SAGPLLVPFT LNFTITNLQY EEDMRHPGSR KFNTTERVLQ GLLKPLFKST

12910 12920 12930 12940 12950 12960

SVGPLYSGCR LTLLRSEKDG AATGVDAICT HRLDPKSPGV DREQLYWELS QLTNGIKELG

12970 12980 12990 13000 13010 13020

PYTLDRNSLY VNGFTHQTSA PNTSTPGTST VDLGTSGTPS SLPSPTSAGP LLVPFTLNFT

13030 13040 13050 13060 13070 13080

ITNLQYEEDM HHPGSRKFNT TERVLQGLLG PMFKNTSVGL LYSGCRLTLL RPEKNGAATG

13090 13100 13110 13120 13130 13140

MDAICSHRLD PKSPGLNREQ LYWELSQLTH GIKELGPYTL DRNSLYVNGF THRSSVAPTS

13150 13160 13170 13180 13190 13200

TPGTSTVDLG TSGTPSSLPS PTTAVPLLVP FTLNFTITNL QYGEDMRHPG SRKFNTTERV

13210 13220 13230 13240 13250 13260

LQGLLGPLFK NSSVGPLYSG CRLISLRSEK DGAATGVDAI CTHHLNPQSP GLDREQLYWQ

13270 13280 13290 13300 13310 13320

LSQMTNGIKE LGPYTLDRNS LYVNGFTHRS SGLTTSTPWT STVDLGTSGT PSPVPSPTTA

13330 13340 13350 13360 13370 13380

GPLLVPFTLN FTITNLQYEE DMHRPGSRKF NTTERVLQGL LSPIFKNSSV GPLYSGCRLT

13390 13400 13410 13420 13430 13440

SLRPEKDGAA TGMDAVCLYH PNPKRPGLDR EQLYWELSQL THNITELGPY SLDRDSLYVN

13450 13460 13470 13480 13490 13500

GFTHQNSVPT TSTPGTSTVY WATTGTPSSF PGHTEPGPLL IPFTFNFTIT NLHYEENMQH

13510 13520 13530 13540 13550 13560

PGSRKFNTTE RVLQGLLKPL FKNTSVGPLY SGCRLTSLRP EKDGAATGMD AVCLYHPNPK

13570 13580 13590 13600 13610 13620

RPGLDREQLY WELSQLTHNI TELGPYSLDR DSLYVNGFTH QNSVPTTSTP GTSTVYWATT

13630 13640 13650 13660 13670 13680

GTPSSFPGHT EPGPLLIPFT FNFTITNLHY EENMQHPGSR KFNTTERVLQ GLLKPLFKNT

13690 13700 13710 13720 13730 13740

SVGPLYSGCR LTLLRPEKHE AATGVDTICT HRVDPIGPGL DRERLYWELS QLTNSITELG

13750 13760 13770 13780 13790 13800

PYTLDRDSLY VNGFNPRSSV PTTSTPGTST VHLATSGTPS SLPGHTAPVP LLIPFTLNFT

13810 13820 13830 13840 13850 13860

ITNLHYEENM QHPGSRKFNT TERVLQGLLK PLFKNTSVGP LYSGCRLTLL RPEKHEAATG

13870 13880 13890 13900 13910 13920

VDTICTHRVD PIGPGLXXEX LYWELSXLTX XIXELGPYTL DRXSLYVNGF THXXSXPTTS

13930 13940 13950 13960 13970 13980

TPGTSTVXXG TSGTPSSXPX XTSAGPLLVP FTLNFTITNL QYEEDMHHPG SRKFNTTERV

13990 14000 14010 14020 14030 14040

LQGLLGPMFK NTSVGLLYSG CRLTLLRPEK NGAATGMDAI CSHRLDPKSP GLDREQLYWE

14050 14060 14070 14080 14090 14100

LSQLTHGIKE LGPYTLDRNS LYVNGFTHRS SVAPTSTPGT STVDLGTSGT PSSLPSPTTA

14110 14120 14130 14140 14150 14160

VPLLVPFTLN FTITNLQYGE DMRHPGSRKF NTTERVLQGL LGPLFKNSSV GPLYSGCRLI

14170 14180 14190 14200 14210 14220

SLRSEKDGAA TGVDAICTHH LNPQSPGLDR EQLYWQLSQM TNGIKELGPY TLDRNSLYVN

14230 14240 14250 14260 14270 14280

GFTHRSSGLT TSTPWTSTVD LGTSGTPSPV PSPTTAGPLL VPFTLNFTIT NLQYEEDMHR

14290 14300 14310 14320 14330 14340

PGSRKFNATE RVLQGLLSPI FKNSSVGPLY SGCRLTSLRP EKDGAATGMD AVCLYHPNPK

14350 14360 14370 14380 14390 14400

RPGLDREQLY WELSQLTHNI TELGPYSLDR DSLYVNGFTH QSSMTTTRTP DTSTMHLATS

14410 14420 14430 14440 14450 14460

RTPASLSGPT TASPLLVLFT INCTITNLQY EEDMRRTGSR KFNTMESVLQ GLLKPLFKNT

14470 14480 14490 14500 14510 14520

SVGPLYSGCR LTLLRPKKDG AATGVDAICT HRLDPKSPGL NREQLYWELS KLTNDIEELG

14530 14540 14550 14560 14570 14580

PYTLDRNSLY VNGFTHQSSV STTSTPGTST VDLRTSGTPS SLSSPTIMXX XPLLXPFTXN

14590 14600 14610 14620 14630 14640

XTITNLXXXX XMXXPGSRKF NTTERVLQGL LRPLFKNTSV SSLYSGCRLT LLRPEKDGAA

14650 14660 14670 14680 14690 14700

TRVDAACTYR PDPKSPGLDR EQLYWELSQL THSITELGPY TLDRVSLYVN GFNPRSSVPT

14710 14720 14730 14740 14750 14760

TSTPGTSTVH LATSGTPSSL PGHTXXXPLL XPFTXNXTIT NLXXXXXMXX PGSRKFNTTE

14770 14780 14790 14800 14810 14820

RVLQGLLKPL FRNSSLEYLY SGCRLASLRP EKDSSAMAVD AICTHRPDPE DLGLDRERLY

14830 14840 14850 14860 14870 14880

WELSNLTNGI QELGPYTLDR NSLYVNGFTH RSSGLTTSTP WTSTVDLGTS GTPSPVPSPT

14890 14900 14910 14920 14930 14940

TAGPLLVPFT LNFTITNLQY EEDMHRPGSR RFNTTERVLQ GLLTPLFKNT SVGPLYSGCR

14950 14960 14970 14980 14990 15000

LTLLRPEKQE AATGVDTICT HRVDPIGPGL DRERLYWELS QLTNSITELG PYTLDRDSLY

15010 15020 15030 15040 15050 15060

VNGFNPWSSV PTTSTPGTST VHLATSGTPS SLPGHTAPVP LLIPFTLNFT ITDLHYEENM

15070 15080 15090 15100 15110 15120

QHPGSRKFNT TERVLQGLLK PLFKSTSVGP LYSGCRLTLL RPEKHGAATG VDAICTLRLD

15130 15140 15150 15160 15170 15180

PTGPGLDRER LYWELSQLTN SVTELGPYTL DRDSLYVNGF THRSSVPTTS IPGTSAVHLE

15190 15200 15210 15220 15230 15240

TSGTPASLPG HTAPGPLLVP FTLNFTITNL QYEEDMRHPG SRKFSTTERV LQGLLKPLFK

15250 15260 15270 15280 15290 15300

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15370 15380 15390 15400 15410 15420

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15430 15440 15450 15460 15470 15480

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15490 15500 15510 15520 15530 15540

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15550 15560 15570 15580 15590 15600

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15610 15620 15630 15640 15650 15660

WELSKLTRGI IELGPYLLDR GSLYVNGFTH RTSVPTTSTP GTSTVDLGTS GTPFSLPSPA

15670 15680 15690 15700 15710 15720

XXXPLLXPFT XNXTITNLXX XXXMXXPGSR KFNTTERVLQ TLLGPMFKNT SVGLLYSGCR

15730 15740 15750 15760 15770 15780

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15790 15800 15810 15820 15830 15840

VNGFTHWIPV PTSSTPGTST VDLGSGTPSS LPSPTTAGPL LVPFTLNFTI TNLKYEEDMH

15850 15860 15870 15880 15890 15900

CPGSRKFNTT ERVLQSLLGP MFKNTSVGPL YSGCRLTLLR SEKDGAATGV DAICTHRLDP

15910 15920 15930 15940 15950 15960

KSPGVDREQL YWELSQLTNG IKELGPYTLD RNSLYVNGFT HQTSAPNTST PGTSTVDLGT

15970 15980 15990 16000 16010 16020

SGTPSSLPSP TXXXPLLXPF TXNXTITNLX XXXXMXXPGS RKFNTTEXVL QGLLXPXFKN

16030 16040 16050 16060 16070 16080

XSVGXLYSGC RLTXLRXEKX GAATGXDAIC XHXXXPKXPG LXXEXLYWEL SXLTXXIXEL

16090 16100 16110 16120 16130 16140

GPYTLDRXSL YVNGFTHWIP VPTSSTPGTS TVDLGSGTPS SLPSPTTAGP LLVPFTLNFT

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16210 16220 16230 16240 16250 16260

VDAICTHRVD PKSPGVDREQ LYWELSQLTN GIKELGPYTL DRNSLYVNGF THQTSAPNTS

16270 16280 16290 16300 16310 16320

TPGTSTVXXG TSGTPSSXPX XTSAGPLLVP FTLNFTITNL QYEEDMHHPG SRKFNTTERV

16330 16340 16350 16360 16370 16380

LQGLLGPMFK NTSVGLLYSG CRLTLLRPEK NGATTGMDAI CTHRLDPKSP GLXXEXLYWE

16390 16400 16410 16420 16430 16440

LSXLTXXIXE LGPYTLDRXS LYVNGFTHXX SXPTTSTPGT STVXXGTSGT PSSXPXXTXX

16450 16460 16470 16480 16490 16500

XPLLXPFTXN XTITNLXXXX XMXXPGSRKF NTTERVLQGL LKPLFRNSSL EYLYSGCRLA

16510 16520 16530 16540 16550 16560

SLRPEKDSSA MAVDAICTHR PDPEDLGLDR ERLYWELSNL TNGIQELGPY TLDRNSLYVN

16570 16580 16590 16600 16610 16620

GFTHRSSMPT TSTPGTSTVD VGTSGTPSSS PSPTTAGPLL IPFTLNFTIT NLQYGEDMGH

16630 16640 16650 16660 16670 16680

PGSRKFNTTE RVLQGLLGPI FKNTSVGPLY SGCRLTSLRS EKDGAATGVD AICIHHLDPK

16690 16700 16710 16720 16730 16740

SPGLNRERLY WELSQLTNGI KELGPYTLDR NSLYVNGFTH RTSVPTTSTP GTSTVDLGTS

16750 16760 16770 16780 16790 16800

GTPFSLPSPA TAGPLLVLFT LNFTITNLKY EEDMHRPGSR KFNTTERVLQ TLLGPMFKNT

16810 16820 16830 16840 16850 16860

SVGLLYSGCR LTLLRSEKDG AATGVDAICT HRLDPKSPGL XXEXLYWELS XLTXXIXELG

16870 16880 16890 16900 16910 16920

PYTLDRXSLY VNGFTHXXSX PTTSTPGTST VXXGTSGTPS SXPXXTXXXP LLXPFTXNXT

16930 16940 16950 16960 16970 16980

ITNLXXXXXM XXPGSRKFNT TERVLQGLLR PVFKNTSVGP LYSGCRLTLL RPKKDGAATK

16990 17000 17010 17020 17030 17040

VDAICTYRPD PKSPGLDREQ LYWELSQLTH SITELGPYTQ DRDSLYVNGF THRSSVPTTS

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17110 17120 17130 17140 17150 17160

LQGLLTPLFK NTSVGPLYSG CRLTLLRPEK QEAATGVDTI CTHRVDPIGP GLDRERLYWE

17170 17180 17190 17200 17210 17220

LSQLTNSITE LGPYTLDRDS LYVDGFNPWS SVPTTSTPGT STVHLATSGT PSPLPGHTAP

17230 17240 17250 17260 17270 17280

VPLLIPFTLN FTITDLHYEE NMQHPGSRKF NTTERVLQGL LKPLFKSTSV GPLYSGCRLT

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17470 17480 17490 17500 17510 17520

SPGLXXEXLY WELSXLTXXI XELGPYTLDR XSLYVNGFTH XXSXPTTSTP GTSTVXXGTS

17530 17540 17550 17560 17570 17580

GTPSSXPXXT XXXPLLXPFT XNXTITNLXX XXXMXXPGSR KFNTTEXVLQ GLLXPXFKNX

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LQGLLXPXFK NXSVGXLYSG CRLTXLRXEK XGAATGXDAI CXHXXXPKXP GLXXEXLYWE

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18250 18260 18270 18280 18290 18300

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18370 18380 18390 18400 18410 18420

SVGPLYSGCR LTLLRPEKQE AATGVDTICT HRVDPIGPGL XXEXLYWELS XLTXXIXELG

18430 18440 18450 18460 18470 18480

PYTLDRXSLY VNGFTHXXSX PTTSTPGTST VXXGTSGTPS SXPXXTXXXP LLXPFTXNXT

18490 18500 18510 18520 18530 18540

ITNLXXXXXM XXPGSRKFNT TEXVLQGLLX PXFKNXSVGX LYSGCRLTXL RXEKXGAATG

18550 18560 18570 18580 18590 18600

XDAICXHXXX PKXPGLXXEX LYWELSXLTX XIXELGPYTL DRXSLYVNGF THRSSVPTTS

18610 18620 18630 18640 18650 18660

SPGTSTVHLA TSGTPSSLPG HTAPVPLLIP FTLNFTITNL HYEENMQHPG SRKFNTTERV

18670 18680 18690 18700 18710 18720

LQGLLKPLFK STSVGPLYSG CRLTLLRPEK HGAATGVDAI CTLRLDPTGP GLXXEXLYWE

18730 18740 18750 18760 18770 18780

LSXLTXXIXE LGPYTLDRXS LYVNGFTHXX SXPTTSTPGT STVXXGTSGT PSSXPXXTXX

18790 18800 18810 18820 18830 18840

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18850 18860 18870 18880 18890 18900

XLRXEKXGAA TGXDAICXHX XXPKXPGLXX EXLYWELSXL TXXIXELGPY TLDRXSLYVN

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18970 18980 18990 19000 19010 19020

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19030 19040 19050 19060 19070 19080

RPGLDREQLY CELSQLTHNI TELGPYSLDR DSLYVNGFTH QNSVPTTSTP GTSTVYWATT

19090 19100 19110 19120 19130 19140

GTPSSFPGHT XXXPLLXPFT XNXTITNLXX XXXMXXPGSR KFNTTEXVLQ GLLXPXFKNX

19150 19160 19170 19180 19190 19200

SVGXLYSGCR LTXLRXEKXG AATGXDAICX HXXXPKXPGL XXEXLYWELS XLTXXIXELG

19210 19220 19230 19240 19250 19260

PYTLDRXSLY VNGFTHWSSG LTTSTPWTST VDLGTSGTPS PVPSPTTAGP LLVPFTLNFT

19270 19280 19290 19300 19310 19320

ITNLQYEEDM HRPGSRKFNA TERVLQGLLS PIFKNTSVGP LYSGCRLTLL RPEKQEAATG

19330 19340 19350 19360 19370 19380

VDTICTHRVD PIGPGLXXEX LYWELSXLTX XIXELGPYTL DRXSLYVNGF THXXSXPTTS

19390 19400 19410 19420 19430 19440

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LQGLLXPXFK NXSVGXLYSG CRLTXLRXEK XGAATGXDAI CXHXXXPKXP GLXXEXLYWE

19510 19520 19530 19540 19550 19560

LSXLTXXIXE LGPYTLDRXS LYVNGFTHRS FGLTTSTPWT STVDLGTSGT PSPVPSPTTA

19570 19580 19590 19600 19610 19620

GPLLVPFTLN FTITNLQYEE DMHRPGSRKF NTTERVLQGL LTPLFRNTSV SSLYSGCRLT

19630 19640 19650 19660 19670 19680

LLRPEKDGAA TRVDAVCTHR PDPKSPGLXX EXLYWELSXL TXXIXELGPY TLDRXSLYVN

19690 19700 19710 19720 19730 19740

GFTHXXSXPT TSTPGTSTVX XGTSGTPSSX PXXTXXXPLL XPFTXNXTIT NLXXXXXMXX

19750 19760 19770 19780 19790 19800

PGSRKFNTTE XVLQGLLXPX FKNXSVGXLY SGCRLTXLRX EKXGAATGXD AICXHXXXPK

19810 19820 19830 19840 19850 19860

XPGLXXEXLY WELSXLTXXI XELGPYTLDR XSLYVNGFTH WIPVPTSSTP GTSTVDLGSG

19870 19880 19890 19900 19910 19920

TPSSLPSPTT AGPLLVPFTL NFTITNLQYG EDMGHPGSRK FNTTERVLQG LLGPIFKNTS

19930 19940 19950 19960 19970 19980

VGPLYSGCRL TSLRSEKDGA ATGVDAICIH HLDPKSPGLX XEXLYWELSX LTXXIXELGP

19990 20000 20010 20020 20030 20040

YTLDRXSLYV NGFTHXXSXP TTSTPGTSTV XXGTSGTPSS XPXXTXXXPL LXPFTXNXTI

20050 20060 20070 20080 20090 20100

TNLXXXXXMX XPGSRKFNTT EXVLQGLLXP XFKNXSVGXL YSGCRLTXLR XEKXGAATGX

20110 20120 20130 20140 20150 20160

DAICXHXXXP KXPGLXXEXL YWELSXLTXX IXELGPYTLD RXSLYVNGFT HQTFAPNTST

20170 20180 20190 20200 20210 20220

PGTSTVDLGT SGTPSSLPSP TSAGPLLVPF TLNFTITNLQ YEEDMHHPGS RKFNTTERVL

20230 20240 20250 20260 20270 20280

QGLLGPMFKN TSVGLLYSGC RLTLLRPEKN GAATRVDAVC THRPDPKSPG LXXEXLYWEL

20290 20300 20310 20320 20330 20340

SXLTXXIXEL GPYTLDRXSL YVNGFTHXXS XPTTSTPGTS TVXXGTSGTP SSXPXXTAPV

20350 20360 20370 20380 20390 20400

PLLIPFTLNF TITNLHYEEN MQHPGSRKFN TTERVLQGLL KPLFKSTSVG PLYSGCRLTL

20410 20420 20430 20440 20450 20460

LRPEKHGAAT GVDAICTLRL DPTGPGLDRE RLYWELSQLT NSVTELGPYT LDRDSLYVNG

20470 20480 20490 20500 20510 20520

FTQRSSVPTT SIPGTSAVHL ETSGTPASLP GHTAPGPLLV PFTLNFTITN LQYEVDMRHP

20530 20540 20550 20560 20570 20580

GSRKFNTTER VLQGLLKPLF KSTSVGPLYS GCRLTLLRPE KRGAATGVDT ICTHRLDPLN

20590 20600 20610 20620 20630 20640

PGLDREQLYW ELSKLTRGII ELGPYLLDRG SLYVNGFTHR NFVPITSTPG TSTVHLGTSE

20650 20660 20670 20680 20690 20700

TPSSLPRPIV PGPLLVPFTL NFTITNLQYE EAMRHPGSRK FNTTERVLQG LLRPLFKNTS

20710 20720 20730 20740 20750 20760

IGPLYSSCRL TLLRPEKDKA ATRVDAICTH HPDPQSPGLN REQLYWELSQ LTHGITELGP

20770 20780 20790 20800 20810 20820

YTLDRDSLYV DGFTHWSPIP TTSTPGTSIV NLGTSGIPPS LPETTXXXPL LXPFTXNXTI

20830 20840 20850 20860 20870 20880

TNLXXXXXMX XPGSRKFNTT ERVLQGLLKP LFKSTSVGPL YSGCRLTLLR PEKDGVATRV

20890 20900 20910 20920 20930 20940

DAICTHRPDP KIPGLDRQQL YWELSQLTHS ITELGPYTLD RDSLYVNGFT QRSSVPTTST

20950 20960 20970 20980 20990 21000

PGTFTVQPET SETPSSLPGP TATGPVLLPF TLNFTITNLQ YEEDMHRPGS RKFNTTERVL

21010 21020 21030 21040 21050 21060

QGLLMPLFKN TSVSSLYSGC RLTLLRPEKD GAATRVDAVC THRPDPKSPG LDRERLYWKL

21070 21080 21090 21100 21110 21120

SQLTHGITEL GPYTLDRHSL YVNGFTHQSS MTTTRTPDTS TMHLATSRTP ASLSGPTTAS

21130 21140 21150 21160 21170 21180

PLLVLFTINF TITNLRYEEN MHHPGSRKFN TTERVLQGLL RPVFKNTSVG PLYSGCRLTL

21190 21200 21210 21220 21230 21240

LRPKKDGAAT KVDAICTYRP DPKSPGLDRE QLYWELSQLT HSITELGPYT LDRDSLYVNG

21250 21260 21270 21280 21290 21300

FTQRSSVPTT SIPGTPTVDL GTSGTPVSKP GPSAASPLLV LFTLNFTITN LRYEENMQHP

21310 21320 21330 21340 21350 21360

GSRKFNTTER VLQGLLRSLF KSTSVGPLYS GCRLTLLRPE KDGTATGVDA ICTHHPDPKS

21370 21380 21390 21400 21410 21420

PRLDREQLYW ELSQLTHNIT ELGHYALDND SLFVNGFTHR SSVSTTSTPG TPTVYLGASK

21430 21440 21450 21460 21470 21480

TPASIFGPSA ASHLLILFTL NFTITNLRYE ENMWPGSRKF NTTERVLQGL LRPLFKNTSV

21490 21500 21510 21520 21530 21540

GPLYSGSRLT LLRPEKDGEA TGVDAICTHR PDPTGPGLDR EQLYLELSQL THSITELGPY

21550 21560 21570 21580 21590 21600

TLDRDSLYVN GFTHRSSVPT TSTGVVSEEP FTLNFTINNL RYMADMGQPG SLKFNITDNV

21610 21620 21630 21640 21650 21660

MKHLLSPLFQ RSSLGARYTG CRVIALRSVK NGAETRVDLL CTYLQPLSGP GLPIKQVFHE

21670 21680 21690 21700 21710 21720

LSQQTHGITR LGPYSLDKDS LYLNGYNEPG LDEPPTTPKP ATTFLPPLSE ATTAMGYHLK

21730 21740 21750 21760 21770 21780

TLTLNFTISN LQYSPDMGKG SATFNSTEGV LQHLLRPLFQ KSSMGPFYLG CQLISLRPEK

21790 21800 21810 21820 21830 21840

DGAATGVDTT CTYHPDPVGP GLDIQQLYWE LSQLTHGVTQ LGFYVLDRDS LFINGYAPQN

21850 21860 21870 21880 21890 21900

LSIRGEYQIN FHIVNWNLSN PDPTSSEYIT LLRDIQDKVT TLYKGSQLHD TFRFCLVTNL

21910 21920 21930 21940 21950 21960

TMDSVLVTVK ALFSSNLDPS LVEQVFLDKT LNASFHWLGS TYQLVDIHVT EMESSVYQPT

21970 21980 21990 22000 22010 22020

SSSSTQHFYL NFTITNLPYS QDKAQPGTTN YQRNKRNIED ALNQLFRNSS IKSYFSDCQV

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     22030       22040       22050       22060       22070       22080
STFRSVPNRH HTGVDSLCNF SPLARRVDRV AIYEEFLRMT RNGTQLQNFT LDRSSVLVDG
     22090       22100       22110       22120       22130       22140
YSPNRNEPLT GNSDLPFWAV ILIGLAGLLG LITCLICGVL VTTRRRKKEG EYNVQQQCPG
     22150
YYQSHLDLED LQ
```

[0079] Most preferably, the Mucin-16 assay detects one or more soluble forms of Mucin-16. Mucin-16 is a single-pass type I membrane protein having a large extracellular domain, most or all of which is present in soluble forms of Mucin-16 generated either through alternative splicing event which deletes all or a portion of the transmembrane domain, or by proteolysis of the membrane-bound form. In the case of an immunoassay, one or more antibodies that bind to epitopes within this extracellular domain may be used to detect these soluble form(s). The following domains have been identified in Mucin-16:

Residues	Length	Domain ID
1-22152	22152	Mucin-16
1-22096	22906	extracellular
22907-22117	21	transmembrane
22128-22152	35	cytoplasmic

[0080] As used herein, the term “Carcinoembryonic antigen-related cell adhesion molecule 5” refers to one or polypeptides present in a biological sample that are derived from the Carcinoembryonic antigen-related cell adhesion molecule 5 precursor (Swiss-Prot P06731 (SEQ ID NO: 13)).

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        10          20          30          40          50          60
MESPSAPPHR WCIPWQRLLL TASLLTFWNP PTTAKLTIES TPFNVAEGKE VLLLVHNLPQ
        70          80          90         100         110         120
HLFGYSWYKG ERVDGNRQII GYVIGTQQAT PGPAYSGREI IYPNASLLIQ NIIQNDTGFY
       130         140         150         160         170         180
TLHVIKSDLV NEEATGQFRV YPELPKPSIS SNNSKPVEDK DAVAFTCEPE TQDATYLWWV
       190         200         210         220         230         240
```

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NNQSLPVSPR LQLSNGNRTL TLFNVTRNDT ASYKCETQNP VSARRSDSVI LNVLYGPDAP
       250        260        270        280        290        300
TISPLNTSYR SGENLNLSCH AASNPPAQYS WFVNGTFQQS TQELFIPNIT VNNSGSYTCQ
       310        320        330        340        350        360
AHNSDTGLNR TTVTTITVYA EPPKPFITSN NSNPVEDEDA VALTCEPEIQ NTTYLWWVNN
       370        380        390        400        410        420
QSLPVSPRLQ LSNDNRTLTL LSVTRNDVGP YECGIQNELS VDHSDPVILN VLYGPDDPTI
       430        440        450        460        470        480
SPSYTYYRPG VNLSLSCHAA SNPPAQYSWL IDGNIQQHTQ ELFISNITEK NSGLYTCQAN
       490        500        510        520        530        540
NSASGHSRTT VKTITVSAEL PKPSISSNNS KPVEDKDAVA FTCEPEAQNT TYLWWVNGQS
       550        560        570        580        590        600
LPVSPRLQLS NGNRTLTLFN VTRNDARAYV CGIQNSVSAN RSDPVTLDVL YGPDTPIISP
       610        620        630        640        650        660
PDSSYLSGAN LNLSCHSASN PSPQYSWRIN GIPQQHTQVL FIAKITPNNN GTYACFVSNL
       670        680        690        700
ATGRNNSIVK SITVSASGTS PGLSAGATVG IMIGVLVGVA LI
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[0081] The following domains have been identified in Carcinoembryonic antigen-related cell adhesion molecule 5:

Residues	Length	Domain ID
1-34	34	Signal sequence
35-685	5	Carcinoembryonic antigen-related cell adhesion molecule 5
686-702	17	Propeptide

[0082] As used herein, the term “cellular tumor antigen p53” refers to one or more polypeptides present in a biological sample that are derived from the cellular tumor antigen p53 precursor (Swiss-Prot P04637 (SEQ ID NO: 14)).

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        10         20         30         40         50         60
MEEPQSDPSV EPPLSQETFS DLWKLLPENN VLSPLPSQAM DDLMLSPDDI EQWFTEDPGP
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        70          80          90         100         110         120
DEAPRMPEAA PRVAPAPAAP TPAAPAPAPS WPLSSSVPSQ KTYQGSYGFR LGFLHSGTAK
       130         140         150         160         170         180
SVTCTYSPAL NKMFCQLAKT CPVQLWVDST PPPGTRVRAM AIYKQSQHMT EVVRRCPHHE
       190         200         210         220         230         240
RCSDSDGLAP PQHLIRVEGN LRVEYLDDRN TFRHSVVVPY EPPEVGSDCT TIHYNYMCNS
       250         260         270         280         290         300
SCMGGMNRRP ILTIITLEDS SGNLLGRNSF EVRVCACPGR DRRTEEENLR KKGEPHHELP
       310         320         330         340         350         360
PGSTKRALPN NTSSSPQPKK KPLDGEYFTL QIRGRERFEM FRELNEALEL KDAQAGKEPG
       370         380         390
GSRAHSSHLK SKKGQSTSRH KKLMFKTEGP DSD
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[0083] Isoform 2 of cellular tumor antigen p53 has the following changes from this isoform 1 sequence:

332-341: IRGRERFEMF (SEQ ID NO: 15) → DGTSFQKENC (SEQ ID NO: 16)

342-393: Missing

[0084] As used herein, the term "relating a signal to the presence or amount" of an analyte reflects this understanding. Assay signals are typically related to the presence or amount of an analyte through the use of a standard curve calculated using known concentrations of the analyte of interest. As the term is used herein, an assay is "configured to detect" an analyte if an assay can generate a detectable signal indicative of the presence or amount of a physiologically relevant concentration of the analyte. Because an antibody epitope is on the order of 8 amino acids, an immunoassay configured to detect a marker of interest will also detect polypeptides related to the marker sequence, so long as those polypeptides contain the epitope(s) necessary to bind to the antibody or antibodies used in the assay. The term "related marker" as used herein with regard to a biomarker such as one of the kidney injury markers described herein refers to one or more fragments, variants, etc., of a particular marker or its biosynthetic parent that may be detected as a surrogate for the marker itself or as independent biomarkers. The term also refers to one or more polypeptides present in a biological

sample that are derived from the biomarker precursor complexed to additional species, such as binding proteins, receptors, heparin, lipids, sugars, *etc.*

[0085] In this regard, the skilled artisan will understand that the signals obtained from an immunoassay are a direct result of complexes formed between one or more antibodies and the target biomolecule (*i.e.*, the analyte) and polypeptides containing the necessary epitope(s) to which the antibodies bind. While such assays may detect the full length biomarker and the assay result be expressed as a concentration of a biomarker of interest, the signal from the assay is actually a result of all such "immunoreactive" polypeptides present in the sample. Expression of biomarkers may also be determined by means other than immunoassays, including protein measurements (such as dot blots, western blots, chromatographic methods, mass spectrometry, *etc.*) and nucleic acid measurements (mRNA quatitation). This list is not meant to be limiting.

[0086] The term "positive going" marker as that term is used herein refer to a marker that is determined to be elevated in subjects suffering from a disease or condition, relative to subjects not suffering from that disease or condition. The term "negative going" marker as that term is used herein refer to a marker that is determined to be reduced in subjects suffering from a disease or condition, relative to subjects not suffering from that disease or condition.

[0087] The term "subject" as used herein refers to a human or non-human organism. Thus, the methods and compositions described herein are applicable to both human and veterinary disease. Further, while a subject is preferably a living organism, the invention described herein may be used in post-mortem analysis as well. Preferred subjects are humans, and most preferably "patients," which as used herein refers to living humans that are receiving medical care for a disease or condition. This includes persons with no defined illness who are being investigated for signs of pathology.

[0088] Preferably, an analyte is measured in a sample. Such a sample may be obtained from a subject, or may be obtained from biological materials intended to be provided to the subject. For example, a sample may be obtained from a kidney being evaluated for possible transplantation into a subject, and an analyte measurement used to evaluate the kidney for preexisting damage. Preferred samples are body fluid samples.

[0089] The term "body fluid sample" as used herein refers to a sample of bodily fluid obtained for the purpose of diagnosis, prognosis, classification or evaluation of a subject

of interest, such as a patient or transplant donor. In certain embodiments, such a sample may be obtained for the purpose of determining the outcome of an ongoing condition or the effect of a treatment regimen on a condition. Preferred body fluid samples include blood, serum, plasma, cerebrospinal fluid, urine, saliva, sputum, and pleural effusions. In addition, one of skill in the art would realize that certain body fluid samples would be more readily analyzed following a fractionation or purification procedure, for example, separation of whole blood into serum or plasma components.

[0090] The term "diagnosis" as used herein refers to methods by which the skilled artisan can estimate and/or determine the probability ("a likelihood") of whether or not a patient is suffering from a given disease or condition. In the case of the present invention, "diagnosis" includes using the results of an assay, most preferably an immunoassay, for a kidney injury marker of the present invention, optionally together with other clinical characteristics, to arrive at a diagnosis (that is, the occurrence or nonoccurrence) of an acute renal injury or ARF for the subject from which a sample was obtained and assayed. That such a diagnosis is "determined" is not meant to imply that the diagnosis is 100% accurate. Many biomarkers are indicative of multiple conditions. The skilled clinician does not use biomarker results in an informational vacuum, but rather test results are used together with other clinical indicia to arrive at a diagnosis. Thus, a measured biomarker level on one side of a predetermined diagnostic threshold indicates a greater likelihood of the occurrence of disease in the subject relative to a measured level on the other side of the predetermined diagnostic threshold.

[0091] Similarly, a prognostic risk signals a probability ("a likelihood") that a given course or outcome will occur. A level or a change in level of a prognostic indicator, which in turn is associated with an increased probability of morbidity (e.g., worsening renal function, future ARF, or death) is referred to as being "indicative of an increased likelihood" of an adverse outcome in a patient.

[0092] Marker Assays

[0093] In general, immunoassays involve contacting a sample containing or suspected of containing a biomarker of interest with at least one antibody that specifically binds to the biomarker. A signal is then generated indicative of the presence or amount of complexes formed by the binding of polypeptides in the sample to the antibody or other binding species. The signal is then related to the presence or amount of the biomarker in

the sample. Numerous methods and devices are well known to the skilled artisan for the detection and analysis of biomarkers. *See, e.g.*, U.S. Patents 6,143,576; 6,113,855; 6,019,944; 5,985,579; 5,947,124; 5,939,272; 5,922,615; 5,885,527; 5,851,776; 5,824,799; 5,679,526; 5,525,524; and 5,480,792, and *The Immunoassay Handbook*, David Wild, ed. Stockton Press, New York, 1994, each of which is hereby incorporated by reference in its entirety, including all tables, figures and claims.

[0094] The assay devices and methods known in the art can utilize labeled molecules in various sandwich, competitive, or non-competitive assay formats, to generate a signal that is related to the presence or amount of the biomarker of interest. Suitable assay formats also include chromatographic, mass spectrographic, and protein "blotting" methods. Additionally, certain methods and devices, such as biosensors and optical immunoassays, may be employed to determine the presence or amount of analytes without the need for a labeled molecule. *See, e.g.*, U.S. Patents 5,631,171; and 5,955,377, each of which is hereby incorporated by reference in its entirety, including all tables, figures and claims. One skilled in the art also recognizes that robotic instrumentation including but not limited to Beckman ACCESS®, Abbott AXSYM®, Roche ELECSYS®, Dade Behring STRATUS® systems are among the immunoassay analyzers that are capable of performing immunoassays. But any suitable immunoassay may be utilized, for example, enzyme-linked immunoassays (ELISA), radioimmunoassays (RIAs), competitive binding assays, and the like.

[0095] Antibodies or other polypeptides may be immobilized onto a variety of solid supports for use in assays. Solid phases that may be used to immobilize specific binding members include include those developed and/or used as solid phases in solid phase binding assays. Examples of suitable solid phases include membrane filters, cellulose-based papers, beads (including polymeric, latex and paramagnetic particles), glass, silicon wafers, microparticles, nanoparticles, TentaGels, AgroGels, PEGA gels, SPOCC gels, and multiple-well plates. An assay strip could be prepared by coating the antibody or a plurality of antibodies in an array on solid support. This strip could then be dipped into the test sample and then processed quickly through washes and detection steps to generate a measurable signal, such as a colored spot. Antibodies or other polypeptides may be bound to specific zones of assay devices either by conjugating directly to an assay device surface, or by indirect binding. In an example of the later case, antibodies or other

polypeptides may be immobilized on particles or other solid supports, and that solid support immobilized to the device surface.

[0096] Biological assays require methods for detection, and one of the most common methods for quantitation of results is to conjugate a detectable label to a protein or nucleic acid that has affinity for one of the components in the biological system being studied. Detectable labels may include molecules that are themselves detectable (*e.g.*, fluorescent moieties, electrochemical labels, metal chelates, *etc.*) as well as molecules that may be indirectly detected by production of a detectable reaction product (*e.g.*, enzymes such as horseradish peroxidase, alkaline phosphatase, *etc.*) or by a specific binding molecule which itself may be detectable (e.g., biotin, digoxigenin, maltose, oligohistidine, 2,4-dintrobenzene, phenylarsenate, ssDNA, dsDNA, etc.).

[0097] Preparation of solid phases and detectable label conjugates often comprise the use of chemical cross-linkers. Cross-linking reagents contain at least two reactive groups, and are divided generally into homofunctional cross-linkers (containing identical reactive groups) and heterofunctional cross-linkers (containing non-identical reactive groups). Homobifunctional cross-linkers that couple through amines, sulfhydryls or react non-specifically are available from many commercial sources. Maleimides, alkyl and aryl halides, alpha-haloacyls and pyridyl disulfides are thiol reactive groups. Maleimides, alkyl and aryl halides, and alpha-haloacyls react with sulfhydryls to form thiol ether bonds, while pyridyl disulfides react with sulfhydryls to produce mixed disulfides. The pyridyl disulfide product is cleavable. Imidoesters are also very useful for protein-protein cross-links. A variety of heterobifunctional cross-linkers, each combining different attributes for successful conjugation, are commercially available.

[0098] In certain aspects, the present invention provides kits for the analysis of the described kidney injury markers. The kit comprises reagents for the analysis of at least one test sample which comprise at least one antibody that a kidney injury marker. The kit can also include devices and instructions for performing one or more of the diagnostic and/or prognostic correlations described herein. Preferred kits will comprise an antibody pair for performing a sandwich assay, or a labeled species for performing a competitive assay, for the analyte. Preferably, an antibody pair comprises a first antibody conjugated to a solid phase and a second antibody conjugated to a detectable label, wherein each of the first and second antibodies that bind a kidney injury marker. Most preferably each of the antibodies are monoclonal antibodies. The instructions for use of the kit and

performing the correlations can be in the form of labeling, which refers to any written or recorded material that is attached to, or otherwise accompanies a kit at any time during its manufacture, transport, sale or use. For example, the term labeling encompasses advertising leaflets and brochures, packaging materials, instructions, audio or video cassettes, computer discs, as well as writing imprinted directly on kits.

[0099] Antibodies

[0100] The term "antibody" as used herein refers to a peptide or polypeptide derived from, modeled after or substantially encoded by an immunoglobulin gene or immunoglobulin genes, or fragments thereof, capable of specifically binding an antigen or epitope. *See, e.g.* Fundamental Immunology, 3rd Edition, W.E. Paul, ed., Raven Press, N.Y. (1993); Wilson (1994; J. Immunol. Methods 175:267-273; Yarmush (1992) J. Biochem. Biophys. Methods 25:85-97. The term antibody includes antigen-binding portions, i.e., "antigen binding sites," (e.g., fragments, subsequences, complementarity determining regions (CDRs)) that retain capacity to bind antigen, including (i) a Fab fragment, a monovalent fragment consisting of the VL, VH, CL and CHl domains; (ii) a F(ab')2 fragment, a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region; (iii) a Fd fragment consisting of the VH and CHl domains; (iv) a Fv fragment consisting of the VL and VH domains of a single arm of an antibody, (v) a dAb fragment (Ward et al., (1989) Nature 341:544-546), which consists of a VH domain; and (vi) an isolated complementarity determining region (CDR). Single chain antibodies are also included by reference in the term "antibody."

[0101] Antibodies used in the immunoassays described herein preferably specifically bind to a kidney injury marker of the present invention. The term "specifically binds" is not intended to indicate that an antibody binds exclusively to its intended target since, as noted above, an antibody binds to any polypeptide displaying the epitope(s) to which the antibody binds. Rather, an antibody "specifically binds" if its affinity for its intended target is about 5-fold greater when compared to its affinity for a non-target molecule which does not display the appropriate epitope(s). Preferably the affinity of the antibody will be at least about 5 fold, preferably 10 fold, more preferably 25-fold, even more preferably 50-fold, and most preferably 100-fold or more, greater for a target molecule than its affinity for a non-target molecule. In preferred embodiments, Preferred antibodies bind with affinities of at least about 10^7 M^{-1}, and preferably between about 10^8 M^{-1} to about 10^9 M^{-1}, about 10^9 M^{-1} to about 10^{10} M^{-1}, or about 10^{10} M^{-1} to about 10^{12} M^{-1} .

[0102] Affinity is calculated as $K_d = k_{off}/k_{on}$ (k_{off} is the dissociation rate constant, K_{on} is the association rate constant and K_d is the equilibrium constant). Affinity can be determined at equilibrium by measuring the fraction bound (r) of labeled ligand at various concentrations (c). The data are graphed using the Scatchard equation: r/c = K(n-r): where r = moles of bound ligand/mole of receptor at equilibrium; c = free ligand concentration at equilibrium; K = equilibrium association constant; and n = number of ligand binding sites per receptor molecule. By graphical analysis, r/c is plotted on the Y-axis versus r on the X-axis, thus producing a Scatchard plot. Antibody affinity measurement by Scatchard analysis is well known in the art. *See, e.g.*, van Erp *et al., J. Immunoassay* 12: 425-43, 1991; Nelson and Griswold, *Comput. Methods Programs Biomed.* 27: 65-8, 1988.

[0103] The term "epitope" refers to an antigenic determinant capable of specific binding to an antibody. Epitopes usually consist of chemically active surface groupings of molecules such as amino acids or sugar side chains and usually have specific three dimensional structural characteristics, as well as specific charge characteristics. Conformational and nonconformational epitopes are distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

[0104] Numerous publications discuss the use of phage display technology to produce and screen libraries of polypeptides for binding to a selected analyte. *See, e.g*, Cwirla *et al., Proc. Natl. Acad. Sci. USA* 87, 6378-82, 1990; Devlin *et al., Science* 249, 404-6, 1990, Scott and Smith, *Science* 249, 386-88, 1990; and Ladner *et al.*, U.S. Pat. No. 5,571,698. A basic concept of phage display methods is the establishment of a physical association between DNA encoding a polypeptide to be screened and the polypeptide. This physical association is provided by the phage particle, which displays a polypeptide as part of a capsid enclosing the phage genome which encodes the polypeptide. The establishment of a physical association between polypeptides and their genetic material allows simultaneous mass screening of very large numbers of phage bearing different polypeptides. Phage displaying a polypeptide with affinity to a target bind to the target and these phage are enriched by affinity screening to the target. The identity of polypeptides displayed from these phage can be determined from their respective genomes. Using these methods a polypeptide identified as having a binding affinity for a desired target can then be synthesized in bulk by conventional means. *See, e.g.*, U.S. Patent No. 6,057,098, which is hereby incorporated in its entirety, including all tables, figures, and claims.

[0105] The antibodies that are generated by these methods may then be selected by first screening for affinity and specificity with the purified polypeptide of interest and, if required, comparing the results to the affinity and specificity of the antibodies with polypeptides that are desired to be excluded from binding. The screening procedure can involve immobilization of the purified polypeptides in separate wells of microtiter plates. The solution containing a potential antibody or groups of antibodies is then placed into the respective microtiter wells and incubated for about 30 min to 2 h. The microtiter wells are then washed and a labeled secondary antibody (for example, an anti-mouse antibody conjugated to alkaline phosphatase if the raised antibodies are mouse antibodies) is added to the wells and incubated for about 30 min and then washed. Substrate is added to the wells and a color reaction will appear where antibody to the immobilized polypeptide(s) are present.

[0106] The antibodies so identified may then be further analyzed for affinity and specificity in the assay design selected. In the development of immunoassays for a target protein, the purified target protein acts as a standard with which to judge the sensitivity and specificity of the immunoassay using the antibodies that have been selected. Because the binding affinity of various antibodies may differ; certain antibody pairs (e.g., in sandwich assays) may interfere with one another sterically, etc., assay performance of an antibody may be a more important measure than absolute affinity and specificity of an antibody.

[0107] While the present application describes antibody-based binding assays in detail, alternatives to antibodies as binding species in assays are well known in the art. These include receptors for a particular target, aptamers, etc. Aptamers are oligonucleic acid or peptide molecules that bind to a specific target molecule. Aptamers are usually created by selecting them from a large random sequence pool, but natural aptamers also exist. High-affinity aptamers containing modified nucleotides conferring improved characteristics on the ligand, such as improved in vivo stability or improved delivery characteristics. Examples of such modifications include chemical substitutions at the ribose and/or phosphate and/or base positions, and may include amino acid side chain functionalities.

[0108] Assay Correlations

[0109] The term "correlating" as used herein in reference to the use of biomarkers refers to comparing the presence or amount of the biomarker(s) in a patient to its presence or amount in persons known to suffer from, or known to be at risk of, a given condition; or in persons known to be free of a given condition. Often, this takes the form of comparing an assay result in the form of a biomarker concentration to a predetermined threshold selected to be indicative of the occurrence or nonoccurrence of a disease or the likelihood of some future outcome.

[0110] Selecting a diagnostic threshold involves, among other things, consideration of the probability of disease, distribution of true and false diagnoses at different test thresholds, and estimates of the consequences of treatment (or a failure to treat) based on the diagnosis. For example, when considering administering a specific therapy which is highly efficacious and has a low level of risk, few tests are needed because clinicians can accept substantial diagnostic uncertainty. On the other hand, in situations where treatment options are less effective and more risky, clinicians often need a higher degree of diagnostic certainty. Thus, cost/benefit analysis is involved in selecting a diagnostic threshold.

[0111] Suitable thresholds may be determined in a variety of ways. For example, one recommended diagnostic threshold for the diagnosis of acute myocardial infarction using cardiac troponin is the 97.5th percentile of the concentration seen in a normal population. Another method may be to look at serial samples from the same patient, where a prior "baseline" result is used to monitor for temporal changes in a biomarker level.

[0112] Population studies may also be used to select a decision threshold. Reciever Operating Characteristic ("ROC") arose from the field of signal dectection therory developed during World War II for the analysis of radar images, and ROC analysis is often used to select a threshold able to best distinguish a "diseased" subpopulation from a "nondiseased" subpopulation. A false positive in this case occurs when the person tests positive, but actually does not have the disease. A false negative, on the other hand, occurs when the person tests negative, suggesting they are healthy, when they actually do have the disease. To draw a ROC curve, the true positive rate (TPR) and false positive rate (FPR) are determined as the decision threshold is varied continuously. Since TPR is equivalent with sensitivity and FPR is equal to 1 - specificity, the ROC graph is sometimes called the sensitivity vs (1 - specificity) plot. A perfect test will have an area

under the ROC curve of 1.0; a random test will have an area of 0.5. A threshold is selected to provide an acceptable level of specificity and sensitivity.

[0113] In this context, "diseased" is meant to refer to a population having one characteristic (the presence of a disease or condition or the occurrence of some outcome) and "nondiseased" is meant to refer to a population lacking the characteristic. While a single decision threshold is the simplest application of such a method, multiple decision thresholds may be used. For example, below a first threshold, the absence of disease may be assigned with relatively high confidence, and above a second threshold the presence of disease may also be assigned with relatively high confidence. Between the two thresholds may be considered indeterminate. This is meant to be exemplary in nature only.

[0114] In addition to threshold comparisons, other methods for correlating assay results to a patient classification (occurrence or nonoccurrence of disease, likelihood of an outcome, etc.) include decision trees, rule sets, Bayesian methods, and neural network methods. These methods can produce probability values representing the degree to which a subject belongs to one classification out of a plurality of classifications.

[0115] Measures of test accuracy may be obtained as described in Fischer *et al., Intensive Care Med.* 29: 1043-51, 2003, and used to determine the effectiveness of a given biomarker. These measures include sensitivity and specificity, predictive values, likelihood ratios, diagnostic odds ratios, and ROC curve areas. The area under the curve ("AUC") of a ROC plot is equal to the probability that a classifier will rank a randomly chosen positive instance higher than a randomly chosen negative one. The area under the ROC curve may be thought of as equivalent to the Mann-Whitney U test, which tests for the median difference between scores obtained in the two groups considered if the groups are of continuous data, or to the Wilcoxon test of ranks.

[0116] As discussed above, suitable tests may exhibit one or more of the following results on these various measures: a specificity of greater than 0.5, preferably at least 0.6, more preferably at least 0.7, still more preferably at least 0.8, even more preferably at least 0.9 and most preferably at least 0.95, with a corresponding sensitivity greater than 0.2, preferably greater than 0.3, more preferably greater than 0.4, still more preferably at least 0.5, even more preferably 0.6, yet more preferably greater than 0.7, still more preferably greater than 0.8, more preferably greater than 0.9, and most preferably greater than 0.95; a sensitivity of greater than 0.5, preferably at least 0.6, more preferably at least

0.7, still more preferably at least 0.8, even more preferably at least 0.9 and most preferably at least 0.95, with a corresponding specificity greater than 0.2, preferably greater than 0.3, more preferably greater than 0.4, still more preferably at least 0.5, even more preferably 0.6, yet more preferably greater than 0.7, still more preferably greater than 0.8, more preferably greater than 0.9, and most preferably greater than 0.95; at least 75% sensitivity, combined with at least 75% specificity; a ROC curve area of greater than 0.5, preferably at least 0.6, more preferably 0.7, still more preferably at least 0.8, even more preferably at least 0.9, and most preferably at least 0.95; an odds ratio different from 1, preferably at least about 2 or more or about 0.5 or less, more preferably at least about 3 or more or about 0.33 or less, still more preferably at least about 4 or more or about 0.25 or less, even more preferably at least about 5 or more or about 0.2 or less, and most preferably at least about 10 or more or about 0.1 or less; a positive likelihood ratio (calculated as sensitivity/(1-specificity)) of greater than 1, at least 2, more preferably at least 3, still more preferably at least 5, and most preferably at least 10; and or a negative likelihood ratio (calculated as (1-sensitivity)/specificity) of less than 1, less than or equal to 0.5, more preferably less than or equal to 0.3, and most preferably less than or equal to 0.1

[0117] Additional clinical indicia may be combined with the kidney injury marker assay result(s) of the present invention. These include other biomarkers related to renal status. Examples include the following, which recite the common biomarker name, followed by the Swiss-Prot entry number for that biomarker or its parent: Actin (P68133); Adenosine deaminase binding protein (DPP4, P27487); Alpha-1-acid glycoprotein 1 (P02763); Alpha-1-microglobulin (P02760); Albumin (P02768); Angiotensinogenase (Renin, P00797); Annexin A2 (P07355); Beta-glucuronidase (P08236); B-2-microglobulin (P61679); Beta-galactosidase (P16278); BMP-7 (P18075); Brain natriuretic peptide (proBNP, BNP-32, NTproBNP; P16860); Calcium-binding protein Beta (S100-beta, P04271); Carbonic anhydrase (Q16790); Casein Kinase 2 (P68400); Ceruloplasmin (P00450); Clusterin (P10909); Complement C3 (P01024); Cysteine-rich protein (CYR61, O00622); Cytochrome C (P99999); Epidermal growth factor (EGF, P01133); Endothelin-1 (P05305); Exosomal Fetuin-A (P02765); Fatty acid-binding protein, heart (FABP3, P05413); Fatty acid-binding protein, liver (P07148); Ferritin (light chain, P02793; heavy chain P02794); Fructose-1,6-biphosphatase (P09467); GRO-alpha (CXCL1, (P09341); Growth Hormone (P01241); Hepatocyte growth factor (P14210);

Insulin-like growth factor I (P01343); Immunoglobulin G; Immunoglobulin Light Chains (Kappa and Lambda); Interferon gamma (P01308); Lysozyme (P61626); Interleukin-1alpha (P01583); Interleukin-2 (P60568); Interleukin-4 (P60568); Interleukin-9 (P15248); Interleukin-12p40 (P29460); Interleukin-13 (P35225); Interleukin-16 (Q14005); L1 cell adhesion molecule (P32004); Lactate dehydrogenase (P00338); Leucine Aminopeptidase (P28838); Meprin A-alpha subunit (Q16819); Meprin A-beta subunit (Q16820); Midkine (P21741); MIP2-alpha (CXCL2, P19875); MMP-2 (P08253); MMP-9 (P14780); Netrin-1 (O95631); Neutral endopeptidase (P08473); Osteopontin (P10451); Renal papillary antigen 1 (RPA1); Renal papillary antigen 2 (RPA2); Retinol binding protein (P09455); Ribonuclease; S100 calcium-binding protein A6 (P06703); Serum Amyloid P Component (P02743); Sodium/Hydrogen exchanger isoform (NHE3, P48764); Spermidine/spermine N1-acetyltransferase (P21673); TGF-Beta1 (P01137); Transferrin (P02787); Trefoil factor 3 (TFF3, Q07654); Toll-Like protein 4 (O00206); Total protein; Tubulointerstitial nephritis antigen (Q9UJW2); Uromodulin (Tamm-Horsfall protein, P07911).

[0118] For purposes of risk stratification, Adiponectin (Q15848); Alkaline phosphatase (P05186); Aminopeptidase N (P15144); CalbindinD28k (P05937); Cystatin C (P01034); 8 subunit of F1FO ATPase (P03928); Gamma-glutamyltransferase (P19440); GSTa (alpha-glutathione-S-transferase, P08263); GSTpi (Glutathione-S-transferase P; GST class-pi; P09211); IGFBP-1 (P08833); IGFBP-2 (P18065); IGFBP-6 (P24592); Integral membrane protein 1 (Itm1, P46977); Interleukin-6 (P05231); Interleukin-8 (P10145); Interleukin-18 (Q14116); IP-10 (10 kDa interferon-gamma-induced protein, P02778); IRPR (IFRD1, O00458); Isovaleryl-CoA dehydrogenase (IVD, P26440); I-TAC/CXCL11 (O14625); Keratin 19 (P08727); Kim-1 (Hepatitis A virus cellular receptor 1, O43656); L-arginine:glycine amidinotransferase (P50440); Leptin (P41159); Lipocalin2 (NGAL, P80188); MCP-1 (P13500); MIG (Gamma-interferon-induced monokine Q07325); MIP-1a (P10147); MIP-3a (P78556); MIP-1beta (P13236); MIP-1d (Q16663); NAG (N-acetyl-beta-D-glucosaminidase, P54802); Organic ion transporter (OCT2, O15244); Osteoprotegerin (O14788); P8 protein (O60356); Plasminogen activator inhibitor 1 (PAI-1, P05121); ProANP(1-98) (P01160); Protein phosphatase 1-beta (PPI-beta, P62140); Rab GDI-beta (P50395); Renal kallikrein (Q86U61); RT1.B-1 (alpha) chain of the integral membrane protein (Q5Y7A8); Soluble tumor necrosis factor receptor superfamily member 1A (sTNFR-I, P19438); Soluble tumor necrosis factor receptor superfamily member 1B (sTNFR-II, P20333); Tissue inhibitor of

metalloproteinases 3 (TIMP-3, P35625); uPAR (Q03405) may be combined with the kidney injury marker assay result(s) of the present invention.

[0119] Other clinical indicia which may be combined with the kidney injury marker assay result(s) of the present invention includes demographic information (e.g., weight, sex, age, race), medical history (e.g., family history, type of surgery, pre-existing disease such as aneurism, congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, or sepsis, type of toxin exposure such as NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin, myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin), clinical variables (*e.g.*, blood pressure, temperature, respiration rate), risk scores (APACHE score, PREDICT score, TIMI Risk Score for UA/NSTEMI, Framingham Risk Score), a urine total protein measurement, a glomerular filtration rate, an estimated glomerular filtration rate, a urine production rate, a serum or plasma creatinine concentration, a renal papillary antigen 1 (RPA1) measurement; a renal papillary antigen 2 (RPA2) measurement; a urine creatinine concentration, a fractional excretion of sodium, a urine sodium concentration, a urine creatinine to serum or plasma creatinine ratio, a urine specific gravity, a urine osmolality, a urine urea nitrogen to plasma urea nitrogen ratio, a plasma BUN to creatnine ratio, and/or a renal failure index calculated as urine sodium / (urine creatinine / plasma creatinine). Other measures of renal function which may be combined with the kidney injury marker assay result(s) are described hereinafter and in Harrison's Principles of Internal Medicine, 17th Ed., McGraw Hill, New York, pages 1741-1830, and Current Medical Diagnosis & Treatment 2008, 47th Ed, McGraw Hill, New York, pages 785-815, each of which are hereby incorporated by reference in their entirety.

[0120] Combining assay results/clinical indicia in this manner can comprise the use of multivariate logistical regression, loglinear modeling, neural network analysis, n-of-m analysis, decision tree analysis, etc. This list is not meant to be limiting.

[0121] Diagnosis of Acute Renal Failure

[0122] As noted above, the terms "acute renal (or kidney) injury" and "acute renal (or kidney) failure" as used herein are defined in part in terms of changes in serum creatinine from a baseline value. Most definitions of ARF have common elements, including the use of serum creatinine and, often, urine output. Patients may present with renal dysfunction

without an available baseline measure of renal function for use in this comparison. In such an event, one may estimate a baseline serum creatinine value by assuming the patient initially had a normal GFR. Glomerular filtration rate (GFR) is the volume of fluid filtered from the renal (kidney) glomerular capillaries into the Bowman's capsule per unit time. Glomerular filtration rate (GFR) can be calculated by measuring any chemical that has a steady level in the blood, and is freely filtered but neither reabsorbed nor secreted by the kidneys. GFR is typically expressed in units of ml/min:

$$GFR = \frac{\text{Urine Concentration} \times \text{Urine Flow}}{\text{Plasma Concentration}}$$

[0123] By normalizing the GFR to the body surface area, a GFR of approximately 75–100 ml/min per 1.73 m^2 can be assumed. The rate therefore measured is the quantity of the substance in the urine that originated from a calculable volume of blood.

[0124] There are several different techniques used to calculate or estimate the glomerular filtration rate (GFR or eGFR). In clinical practice, however, creatinine clearance is used to measure GFR. Creatinine is produced naturally by the body (creatinine is a metabolite of creatine, which is found in muscle). It is freely filtered by the glomerulus, but also actively secreted by the renal tubules in very small amounts such that creatinine clearance overestimates actual GFR by 10-20%. This margin of error is acceptable considering the ease with which creatinine clearance is measured.

[0125] Creatinine clearance (CCr) can be calculated if values for creatinine's urine concentration (U_{Cr}), urine flow rate (V), and creatinine's plasma concentration (P_{Cr}) are known. Since the product of urine concentration and urine flow rate yields creatinine's excretion rate, creatinine clearance is also said to be its excretion rate ($U_{Cr} \times V$) divided by its plasma concentration. This is commonly represented mathematically as:

$$C_{Cr} = \frac{U_{Cr} \times V}{P_{Cr}}$$

[0126] Commonly a 24 hour urine collection is undertaken, from empty-bladder one morning to the contents of the bladder the following morning, with a comparative blood test then taken:

$$C_{Cr} = \frac{U_{Cr} \times \text{24-hour volume}}{P_{Cr} \times 24 \times 60mins}$$

[0127] To allow comparison of results between people of different sizes, the CCr is often corrected for the body surface area (BSA) and expressed compared to the average sized man as ml/min/1.73 m2. While most adults have a BSA that approaches 1.7 (1.6-1.9), extremely obese or slim patients should have their CCr corrected for their actual BSA:

$$C_{Cr-corrected} = \frac{C_{Cr} \times 1.73}{BSA}$$

[0128] The accuracy of a creatinine clearance measurement (even when collection is complete) is limited because as glomerular filtration rate (GFR) falls creatinine secretion is increased, and thus the rise in serum creatinine is less. Thus, creatinine excretion is much greater than the filtered load, resulting in a potentially large overestimation of the GFR (as much as a twofold difference). However, for clinical purposes it is important to determine whether renal function is stable or getting worse or better. This is often determined by monitoring serum creatinine alone. Like creatinine clearance, the serum creatinine will not be an accurate reflection of GFR in the non-steady-state condition of ARF. Nonetheless, the degree to which serum creatinine changes from baseline will reflect the change in GFR. Serum creatinine is readily and easily measured and it is specific for renal function.

[0129] For purposes of determining urine output on a Urine output on a mL/kg/hr basis, hourly urine collection and measurement is adequate. In the case where, for example, only a cumulative 24-h output was available and no patient weights are provided, minor modifications of the RIFLE urine output criteria have been described. For example, Bagshaw *et al., Nephrol. Dial. Transplant.* 23: 1203–1210, 2008, assumes an average patient weight of 70 kg, and patients are assigned a RIFLE classification based on the following: <35 mL/h (Risk), <21 mL/h (Injury) or <4 mL/h (Failure).

[0130] Selecting a Treatment Regimen

[0131] Once a diagnosis is obtained, the clinician can readily select a treatment regimen that is compatible with the diagnosis, such as initiating renal replacement therapy, withdrawing delivery of compounds that are known to be damaging to the

kidney, kidney transplantation, delaying or avoiding procedures that are known to be damaging to the kidney, modifying diuretic administration, initiating goal directed therapy, etc. The skilled artisan is aware of appropriate treatments for numerous diseases discussed in relation to the methods of diagnosis described herein. See, e.g., Merck Manual of Diagnosis and Therapy, 17th Ed. Merck Research Laboratories, Whitehouse Station, NJ, 1999. In addition, since the methods and compositions described herein provide prognostic information, the markers of the present invention may be used to monitor a course of treatment. For example, improved or worsened prognostic state may indicate that a particular treatment is or is not efficacious.

[0132] One skilled in the art readily appreciates that the present invention is well adapted to carry out the objects and obtain the ends and advantages mentioned, as well as those inherent therein. The examples provided herein are representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention.

[0133] Example 1: Contrast-induced nephropathy sample collection

[0134] The objective of this sample collection study is to collect samples of plasma and urine and clinical data from patients before and after receiving intravascular contrast media. Approximately 250 adults undergoing radiographic/angiographic procedures involving intravascular administration of iodinated contrast media are enrolled. To be enrolled in the study, each patient must meet all of the following inclusion criteria and none of the following exclusion criteria:

Inclusion Criteria

males and females 18 years of age or older;

undergoing a radiographic / angiographic procedure (such as a CT scan or coronary intervention) involving the intravascular administration of contrast media;

expected to be hospitalized for at least 48 hours after contrast administration.

able and willing to provide written informed consent for study participation and to comply with all study procedures.

Exclusion Criteria

renal transplant recipients;

acutely worsening renal function prior to the contrast procedure;

already receiving dialysis (either acute or chronic) or in imminent need of dialysis at enrollment;

expected to undergo a major surgical procedure (such as involving cardiopulmonary bypass) or an additional imaging procedure with contrast media with significant risk for further renal insult within the 48 hrs following contrast administration;

participation in an interventional clinical study with an experimental therapy within the previous 30 days;

known infection with human immunodeficiency virus (HIV) or a hepatitis virus.

[0135] Immediately prior to the first contrast administration (and after any pre-procedure hydration), an EDTA anti-coagulated blood sample (10 mL) and a urine sample (10 mL) are collected from each patient. Blood and urine samples are then collected at 4 (±0.5), 8 (±1), 24 (±2) 48 (±2), and 72 (±2) hrs following the last administration of contrast media during the index contrast procedure. Blood is collected via direct venipuncture or via other available venous access, such as an existing femoral sheath, central venous line, peripheral intravenous line or hep-lock. These study blood samples are processed to plasma at the clinical site, frozen and shipped to Astute Medical, Inc., San Diego, CA. The study urine samples are frozen and shipped to Astute Medical, Inc.

[0136] Serum creatinine is assessed at the site immediately prior to the first contrast administration (after any pre-procedure hydration) and at 4 (±0.5), 8 (±1), 24 (±2) and 48 (±2)), and 72 (±2) hours following the last administration of contrast (ideally at the same time as the study samples are obtained). In addition, each patient's status is evaluated through day 30 with regard to additional serum and urine creatinine measurements, a need for dialysis, hospitalization status, and adverse clinical outcomes (including mortality).

[0137] Prior to contrast administration, each patient is assigned a risk based on the following assessment: systolic blood pressure <80 mm Hg = 5 points; intra-arterial balloon pump = 5 points; congestive heart failure (Class III-IV or history of pulmonary edema) = 5 points; age >75 yrs = 4 points; hematocrit level <39% for men, <35% for women = 3 points; diabetes = 3 points; contrast media volume = 1 point for each 100 mL; serum creatinine level >1.5 g/dL = 4 points OR estimated GFR 40–60 mL/min/1.73 m^2 = 2 points, 20–40 mL/min/1.73 m^2 = 4 points, < 20 mL/min/1.73 m^2 = 6 points. The risks

assigned are as follows: risk for CIN and dialysis: 5 or less total points = risk of CIN - 7.5%, risk of dialysis - 0.04%; 6–10 total points = risk of CIN - 14%, risk of dialysis - 0.12%; 11–16 total points = risk of CIN - 26.1%, risk of dialysis - 1.09%; >16 total points = risk of CIN - 57.3%, risk of dialysis - 12.8%.

[0138] Example 2: Cardiac surgery sample collection

[0139] The objective of this sample collection study is to collect samples of plasma and urine and clinical data from patients before and after undergoing cardiovascular surgery, a procedure known to be potentially damaging to kidney function. Approximately 900 adults undergoing such surgery are enrolled. To be enrolled in the study, each patient must meet all of the following inclusion criteria and none of the following exclusion criteria:

Inclusion Criteria

males and females 18 years of age or older;

undergoing cardiovascular surgery;

Toronto/Ottawa Predictive Risk Index for Renal Replacement risk score of at least 2 (Wijeysundera *et al., JAMA* 297: 1801-9, 2007); and

able and willing to provide written informed consent for study participation and to comply with all study procedures.

Exclusion Criteria

known pregnancy;

previous renal transplantation;

acutely worsening renal function prior to enrollment (e.g., any category of

RIFLE criteria);

already receiving dialysis (either acute or chronic) or in imminent need of dialysis at enrollment;

currently enrolled in another clinical study or expected to be enrolled in another clinical study within 7 days of cardiac surgery that involves drug infusion or a therapeutic intervention for AKI;

known infection with human immunodeficiency virus (HIV) or a hepatitis virus.

[0140] Within 3 hours prior to the first incision (and after any pre-procedure hydration), an EDTA anti-coagulated blood sample (10 mL), whole blood (3 mL), and a urine sample (35 mL) are collected from each patient. Blood and urine samples are then collected at 3 (±0.5), 6 (±0.5), 12 (±1), 24 (±2) and 48 (±2) hrs following the procedure and then daily on days 3 through 7 if the subject remains in the hospital. Blood is collected via direct venipuncture or via other available venous access, such as an existing femoral sheath, central venous line, peripheral intravenous line or hep-lock. These study blood samples are frozen and shipped to Astute Medical, Inc., San Diego, CA. The study urine samples are frozen and shipped to Astute Medical, Inc.

[0141] Example 3: Acutely ill subject sample collection

[0142] The objective of this study is to collect samples from acutely ill patients. Approximately 900 adults expected to be in the ICU for at least 48 hours will be enrolled. To be enrolled in the study, each patient must meet all of the following inclusion criteria and none of the following exclusion criteria:

Inclusion Criteria

males and females 18 years of age or older;

Study population 1: approximately 300 patients that have at least one of:

shock (SBP < 90 mmHg and/or need for vasopressor support to maintain MAP > 60 mmHg and/or documented drop in SBP of at least 40 mmHg); and

sepsis;

Study population 2: approximately 300 patients that have at least one of:

IV antibiotics ordered in computerized physician order entry (CPOE) within 24 hours of enrollment;

contrast media exposure within 24 hours of enrollment;

increased Intra-Abdominal Pressure with acute decompensated heart failure; and

severe trauma as the primary reason for ICU admission and likely to be hospitalized in the ICU for 48 hours after enrollment;

Study population 3: approximately 300 patients expected to be hospitalized through acute care setting (ICU or ED) with a known risk factor for acute renal injury (*e.g.* sepsis, hypotension/shock (Shock = systolic BP < 90 mmHg and/or the need for vasopressor

support to maintain a MAP > 60 mmHg and/or a documented drop in SBP > 40 mmHg), major trauma, hemorrhage, or major surgery); and/or expected to be hospitalized to the ICU for at least 24 hours after enrollment.

Exclusion Criteria

known pregnancy;

institutionalized individuals;

previous renal transplantation;

known acutely worsening renal function prior to enrollment (e.g., any category of RIFLE criteria);

received dialysis (either acute or chronic) within 5 days prior to enrollment or in imminent need of dialysis at the time of enrollment;

known infection with human immunodeficiency virus (HIV) or a hepatitis virus;

meets only the SBP < 90 mmHg inclusion criterion set forth above, and does not have shock in the attending physician's or principal investigator's opinion.

[0143] After providing informed consent, an EDTA anti-coagulated blood sample (10 mL) and a urine sample (25-30 mL) are collected from each patient. Blood and urine samples are then collected at 4 (± 0.5) and 8 (± 1) hours after contrast administration (if applicable); at 12 (± 1), 24 (± 2), and 48 (± 2) hours after enrollment, and thereafter daily up to day 7 to day 14 while the subject is hospitalized. Blood is collected via direct venipuncture or via other available venous access, such as an existing femoral sheath, central venous line, peripheral intravenous line or hep-lock. These study blood samples are processed to plasma at the clinical site, frozen and shipped to Astute Medical, Inc., San Diego, CA. The study urine samples are frozen and shipped to Astute Medical, Inc.

[0144] Example 4. Immunoassay format

[0145] Analytes are measured using standard sandwich enzyme immunoassay techniques. A first antibody which binds the analyte is immobilized in wells of a 96 well polystyrene microplate. Analyte standards and test samples are pipetted into the appropriate wells and any analyte present is bound by the immobilized antibody. After washing away any unbound substances, a horseradish peroxidase-conjugated second antibody which binds the analyte is added to the wells, thereby forming sandwich

complexes with the analyte (if present) and the first antibody. Following a wash to remove any unbound antibody-enzyme reagent, a substrate solution comprising tetramethylbenzidine and hydrogen peroxide is added to the wells. Color develops in proportion to the amount of analyte present in the sample. The color development is stopped and the intensity of the color is measured at 540 nm or 570 nm. An analyte concentration is assigned to the test sample by comparison to a standard curve determined from the analyte standards.

[0146] Example 5. Apparently Healthy Donor and Chronic Disease Patient Samples

[0147] Human urine samples from donors with no known chronic or acute disease ("Apparently Healthy Donors") were purchased from two vendors (Golden West Biologicals, Inc., 27625 Commerce Center Dr., Temecula, CA 92590 and Virginia Medical Research, Inc., 915 First Colonial Rd., Virginia Beach, VA 23454). The urine samples were shipped and stored frozen at less than -20° C. The vendors supplied demographic information for the individual donors including gender, race (Black /White), smoking status and age.

[0148] Human urine samples from donors with various chronic diseases ("Chronic Disease Patients") including congestive heart failure, coronary artery disease, chronic kidney disease, chronic obstructive pulmonary disease, diabetes mellitus and hypertension were purchased from Virginia Medical Research, Inc., 915 First Colonial Rd., Virginia Beach, VA 23454. The urine samples were shipped and stored frozen at less than -20 degrees centigrade. The vendor provided a case report form for each individual donor with age, gender, race (Black/White), smoking status and alcohol use, height, weight, chronic disease(s) diagnosis, current medications and previous surgeries.

[0149] Example 6. Use of Kidney Injury Markers for evaluating renal status in patients

[0150] Patients from the intensive care unit (ICU) were enrolled in the following study. Each patient was classified by kidney status as non-injury (0), risk of injury (R), injury (I), and failure (F) according to the maximum stage reached within 7 days of enrollment as determined by the RIFLE criteria. EDTA anti-coagulated blood samples (10 mL) and a urine samples (25-30 mL) were collected from each patient at enrollment, 4 (± 0.5) and 8 (± 1) hours after contrast administration (if applicable); at 12 (± 1), 24 (±

2), and 48 (± 2) hours after enrollment, and thereafter daily up to day 7 to day 14 while the subject is hospitalized. Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, Carcinoembryonic antigen-related cell adhesion molecule 5, and Cellular tumor antigen p53 were each measured by standard immunoassay methods using commercially available assay reagents in the urine samples and the plasma component of the blood samples collected. Concentrations were reported as follows: Tumor necrosis factor receptor superfamily member 10B – ng/ml, Cadherin-16 – ng/ml, Caspase-9 – ng/ml, Bcl2 antagonist of cell death – absorbance units, Caspase-1 – pg/ml, Cadherin-1 – pg/ml, Poly [ADP-ribose] polymerase 1 – ng/ml, Cyclin-dependent kinase inhibitor 1 – pg/ml, Cadherin-5 – ng/ml, Myoglobin – ng/ml, Apolipoprotein A-II – ng/ml, Mucin-16, Carcinoembryonic antigen-related cell adhesion molecule 5, and Cellular tumor antigen p53 – U/ml, Carcinoembryonic antigen-related cell adhesion molecule 5 – ng/ml, and Cellular tumor antigen p53 – ng/ml.

[0151] Two cohorts were defined as described in the introduction to each of the following tables. In the following tables, the time "prior max stage" represents the time at which a sample is collected, relative to the time a particular patient reaches the lowest disease stage as defined for that cohort, binned into three groups which are +/- 12 hours. For example, "24 hr prior" which uses 0 vs R, I, F as the two cohorts would mean 24 hr (+/- 12 hours) prior to reaching stage R (or I if no sample at R, or F if no sample at R or I).

[0152] A receiver operating characteristic (ROC) curve was generated for each biomarker measured and the area under each ROC curve (AUC) was determined. Patients in Cohort 2 were also separated according to the reason for adjudication to cohort 2 as being based on serum creatinine measurements (sCr), being based on urine output (UO), or being based on either serum creatinine measurements or urine output. Using the same example discussed above (0 vs R, I, F), for those patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements alone, the stage 0 cohort may have included patients adjudicated to stage R, I, or F on the basis of urine output; for those patients adjudicated to stage R, I, or F on the basis of urine output alone, the stage 0 cohort may have included patients adjudicated to stage R, I, or F on the basis of serum creatinine measurements; and for those patients adjudicated to stage R, I, or F on the basis

of serum creatinine measurements or urine output, the stage 0 cohort contains only patients in stage 0 for both serum creatinine measurements and urine output. Also, in the data for patients adjudicated on the basis of serum creatinine measurements or urine output, the adjudication method which yielded the most severe RIFLE stage was used.

[0153] The ability to distinguish cohort 1 from Cohort 2 was determined using ROC analysis. SE is the standard error of the AUC, n is the number of sample or individual patients ("pts," as indicated). Standard errors were calculated as described in Hanley, J. A., and McNeil, B.J., The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology (1982) 143: 29-36; p values were calculated with a two-tailed Z-test, and are reported as $p<0.05$ in tables 1-6 and $p<0.10$ in tables 7-14. An AUC < 0.5 is indicative of a negative going marker for the comparison, and an AUC > 0.5 is indicative of a positive going marker for the comparison.

[0154] Various threshold (or "cutoff") concentrations were selected, and the associated sensitivity and specificity for distinguishing cohort 1 from cohort 2 were determined. OR is the odds ratio calculated for the particular cutoff concentration, and 95% CI is the confidence interval for the odds ratio.

[0155] Table 1: Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Apolipoprotein A-II

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	71.6	85.6	71.6	72.2	71.6	75.2
Average	199	234	199	394	199	136
Stdev	723	763	723	2590	723	224
p(t-test)		0.70		0.21		0.58
Min	2.08	4.67	2.08	9.26	2.08	1.00E-9
Max	6400	6400	6400	24300	6400	1420
n (Samp)	366	74	366	88	366	41
n (Patient)	196	74	196	88	196	41

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	75.8	85.0	75.8	85.9	75.8	75.2
Average	201	358	201	131	201	120
Stdev	1050	1220	1050	145	1050	127
p(t-test)		0.45		0.69		0.71
Min	1.00E-9	4.67	1.00E-9	9.44	1.00E-9	5.58
Max	24300	6400	24300	677	24300	488
n (Samp)	750	27	750	37	750	23
n (Patient)	294	27	294	37	294	23

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	72.9	95.4	72.9	82.5	72.9	117
Average	219	249	219	483	219	174
Stdev	774	808	774	2820	774	260
p(t-test)		0.78		0.16		0.73
Min	2.08	18.9	2.08	9.26	2.08	1.00E-9
Max	6400	6400	6400	24300	6400	1420
n (Samp)	297	65	297	74	297	35
n (Patient)	132	65	132	74	132	35

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.57	0.54	0.59	0.53	0.54	0.56	0.53	0.51	0.60
SE	0.038	0.058	0.040	0.035	0.050	0.038	0.048	0.062	0.053
p	0.066	0.54	0.019	0.47	0.45	0.11	0.57	0.82	0.068
nCohort 1	366	750	297	366	750	297	366	750	297
nCohort 2	74	27	65	88	37	74	41	23	35
Cutoff 1	53.4	58.0	64.3	46.8	58.2	56.1	46.8	47.2	68.6
Sens 1	70%	70%	71%	70%	70%	70%	71%	74%	71%
Spec 1	38%	36%	45%	32%	37%	38%	32%	28%	48%
Cutoff 2	36.3	34.3	48.8	40.5	33.2	44.5	28.5	41.3	37.4
Sens 2	81%	81%	80%	81%	81%	81%	80%	83%	80%
Spec 2	20%	16%	31%	24%	15%	25%	12%	23%	19%
Cutoff 3	33.5	26.3	36.2	28.5	26.3	33.2	21.0	27.1	23.1
Sens 3	91%	93%	91%	91%	92%	91%	90%	91%	91%
Spec 3	17%	9%	16%	12%	9%	14%	7%	10%	8%
Cutoff 4	107	114	113	107	114	113	107	114	113
Sens 4	39%	41%	42%	34%	41%	41%	39%	35%	54%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	135	148	144	135	148	144	135	148	144
Sens 5	32%	26%	34%	26%	30%	31%	32%	17%	46%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	226	227	292	226	227	292	226	227	292
Sens 6	18%	15%	14%	10%	11%	9%	12%	13%	9%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	0.67	0.42	1.2	1.4	0.58	1.1	0.46	1.4	0.60
p Value	0.32	0.21	0.68	0.33	0.31	0.87	0.14	0.56	0.39
95% CI of	0.30	0.11	0.51	0.72	0.21	0.50	0.17	0.44	0.19
OR Quart2	1.5	1.6	2.8	2.7	1.6	2.3	1.3	4.5	1.9
OR Quart 3	1.2	1.1	1.7	0.88	0.79	0.99	0.72	0.80	0.60
p Value	0.59	0.79	0.22	0.72	0.62	0.97	0.48	0.74	0.39
95% CI of	0.60	0.41	0.73	0.43	0.30	0.46	0.29	0.21	0.19
OR Quart3	2.5	3.2	3.8	1.8	2.0	2.1	1.8	3.0	1.9
OR Quart 4	1.6	1.3	2.6	1.5	1.3	1.7	1.2	1.4	2.4
p Value	0.17	0.62	0.018	0.20	0.53	0.12	0.69	0.57	0.056
95% CI of	0.81	0.47	1.2	0.80	0.56	0.86	0.52	0.44	0.98
OR Quart4	3.2	3.5	5.6	3.0	3.1	3.5	2.7	4.5	6.0

Bcl2 antagonist of cell death

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.00173	0.00173	nd	nd	nd	nd
Average	0.0412	0.00246	nd	nd	nd	nd

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Stdev	0.150	0.00254	nd	nd	nd	nd
p(t-test)		0.38	nd	nd	nd	nd
Min	0.00173	0.00173	nd	nd	nd	nd
Max	0.833	0.0105	nd	nd	nd	nd
n (Samp)	54	12	nd	nd	nd	nd
n (Patient)	36	12	nd	nd	nd	nd

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.00173	0.00173	nd	nd	nd	nd
Average	0.0279	0.00319	nd	nd	nd	nd
Stdev	0.122	0.00359	nd	nd	nd	nd
p(t-test)		0.62	nd	nd	nd	nd
Min	0.00173	0.00173	nd	nd	nd	nd
Max	0.833	0.0105	nd	nd	nd	nd
n (Samp)	84	6	nd	nd	nd	nd
n (Patient)	59	6	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.00173	0.00173	nd	nd	nd	nd
Average	0.0457	0.00173	nd	nd	nd	nd
Stdev	0.172	0	nd	nd	nd	nd
p(t-test)		0.38	nd	nd	nd	nd
Min	0.00173	0.00173	nd	nd	nd	nd
Max	0.833	0.00173	nd	nd	nd	nd
n (Samp)	40	12	nd	nd	nd	nd
n (Patient)	26	12	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.38	0.43	0.39	nd	nd	nd	nd	nd	nd
SE	0.094	0.13	0.097	nd	nd	nd	nd	nd	nd
p	0.20	0.60	0.24	nd	nd	nd	nd	nd	nd
nCohort 1	54	84	40	nd	nd	nd	nd	nd	nd
nCohort 2	12	6	12	nd	nd	nd	nd	nd	nd
Cutoff 1	0	0	0	nd	nd	nd	nd	nd	nd
Sens 1	100%	100%	100%	nd	nd	nd	nd	nd	nd
Spec 1	0%	0%	0%	nd	nd	nd	nd	nd	nd
Cutoff 2	0	0	0	nd	nd	nd	nd	nd	nd
Sens 2	100%	100%	100%	nd	nd	nd	nd	nd	nd
Spec 2	0%	0%	0%	nd	nd	nd	nd	nd	nd
Cutoff 3	0	0	0	nd	nd	nd	nd	nd	nd
Sens 3	100%	100%	100%	nd	nd	nd	nd	nd	nd
Spec 3	0%	0%	0%	nd	nd	nd	nd	nd	nd
Cutoff 4	0.00509	0.00173	0.00173	nd	nd	nd	nd	nd	nd
Sens 4	8%	17%	0%	nd	nd	nd	nd	nd	nd
Spec 4	70%	71%	78%	nd	nd	nd	nd	nd	nd
Cutoff 5	0.0148	0.00943	0.00509	nd	nd	nd	nd	nd	nd
Sens 5	0%	17%	0%	nd	nd	nd	nd	nd	nd
Spec 5	83%	82%	80%	nd	nd	nd	nd	nd	nd
Cutoff 6	0.0354	0.0235	0.0148	nd	nd	nd	nd	nd	nd
Sens 6	0%	0%	0%	nd	nd	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Spec 6	91%	92%	90%	nd	nd	nd	nd	nd	nd
OR Quart 2	9.6	4.9	>0	nd	nd	nd	nd	nd	nd
p Value	0.050	0.17	<na	nd	nd	nd	nd	nd	nd
95% CI of	1.0	0.50	>na	nd	nd	nd	nd	nd	nd
OR Quart2	92	48	na	nd	nd	nd	nd	nd	nd
OR Quart 3	3.4	1.0	>160	nd	nd	nd	nd	nd	nd
p Value	0.31	1.0	<5.9E-4	nd	nd	nd	nd	nd	nd
95% CI of	0.32	0.059	>8.8	nd	nd	nd	nd	nd	nd
OR Quart3	37	17	na	nd	nd	nd	nd	nd	nd
OR Quart 4	2.3	0	>0	nd	nd	nd	nd	nd	nd
p Value	0.52	na	<na	nd	nd	nd	nd	nd	nd
95% CI of	0.19	na	>na	nd	nd	nd	nd	nd	nd
OR Quart4	28	na	na	nd	nd	nd	nd	nd	nd

Caspase-9

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.469	0.955	nd	nd	nd	nd
Average	1.11	0.937	nd	nd	nd	nd
Stdev	2.89	1.01	nd	nd	nd	nd
p(t-test)		0.84	nd	nd	nd	nd
Min	0.0360	0.0360	nd	nd	nd	nd
Max	19.5	3.69	nd	nd	nd	nd
n (Samp)	54	12	nd	nd	nd	nd
n (Patient)	36	12	nd	nd	nd	nd

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.469	1.05	nd	nd	nd	nd
Average	1.08	1.44	nd	nd	nd	nd
Stdev	2.44	1.42	nd	nd	nd	nd
p(t-test)		0.73	nd	nd	nd	nd
Min	0.0360	0.0360	nd	nd	nd	nd
Max	19.5	3.92	nd	nd	nd	nd
n (Samp)	86	6	nd	nd	nd	nd
n (Patient)	60	6	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.586	0.790	nd	nd	nd	nd
Average	1.35	0.929	nd	nd	nd	nd
Stdev	3.31	0.998	nd	nd	nd	nd
p(t-test)		0.67	nd	nd	nd	nd
Min	0.0360	0.0360	nd	nd	nd	nd
Max	19.5	3.69	nd	nd	nd	nd
n (Samp)	40	12	nd	nd	nd	nd
n (Patient)	26	12	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.59	0.66	0.56	nd	nd	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
SE	0.094	0.13	0.097	nd	nd	nd	nd	nd	nd
p	0.32	0.20	0.52	nd	nd	nd	nd	nd	nd
nCohort 1	54	86	40	nd	nd	nd	nd	nd	nd
nCohort 2	12	6	12	nd	nd	nd	nd	nd	nd
Cutoff 1	0.208	0.330	0.208	nd	nd	nd	nd	nd	nd
Sens 1	75%	83%	83%	nd	nd	nd	nd	nd	nd
Spec 1	37%	38%	28%	nd	nd	nd	nd	nd	nd
Cutoff 2	0	0.330	0.208	nd	nd	nd	nd	nd	nd
Sens 2	100%	83%	83%	nd	nd	nd	nd	nd	nd
Spec 2	0%	38%	28%	nd	nd	nd	nd	nd	nd
Cutoff 3	0	0	0	nd	nd	nd	nd	nd	nd
Sens 3	100%	100%	100%	nd	nd	nd	nd	nd	nd
Spec 3	0%	0%	0%	nd	nd	nd	nd	nd	nd
Cutoff 4	0.703	0.811	0.781	nd	nd	nd	nd	nd	nd
Sens 4	58%	67%	50%	nd	nd	nd	nd	nd	nd
Spec 4	70%	71%	72%	nd	nd	nd	nd	nd	nd
Cutoff 5	1.04	1.04	0.868	nd	nd	nd	nd	nd	nd
Sens 5	33%	50%	50%	nd	nd	nd	nd	nd	nd
Spec 5	81%	80%	80%	nd	nd	nd	nd	nd	nd
Cutoff 6	1.76	2.17	2.17	nd	nd	nd	nd	nd	nd
Sens 6	8%	17%	8%	nd	nd	nd	nd	nd	nd
Spec 6	91%	91%	90%	nd	nd	nd	nd	nd	nd
OR Quart 2	0.58	1.0	1.6	nd	nd	nd	nd	nd	nd
p Value	0.58	1.0	0.62	nd	nd	nd	nd	nd	nd
95% CI of	0.083	0.059	0.23	nd	nd	nd	nd	nd	nd
OR Quart2	4.0	17	12	nd	nd	nd	nd	nd	nd
OR Quart 3	0.29	1.0	1.0	nd	nd	nd	nd	nd	nd
p Value	0.31	1.0	1.0	nd	nd	nd	nd	nd	nd
95% CI of	0.027	0.059	0.12	nd	nd	nd	nd	nd	nd
OR Quart3	3.1	17	8.4	nd	nd	nd	nd	nd	nd
OR Quart 4	2.4	3.3	3.4	nd	nd	nd	nd	nd	nd
p Value	0.29	0.32	0.20	nd	nd	nd	nd	nd	nd
95% CI of	0.48	0.32	0.53	nd	nd	nd	nd	nd	nd
OR Quart4	12	34	22	nd	nd	nd	nd	nd	nd

Cadherin-1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	48800	32700	48800	111000	nd	nd
Average	84900	79300	84900	143000	nd	nd
Stdev	121000	100000	121000	147000	nd	nd
p(t-test)		0.86		0.091	nd	nd
Min	160	1620	160	1660	nd	nd
Max	744000	363000	744000	543000	nd	nd
n (Samp)	52	20	52	20	nd	nd
n (Patient)	41	20	41	20	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	37500	50200	37500	111000	nd	nd
Average	75900	91900	75900	146000	nd	nd
Stdev	124000	107000	124000	140000	nd	nd
p(t-test)		0.65		0.046	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Min	160	1620	160	2220	nd	nd
Max	744000	363000	744000	543000	nd	nd
n (Samp)	42	16	42	21	nd	nd
n (Patient)	33	16	33	21	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.45	nd	0.55	0.64	nd	0.71	nd	nd	nd
SE	0.077	nd	0.086	0.076	nd	0.073	nd	nd	nd
p	0.55	nd	0.58	0.064	nd	0.0041	nd	nd	nd
nCohort 1	52	nd	42	52	nd	42	nd	nd	nd
nCohort 2	20	nd	16	20	nd	21	nd	nd	nd
Cutoff 1	10500	nd	21400	51100	nd	54200	nd	nd	nd
Sens 1	70%	nd	75%	70%	nd	71%	nd	nd	nd
Spec 1	15%	nd	36%	54%	nd	60%	nd	nd	nd
Cutoff 2	9800	nd	10400	28500	nd	36500	nd	nd	nd
Sens 2	80%	nd	81%	80%	nd	81%	nd	nd	nd
Spec 2	13%	nd	24%	38%	nd	50%	nd	nd	nd
Cutoff 3	4310	nd	3350	8380	nd	11700	nd	nd	nd
Sens 3	90%	nd	94%	90%	nd	90%	nd	nd	nd
Spec 3	8%	nd	10%	12%	nd	29%	nd	nd	nd
Cutoff 4	94000	nd	80700	94000	nd	80700	nd	nd	nd
Sens 4	25%	nd	38%	55%	nd	62%	nd	nd	nd
Spec 4	71%	nd	71%	71%	nd	71%	nd	nd	nd
Cutoff 5	134000	nd	122000	134000	nd	122000	nd	nd	nd
Sens 5	20%	nd	31%	40%	nd	48%	nd	nd	nd
Spec 5	81%	nd	81%	81%	nd	81%	nd	nd	nd
Cutoff 6	152000	nd	144000	152000	nd	144000	nd	nd	nd
Sens 6	15%	nd	19%	35%	nd	33%	nd	nd	nd
Spec 6	90%	nd	90%	90%	nd	90%	nd	nd	nd
OR Quart 2	0.74	nd	0.62	1.4	nd	0.92	nd	nd	nd
p Value	0.70	nd	0.59	0.67	nd	0.93	nd	nd	nd
95% CI of	0.16	nd	0.11	0.27	nd	0.16	nd	nd	nd
OR Quart2	3.4	nd	3.5	7.5	nd	5.5	nd	nd	nd
OR Quart 3	0.74	nd	0.68	1.9	nd	1.8	nd	nd	nd
p Value	0.70	nd	0.66	0.43	nd	0.48	nd	nd	nd
95% CI of	0.16	nd	0.12	0.38	nd	0.35	nd	nd	nd
OR Quart3	3.4	nd	3.8	9.6	nd	9.5	nd	nd	nd
OR Quart 4	1.7	nd	1.7	4.0	nd	6.7	nd	nd	nd
p Value	0.48	nd	0.52	0.080	nd	0.022	nd	nd	nd
95% CI of	0.41	nd	0.35	0.85	nd	1.3	nd	nd	nd
OR Quart4	6.7	nd	7.9	19	nd	34	nd	nd	nd

Cadherin-5

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.00224	0.00224	nd	nd	nd	nd
Average	0.0957	0.0142	nd	nd	nd	nd
Stdev	0.210	0.0183	nd	nd	nd	nd
p(t-test)		0.28	nd	nd	nd	nd
Min	0.00224	0.00224	nd	nd	nd	nd
Max	1.10	0.0502	nd	nd	nd	nd
n (Samp)	47	8	nd	nd	nd	nd

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
n (Patient)	30	8	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.00224	0.00224	nd	nd	nd	nd
Average	0.0806	0.00753	nd	nd	nd	nd
Stdev	0.218	0.0108	nd	nd	nd	nd
p(t-test)		0.32	nd	nd	nd	nd
Min	0.00224	0.00224	nd	nd	nd	nd
Max	1.10	0.0309	nd	nd	nd	nd
n (Samp)	34	9	nd	nd	nd	nd
n (Patient)	20	9	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.46	nd	0.44	nd	nd	nd	nd	nd	nd
SE	0.11	nd	0.11	nd	nd	nd	nd	nd	nd
p	0.72	nd	0.62	nd	nd	nd	nd	nd	nd
nCohort 1	47	nd	34	nd	nd	nd	nd	nd	nd
nCohort 2	8	nd	9	nd	nd	nd	nd	nd	nd
Cutoff 1	0	nd	0	nd	nd	nd	nd	nd	nd
Sens 1	100%	nd	100%	nd	nd	nd	nd	nd	nd
Spec 1	0%	nd	0%	nd	nd	nd	nd	nd	nd
Cutoff 2	0	nd	0	nd	nd	nd	nd	nd	nd
Sens 2	100%	nd	100%	nd	nd	nd	nd	nd	nd
Spec 2	0%	nd	0%	nd	nd	nd	nd	nd	nd
Cutoff 3	0	nd	0	nd	nd	nd	nd	nd	nd
Sens 3	100%	nd	100%	nd	nd	nd	nd	nd	nd
Spec 3	0%	nd	0%	nd	nd	nd	nd	nd	nd
Cutoff 4	0.0405	nd	0.00224	nd	nd	nd	nd	nd	nd
Sens 4	12%	nd	22%	nd	nd	nd	nd	nd	nd
Spec 4	72%	nd	71%	nd	nd	nd	nd	nd	nd
Cutoff 5	0.137	nd	0.127	nd	nd	nd	nd	nd	nd
Sens 5	0%	nd	0%	nd	nd	nd	nd	nd	nd
Spec 5	81%	nd	82%	nd	nd	nd	nd	nd	nd
Cutoff 6	0.329	nd	0.239	nd	nd	nd	nd	nd	nd
Sens 6	0%	nd	0%	nd	nd	nd	nd	nd	nd
Spec 6	91%	nd	91%	nd	nd	nd	nd	nd	nd
OR Quart 2	2.2	nd	0	nd	nd	nd	nd	nd	nd
p Value	0.55	nd	na	nd	nd	nd	nd	nd	nd
95% CI of	0.17	nd	na	nd	nd	nd	nd	nd	nd
OR Quart2	27	nd	na	nd	nd	nd	nd	nd	nd
OR Quart 3	3.5	nd	5.4	nd	nd	nd	nd	nd	nd
p Value	0.30	nd	0.088	nd	nd	nd	nd	nd	nd
95% CI of	0.32	nd	0.78	nd	nd	nd	nd	nd	nd
OR Quart3	39	nd	38	nd	nd	nd	nd	nd	nd
OR Quart 4	2.4	nd	0.50	nd	nd	nd	nd	nd	nd
p Value	0.51	nd	0.60	nd	nd	nd	nd	nd	nd
95% CI of	0.19	nd	0.038	nd	nd	nd	nd	nd	nd
OR Quart4	30	nd	6.5	nd	nd	nd	nd	nd	nd

Cyclin-dependent kinase inhibitor 1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.713	0.116	0.713	1.98	0.713	1.09
Average	103	8.88	103	19.5	103	5.00
Stdev	670	19.5	670	49.0	670	9.16
p(t-test)		0.33		0.35		0.47
Min	1.14E-14	1.70E-14	1.14E-14	1.70E-14	1.14E-14	1.70E-14
Max	6950	112	6950	327	6950	42.0
n (Samp)	165	48	165	56	165	25
n (Patient)	102	48	102	56	102	25

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.09	5.28	1.09	10.7	1.09	2.45
Average	62.4	15.7	62.4	19.5	62.4	6.76
Stdev	482	28.6	482	21.2	482	12.3
p(t-test)		0.70		0.69		0.68
Min	1.14E-14	0.116	1.14E-14	1.70E-14	1.14E-14	1.70E-14
Max	6950	112	6950	71.0	6950	44.1
n (Samp)	325	16	325	20	325	13
n (Patient)	168	16	168	20	168	13

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.850	0.116	0.850	2.45	0.850	1.09
Average	119	24.9	119	23.7	119	10.5
Stdev	729	97.5	729	60.2	729	24.6
p(t-test)		0.39		0.35		0.48
Min	1.14E-14	1.70E-14	1.14E-14	0.116	1.14E-14	0.116
Max	6950	630	6950	327	6950	112
n (Samp)	139	46	139	51	139	23
n (Patient)	85	46	85	51	85	23

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.45	0.61	0.45	0.53	0.62	0.54	0.46	0.46	0.49
SE	0.048	0.077	0.050	0.045	0.069	0.048	0.063	0.084	0.065
p	0.35	0.16	0.28	0.51	0.088	0.44	0.58	0.60	0.89
nCohort 1	165	325	139	165	325	139	165	325	139
nCohort 2	48	16	46	56	20	51	25	13	23
Cutoff 1	1.70E-14	0.850	1.70E-14	1.70E-14	0.850	1.14E-14	1.70E-14	1.70E-14	1.14E-14
Sens 1	98%	75%	98%	96%	75%	100%	96%	92%	100%
Spec 1	2%	50%	2%	2%	50%	2%	2%	2%	2%
Cutoff 2	1.70E-14	0.116	1.70E-14	1.70E-14	1.70E-14	1.14E-14	1.70E-14	1.70E-14	1.14E-14
Sens 2	98%	81%	98%	96%	90%	100%	96%	92%	100%
Spec 2	2%	43%	2%	2%	2%	2%	2%	2%	2%
Cutoff 3	1.70E-14	1.14E-14	1.70E-14	1.70E-14	1.70E-14	1.14E-14	1.70E-14	1.70E-14	1.14E-14
Sens 3	98%	100%	98%	96%	90%	100%	96%	92%	100%
Spec 3	2%	2%	2%	2%	2%	2%	2%	2%	2%
Cutoff 4	7.84	9.28	9.28	7.84	9.28	9.28	7.84	9.28	9.28
Sens 4	23%	25%	26%	38%	50%	35%	24%	15%	22%
Spec 4	70%	71%	71%	70%	71%	71%	70%	71%	71%
Cutoff 5	18.3	15.5	22.7	18.3	15.5	22.7	18.3	15.5	22.7
Sens 5	17%	25%	15%	25%	45%	20%	4%	15%	13%
Spec 5	80%	80%	81%	80%	80%	81%	80%	80%	81%

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Cutoff 6	60.3	44.8	73.1	60.3	44.8	73.1	60.3	44.8	73.1
Sens 6	2%	6%	4%	7%	10%	6%	0%	0%	4%
Spec 6	90%	90%	91%	90%	90%	91%	90%	90%	91%
OR Quart 2	1.3	0.33	1.0	0.25	0.19	0.60	4.6	2.6	2.7
p Value	0.60	0.34	0.96	0.0079	0.13	0.31	0.027	0.26	0.13
95% CI of	0.50	0.033	0.38	0.091	0.022	0.23	1.2	0.50	0.75
OR Quart2	3.3	3.2	2.8	0.70	1.7	1.6	18	14	9.6
OR Quart 3	0.78	2.8	1.2	0.77	0.79	1.1	0	0	0.23
p Value	0.64	0.13	0.76	0.53	0.73	0.82	na	na	0.20
95% CI of	0.28	0.73	0.44	0.34	0.20	0.45	na	na	0.025
OR Quart3	2.2	11	3.1	1.7	3.0	2.7	na	na	2.2
OR Quart 4	2.3	1.3	1.8	0.90	2.1	1.2	4.6	3.2	2.7
p Value	0.073	0.71	0.22	0.79	0.19	0.70	0.027	0.16	0.13
95% CI of	0.93	0.29	0.71	0.40	0.69	0.49	1.2	0.63	0.75
OR Quart4	5.5	6.1	4.5	2.0	6.4	2.9	18	16	9.6

Carcinoembryonic antigen-related cell adhesion molecule 5

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.646	1.40	0.646	1.30	0.646	1.38
Average	2.04	4.66	2.04	4.98	2.04	4.81
Stdev	4.06	7.77	4.06	10.7	4.06	9.92
p(t-test)		6.7E-4		7.2E-4		0.0064
Min	0.00336	0.00336	0.00336	0.0411	0.00336	0.0844
Max	43.4	29.4	43.4	54.4	43.4	47.4
n (Samp)	253	48	253	57	253	26
n (Patient)	102	48	102	57	102	26

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.947	1.48	0.947	1.66	0.947	2.29
Average	12.1	3.83	12.1	7.05	12.1	3.90
Stdev	192	5.63	192	12.5	192	4.53
p(t-test)		0.86		0.90		0.88
Min	0.00336	0.00336	0.00336	0.0411	0.00336	0.173
Max	4070	21.1	4070	51.3	4070	15.3
n (Samp)	447	16	447	21	447	13
n (Patient)	170	16	170	21	170	13

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.625	1.44	0.625	1.25	0.625	1.35
Average	2.35	4.89	2.35	4.76	2.35	4.02
Stdev	4.80	7.57	4.80	10.6	4.80	9.89
p(t-test)		0.0038		0.015		0.16
Min	0.00336	0.00336	0.00336	0.0946	0.00336	0.00336
Max	43.4	29.4	43.4	54.4	43.4	47.4
n (Samp)	212	47	212	52	212	25
n (Patient)	85	47	85	52	85	25

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.62	0.56	0.64	0.61	0.62	0.61	0.60	0.65	0.55

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
SE	0.046	0.076	0.047	0.043	0.067	0.045	0.061	0.084	0.062
p	0.012	0.44	0.0036	0.0089	0.081	0.014	0.11	0.068	0.41
nCohort 1	253	447	212	253	447	212	253	447	212
nCohort 2	48	16	47	57	21	52	26	13	25
Cutoff 1	0.540	0.414	0.550	0.607	1.10	0.607	0.456	1.06	0.456
Sens 1	71%	75%	70%	70%	71%	71%	73%	77%	72%
Spec 1	45%	32%	46%	48%	53%	49%	42%	53%	43%
Cutoff 2	0.383	0.271	0.485	0.394	0.394	0.444	0.303	0.849	0.303
Sens 2	81%	81%	81%	81%	81%	81%	81%	85%	80%
Spec 2	37%	23%	43%	38%	31%	42%	31%	47%	32%
Cutoff 3	0.146	0.102	0.148	0.173	0.0990	0.211	0.146	0.211	0.0990
Sens 3	92%	94%	91%	91%	90%	90%	92%	92%	92%
Spec 3	13%	7%	12%	16%	7%	20%	13%	17%	8%
Cutoff 4	1.54	1.91	1.54	1.54	1.91	1.54	1.54	1.91	1.54
Sens 4	38%	44%	43%	44%	48%	42%	42%	54%	32%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	2.53	3.14	2.77	2.53	3.14	2.77	2.53	3.14	2.77
Sens 5	35%	44%	34%	28%	33%	25%	27%	31%	16%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	5.50	8.51	6.40	5.50	8.51	6.40	5.50	8.51	6.40
Sens 6	21%	12%	23%	18%	19%	17%	19%	15%	12%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	2.2	0.74	1.8	1.6	0.66	1.3	0.57	0.50	0.58
p Value	0.14	0.69	0.30	0.36	0.65	0.61	0.46	0.57	0.47
95% CI of	0.78	0.16	0.60	0.60	0.11	0.48	0.13	0.044	0.13
OR Quart2	6.2	3.4	5.2	4.1	4.0	3.5	2.5	5.5	2.5
OR Quart 3	2.4	0.49	2.2	3.0	2.8	3.2	2.1	2.6	2.8
p Value	0.093	0.41	0.14	0.015	0.14	0.013	0.19	0.27	0.074
95% CI of	0.86	0.087	0.77	1.2	0.72	1.3	0.69	0.49	0.90
OR Quart3	6.7	2.7	6.2	7.4	11	7.8	6.6	14	8.4
OR Quart 4	3.3	1.8	4.0	2.4	2.8	2.0	1.7	2.6	0.98
p Value	0.018	0.37	0.0064	0.058	0.14	0.17	0.40	0.27	0.98
95% CI of	1.2	0.51	1.5	0.97	0.72	0.76	0.51	0.49	0.27
OR Quart4	8.9	6.3	11	6.0	11	5.0	5.3	14	3.6

Myoglobin

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.21	0.965	1.21	0.546	1.21	0.330
Average	26.0	38.3	26.0	70.8	26.0	47.2
Stdev	82.5	97.7	82.5	151	82.5	131
p(t-test)		0.36		0.0021		0.24
Min	0.000105	0.000105	0.000105	0.0276	0.000105	0.0254
Max	618	469	618	618	618	469
n (Samp)	253	48	253	57	253	26
n (Patient)	102	48	102	57	102	26

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.608	0.186	0.608	0.375	0.608	0.349
Average	32.4	66.7	32.4	58.7	32.4	62.5
Stdev	99.0	156	99.0	131	99.0	173
p(t-test)		0.18		0.24		0.29
Min	0.000105	0.000105	0.000105	0.0375	0.000105	0.0567

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Max	618	469	618	442	618	618
n (Samp)	447	16	447	21	447	13
n (Patient)	170	16	170	21	170	13

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.23	1.00	1.23	0.855	1.23	0.366
Average	29.6	29.5	29.6	76.5	29.6	68.8
Stdev	90.0	76.4	90.0	160	90.0	155
p(t-test)		0.99		0.0051		0.062
Min	0.00616	0.0266	0.00616	0.000105	0.00616	0.0254
Max	618	469	618	618	618	469
n (Samp)	212	47	212	52	212	25
n (Patient)	85	47	85	52	85	25

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.51	0.48	0.51	0.50	0.53	0.51	0.45	0.52	0.50
SE	0.046	0.074	0.047	0.042	0.066	0.045	0.061	0.082	0.061
p	0.85	0.84	0.87	0.94	0.66	0.84	0.44	0.76	0.97
nCohort 1	253	447	212	253	447	212	253	447	212
nCohort 2	48	16	47	57	21	52	26	13	25
Cutoff 1	0.0819	0.0422	0.0832	0.0855	0.0849	0.0855	0.0877	0.132	0.118
Sens 1	71%	75%	70%	70%	71%	71%	73%	77%	72%
Spec 1	19%	16%	19%	19%	26%	19%	19%	33%	24%
Cutoff 2	0.0394	0.0333	0.0485	0.0746	0.0556	0.0767	0.0667	0.0667	0.0832
Sens 2	81%	81%	81%	81%	81%	81%	81%	85%	80%
Spec 2	11%	12%	11%	18%	21%	18%	17%	23%	19%
Cutoff 3	0.0329	0	0.0333	0.0337	0.0399	0.0333	0.0296	0.0584	0.0296
Sens 3	92%	100%	91%	91%	90%	90%	92%	92%	92%
Spec 3	8%	0%	7%	8%	15%	7%	6%	22%	5%
Cutoff 4	6.79	5.77	7.09	6.79	5.77	7.09	6.79	5.77	7.09
Sens 4	44%	44%	43%	35%	38%	37%	23%	31%	32%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	16.7	16.8	18.6	16.7	16.8	18.6	16.7	16.8	18.6
Sens 5	31%	38%	26%	32%	29%	31%	19%	15%	28%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	45.5	63.4	54.1	45.5	63.4	54.1	45.5	63.4	54.1
Sens 6	19%	12%	13%	21%	19%	23%	12%	15%	16%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	0.33	0	0.33	0.47	1.0	0.42	0.65	1.7	0.47
p Value	0.020	na	0.025	0.068	1.0	0.056	0.51	0.48	0.24
95% CI of	0.13	na	0.13	0.21	0.31	0.17	0.17	0.40	0.13
OR Quart2	0.84	na	0.87	1.1	3.2	1.0	2.4	7.3	1.7
OR Quart 3	0.33	0.41	0.39	0.33	0.32	0.37	1.4	0.66	0.60
p Value	0.020	0.21	0.045	0.015	0.17	0.032	0.57	0.65	0.40
95% CI of	0.13	0.10	0.15	0.14	0.064	0.15	0.45	0.11	0.18
OR Quart3	0.84	1.6	0.98	0.81	1.6	0.92	4.2	4.0	2.0
OR Quart 4	0.84	0.86	0.83	0.86	1.2	0.93	1.4	1.0	1.0
p Value	0.66	0.79	0.65	0.68	0.78	0.84	0.56	1.0	0.97
95% CI of	0.39	0.28	0.37	0.41	0.38	0.43	0.46	0.20	0.36
OR Quart4	1.8	2.6	1.8	1.8	3.6	2.0	4.3	5.1	2.9

Mucin-16

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.619	0.753	0.619	0.547	nd	nd
Average	1.06	1.12	1.06	23.1	nd	nd
Stdev	1.28	0.983	1.28	96.4	nd	nd
p(t-test)		0.85		0.10	nd	nd
Min	0.141	1.00E-9	0.141	0.223	nd	nd
Max	6.37	3.40	6.37	433	nd	nd
n (Samp)	52	20	52	20	nd	nd
n (Patient)	41	20	41	20	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.547	0.654	0.547	0.684	nd	nd
Average	0.951	1.00	0.951	22.0	nd	nd
Stdev	1.18	0.898	1.18	94.1	nd	nd
p(t-test)		0.87		0.15	nd	nd
Min	0.0565	1.00E-9	0.0565	0.223	nd	nd
Max	6.37	2.82	6.37	433	nd	nd
n (Samp)	42	16	42	21	nd	nd
n (Patient)	33	16	33	21	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.54	nd	0.54	0.49	nd	0.56	nd	nd	nd
SE	0.077	nd	0.086	0.077	nd	0.078	nd	nd	nd
p	0.61	nd	0.67	0.87	nd	0.48	nd	nd	nd
nCohort 1	52	nd	42	52	nd	42	nd	nd	nd
nCohort 2	20	nd	16	20	nd	21	nd	nd	nd
Cutoff 1	0.479	nd	0.412	0.344	nd	0.384	nd	nd	nd
Sens 1	70%	nd	75%	70%	nd	71%	nd	nd	nd
Spec 1	37%	nd	36%	17%	nd	29%	nd	nd	nd
Cutoff 2	0.223	nd	0.223	0.278	nd	0.278	nd	nd	nd
Sens 2	85%	nd	81%	90%	nd	90%	nd	nd	nd
Spec 2	4%	nd	7%	10%	nd	12%	nd	nd	nd
Cutoff 3	0.146	nd	0.0565	0.278	nd	0.278	nd	nd	nd
Sens 3	90%	nd	94%	90%	nd	90%	nd	nd	nd
Spec 3	4%	nd	2%	10%	nd	12%	nd	nd	nd
Cutoff 4	0.937	nd	0.859	0.937	nd	0.859	nd	nd	nd
Sens 4	45%	nd	38%	30%	nd	43%	nd	nd	nd
Spec 4	71%	nd	71%	71%	nd	71%	nd	nd	nd
Cutoff 5	1.24	nd	1.09	1.24	nd	1.09	nd	nd	nd
Sens 5	40%	nd	38%	30%	nd	33%	nd	nd	nd
Spec 5	81%	nd	81%	81%	nd	81%	nd	nd	nd
Cutoff 6	1.87	nd	1.68	1.87	nd	1.68	nd	nd	nd
Sens 6	20%	nd	19%	25%	nd	24%	nd	nd	nd
Spec 6	90%	nd	90%	90%	nd	90%	nd	nd	nd
OR Quart 2	0.74	nd	0.62	0.40	nd	0.50	nd	nd	nd
p Value	0.70	nd	0.59	0.26	nd	0.38	nd	nd	nd
95% CI of	0.16	nd	0.11	0.082	nd	0.11	nd	nd	nd
OR Quart2	3.4	nd	3.5	1.9	nd	2.3	nd	nd	nd
OR Quart 3	0.52	nd	0.68	0.77	nd	0.50	nd	nd	nd
p Value	0.43	nd	0.66	0.72	nd	0.38	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
95% CI of	0.10	nd	0.12	0.19	nd	0.11	nd	nd	nd
OR Quart3	2.6	nd	3.8	3.2	nd	2.3	nd	nd	nd
OR Quart 4	2.1	nd	1.7	1.0	nd	1.2	nd	nd	nd
p Value	0.30	nd	0.52	1.0	nd	0.83	nd	nd	nd
95% CI of	0.52	nd	0.35	0.25	nd	0.28	nd	nd	nd
OR Quart4	8.3	nd	7.9	4.0	nd	4.9	nd	nd	nd

Poly [ADP-ribose] polymerase 1 (cleaved)

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	0.00439
Average	0.00474	0.00294	0.00474	0.00432	0.00474	0.00271
Stdev	0.00688	0.00538	0.00688	0.00586	0.00688	0.00261
p(t-test)		0.11		0.70		0.16
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	0.0357	0.0144	0.0357	0.0183	0.0357	0.00723
n (Samp)	118	47	118	54	118	24
n (Patient)	97	47	97	54	97	24

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Average	0.00375	0.00338	0.00375	0.00301	0.00375	0.00350
Stdev	0.00582	0.00600	0.00582	0.00648	0.00582	0.00540
p(t-test)		0.82		0.60		0.89
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	0.0357	0.0144	0.0357	0.0253	0.0357	0.0144
n (Samp)	263	14	263	19	263	12
n (Patient)	159	14	159	19	159	12

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	1.00E-9	1.00E-9	0.00340	1.00E-9	0.00471
Average	0.00356	0.00258	0.00356	0.00527	0.00356	0.00448
Stdev	0.00628	0.00494	0.00628	0.00622	0.00628	0.00455
p(t-test)		0.36		0.12		0.51
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	0.0357	0.0144	0.0357	0.0183	0.0357	0.0144
n (Samp)	105	45	105	49	105	23
n (Patient)	84	45	84	49	84	23

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.43	0.46	0.47	0.51	0.45	0.59	0.50	0.50	0.62
SE	0.050	0.081	0.052	0.048	0.070	0.050	0.065	0.086	0.068
p	0.18	0.63	0.51	0.85	0.52	0.060	0.97	0.97	0.071
nCohort 1	118	263	105	118	263	105	118	263	105
nCohort 2	47	14	45	54	19	49	24	12	23
Cutoff 1	0	0	0	0	0	0	0	0	0
Sens 1	100%	100%	100%	100%	100%	100%	100%	100%	100%
Spec 1	0%	0%	0%	0%	0%	0%	0%	0%	0%

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Cutoff 2	0	0	0	0	0	0	0	0	0
Sens 2	100%	100%	100%	100%	100%	100%	100%	100%	100%
Spec 2	0%	0%	0%	0%	0%	0%	0%	0%	0%
Cutoff 3	0	0	0	0	0	0	0	0	0
Sens 3	100%	100%	100%	100%	100%	100%	100%	100%	100%
Spec 3	0%	0%	0%	0%	0%	0%	0%	0%	0%
Cutoff 4	0.00598	0.00471	0.00406	0.00598	0.00471	0.00406	0.00598	0.00471	0.00406
Sens 4	17%	21%	24%	24%	16%	47%	4%	17%	61%
Spec 4	70%	74%	70%	70%	74%	70%	70%	74%	70%
Cutoff 5	0.0141	0.00723	0.00681	0.0141	0.00723	0.00681	0.0141	0.00723	0.00681
Sens 5	11%	21%	13%	19%	11%	31%	0%	17%	17%
Spec 5	81%	81%	80%	81%	81%	80%	81%	81%	80%
Cutoff 6	0.0144	0.0144	0.0144	0.0144	0.0144	0.0144	0.0144	0.0144	0.0144
Sens 6	0%	0%	0%	2%	5%	2%	0%	0%	0%
Spec 6	95%	97%	99%	95%	97%	99%	95%	97%	99%
OR Quart 2	0.59	0.33	1.3	2.3	1.0	1.3	18	1.5	1.0
p Value	0.39	0.34	0.56	0.073	0.99	0.63	0.0069	0.65	1.0
95% CI of	0.18	0.033	0.50	0.93	0.20	0.45	2.2	0.25	0.23
OR Quart2	2.0	3.2	3.6	5.7	5.2	3.7	150	9.4	4.4
OR Quart 3	7.4	3.4	1.0	1.3	4.6	2.2	5.6	3.8	2.3
p Value	8.9E-5	0.080	1.0	0.63	0.022	0.13	0.12	0.11	0.21
95% CI of	2.7	0.87	0.36	0.49	1.2	0.79	0.62	0.76	0.62
OR Quart3	20	13	2.8	3.2	17	6.1	51	19	8.7
OR Quart 4	1.0	0.33	1.5	1.0	0.33	2.9	7.2	0	2.0
p Value	0.96	0.34	0.41	1.0	0.34	0.038	0.074	na	0.33
95% CI of	0.35	0.033	0.56	0.38	0.033	1.1	0.82	na	0.51
OR Quart4	3.1	3.2	4.1	2.6	3.2	7.9	64	na	7.5

KSP-Cadherin

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.03	1.24	1.03	1.15	nd	nd
Average	1.47	1.58	1.47	1.90	nd	nd
Stdev	1.59	1.15	1.59	1.74	nd	nd
p(t-test)		0.71		0.25	nd	nd
Min	0.00263	0.0646	0.00263	0.291	nd	nd
Max	11.9	4.63	11.9	7.51	nd	nd
n (Samp)	85	32	85	25	nd	nd
n (Patient)	68	32	68	25	nd	nd

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.10	0.683	1.10	1.04	nd	nd
Average	1.58	1.36	1.58	1.60	nd	nd
Stdev	1.55	1.28	1.55	1.45	nd	nd
p(t-test)		0.66		0.98	nd	nd
Min	0.00263	0.0646	0.00263	0.291	nd	nd
Max	11.9	3.49	11.9	4.08	nd	nd
n (Samp)	152	10	152	6	nd	nd
n (Patient)	114	10	114	6	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.02	1.40	1.02	1.61	nd	nd
Average	1.55	1.73	1.55	2.07	nd	nd
Stdev	1.72	1.11	1.72	1.77	nd	nd
p(t-test)		0.61		0.19	nd	nd
Min	0.00263	0.557	0.00263	0.371	nd	nd
Max	11.9	4.63	11.9	7.51	nd	nd
n (Samp)	73	27	73	25	nd	nd
n (Patient)	59	27	59	25	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.57	0.44	0.62	0.58	0.50	0.60	nd	nd	nd
SE	0.061	0.097	0.065	0.067	0.12	0.068	nd	nd	nd
p	0.25	0.53	0.068	0.26	1.00	0.12	nd	nd	nd
nCohort 1	85	152	73	85	152	73	nd	nd	nd
nCohort 2	32	10	27	25	6	25	nd	nd	nd
Cutoff 1	0.946	0.622	0.996	0.845	0.569	0.845	nd	nd	nd
Sens 1	72%	70%	70%	72%	83%	72%	nd	nd	nd
Spec 1	46%	25%	48%	40%	22%	41%	nd	nd	nd
Cutoff 2	0.734	0.380	0.935	0.569	0.569	0.723	nd	nd	nd
Sens 2	81%	80%	81%	80%	83%	80%	nd	nd	nd
Spec 2	35%	14%	47%	22%	22%	34%	nd	nd	nd
Cutoff 3	0.555	0.0646	0.739	0.398	0.252	0.426	nd	nd	nd
Sens 3	91%	90%	93%	92%	100%	92%	nd	nd	nd
Spec 3	21%	3%	36%	15%	8%	16%	nd	nd	nd
Cutoff 4	1.66	1.69	1.71	1.66	1.69	1.71	nd	nd	nd
Sens 4	28%	40%	30%	40%	33%	40%	nd	nd	nd
Spec 4	71%	70%	71%	71%	70%	71%	nd	nd	nd
Cutoff 5	2.10	2.45	2.19	2.10	2.45	2.19	nd	nd	nd
Sens 5	25%	30%	26%	36%	33%	36%	nd	nd	nd
Spec 5	80%	80%	81%	80%	80%	81%	nd	nd	nd
Cutoff 6	2.74	3.39	3.17	2.74	3.39	3.17	nd	nd	nd
Sens 6	16%	10%	11%	16%	17%	20%	nd	nd	nd
Spec 6	91%	90%	90%	91%	90%	90%	nd	nd	nd
OR Quart 2	2.2	0.32	16	0.76	0.47	0.95	nd	nd	nd
p Value	0.22	0.34	0.012	0.69	0.55	0.94	nd	nd	nd
95% CI of	0.62	0.032	1.9	0.20	0.041	0.24	nd	nd	nd
OR Quart2	7.5	3.3	140	2.9	5.5	3.8	nd	nd	nd
OR Quart 3	2.5	1.0	14	0.80	0.49	1.3	nd	nd	nd
p Value	0.14	1.0	0.018	0.74	0.56	0.73	nd	nd	nd
95% CI of	0.74	0.19	1.6	0.21	0.042	0.33	nd	nd	nd
OR Quart3	8.6	5.3	120	3.0	5.6	4.9	nd	nd	nd
OR Quart 4	1.7	1.0	9.3	1.7	0.97	2.1	nd	nd	nd
p Value	0.39	0.97	0.045	0.41	0.98	0.24	nd	nd	nd
95% CI of	0.50	0.19	1.1	0.50	0.13	0.59	nd	nd	nd
OR Quart4	6.1	5.4	83	5.5	7.3	7.7	nd	nd	nd

Tumor necrosis factor receptor superfamily member 10B

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.124	0.573	0.124	0.395	nd	nd
Average	0.891	1.21	0.891	1.09	nd	nd
Stdev	1.49	1.55	1.49	1.82	nd	nd

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
p(t-test)		0.43		0.64	nd	nd
Min	0.00360	0.0182	0.00360	0.00464	nd	nd
Max	6.71	4.65	6.71	6.48	nd	nd
n (Samp)	52	20	52	20	nd	nd
n (Patient)	41	20	41	20	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.106	0.709	0.106	0.464	nd	nd
Average	0.595	1.40	0.595	1.25	nd	nd
Stdev	1.03	1.68	1.03	1.96	nd	nd
p(t-test)		0.031		0.087	nd	nd
Min	0.00360	0.0573	0.00360	0.0172	nd	nd
Max	4.38	4.65	4.38	6.48	nd	nd
n (Samp)	42	16	42	21	nd	nd
n (Patient)	33	16	33	21	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.64	nd	0.71	0.62	nd	0.68	nd	nd	nd
SE	0.076	nd	0.081	0.076	nd	0.074	nd	nd	nd
p	0.064	nd	0.0099	0.12	nd	0.014	nd	nd	nd
nCohort 1	52	nd	42	52	nd	42	nd	nd	nd
nCohort 2	20	nd	16	20	nd	21	nd	nd	nd
Cutoff 1	0.182	nd	0.107	0.154	nd	0.154	nd	nd	nd
Sens 1	70%	nd	75%	70%	nd	71%	nd	nd	nd
Spec 1	54%	nd	52%	52%	nd	55%	nd	nd	nd
Cutoff 2	0.0761	nd	0.0761	0.141	nd	0.141	nd	nd	nd
Sens 2	80%	nd	81%	80%	nd	81%	nd	nd	nd
Spec 2	40%	nd	40%	52%	nd	55%	nd	nd	nd
Cutoff 3	0.0591	nd	0.0591	0.0796	nd	0.101	nd	nd	nd
Sens 3	90%	nd	94%	90%	nd	90%	nd	nd	nd
Spec 3	38%	nd	38%	44%	nd	48%	nd	nd	nd
Cutoff 4	0.786	nd	0.398	0.786	nd	0.398	nd	nd	nd
Sens 4	45%	nd	56%	30%	nd	52%	nd	nd	nd
Spec 4	71%	nd	71%	71%	nd	71%	nd	nd	nd
Cutoff 5	1.56	nd	0.819	1.56	nd	0.819	nd	nd	nd
Sens 5	25%	nd	50%	15%	nd	33%	nd	nd	nd
Spec 5	81%	nd	81%	81%	nd	81%	nd	nd	nd
Cutoff 6	3.11	nd	2.19	3.11	nd	2.19	nd	nd	nd
Sens 6	15%	nd	25%	10%	nd	14%	nd	nd	nd
Spec 6	90%	nd	90%	90%	nd	90%	nd	nd	nd
OR Quart 2	8.5	nd	>7.0	11	nd	11	nd	nd	nd
p Value	0.061	nd	<0.097	0.036	nd	0.038	nd	nd	nd
95% CI of	0.90	nd	>0.71	1.2	nd	1.1	nd	nd	nd
OR Quart2	80	nd	na	100	nd	100	nd	nd	nd
OR Quart 3	11	nd	>3.8	11	nd	8.4	nd	nd	nd
p Value	0.036	nd	<0.27	0.036	nd	0.066	nd	nd	nd
95% CI of	1.2	nd	>0.35	1.2	nd	0.87	nd	nd	nd
OR Quart3	100	nd	na	100	nd	81	nd	nd	nd
OR Quart 4	8.5	nd	>16	6.5	nd	11	nd	nd	nd
p Value	0.061	nd	<0.017	0.10	nd	0.038	nd	nd	nd
95% CI of	0.90	nd	>1.7	0.68	nd	1.1	nd	nd	nd
OR Quart4	80	nd	na	63	nd	100	nd	nd	nd

[0156] Table 2: Comparison of marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in urine samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

Apolipoprotein A-II

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	73.2	102	73.2	116	73.2	81.7
Average	185	272	185	697	185	87.4
Stdev	645	1020	645	3530	645	69.4
p(t-test)		0.44		0.0018		0.44
Min	2.08	8.69	2.08	10.8	2.08	1.00E-9
Max	6400	6400	6400	24300	6400	301
n (Samp)	685	38	685	47	685	26
n (Patient)	283	38	283	47	283	26

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	76.6	106	76.6	127	76.6	98.8
Average	198	891	198	176	198	108
Stdev	990	2230	990	158	990	84.1
p(t-test)		0.053		0.93		0.74
Min	1.00E-9	34.5	1.00E-9	24.0	1.00E-9	6.18
Max	24300	6400	24300	613	24300	288
n (Samp)	891	8	891	13	891	13
n (Patient)	334	8	334	13	334	13

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	76.6	107	76.6	131	76.6	98.7
Average	195	297	195	789	195	105
Stdev	649	1060	649	3780	649	74.2
p(t-test)		0.39		0.0017		0.52
Min	2.08	8.69	2.08	10.8	2.08	1.00E-9
Max	6400	6400	6400	24300	6400	301
n (Samp)	553	35	553	41	553	22
n (Patient)	202	35	202	41	202	22

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.59	0.60	0.60	0.66	0.66	0.67	0.47	0.51	0.53
SE	0.050	0.11	0.052	0.045	0.083	0.048	0.059	0.081	0.064
p	0.069	0.36	0.053	3.3E-4	0.055	2.3E-4	0.60	0.87	0.61
nCohort 1	685	891	553	685	891	553	685	891	553
nCohort 2	38	8	35	47	13	41	26	13	22
Cutoff 1	70.0	59.9	76.9	85.8	85.8	99.4	39.3	39.3	56.5
Sens 1	71%	75%	71%	70%	77%	71%	73%	77%	73%
Spec 1	48%	37%	50%	59%	56%	63%	22%	21%	35%
Cutoff 2	56.5	49.4	69.8	66.5	66.5	72.6	31.3	31.3	43.2
Sens 2	82%	88%	80%	81%	85%	80%	81%	85%	82%

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Spec 2	38%	30%	45%	46%	43%	47%	14%	13%	22%
Cutoff 3	33.5	34.3	33.5	43.2	43.2	44.8	11.0	16.2	27.1
Sens 3	92%	100%	91%	91%	92%	90%	92%	92%	91%
Spec 3	16%	16%	14%	26%	24%	24%	2%	3%	9%
Cutoff 4	110	122	118	110	122	118	110	122	118
Sens 4	42%	50%	46%	53%	62%	54%	31%	38%	36%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	148	154	154	148	154	154	148	154	154
Sens 5	18%	38%	20%	38%	31%	41%	19%	23%	14%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	226	229	248	226	229	248	226	229	248
Sens 6	11%	12%	11%	21%	31%	24%	4%	8%	5%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	1.2	2.0	1.2	1.4	0.50	0.49	1.3	0	0.79
p Value	0.79	0.57	0.76	0.56	0.57	0.31	0.59	na	0.73
95% CI of	0.38	0.18	0.36	0.44	0.045	0.12	0.46	na	0.21
OR Quart2	3.5	22	4.1	4.5	5.5	2.0	4.0	na	3.0
OR Quart 3	2.2	2.0	2.5	3.2	2.5	2.3	0.49	0.59	1.2
p Value	0.11	0.57	0.090	0.028	0.27	0.10	0.32	0.48	0.77
95% CI of	0.83	0.18	0.87	1.1	0.49	0.84	0.12	0.14	0.36
OR Quart3	6.0	22	7.4	8.9	13	6.2	2.0	2.5	4.0
OR Quart 4	2.1	3.0	2.5	4.4	2.5	3.5	1.5	1.0	1.4
p Value	0.16	0.34	0.090	0.0040	0.27	0.010	0.43	1.0	0.57
95% CI of	0.76	0.31	0.87	1.6	0.49	1.3	0.53	0.29	0.44
OR Quart4	5.6	29	7.4	12	13	8.9	4.4	3.5	4.6

Caspase-1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.02	0.826	nd	nd	nd	nd
Average	1.20	0.896	nd	nd	nd	nd
Stdev	1.22	0.687	nd	nd	nd	nd
p(t-test)		0.49	nd	nd	nd	nd
Min	0.0223	0.0223	nd	nd	nd	nd
Max	4.68	2.33	nd	nd	nd	nd
n (Samp)	55	8	nd	nd	nd	nd
n (Patient)	35	8	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.09	0.826	nd	nd	nd	nd
Average	1.20	0.896	nd	nd	nd	nd
Stdev	1.19	0.687	nd	nd	nd	nd
p(t-test)		0.50	nd	nd	nd	nd
Min	0.0223	0.0223	nd	nd	nd	nd
Max	4.46	2.33	nd	nd	nd	nd
n (Samp)	41	8	nd	nd	nd	nd
n (Patient)	24	8	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.46	nd	0.46	nd	nd	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
SE	0.11	nd	0.11	nd	nd	nd	nd	nd	nd
p	0.74	nd	0.76	nd	nd	nd	nd	nd	nd
nCohort 1	55	nd	41	nd	nd	nd	nd	nd	nd
nCohort 2	8	nd	8	nd	nd	nd	nd	nd	nd
Cutoff 1	0.496	nd	0.496	nd	nd	nd	nd	nd	nd
Sens 1	75%	nd	75%	nd	nd	nd	nd	nd	nd
Spec 1	40%	nd	41%	nd	nd	nd	nd	nd	nd
Cutoff 2	0.298	nd	0.298	nd	nd	nd	nd	nd	nd
Sens 2	88%	nd	88%	nd	nd	nd	nd	nd	nd
Spec 2	36%	nd	37%	nd	nd	nd	nd	nd	nd
Cutoff 3	0	nd	0	nd	nd	nd	nd	nd	nd
Sens 3	100%	nd	100%	nd	nd	nd	nd	nd	nd
Spec 3	0%	nd	0%	nd	nd	nd	nd	nd	nd
Cutoff 4	1.54	nd	1.54	nd	nd	nd	nd	nd	nd
Sens 4	12%	nd	12%	nd	nd	nd	nd	nd	nd
Spec 4	71%	nd	71%	nd	nd	nd	nd	nd	nd
Cutoff 5	2.07	nd	2.07	nd	nd	nd	nd	nd	nd
Sens 5	12%	nd	12%	nd	nd	nd	nd	nd	nd
Spec 5	82%	nd	85%	nd	nd	nd	nd	nd	nd
Cutoff 6	2.59	nd	2.59	nd	nd	nd	nd	nd	nd
Sens 6	0%	nd	0%	nd	nd	nd	nd	nd	nd
Spec 6	91%	nd	90%	nd	nd	nd	nd	nd	nd
OR Quart 2	1.0	nd	2.4	nd	nd	nd	nd	nd	nd
p Value	1.0	nd	0.50	nd	nd	nd	nd	nd	nd
95% CI of	0.057	nd	0.19	nd	nd	nd	nd	nd	nd
OR Quart2	18	nd	31	nd	nd	nd	nd	nd	nd
OR Quart 3	6.8	nd	6.0	nd	nd	nd	nd	nd	nd
p Value	0.099	nd	0.14	nd	nd	nd	nd	nd	nd
95% CI of	0.69	nd	0.56	nd	nd	nd	nd	nd	nd
OR Quart3	67	nd	64	nd	nd	nd	nd	nd	nd
OR Quart 4	1.1	nd	1.1	nd	nd	nd	nd	nd	nd
p Value	0.96	nd	0.95	nd	nd	nd	nd	nd	nd
95% CI of	0.061	nd	0.061	nd	nd	nd	nd	nd	nd
OR Quart4	19	nd	20	nd	nd	nd	nd	nd	nd

Caspase-9

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.469	0.547	nd	nd	nd	nd
Average	0.965	0.998	nd	nd	nd	nd
Stdev	2.44	1.52	nd	nd	nd	nd
p(t-test)		0.97	nd	nd	nd	nd
Min	0.0360	0.0360	nd	nd	nd	nd
Max	19.5	4.64	nd	nd	nd	nd
n (Samp)	78	8	nd	nd	nd	nd
n (Patient)	56	8	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.469	0.547	nd	nd	nd	nd
Average	1.12	0.998	nd	nd	nd	nd
Stdev	2.73	1.52	nd	nd	nd	nd
p(t-test)		0.90	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Min	0.0360	0.0360	nd	nd	nd	nd
Max	19.5	4.64	nd	nd	nd	nd
n (Samp)	61	8	nd	nd	nd	nd
n (Patient)	43	8	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.54	nd	0.50	nd	nd	nd	nd	nd	nd
SE	0.11	nd	0.11	nd	nd	nd	nd	nd	nd
p	0.73	nd	0.98	nd	nd	nd	nd	nd	nd
nCohort 1	78	nd	61	nd	nd	nd	nd	nd	nd
nCohort 2	8	nd	8	nd	nd	nd	nd	nd	nd
Cutoff 1	0.208	nd	0.208	nd	nd	nd	nd	nd	nd
Sens 1	75%	nd	75%	nd	nd	nd	nd	nd	nd
Spec 1	36%	nd	28%	nd	nd	nd	nd	nd	nd
Cutoff 2	0	nd	0	nd	nd	nd	nd	nd	nd
Sens 2	100%	nd	100%	nd	nd	nd	nd	nd	nd
Spec 2	0%	nd	0%	nd	nd	nd	nd	nd	nd
Cutoff 3	0	nd	0	nd	nd	nd	nd	nd	nd
Sens 3	100%	nd	100%	nd	nd	nd	nd	nd	nd
Spec 3	0%	nd	0%	nd	nd	nd	nd	nd	nd
Cutoff 4	0.781	nd	0.781	nd	nd	nd	nd	nd	nd
Sens 4	38%	nd	38%	nd	nd	nd	nd	nd	nd
Spec 4	72%	nd	70%	nd	nd	nd	nd	nd	nd
Cutoff 5	0.955	nd	0.955	nd	nd	nd	nd	nd	nd
Sens 5	25%	nd	25%	nd	nd	nd	nd	nd	nd
Spec 5	81%	nd	80%	nd	nd	nd	nd	nd	nd
Cutoff 6	1.66	nd	1.49	nd	nd	nd	nd	nd	nd
Sens 6	12%	nd	12%	nd	nd	nd	nd	nd	nd
Spec 6	91%	nd	90%	nd	nd	nd	nd	nd	nd
OR Quart 2	0.95	nd	0.47	nd	nd	nd	nd	nd	nd
p Value	0.96	nd	0.55	nd	nd	nd	nd	nd	nd
95% CI of	0.12	nd	0.038	nd	nd	nd	nd	nd	nd
OR Quart2	7.4	nd	5.7	nd	nd	nd	nd	nd	nd
OR Quart 3	1.0	nd	1.0	nd	nd	nd	nd	nd	nd
p Value	1.0	nd	1.0	nd	nd	nd	nd	nd	nd
95% CI of	0.13	nd	0.12	nd	nd	nd	nd	nd	nd
OR Quart3	7.9	nd	8.1	nd	nd	nd	nd	nd	nd
OR Quart 4	0.95	nd	1.5	nd	nd	nd	nd	nd	nd
p Value	0.96	nd	0.68	nd	nd	nd	nd	nd	nd
95% CI of	0.12	nd	0.22	nd	nd	nd	nd	nd	nd
OR Quart4	7.4	nd	10	nd	nd	nd	nd	nd	nd

Cadherin-1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	57300	62400	nd	nd
Average	nd	nd	102000	78500	nd	nd
Stdev	nd	nd	128000	81700	nd	nd
p(t-test)	nd	nd		0.47	nd	nd
Min	nd	nd	160	1620	nd	nd
Max	nd	nd	744000	260000	nd	nd
n (Samp)	nd	nd	96	16	nd	nd

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
n (Patient)	nd	nd	73	16	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	58600	59500	nd	nd
Average	nd	nd	104000	82000	nd	nd
Stdev	nd	nd	134000	82800	nd	nd
p(t-test)	nd	nd		0.54	nd	nd
Min	nd	nd	160	1620	nd	nd
Max	nd	nd	744000	260000	nd	nd
n (Samp)	nd	nd	81	15	nd	nd
n (Patient)	nd	nd	61	15	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	nd	nd	nd	0.44	nd	0.47	nd	nd	nd
SE	nd	nd	nd	0.080	nd	0.082	nd	nd	nd
p	nd	nd	nd	0.49	nd	0.72	nd	nd	nd
nCohort 1	nd	nd	nd	96	nd	81	nd	nd	nd
nCohort 2	nd	nd	nd	16	nd	15	nd	nd	nd
Cutoff 1	nd	nd	nd	12500	nd	12900	nd	nd	nd
Sens 1	nd	nd	nd	75%	nd	73%	nd	nd	nd
Spec 1	nd	nd	nd	19%	nd	22%	nd	nd	nd
Cutoff 2	nd	nd	nd	9460	nd	11700	nd	nd	nd
Sens 2	nd	nd	nd	81%	nd	80%	nd	nd	nd
Spec 2	nd	nd	nd	11%	nd	22%	nd	nd	nd
Cutoff 3	nd	nd	nd	1660	nd	1660	nd	nd	nd
Sens 3	nd	nd	nd	94%	nd	93%	nd	nd	nd
Spec 3	nd	nd	nd	2%	nd	2%	nd	nd	nd
Cutoff 4	nd	nd	nd	128000	nd	125000	nd	nd	nd
Sens 4	nd	nd	nd	25%	nd	27%	nd	nd	nd
Spec 4	nd	nd	nd	71%	nd	70%	nd	nd	nd
Cutoff 5	nd	nd	nd	141000	nd	144000	nd	nd	nd
Sens 5	nd	nd	nd	25%	nd	27%	nd	nd	nd
Spec 5	nd	nd	nd	80%	nd	80%	nd	nd	nd
Cutoff 6	nd	nd	nd	219000	nd	219000	nd	nd	nd
Sens 6	nd	nd	nd	6%	nd	7%	nd	nd	nd
Spec 6	nd	nd	nd	91%	nd	90%	nd	nd	nd
OR Quart 2	nd	nd	nd	1.3	nd	1.0	nd	nd	nd
p Value	nd	nd	nd	0.72	nd	1.0	nd	nd	nd
95% CI of	nd	nd	nd	0.31	nd	0.22	nd	nd	nd
OR Quart2	nd	nd	nd	5.5	nd	4.6	nd	nd	nd
OR Quart 3	nd	nd	nd	0	nd	0.45	nd	nd	nd
p Value	nd	nd	nd	na	nd	0.39	nd	nd	nd
95% CI of	nd	nd	nd	na	nd	0.075	nd	nd	nd
OR Quart3	nd	nd	nd	na	nd	2.8	nd	nd	nd
OR Quart 4	nd	nd	nd	2.0	nd	1.3	nd	nd	nd
p Value	nd	nd	nd	0.32	nd	0.71	nd	nd	nd
95% CI of	nd	nd	nd	0.51	nd	0.31	nd	nd	nd
OR Quart4	nd	nd	nd	7.8	nd	5.6	nd	nd	nd

Cyclin-dependent kinase inhibitor 1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.09	3.35	1.09	4.76	1.09	2.45
Average	62.1	42.8	62.1	57.1	62.1	13.0
Stdev	497	133	497	173	497	18.2
p(t-test)		0.85		0.95		0.68
Min	1.14E-14	1.70E-14	1.14E-14	0.116	1.14E-14	0.116
Max	6950	630	6950	907	6950	52.9
n (Samp)	302	24	302	35	302	17
n (Patient)	164	24	164	35	164	17

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	1.23	7.84	1.23	9.80
Average	nd	nd	58.3	15.2	58.3	15.4
Stdev	nd	nd	447	17.6	447	16.5
p(t-test)	nd	nd		0.80		0.80
Min	nd	nd	1.14E-14	0.116	1.14E-14	0.116
Max	nd	nd	6950	42.1	6950	39.2
n (Samp)	nd	nd	380	7	380	7
n (Patient)	nd	nd	196	7	196	7

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.850	3.35	0.850	2.87	0.850	2.66
Average	70.1	42.8	70.1	62.4	70.1	12.3
Stdev	538	133	538	183	538	17.6
p(t-test)		0.80		0.94		0.67
Min	1.14E-14	1.70E-14	1.14E-14	0.116	1.14E-14	0.116
Max	6950	630	6950	907	6950	52.9
n (Samp)	257	24	257	31	257	16
n (Patient)	134	24	134	31	134	16

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.55	nd	0.54	0.59	0.64	0.58	0.55	0.60	0.59
SE	0.063	nd	0.063	0.053	0.11	0.056	0.074	0.11	0.077
p	0.46	nd	0.50	0.080	0.21	0.16	0.49	0.36	0.24
nCohort 1	302	nd	257	302	380	257	302	380	257
nCohort 2	24	nd	24	35	7	31	17	7	16
Cutoff 1	1.70E-14	nd	1.70E-14	0.713	6.55	1.70E-14	1.70E-14	2.02	0.116
Sens 1	96%	nd	96%	71%	71%	100%	100%	71%	75%
Spec 1	2%	nd	2%	47%	65%	2%	2%	52%	45%
Cutoff 2	1.70E-14	nd	1.70E-14	1.70E-14	0.850	1.70E-14	1.70E-14	1.70E-14	1.70E-14
Sens 2	96%	nd	96%	100%	86%	100%	100%	100%	100%
Spec 2	2%	nd	2%	2%	47%	2%	2%	2%	2%
Cutoff 3	1.70E-14	nd	1.70E-14	1.70E-14	1.70E-14	1.70E-14	1.70E-14	1.70E-14	1.70E-14
Sens 3	96%	nd	96%	100%	100%	100%	100%	100%	100%
Spec 3	2%	nd	2%	2%	2%	2%	2%	2%	2%
Cutoff 4	7.84	nd	7.29	7.84	9.35	7.29	7.84	9.35	7.29
Sens 4	38%	nd	38%	43%	29%	42%	41%	57%	44%
Spec 4	70%	nd	70%	70%	71%	70%	70%	71%	70%
Cutoff 5	16.1	nd	13.9	16.1	18.3	13.9	16.1	18.3	13.9
Sens 5	21%	nd	21%	29%	29%	32%	24%	43%	31%

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Spec 5	80%	nd	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	43.4	nd	44.8	43.4	48.9	44.8	43.4	48.9	44.8
Sens 6	12%	nd	12%	11%	0%	13%	12%	0%	12%
Spec 6	90%	nd	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	0.23	nd	0	1.4	0.99	2.9	>7.6	0	0.24
p Value	0.067	nd	na	0.55	0.99	0.13	<0.061	na	0.21
95% CI of	0.047	nd	na	0.44	0.061	0.73	>0.91	na	0.026
OR Quart2	1.1	nd	na	4.7	16	11	na	na	2.2
OR Quart 3	0.86	nd	0.87	2.6	3.0	3.3	>3.1	0.99	1.3
p Value	0.79	nd	0.80	0.082	0.34	0.084	<0.33	0.99	0.73
95% CI of	0.30	nd	0.32	0.88	0.31	0.85	>0.31	0.14	0.33
OR Quart3	2.5	nd	2.4	7.8	30	13	na	7.2	4.9
OR Quart 4	0.85	nd	0.74	2.3	2.0	4.1	>7.6	1.5	1.5
p Value	0.77	nd	0.58	0.13	0.57	0.035	<0.061	0.66	0.53
95% CI of	0.29	nd	0.26	0.78	0.18	1.1	>0.91	0.25	0.41
OR Quart4	2.5	nd	2.1	7.1	22	16	na	9.2	5.7

Carcinoembryonic antigen-related cell adhesion molecule 5

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.852	1.70	0.852	2.56	0.852	1.46
Average	12.6	4.03	12.6	5.68	12.6	4.91
Stdev	199	4.99	199	9.51	199	11.3
p(t-test)		0.83		0.84		0.87
Min	0.00336	0.00336	0.00336	0.0950	0.00336	0.148
Max	4070	19.5	4070	50.6	4070	47.4
n (Samp)	419	26	419	34	419	17
n (Patient)	164	26	164	34	164	17

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	0.978	3.62	0.978	5.87
Average	nd	nd	11.1	5.25	11.1	6.39
Stdev	nd	nd	180	7.06	180	4.92
p(t-test)	nd	nd		0.93		0.94
Min	nd	nd	0.00336	0.102	0.00336	0.173
Max	nd	nd	4070	22.0	4070	14.6
n (Samp)	nd	nd	511	8	511	7
n (Patient)	nd	nd	198	8	198	7

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.852	1.48	0.852	2.42	0.852	1.12
Average	14.6	3.87	14.6	5.34	14.6	4.41
Stdev	216	5.02	216	9.63	216	11.3
p(t-test)		0.80		0.81		0.85
Min	0.00336	0.0573	0.00336	0.00336	0.00336	0.148
Max	4070	19.5	4070	50.6	4070	47.4
n (Samp)	355	26	355	30	355	17
n (Patient)	134	26	134	30	134	17

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.63	nd	0.61	0.67	0.65	0.66	0.57	0.76	0.54
SE	0.060	nd	0.061	0.052	0.11	0.056	0.074	0.11	0.073
p	0.029	nd	0.059	0.0014	0.16	0.0056	0.34	0.016	0.58
nCohort 1	419	nd	355	419	511	355	419	511	355
nCohort 2	26	nd	26	34	8	30	17	7	17
Cutoff 1	0.969	nd	0.816	0.942	2.26	0.942	0.607	3.47	0.491
Sens 1	73%	nd	73%	71%	75%	70%	71%	71%	71%
Spec 1	53%	nd	50%	52%	73%	51%	43%	80%	39%
Cutoff 2	0.590	nd	0.590	0.546	0.214	0.684	0.279	2.55	0.279
Sens 2	81%	nd	81%	82%	88%	80%	82%	86%	82%
Spec 2	42%	nd	43%	41%	17%	47%	25%	74%	25%
Cutoff 3	0.150	nd	0.150	0.214	0.0990	0.444	0.150	0.172	0.150
Sens 3	92%	nd	92%	91%	100%	90%	94%	100%	94%
Spec 3	12%	nd	12%	18%	7%	37%	12%	14%	12%
Cutoff 4	1.76	nd	1.84	1.76	1.97	1.84	1.76	1.97	1.84
Sens 4	50%	nd	46%	59%	75%	57%	41%	86%	29%
Spec 4	70%	nd	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	3.16	nd	3.25	3.16	3.51	3.25	3.16	3.51	3.25
Sens 5	38%	nd	35%	44%	50%	40%	24%	57%	18%
Spec 5	80%	nd	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	8.38	nd	8.86	8.38	8.51	8.86	8.38	8.51	8.86
Sens 6	15%	nd	12%	15%	12%	13%	12%	29%	6%
Spec 6	90%	nd	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	1.3	nd	1.7	1.5	0	2.4	0.74	0	1.7
p Value	0.70	nd	0.47	0.52	na	0.21	0.70	na	0.47
95% CI of	0.29	nd	0.40	0.42	na	0.61	0.16	na	0.40
OR Quart2	6.2	nd	7.3	5.6	na	9.7	3.4	na	7.3
OR Quart 3	3.2	nd	3.2	2.1	0.99	2.4	1.3	1.0	1.7
p Value	0.090	nd	0.088	0.24	0.99	0.21	0.73	1.0	0.47
95% CI of	0.84	nd	0.84	0.61	0.14	0.61	0.33	0.062	0.40
OR Quart3	12	nd	12	7.1	7.2	9.7	4.8	16	7.3
OR Quart 4	3.5	nd	3.2	4.4	2.0	4.8	1.3	5.1	1.3
p Value	0.061	nd	0.091	0.0096	0.42	0.017	0.73	0.14	0.70
95% CI of	0.94	nd	0.83	1.4	0.36	1.3	0.33	0.59	0.29
OR Quart4	13	nd	12	14	11	17	4.8	44	6.2

Myoglobin

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.860	0.477	0.860	0.126	0.860	0.176
Average	35.5	18.1	35.5	44.2	35.5	6.85
Stdev	103	38.1	103	130	103	15.5
p(t-test)		0.39		0.64		0.25
Min	0.000105	0.0151	0.000105	0.000105	0.000105	0.0254
Max	618	163	618	469	618	49.1
n (Samp)	419	26	419	34	419	17
n (Patient)	164	26	164	34	164	17

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	0.599	4.97	0.599	0.349
Average	nd	nd	37.0	95.0	37.0	19.7

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Stdev	nd	nd	109	171	109	28.5
p(t-test)	nd	nd		0.14		0.68
Min	nd	nd	0.000105	0.0561	0.000105	0.0683
Max	nd	nd	618	420	618	71.6
n (Samp)	nd	nd	511	8	511	7
n (Patient)	nd	nd	198	8	198	7

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.885	0.354	0.885	0.108	0.885	0.176
Average	40.5	17.6	40.5	36.1	40.5	5.29
Stdev	112	38.2	112	119	112	12.1
p(t-test)		0.30		0.84		0.20
Min	0.000105	0.0151	0.000105	0.000105	0.000105	0.0254
Max	618	163	618	469	618	49.1
n (Samp)	355	26	355	30	355	17
n (Patient)	134	26	134	30	134	17

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.48	nd	0.45	0.39	0.57	0.38	0.40	0.55	0.39
SE	0.059	nd	0.060	0.053	0.11	0.057	0.074	0.11	0.074
p	0.72	nd	0.36	0.045	0.53	0.031	0.16	0.67	0.15
nCohort 1	419	nd	355	419	511	355	419	511	355
nCohort 2	26	nd	26	34	8	30	17	7	17
Cutoff 1	0.0772	nd	0.0667	0.0584	0.118	0.0562	0.0849	0.132	0.0834
Sens 1	73%	nd	73%	71%	75%	70%	71%	71%	71%
Spec 1	22%	nd	20%	19%	32%	18%	23%	32%	22%
Cutoff 2	0.0511	nd	0.0422	0.0375	0.0589	0.0366	0.0667	0.0849	0.0630
Sens 2	81%	nd	81%	82%	88%	80%	82%	86%	82%
Spec 2	18%	nd	13%	12%	22%	11%	21%	26%	19%
Cutoff 3	0.0375	nd	0.0366	0.0331	0.0556	0.0331	0.0337	0.0667	0.0337
Sens 3	92%	nd	92%	91%	100%	90%	94%	100%	94%
Spec 3	12%	nd	11%	10%	21%	9%	11%	23%	10%
Cutoff 4	7.09	nd	7.24	7.09	6.05	7.24	7.09	6.05	7.24
Sens 4	31%	nd	27%	21%	50%	20%	18%	43%	24%
Spec 4	70%	nd	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	19.0	nd	23.8	19.0	17.9	23.8	19.0	17.9	23.8
Sens 5	19%	nd	19%	15%	25%	13%	12%	43%	6%
Spec 5	80%	nd	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	66.4	nd	79.4	66.4	70.5	79.4	66.4	70.5	79.4
Sens 6	12%	nd	8%	12%	25%	7%	0%	14%	0%
Spec 6	90%	nd	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	0.83	nd	0.66	0.83	0.99	0.66	0.66	3.0	2.0
p Value	0.77	nd	0.53	0.77	0.99	0.53	0.65	0.34	0.42
95% CI of	0.25	nd	0.18	0.25	0.14	0.18	0.11	0.31	0.37
OR Quart2	2.8	nd	2.4	2.8	7.2	2.4	4.0	29	11
OR Quart 3	1.0	nd	1.0	1.2	0.49	0.83	2.1	0	2.0
p Value	0.99	nd	0.99	0.76	0.56	0.77	0.32	na	0.42
95% CI of	0.32	nd	0.31	0.39	0.044	0.25	0.50	na	0.37
OR Quart3	3.2	nd	3.3	3.7	5.5	2.8	8.4	na	11
OR Quart 4	1.6	nd	1.8	3.0	1.5	2.8	2.1	3.0	3.7
p Value	0.42	nd	0.29	0.029	0.66	0.042	0.32	0.34	0.11
95% CI of	0.54	nd	0.61	1.1	0.25	1.0	0.50	0.31	0.75

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
OR Quart4	4.5	nd	5.1	7.9	9.1	7.6	8.4	29	18

Mucin-16

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	0.684	0.822	nd	nd
Average	nd	nd	1.24	28.1	nd	nd
Stdev	nd	nd	1.59	108	nd	nd
p(t-test)	nd	nd		0.014	nd	nd
Min	nd	nd	1.00E-9	0.304	nd	nd
Max	nd	nd	10.1	433	nd	nd
n (Samp)	nd	nd	96	16	nd	nd
n (Patient)	nd	nd	73	16	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	0.623	0.822	nd	nd
Average	nd	nd	1.23	29.9	nd	nd
Stdev	nd	nd	1.64	111	nd	nd
p(t-test)	nd	nd		0.020	nd	nd
Min	nd	nd	1.00E-9	0.304	nd	nd
Max	nd	nd	10.1	433	nd	nd
n (Samp)	nd	nd	81	15	nd	nd
n (Patient)	nd	nd	61	15	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	nd	nd	nd	0.55	nd	0.56	nd	nd	nd
SE	nd	nd	nd	0.080	nd	0.083	nd	nd	nd
p	nd	nd	nd	0.49	nd	0.45	nd	nd	nd
nCohort 1	nd	nd	nd	96	nd	81	nd	nd	nd
nCohort 2	nd	nd	nd	16	nd	15	nd	nd	nd
Cutoff 1	nd	nd	nd	0.412	nd	0.412	nd	nd	nd
Sens 1	nd	nd	nd	75%	nd	73%	nd	nd	nd
Spec 1	nd	nd	nd	32%	nd	36%	nd	nd	nd
Cutoff 2	nd	nd	nd	0.344	nd	0.344	nd	nd	nd
Sens 2	nd	nd	nd	88%	nd	87%	nd	nd	nd
Spec 2	nd	nd	nd	21%	nd	26%	nd	nd	nd
Cutoff 3	nd	nd	nd	0.278	nd	0.278	nd	nd	nd
Sens 3	nd	nd	nd	100%	nd	100%	nd	nd	nd
Spec 3	nd	nd	nd	11%	nd	15%	nd	nd	nd
Cutoff 4	nd	nd	nd	1.17	nd	1.09	nd	nd	nd
Sens 4	nd	nd	nd	25%	nd	33%	nd	nd	nd
Spec 4	nd	nd	nd	71%	nd	70%	nd	nd	nd
Cutoff 5	nd	nd	nd	1.41	nd	1.44	nd	nd	nd
Sens 5	nd	nd	nd	19%	nd	20%	nd	nd	nd
Spec 5	nd	nd	nd	80%	nd	80%	nd	nd	nd
Cutoff 6	nd	nd	nd	3.40	nd	3.26	nd	nd	nd
Sens 6	nd	nd	nd	12%	nd	13%	nd	nd	nd
Spec 6	nd	nd	nd	91%	nd	90%	nd	nd	nd
OR Quart 2	nd	nd	nd	0.72	nd	1.0	nd	nd	nd
p Value	nd	nd	nd	0.69	nd	1.0	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
95% CI of	nd	nd	nd	0.15	nd	0.18	nd	nd	nd
OR Quart2	nd	nd	nd	3.6	nd	5.5	nd	nd	nd
OR Quart 3	nd	nd	nd	1.3	nd	1.8	nd	nd	nd
p Value	nd	nd	nd	0.72	nd	0.44	nd	nd	nd
95% CI of	nd	nd	nd	0.31	nd	0.39	nd	nd	nd
OR Quart3	nd	nd	nd	5.5	nd	8.8	nd	nd	nd
OR Quart 4	nd	nd	nd	1.0	nd	1.4	nd	nd	nd
p Value	nd	nd	nd	1.0	nd	0.68	nd	nd	nd
95% CI of	nd	nd	nd	0.22	nd	0.28	nd	nd	nd
OR Quart4	nd	nd	nd	4.5	nd	7.1	nd	nd	nd

Tumor necrosis factor receptor superfamily member 10B

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	0.344	0.306	nd	nd
Average	nd	nd	0.956	1.45	nd	nd
Stdev	nd	nd	1.45	1.97	nd	nd
p(t-test)	nd	nd		0.24	nd	nd
Min	nd	nd	0.00360	0.0172	nd	nd
Max	nd	nd	6.71	5.86	nd	nd
n (Samp)	nd	nd	96	16	nd	nd
n (Patient)	nd	nd	73	16	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	0.343	0.287	nd	nd
Average	nd	nd	0.805	1.42	nd	nd
Stdev	nd	nd	1.26	2.00	nd	nd
p(t-test)	nd	nd		0.12	nd	nd
Min	nd	nd	0.00360	0.0172	nd	nd
Max	nd	nd	6.48	5.86	nd	nd
n (Samp)	nd	nd	81	15	nd	nd
n (Patient)	nd	nd	61	15	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	nd	nd	nd	0.56	nd	0.55	nd	nd	nd
SE	nd	nd	nd	0.080	nd	0.083	nd	nd	nd
p	nd	nd	nd	0.46	nd	0.53	nd	nd	nd
nCohort 1	nd	nd	nd	96	nd	81	nd	nd	nd
nCohort 2	nd	nd	nd	16	nd	15	nd	nd	nd
Cutoff 1	nd	nd	nd	0.109	nd	0.109	nd	nd	nd
Sens 1	nd	nd	nd	75%	nd	73%	nd	nd	nd
Spec 1	nd	nd	nd	35%	nd	36%	nd	nd	nd
Cutoff 2	nd	nd	nd	0.101	nd	0.101	nd	nd	nd
Sens 2	nd	nd	nd	81%	nd	80%	nd	nd	nd
Spec 2	nd	nd	nd	31%	nd	32%	nd	nd	nd
Cutoff 3	nd	nd	nd	0.0198	nd	0.0182	nd	nd	nd
Sens 3	nd	nd	nd	94%	nd	93%	nd	nd	nd
Spec 3	nd	nd	nd	11%	nd	11%	nd	nd	nd
Cutoff 4	nd	nd	nd	0.855	nd	0.819	nd	nd	nd
Sens 4	nd	nd	nd	38%	nd	33%	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Spec 4	nd	nd	nd	71%	nd	70%	nd	nd	nd
Cutoff 5	nd	nd	nd	1.56	nd	0.979	nd	nd	nd
Sens 5	nd	nd	nd	31%	nd	33%	nd	nd	nd
Spec 5	nd	nd	nd	80%	nd	80%	nd	nd	nd
Cutoff 6	nd	nd	nd	3.11	nd	2.25	nd	nd	nd
Sens 6	nd	nd	nd	19%	nd	27%	nd	nd	nd
Spec 6	nd	nd	nd	91%	nd	90%	nd	nd	nd
OR Quart 2	nd	nd	nd	4.3	nd	3.7	nd	nd	nd
p Value	nd	nd	nd	0.086	nd	0.14	nd	nd	nd
95% CI of	nd	nd	nd	0.81	nd	0.66	nd	nd	nd
OR Quart2	nd	nd	nd	23	nd	20	nd	nd	nd
OR Quart 3	nd	nd	nd	0.48	nd	1.0	nd	nd	nd
p Value	nd	nd	nd	0.56	nd	1.0	nd	nd	nd
95% CI of	nd	nd	nd	0.041	nd	0.13	nd	nd	nd
OR Quart3	nd	nd	nd	5.6	nd	7.7	nd	nd	nd
OR Quart 4	nd	nd	nd	3.5	nd	2.9	nd	nd	nd
p Value	nd	nd	nd	0.14	nd	0.23	nd	nd	nd
95% CI of	nd	nd	nd	0.65	nd	0.50	nd	nd	nd
OR Quart4	nd	nd	nd	19	nd	17	nd	nd	nd

Cellular tumor antigen p53

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	1.00E-9	0.000165	nd	nd
Average	nd	nd	0.00163	0.00180	nd	nd
Stdev	nd	nd	0.00319	0.00245	nd	nd
p(t-test)	nd	nd		0.84	nd	nd
Min	nd	nd	1.00E-9	1.00E-9	nd	nd
Max	nd	nd	0.0202	0.00839	nd	nd
n (Samp)	nd	nd	96	16	nd	nd
n (Patient)	nd	nd	73	16	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	1.00E-9	3.53E-5	nd	nd
Average	nd	nd	0.00186	0.00145	nd	nd
Stdev	nd	nd	0.00355	0.00190	nd	nd
p(t-test)	nd	nd		0.66	nd	nd
Min	nd	nd	1.00E-9	1.00E-9	nd	nd
Max	nd	nd	0.0202	0.00470	nd	nd
n (Samp)	nd	nd	81	15	nd	nd
n (Patient)	nd	nd	61	15	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	nd	nd	nd	0.58	nd	0.55	nd	nd	nd
SE	nd	nd	nd	0.080	nd	0.083	nd	nd	nd
p	nd	nd	nd	0.30	nd	0.56	nd	nd	nd
nCohort 1	nd	nd	nd	96	nd	81	nd	nd	nd
nCohort 2	nd	nd	nd	16	nd	15	nd	nd	nd
Cutoff 1	nd	nd	nd	0	nd	0	nd	nd	nd
Sens 1	nd	nd	nd	100%	nd	100%	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Spec 1	nd	nd	nd	0%	nd	0%	nd	nd	nd
Cutoff 2	nd	nd	nd	0	nd	0	nd	nd	nd
Sens 2	nd	nd	nd	100%	nd	100%	nd	nd	nd
Spec 2	nd	nd	nd	0%	nd	0%	nd	nd	nd
Cutoff 3	nd	nd	nd	0	nd	0	nd	nd	nd
Sens 3	nd	nd	nd	100%	nd	100%	nd	nd	nd
Spec 3	nd	nd	nd	0%	nd	0%	nd	nd	nd
Cutoff 4	nd	nd	nd	0.00160	nd	0.00160	nd	nd	nd
Sens 4	nd	nd	nd	38%	nd	33%	nd	nd	nd
Spec 4	nd	nd	nd	73%	nd	72%	nd	nd	nd
Cutoff 5	nd	nd	nd	0.00313	nd	0.00343	nd	nd	nd
Sens 5	nd	nd	nd	38%	nd	20%	nd	nd	nd
Spec 5	nd	nd	nd	81%	nd	80%	nd	nd	nd
Cutoff 6	nd	nd	nd	0.00470	nd	0.00599	nd	nd	nd
Sens 6	nd	nd	nd	6%	nd	0%	nd	nd	nd
Spec 6	nd	nd	nd	92%	nd	91%	nd	nd	nd
OR Quart 2	nd	nd	nd	0.46	nd	0.17	nd	nd	nd
p Value	nd	nd	nd	0.40	nd	0.11	nd	nd	nd
95% CI of	nd	nd	nd	0.077	nd	0.018	nd	nd	nd
OR Quart2	nd	nd	nd	2.8	nd	1.5	nd	nd	nd
OR Quart 3	nd	nd	nd	1.0	nd	0.76	nd	nd	nd
p Value	nd	nd	nd	1.0	nd	0.71	nd	nd	nd
95% CI of	nd	nd	nd	0.22	nd	0.18	nd	nd	nd
OR Quart3	nd	nd	nd	4.5	nd	3.3	nd	nd	nd
OR Quart 4	nd	nd	nd	1.6	nd	1.0	nd	nd	nd
p Value	nd	nd	nd	0.49	nd	1.0	nd	nd	nd
95% CI of	nd	nd	nd	0.41	nd	0.25	nd	nd	nd
OR Quart4	nd	nd	nd	6.6	nd	4.0	nd	nd	nd

[0157] Table 3: Comparison of marker levels in urine samples collected within 12 hours of reaching stage R from Cohort 1 (patients that reached, but did not progress beyond, RIFLE stage R) and from Cohort 2 (patients that reached RIFLE stage I or F).

Apolipoprotein A-II

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	78.2	125	77.5	247	85.8	106
Average	156	187	167	307	149	132
Stdev	303	193	368	295	238	77.5
p(t-test)		0.58		0.30		0.74
Min	4.67	18.9	4.67	23.0	21.4	18.9
Max	2000	845	2000	845	1790	323
n (Samp)	77	33	29	9	61	24
n (Patient)	77	33	29	9	61	24

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.64	0.76	0.60
SE	0.059	0.10	0.070
p	0.016	0.011	0.16
nCohort 1	77	29	61
nCohort 2	33	9	24

	At Enrollment		
	sCr or UO	sCr only	UO only
Cutoff 1	82.3	125	85.8
Sens 1	73%	78%	71%
Spec 1	53%	72%	51%
Cutoff 2	67.3	78.5	65.3
Sens 2	82%	89%	83%
Spec 2	47%	55%	43%
Cutoff 3	58.1	21.6	62.3
Sens 3	91%	100%	92%
Spec 3	42%	10%	41%
Cutoff 4	126	125	148
Sens 4	48%	78%	33%
Spec 4	70%	72%	70%
Cutoff 5	166	166	180
Sens 5	33%	56%	21%
Spec 5	81%	83%	80%
Cutoff 6	314	195	314
Sens 6	12%	56%	4%
Spec 6	91%	93%	90%
OR Quart 2	3.2	0.89	12
p Value	0.12	0.94	0.025
95% CI of	0.75	0.047	1.4
OR Quart2	14	17	110
OR Quart 3	5.5	2.3	15
p Value	0.019	0.53	0.015
95% CI of	1.3	0.17	1.7
OR Quart3	23	31	130
OR Quart 4	5.2	8.0	7.5
p Value	0.023	0.092	0.075
95% CI of	1.3	0.71	0.82
OR Quart4	21	90	69

Myoglobin

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.515	0.0847	nd	nd	0.758	0.0561
Average	42.9	26.9	nd	nd	49.3	3.71
Stdev	122	94.2	nd	nd	131	12.0
p(t-test)		0.57	nd	nd		0.16
Min	0.000105	0.000105	nd	nd	0.0176	0.0145
Max	618	460	nd	nd	618	49.1
n (Samp)	52	24	nd	nd	44	17
n (Patient)	52	24	nd	nd	44	17

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.40	nd	0.30
SE	0.072	nd	0.079
p	0.17	nd	0.011
nCohort 1	52	nd	44
nCohort 2	24	nd	17
Cutoff 1	0.0365	nd	0.0347
Sens 1	71%	nd	71%
Spec 1	15%	nd	14%
Cutoff 2	0.0324	nd	0.0324

	At Enrollment		
	sCr or UO	sCr only	UO only
Sens 2	83%	nd	82%
Spec 2	12%	nd	11%
Cutoff 3	0.0176	nd	0.0176
Sens 3	92%	nd	94%
Spec 3	4%	nd	2%
Cutoff 4	13.5	nd	13.9
Sens 4	21%	nd	6%
Spec 4	71%	nd	70%
Cutoff 5	33.1	nd	34.7
Sens 5	12%	nd	6%
Spec 5	81%	nd	82%
Cutoff 6	63.7	nd	85.7
Sens 6	8%	nd	0%
Spec 6	90%	nd	91%
OR Quart 2	0.75	nd	1.8
p Value	0.70	nd	0.57
95% CI of	0.17	nd	0.25
OR Quart2	3.4	nd	12
OR Quart 3	1.6	nd	3.5
p Value	0.49	nd	0.18
95% CI of	0.41	nd	0.56
OR Quart3	6.5	nd	22
OR Quart 4	2.0	nd	6.1
p Value	0.31	nd	0.048
95% CI of	0.52	nd	1.0
OR Quart4	8.0	nd	37

KSP-Cadherin

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.48	0.809	nd	nd	1.46	0.996
Average	1.74	1.25	nd	nd	1.73	1.18
Stdev	1.18	1.36	nd	nd	1.10	1.26
p(t-test)		0.18	nd	nd		0.21
Min	0.131	0.00263	nd	nd	0.196	0.00263
Max	4.63	4.23	nd	nd	4.63	3.88
n (Samp)	40	16	nd	nd	31	9
n (Patient)	40	16	nd	nd	31	9

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.33	nd	0.31
SE	0.084	nd	0.11
p	0.037	nd	0.081
nCohort 1	40	nd	31
nCohort 2	16	nd	9
Cutoff 1	0.258	nd	0.196
Sens 1	75%	nd	78%
Spec 1	5%	nd	3%
Cutoff 2	0.196	nd	0.00263
Sens 2	81%	nd	89%
Spec 2	5%	nd	0%
Cutoff 3	0.00263	nd	0
Sens 3	94%	nd	100%

	At Enrollment		
	sCr or UO	sCr only	UO only
Spec 3	0%	nd	0%
Cutoff 4	1.84	nd	1.84
Sens 4	25%	nd	22%
Spec 4	70%	nd	71%
Cutoff 5	2.57	nd	2.54
Sens 5	19%	nd	11%
Spec 5	80%	nd	81%
Cutoff 6	3.39	nd	3.11
Sens 6	12%	nd	11%
Spec 6	90%	nd	90%
OR Quart 2	0	nd	0
p Value	na	nd	na
95% CI of	na	nd	na
OR Quart2	na	nd	na
OR Quart 3	1.0	nd	1.7
p Value	1.0	nd	0.61
95% CI of	0.19	nd	0.22
OR Quart3	5.2	nd	13
OR Quart 4	3.3	nd	2.7
p Value	0.13	nd	0.34
95% CI of	0.69	nd	0.36
OR Quart4	16	nd	20

[0158] Table 4: Comparison of the maximum marker levels in urine samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in urine samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

Apolipoprotein A-II

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	76.0	265	76.0	217	76.0	157
Average	241	1760	241	1460	241	225
Stdev	841	5360	841	5260	841	193
p(t-test)		3.5E-4		0.0035		0.95
Min	5.33	27.6	5.33	9.51	5.33	55.6
Max	6400	24300	6400	24300	6400	764
n (Samp)	196	21	196	21	196	11
n (Patient)	196	21	196	21	196	11

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	97.8	268	97.8	265	97.8	216
Average	342	954	342	393	342	213
Stdev	1610	1880	1610	510	1610	68.6
p(t-test)		0.22		0.92		0.84
Min	5.33	27.6	5.33	9.51	5.33	131
Max	24300	6400	24300	1860	24300	288
n (Samp)	294	11	294	11	294	6
n (Patient)	294	11	294	11	294	6

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	87.2	174	87.2	174	87.2	149
Average	294	2240	294	1850	294	227
Stdev	972	6320	972	6230	972	214
p(t-test)		0.0012		0.0086		0.84
Min	5.33	55.6	5.33	45.8	5.33	55.6
Max	6400	24300	6400	24300	6400	764
n (Samp)	132	15	132	15	132	9
n (Patient)	132	15	132	15	132	9

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.80	0.78	0.79	0.77	0.76	0.76	0.78	0.78	0.73
SE	0.059	0.084	0.072	0.062	0.086	0.075	0.084	0.11	0.098
p	2.8E-7	9.4E-4	4.7E-5	8.7E-6	0.0029	5.7E-4	0.0010	0.014	0.019
nCohort 1	196	294	132	196	294	132	196	294	132
nCohort 2	21	11	15	21	11	15	11	6	9
Cutoff 1	148	165	146	148	165	146	146	157	111
Sens 1	71%	73%	73%	71%	73%	73%	73%	83%	78%
Spec 1	80%	74%	77%	80%	74%	77%	79%	71%	63%
Cutoff 2	129	157	129	129	157	129	111	157	100
Sens 2	81%	82%	80%	81%	82%	80%	82%	83%	89%
Spec 2	74%	71%	73%	74%	71%	73%	67%	71%	58%
Cutoff 3	100	135	100	54.2	129	54.3	100	129	54.3
Sens 3	90%	91%	93%	90%	91%	93%	91%	100%	100%
Spec 3	62%	65%	58%	37%	64%	32%	62%	64%	32%
Cutoff 4	124	155	127	124	155	127	124	155	127
Sens 4	81%	82%	80%	81%	82%	80%	73%	83%	67%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	153	200	164	153	200	164	153	200	164
Sens 5	67%	64%	53%	67%	64%	53%	55%	50%	33%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	296	335	312	296	335	312	296	335	312
Sens 6	29%	27%	20%	24%	18%	20%	9%	0%	11%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	1.0	0	>1.0	2.0	0	0.97	>1.0	>0	>1.0
p Value	1.0	na	<1.0	0.57	na	0.98	<1.0	<na	<0.98
95% CI of	0.061	na	>0.060	0.18	na	0.058	>0.061	>na	>0.062
OR Quart2	16	na	na	23	na	16	na	na	na
OR Quart 3	4.2	3.1	>5.6	3.1	3.1	4.2	>2.0	>3.1	>2.1
p Value	0.20	0.33	<0.12	0.33	0.33	0.21	<0.57	<0.33	<0.55
95% CI of	0.46	0.31	>0.62	0.31	0.31	0.45	>0.18	>0.32	>0.18
OR Quart3	39	30	na	31	30	40	na	na	na
OR Quart 4	20	7.5	>12	20	7.5	11	>9.3	>3.1	>7.0
p Value	0.0046	0.063	<0.024	0.0046	0.063	0.026	<0.039	<0.33	<0.079
95% CI of	2.5	0.90	>1.4	2.5	0.90	1.3	>1.1	>0.32	>0.80
OR Quart4	160	63	na	160	63	94	na	na	na

Caspase-1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.28	4.81	1.28	2.33	1.28	0.988
Average	1.56	10.5	1.56	4.46	1.56	1.77
Stdev	1.38	15.7	1.38	6.02	1.38	2.36

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
p(t-test)		0.0057		0.027		0.78
Min	0.0223	0.0223	0.0223	0.0223	0.0223	0.0223
Max	4.68	47.1	4.68	17.3	4.68	6.25
n (Samp)	26	8	26	7	26	6
n (Patient)	26	8	26	7	26	6

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.75	nd	nd	0.64	nd	nd	0.45	nd	nd
SE	0.11	nd	nd	0.12	nd	nd	0.13	nd	nd
p	0.021	nd	nd	0.25	nd	nd	0.72	nd	nd
nCohort 1	26	nd	nd	26	nd	nd	26	nd	nd
nCohort 2	8	nd	nd	7	nd	nd	6	nd	nd
Cutoff 1	2.08	nd	nd	1.02	nd	nd	0	nd	nd
Sens 1	75%	nd	nd	71%	nd	nd	100%	nd	nd
Spec 1	69%	nd	nd	46%	nd	nd	0%	nd	nd
Cutoff 2	0.496	nd	nd	0.496	nd	nd	0	nd	nd
Sens 2	88%	nd	nd	86%	nd	nd	100%	nd	nd
Spec 2	31%	nd	nd	31%	nd	nd	0%	nd	nd
Cutoff 3	0	nd	nd	0	nd	nd	0	nd	nd
Sens 3	100%	nd	nd	100%	nd	nd	100%	nd	nd
Spec 3	0%	nd	nd	0%	nd	nd	0%	nd	nd
Cutoff 4	2.33	nd	nd	2.33	nd	nd	2.33	nd	nd
Sens 4	62%	nd	nd	43%	nd	nd	17%	nd	nd
Spec 4	73%	nd	nd	73%	nd	nd	73%	nd	nd
Cutoff 5	2.59	nd	nd	2.59	nd	nd	2.59	nd	nd
Sens 5	62%	nd	nd	43%	nd	nd	17%	nd	nd
Spec 5	85%	nd	nd	85%	nd	nd	85%	nd	nd
Cutoff 6	3.90	nd	nd	3.90	nd	nd	3.90	nd	nd
Sens 6	50%	nd	nd	29%	nd	nd	17%	nd	nd
Spec 6	92%	nd	nd	92%	nd	nd	92%	nd	nd
OR Quart 2	0.88	nd	nd	1.0	nd	nd	1.0	nd	nd
p Value	0.93	nd	nd	1.0	nd	nd	1.0	nd	nd
95% CI of	0.046	nd	nd	0.052	nd	nd	0.052	nd	nd
OR Quart2	17	nd	nd	19	nd	nd	19	nd	nd
OR Quart 3	1.0	nd	nd	2.3	nd	nd	2.3	nd	nd
p Value	1.0	nd	nd	0.53	nd	nd	0.53	nd	nd
95% CI of	0.052	nd	nd	0.17	nd	nd	0.17	nd	nd
OR Quart3	19	nd	nd	33	nd	nd	33	nd	nd
OR Quart 4	8.8	nd	nd	3.5	nd	nd	2.3	nd	nd
p Value	0.086	nd	nd	0.33	nd	nd	0.53	nd	nd
95% CI of	0.74	nd	nd	0.28	nd	nd	0.17	nd	nd
OR Quart4	100	nd	nd	43	nd	nd	33	nd	nd

Caspase-9

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.549	3.00	0.549	2.16	0.549	1.09
Average	1.25	2.65	1.25	1.79	1.25	1.35
Stdev	3.21	1.71	3.21	1.60	3.21	1.25
p(t-test)		0.24		0.67		0.94
Min	0.0360	0.146	0.0360	0.146	0.0360	0.146
Max	19.5	4.64	19.5	4.64	19.5	3.33

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
n (Samp)	36	8	36	7	36	6
n (Patient)	36	8	36	7	36	6

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.79	nd	nd	0.69	nd	nd	0.64	nd	nd
SE	0.10	nd	nd	0.12	nd	nd	0.13	nd	nd
p	0.0034	nd	nd	0.11	nd	nd	0.27	nd	nd
nCohort 1	36	nd	nd	36	nd	nd	36	nd	nd
nCohort 2	8	nd	nd	7	nd	nd	6	nd	nd
Cutoff 1	1.76	nd	nd	0.473	nd	nd	0.208	nd	nd
Sens 1	75%	nd	nd	71%	nd	nd	83%	nd	nd
Spec 1	89%	nd	nd	50%	nd	nd	33%	nd	nd
Cutoff 2	0.208	nd	nd	0.208	nd	nd	0.208	nd	nd
Sens 2	88%	nd	nd	86%	nd	nd	83%	nd	nd
Spec 2	33%	nd	nd	33%	nd	nd	33%	nd	nd
Cutoff 3	0.135	nd	nd	0.135	nd	nd	0.135	nd	nd
Sens 3	100%	nd	nd	100%	nd	nd	100%	nd	nd
Spec 3	28%	nd	nd	28%	nd	nd	28%	nd	nd
Cutoff 4	0.868	nd	nd	0.868	nd	nd	0.868	nd	nd
Sens 4	75%	nd	nd	57%	nd	nd	50%	nd	nd
Spec 4	72%	nd	nd	72%	nd	nd	72%	nd	nd
Cutoff 5	1.22	nd	nd	1.22	nd	nd	1.22	nd	nd
Sens 5	75%	nd	nd	57%	nd	nd	50%	nd	nd
Spec 5	81%	nd	nd	81%	nd	nd	81%	nd	nd
Cutoff 6	2.17	nd	nd	2.17	nd	nd	2.17	nd	nd
Sens 6	62%	nd	nd	29%	nd	nd	17%	nd	nd
Spec 6	92%	nd	nd	92%	nd	nd	92%	nd	nd
OR Quart 2	>2.4	nd	nd	>2.2	nd	nd	>2.2	nd	nd
p Value	<0.49	nd	nd	<0.54	nd	nd	<0.54	nd	nd
95% CI of	>0.19	nd	nd	>0.17	nd	nd	>0.17	nd	nd
OR Quart2	na	nd	nd	na	nd	nd	na	nd	nd
OR Quart 3	>0	nd	nd	>1.0	nd	nd	>1.1	nd	nd
p Value	<na	nd	nd	<1.0	nd	nd	<0.94	nd	nd
95% CI of	>na	nd	nd	>0.055	nd	nd	>0.060	nd	nd
OR Quart3	na	nd	nd	na	nd	nd	na	nd	nd
OR Quart 4	>13	nd	nd	>5.7	nd	nd	>3.8	nd	nd
p Value	<0.033	nd	nd	<0.15	nd	nd	<0.29	nd	nd
95% CI of	>1.2	nd	nd	>0.52	nd	nd	>0.32	nd	nd
OR Quart4	na	nd	nd	na	nd	nd	na	nd	nd

Cadherin-1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	66800	66800	66800	66800	nd	nd
Average	99700	95000	99700	95000	nd	nd
Stdev	131000	95400	131000	95400	nd	nd
p(t-test)		0.92		0.92	nd	nd
Min	3290	2220	3290	2220	nd	nd
Max	744000	260000	744000	260000	nd	nd
n (Samp)	41	8	41	8	nd	nd
n (Patient)	41	8	41	8	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.49	nd	nd	0.49	nd	nd	nd	nd	nd
SE	0.11	nd	nd	0.11	nd	nd	nd	nd	nd
p	0.91	nd	nd	0.91	nd	nd	nd	nd	nd
nCohort 1	41	nd	nd	41	nd	nd	nd	nd	nd
nCohort 2	8	nd	nd	8	nd	nd	nd	nd	nd
Cutoff 1	16300	nd	nd	16300	nd	nd	nd	nd	nd
Sens 1	75%	nd	nd	75%	nd	nd	nd	nd	nd
Spec 1	17%	nd	nd	17%	nd	nd	nd	nd	nd
Cutoff 2	8380	nd	nd	8380	nd	nd	nd	nd	nd
Sens 2	88%	nd	nd	88%	nd	nd	nd	nd	nd
Spec 2	10%	nd	nd	10%	nd	nd	nd	nd	nd
Cutoff 3	0	nd	nd	0	nd	nd	nd	nd	nd
Sens 3	100%	nd	nd	100%	nd	nd	nd	nd	nd
Spec 3	0%	nd	nd	0%	nd	nd	nd	nd	nd
Cutoff 4	123000	nd	nd	123000	nd	nd	nd	nd	nd
Sens 4	38%	nd	nd	38%	nd	nd	nd	nd	nd
Spec 4	71%	nd	nd	71%	nd	nd	nd	nd	nd
Cutoff 5	138000	nd	nd	138000	nd	nd	nd	nd	nd
Sens 5	25%	nd	nd	25%	nd	nd	nd	nd	nd
Spec 5	80%	nd	nd	80%	nd	nd	nd	nd	nd
Cutoff 6	155000	nd	nd	155000	nd	nd	nd	nd	nd
Sens 6	25%	nd	nd	25%	nd	nd	nd	nd	nd
Spec 6	90%	nd	nd	90%	nd	nd	nd	nd	nd
OR Quart 2	0.30	nd	nd	0.30	nd	nd	nd	nd	nd
p Value	0.33	nd	nd	0.33	nd	nd	nd	nd	nd
95% CI of	0.027	nd	nd	0.027	nd	nd	nd	nd	nd
OR Quart2	3.4	nd	nd	3.4	nd	nd	nd	nd	nd
OR Quart 3	0.30	nd	nd	0.30	nd	nd	nd	nd	nd
p Value	0.33	nd	nd	0.33	nd	nd	nd	nd	nd
95% CI of	0.027	nd	nd	0.027	nd	nd	nd	nd	nd
OR Quart3	3.4	nd	nd	3.4	nd	nd	nd	nd	nd
OR Quart 4	1.1	nd	nd	1.1	nd	nd	nd	nd	nd
p Value	0.91	nd	nd	0.91	nd	nd	nd	nd	nd
95% CI of	0.18	nd	nd	0.18	nd	nd	nd	nd	nd
OR Quart4	7.0	nd	nd	7.0	nd	nd	nd	nd	nd

Cyclin-dependent kinase inhibitor 1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	3.09	14.9	3.09	9.35	3.09	4.76
Average	88.7	37.1	88.7	36.6	88.7	15.2
Stdev	688	81.6	688	81.8	688	16.5
p(t-test)		0.77		0.77		0.75
Min	0.116	0.116	0.116	0.116	0.116	1.64
Max	6950	327	6950	327	6950	44.1
n (Samp)	102	15	102	15	102	9
n (Patient)	102	15	102	15	102	9

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	4.90	18.8	4.90	15.7	nd	nd
Average	69.2	21.5	69.2	20.7	nd	nd
Stdev	541	18.2	541	18.6	nd	nd

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
p(t-test)		0.80		0.80	nd	nd
Min	1.14E-14	0.116	1.14E-14	0.116	nd	nd
Max	6950	44.1	6950	44.1	nd	nd
n (Samp)	168	8	168	8	nd	nd
n (Patient)	168	8	168	8	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	3.29	14.9	3.29	14.9	3.29	4.76
Average	101	50.0	101	50.0	101	14.4
Stdev	753	105	753	105	753	16.4
p(t-test)		0.84		0.84		0.76
Min	0.116	2.45	0.116	2.45	0.116	2.45
Max	6950	327	6950	327	6950	44.1
n (Samp)	85	9	85	9	85	7
n (Patient)	85	9	85	9	85	7

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.66	0.66	0.69	0.65	0.65	0.68	0.63	nd	0.63
SE	0.081	0.11	0.10	0.081	0.11	0.10	0.10	nd	0.12
p	0.050	0.15	0.067	0.062	0.18	0.078	0.22	nd	0.28
nCohort 1	102	168	85	102	168	85	102	nd	85
nCohort 2	15	8	9	15	8	9	9	nd	7
Cutoff 1	2.45	7.35	2.45	2.45	7.35	2.45	2.02	nd	2.45
Sens 1	73%	75%	78%	73%	75%	78%	89%	nd	71%
Spec 1	46%	59%	47%	46%	59%	47%	46%	nd	47%
Cutoff 2	2.02	1.36	2.02	2.02	1.36	2.02	2.02	nd	2.02
Sens 2	87%	88%	100%	87%	88%	100%	89%	nd	100%
Spec 2	46%	40%	47%	46%	40%	47%	46%	nd	47%
Cutoff 3	1.09	1.14E-14	2.02	1.09	1.14E-14	2.02	1.09	nd	2.02
Sens 3	93%	100%	100%	93%	100%	100%	100%	nd	100%
Spec 3	44%	1%	47%	44%	1%	47%	44%	nd	47%
Cutoff 4	12.3	13.6	12.3	12.3	13.6	12.3	12.3	nd	12.3
Sens 4	53%	62%	56%	47%	50%	56%	44%	nd	43%
Spec 4	71%	70%	71%	71%	70%	71%	71%	nd	71%
Cutoff 5	25.7	26.7	25.7	25.7	26.7	25.7	25.7	nd	25.7
Sens 5	33%	38%	33%	33%	38%	33%	33%	nd	29%
Spec 5	80%	80%	80%	80%	80%	80%	80%	nd	80%
Cutoff 6	55.7	56.1	44.8	55.7	56.1	44.8	55.7	nd	44.8
Sens 6	7%	0%	11%	7%	0%	11%	0%	nd	0%
Spec 6	90%	90%	91%	90%	90%	91%	90%	nd	91%
OR Quart 2	4.5	>2.1	>3.3	4.5	>2.1	>3.3	>4.5	nd	>3.4
p Value	0.19	<0.55	<0.32	0.19	<0.55	<0.32	<0.19	nd	<0.30
95% CI of	0.47	>0.18	>0.32	0.47	>0.18	>0.32	>0.47	nd	>0.33
OR Quart2	43	na	na	43	na	na	na	nd	na
OR Quart 3	4.5	>3.2	>3.4	4.5	>3.2	>3.4	>2.1	nd	>2.2
p Value	0.19	<0.32	<0.30	0.19	<0.32	<0.30	<0.56	nd	<0.53
95% CI of	0.47	>0.32	>0.33	0.47	>0.32	>0.33	>0.18	nd	>0.18
OR Quart3	43	na	na	43	na	na	na	nd	na
OR Quart 4	7.0	>3.2	>3.3	7.0	>3.2	>3.3	>3.2	nd	>2.2
p Value	0.081	<0.32	<0.32	0.081	<0.32	<0.32	<0.32	nd	<0.53
95% CI of	0.79	>0.32	>0.32	0.79	>0.32	>0.32	>0.32	nd	>0.18
OR Quart4	62	na	na	62	na	na	na	nd	na

Carcinoembryonic antigen-related cell adhesion molecule 5

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.14	5.45	1.14	2.86	1.14	2.98
Average	3.19	7.89	3.19	7.48	3.19	5.77
Stdev	5.64	11.7	5.64	12.1	5.64	4.90
p(t-test)		0.0094		0.021		0.19
Min	0.00336	0.282	0.00336	0.219	0.00336	0.852
Max	43.4	50.1	43.4	50.1	43.4	14.6
n (Samp)	102	17	102	16	102	9
n (Patient)	102	17	102	16	102	9

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.57	4.46	1.57	3.11	nd	nd
Average	28.3	4.33	28.3	3.91	nd	nd
Stdev	312	3.44	312	3.51	nd	nd
p(t-test)		0.83		0.83	nd	nd
Min	0.00336	0.282	0.00336	0.219	nd	nd
Max	4070	10.9	4070	10.9	nd	nd
n (Samp)	170	8	170	8	nd	nd
n (Patient)	170	8	170	8	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.19	6.79	1.19	4.88	1.19	2.98
Average	3.63	10.4	3.63	10.3	3.63	6.19
Stdev	6.41	14.1	6.41	14.7	6.41	5.50
p(t-test)		0.0070		0.011		0.31
Min	0.00336	0.356	0.00336	0.852	0.00336	0.852
Max	43.4	50.1	43.4	50.1	43.4	14.6
n (Samp)	85	11	85	10	85	7
n (Patient)	85	11	85	10	85	7

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.70	0.62	0.75	0.69	0.57	0.77	0.76	nd	0.74
SE	0.075	0.11	0.089	0.078	0.11	0.091	0.096	nd	0.11
p	0.0072	0.28	0.0055	0.015	0.50	0.0030	0.0080	nd	0.034
nCohort 1	102	170	85	102	170	85	102	nd	85
nCohort 2	17	8	11	16	8	10	9	nd	7
Cutoff 1	2.56	2.59	2.88	2.26	2.26	2.55	2.53	nd	2.53
Sens 1	71%	75%	73%	75%	75%	70%	78%	nd	71%
Spec 1	71%	65%	71%	67%	61%	68%	70%	nd	68%
Cutoff 2	0.816	0.450	1.40	1.44	0.238	2.53	1.44	nd	1.40
Sens 2	82%	88%	82%	81%	88%	80%	89%	nd	86%
Spec 2	42%	20%	56%	58%	8%	68%	58%	nd	56%
Cutoff 3	0.339	0.281	0.816	0.238	0.214	1.40	0.816	nd	0.816
Sens 3	94%	100%	91%	94%	100%	90%	100%	nd	100%
Spec 3	19%	10%	39%	9%	5%	56%	42%	nd	39%
Cutoff 4	2.56	3.33	2.88	2.56	3.33	2.88	2.56	nd	2.88
Sens 4	71%	62%	73%	56%	50%	60%	67%	nd	57%
Spec 4	71%	70%	71%	71%	70%	71%	71%	nd	71%
Cutoff 5	4.03	5.77	5.67	4.03	5.77	5.67	4.03	nd	5.67
Sens 5	53%	25%	55%	44%	25%	50%	44%	nd	43%

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Spec 5	80%	80%	80%	80%	80%	80%	80%	nd	80%
Cutoff 6	8.86	11.0	9.55	8.86	11.0	9.55	8.86	nd	9.55
Sens 6	29%	0%	45%	25%	0%	40%	33%	nd	43%
Spec 6	90%	90%	91%	90%	90%	91%	90%	nd	91%
OR Quart 2	0.30	0	1.0	0.47	0	>1.0	>1.0	nd	>1.0
p Value	0.31	na	1.0	0.54	na	<1.0	<1.0	nd	<0.98
95% CI of	0.029	na	0.059	0.040	na	>0.059	>0.059	nd	>0.062
OR Quart2	3.1	na	17	5.4	na	na	na	nd	na
OR Quart 3	1.3	1.0	3.3	3.5	1.5	>4.6	>4.5	nd	>3.4
p Value	0.72	1.0	0.32	0.15	0.65	<0.19	<0.19	nd	<0.30
95% CI of	0.27	0.13	0.32	0.65	0.24	>0.47	>0.47	nd	>0.33
OR Quart3	6.6	7.4	34	19	9.7	na	na	nd	na
OR Quart 4	3.7	2.0	7.7	4.1	1.5	>6.1	>4.5	nd	>3.4
p Value	0.072	0.42	0.070	0.097	0.67	<0.11	<0.19	nd	<0.30
95% CI of	0.89	0.36	0.85	0.78	0.24	>0.65	>0.47	nd	>0.33
OR Quart4	15	12	70	22	9.4	na	na	nd	na

Myoglobin

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	5.42	18.9	5.42	11.9	5.42	44.9
Average	51.4	149	51.4	155	51.4	174
Stdev	121	203	121	208	121	213
p(t-test)		0.0066		0.0052		0.0076
Min	0.00616	0.0439	0.00616	0.0439	0.00616	0.0772
Max	618	469	618	469	618	469
n (Samp)	102	17	102	16	102	9
n (Patient)	102	17	102	16	102	9

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	3.65	31.9	3.65	29.4	nd	nd
Average	63.1	142	63.1	141	nd	nd
Stdev	142	195	142	196	nd	nd
p(t-test)		0.13		0.14	nd	nd
Min	0.00616	0.0439	0.00616	0.0439	nd	nd
Max	618	469	618	469	nd	nd
n (Samp)	170	8	170	8	nd	nd
n (Patient)	170	8	170	8	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	3.83	0.377	3.83	2.87	3.83	5.36
Average	56.6	143	56.6	152	56.6	150
Stdev	128	203	128	212	128	207
p(t-test)		0.055		0.042		0.081
Min	0.00616	0.0696	0.00616	0.0772	0.00616	0.0772
Max	618	469	618	469	618	469
n (Samp)	85	11	85	10	85	7
n (Patient)	85	11	85	10	85	7

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.57	0.64	0.49	0.57	0.63	0.51	0.62	nd	0.54
SE	0.078	0.11	0.093	0.080	0.11	0.097	0.10	nd	0.12
p	0.36	0.21	0.95	0.36	0.24	0.93	0.25	nd	0.73
nCohort 1	102	170	85	102	170	85	102	nd	85
nCohort 2	17	8	11	16	8	10	9	nd	7
Cutoff 1	0.288	10.2	0.117	0.288	9.39	0.288	0.288	nd	0.288
Sens 1	71%	75%	73%	75%	75%	70%	78%	nd	71%
Spec 1	21%	61%	14%	21%	61%	20%	21%	nd	20%
Cutoff 2	0.0772	0.0780	0.0772	0.117	0.0780	0.117	0.117	nd	0.117
Sens 2	82%	88%	82%	81%	88%	80%	89%	nd	86%
Spec 2	13%	14%	11%	16%	14%	14%	16%	nd	14%
Cutoff 3	0.0606	0.0411	0.0696	0.0606	0.0411	0.0772	0.0606	nd	0.0661
Sens 3	94%	100%	91%	94%	100%	90%	100%	nd	100%
Spec 3	13%	9%	11%	13%	9%	11%	13%	nd	11%
Cutoff 4	17.2	18.6	17.9	17.2	18.6	17.9	17.2	nd	17.9
Sens 4	53%	62%	45%	44%	50%	40%	56%	nd	43%
Spec 4	71%	70%	71%	71%	70%	71%	71%	nd	71%
Cutoff 5	38.9	45.3	55.8	38.9	45.3	55.8	38.9	nd	55.8
Sens 5	47%	38%	36%	44%	38%	40%	56%	nd	43%
Spec 5	80%	80%	80%	80%	80%	80%	80%	nd	80%
Cutoff 6	222	234	232	222	234	232	222	nd	232
Sens 6	29%	25%	27%	31%	25%	30%	33%	nd	29%
Spec 6	90%	90%	91%	90%	90%	91%	90%	nd	91%
OR Quart 2	0.13	0	0	0.13	0	0.21	0.30	nd	0
p Value	0.070	na	na	0.070	na	0.17	0.31	nd	na
95% CI of	0.015	na	na	0.015	na	0.021	0.029	nd	na
OR Quart2	1.2	na	na	1.2	na	2.0	3.0	nd	na
OR Quart 3	0.27	1.0	0.17	0.28	1.0	0.21	0	nd	0.30
p Value	0.13	1.0	0.11	0.15	1.0	0.17	na	nd	0.32
95% CI of	0.050	0.13	0.018	0.052	0.13	0.021	na	nd	0.029
OR Quart3	1.5	7.4	1.5	1.5	7.4	2.0	na	nd	3.2
OR Quart 4	1.4	2.0	1.0	1.2	2.0	0.95	1.7	nd	1.0
p Value	0.59	0.42	1.0	0.81	0.42	0.95	0.48	nd	1.0
95% CI of	0.42	0.36	0.25	0.34	0.36	0.21	0.37	nd	0.18
OR Quart4	4.7	12	4.0	4.0	12	4.4	8.1	nd	5.6

Mucin-16

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.684	1.03	0.684	1.03	nd	nd
Average	1.18	54.9	1.18	54.9	nd	nd
Stdev	1.41	153	1.41	153	nd	nd
p(t-test)		0.023		0.023	nd	nd
Min	0.141	0.304	0.141	0.304	nd	nd
Max	6.37	433	6.37	433	nd	nd
n (Samp)	41	8	41	8	nd	nd
n (Patient)	41	8	41	8	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.65	nd	nd	0.65	nd	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
SE	0.11	nd	nd	0.11	nd	nd	nd	nd	nd
p	0.20	nd	nd	0.20	nd	nd	nd	nd	nd
nCohort 1	41	nd	nd	41	nd	nd	nd	nd	nd
nCohort 2	8	nd	nd	8	nd	nd	nd	nd	nd
Cutoff 1	0.781	nd	nd	0.781	nd	nd	nd	nd	nd
Sens 1	75%	nd	nd	75%	nd	nd	nd	nd	nd
Spec 1	61%	nd	nd	61%	nd	nd	nd	nd	nd
Cutoff 2	0.464	nd	nd	0.464	nd	nd	nd	nd	nd
Sens 2	88%	nd	nd	88%	nd	nd	nd	nd	nd
Spec 2	32%	nd	nd	32%	nd	nd	nd	nd	nd
Cutoff 3	0.278	nd	nd	0.278	nd	nd	nd	nd	nd
Sens 3	100%	nd	nd	100%	nd	nd	nd	nd	nd
Spec 3	10%	nd	nd	10%	nd	nd	nd	nd	nd
Cutoff 4	0.961	nd	nd	0.961	nd	nd	nd	nd	nd
Sens 4	50%	nd	nd	50%	nd	nd	nd	nd	nd
Spec 4	71%	nd	nd	71%	nd	nd	nd	nd	nd
Cutoff 5	1.31	nd	nd	1.31	nd	nd	nd	nd	nd
Sens 5	25%	nd	nd	25%	nd	nd	nd	nd	nd
Spec 5	80%	nd	nd	80%	nd	nd	nd	nd	nd
Cutoff 6	3.42	nd	nd	3.42	nd	nd	nd	nd	nd
Sens 6	12%	nd	nd	12%	nd	nd	nd	nd	nd
Spec 6	90%	nd	nd	90%	nd	nd	nd	nd	nd
OR Quart 2	1.0	nd	nd	1.0	nd	nd	nd	nd	nd
p Value	1.0	nd	nd	1.0	nd	nd	nd	nd	nd
95% CI of	0.055	nd	nd	0.055	nd	nd	nd	nd	nd
OR Quart2	18	nd	nd	18	nd	nd	nd	nd	nd
OR Quart 3	3.7	nd	nd	3.7	nd	nd	nd	nd	nd
p Value	0.29	nd	nd	0.29	nd	nd	nd	nd	nd
95% CI of	0.32	nd	nd	0.32	nd	nd	nd	nd	nd
OR Quart3	42	nd	nd	42	nd	nd	nd	nd	nd
OR Quart 4	3.3	nd	nd	3.3	nd	nd	nd	nd	nd
p Value	0.33	nd	nd	0.33	nd	nd	nd	nd	nd
95% CI of	0.29	nd	nd	0.29	nd	nd	nd	nd	nd
OR Quart4	37	nd	nd	37	nd	nd	nd	nd	nd

Poly [ADP-ribose] polymerase 1 (cleaved)

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	0.0140	1.00E-9	0.0140	1.00E-9	1.00E-9
Average	0.00479	0.0101	0.00479	0.00956	0.00479	0.00605
Stdev	0.00701	0.00857	0.00701	0.00900	0.00701	0.00754
p(t-test)		0.018		0.034		0.65
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	0.0357	0.0253	0.0357	0.0253	0.0357	0.0144
n (Samp)	97	12	97	12	97	7
n (Patient)	97	12	97	12	97	7

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	0.00990	1.00E-9	0.00691	nd	nd
Average	0.00475	0.00992	0.00475	0.00892	nd	nd
Stdev	0.00651	0.00984	0.00651	0.0106	nd	nd
p(t-test)		0.063		0.13	nd	nd

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	nd	nd
Max	0.0357	0.0253	0.0357	0.0253	nd	nd
n (Samp)	159	6	159	6	nd	nd
n (Patient)	159	6	159	6	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	0.0140	1.00E-9	0.0140	1.00E-9	0.00691
Average	0.00380	0.00938	0.00380	0.00938	0.00380	0.00706
Stdev	0.00658	0.00789	0.00658	0.00789	0.00658	0.00773
p(t-test)		0.027		0.027		0.25
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	0.0357	0.0183	0.0357	0.0183	0.0357	0.0144
n (Samp)	84	8	84	8	84	6
n (Patient)	84	8	84	8	84	6

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.67	0.65	0.69	0.64	0.58	0.69	0.52	nd	0.60
SE	0.090	0.12	0.11	0.091	0.12	0.11	0.11	nd	0.13
p	0.059	0.23	0.081	0.13	0.51	0.081	0.87	nd	0.43
nCohort 1	97	159	84	97	159	84	97	nd	84
nCohort 2	12	6	8	12	6	8	7	nd	6
Cutoff 1	0	0	0	0	0	0	0	nd	0
Sens 1	100%	100%	100%	100%	100%	100%	100%	nd	100%
Spec 1	0%	0%	0%	0%	0%	0%	0%	nd	0%
Cutoff 2	0	0	0	0	0	0	0	nd	0
Sens 2	100%	100%	100%	100%	100%	100%	100%	nd	100%
Spec 2	0%	0%	0%	0%	0%	0%	0%	nd	0%
Cutoff 3	0	0	0	0	0	0	0	nd	0
Sens 3	100%	100%	100%	100%	100%	100%	100%	nd	100%
Spec 3	0%	0%	0%	0%	0%	0%	0%	nd	0%
Cutoff 4	0.00598	0.00598	0.00471	0.00598	0.00598	0.00471	0.00598	nd	0.0047
Sens 4									1
Spec 4	58%	50%	62%	58%	50%	62%	43%	nd	50%
	70%	71%	74%	70%	71%	74%	70%	nd	74%
Cutoff 5	0.0144	0.0144	0.0120	0.0144	0.0144	0.0120	0.0144	nd	0.0120
Sens 5	17%	17%	62%	17%	17%	62%	0%	nd	50%
Spec 5	94%	96%	81%	94%	96%	81%	94%	nd	81%
Cutoff 6	0.0144	0.0144	0.0144	0.0144	0.0144	0.0144	0.0144	nd	0.0144
Sens 6	17%	17%	12%	17%	17%	12%	0%	nd	0%
Spec 6	94%	96%	99%	94%	96%	99%	94%	nd	99%
OR Quart 2	1.0	1.0	2.1	1.6	2.1	2.1	3.3	nd	2.0
p Value	1.0	1.0	0.56	0.64	0.56	0.56	0.32	nd	0.58
95% CI of	0.13	0.060	0.18	0.24	0.18	0.18	0.32	nd	0.17
OR Quart2	7.7	17	25	10	24	25	34	nd	24
OR Quart 3	1.0	1.0	0	0	0	0	1.0	nd	0
p Value	1.0	1.0	na	na	na	na	1.0	nd	na
95% CI of	0.13	0.060	na	na	na	na	0.059	nd	na
OR Quart3	7.7	17	na	na	na	na	17	nd	na
OR Quart 4	3.4	3.1	6.1	4.2	3.1	6.1	2.1	nd	3.1
p Value	0.16	0.34	0.11	0.095	0.34	0.11	0.56	nd	0.34
95% CI of	0.62	0.31	0.65	0.78	0.31	0.65	0.18	nd	0.30
OR Quart4	19	31	57	22	31	57	25	nd	33

KSP-Cadherin

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.23	2.26	1.23	2.26	nd	nd
Average	1.66	2.48	1.66	2.48	nd	nd
Stdev	1.71	1.19	1.71	1.19	nd	nd
p(t-test)		0.17		0.17	nd	nd
Min	0.00263	0.562	0.00263	0.562	nd	nd
Max	11.9	4.23	11.9	4.23	nd	nd
n (Samp)	68	9	68	9	nd	nd
n (Patient)	68	9	68	9	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.17	1.87	1.17	1.87	nd	nd
Average	1.76	2.07	1.76	2.07	nd	nd
Stdev	1.84	1.22	1.84	1.22	nd	nd
p(t-test)		0.69		0.69	nd	nd
Min	0.00263	0.562	0.00263	0.562	nd	nd
Max	11.9	4.23	11.9	4.23	nd	nd
n (Samp)	59	6	59	6	nd	nd
n (Patient)	59	6	59	6	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.74	nd	0.64	0.74	nd	0.64	nd	nd	nd
SE	0.099	nd	0.13	0.099	nd	0.13	nd	nd	nd
p	0.017	nd	0.29	0.017	nd	0.29	nd	nd	nd
nCohort 1	68	nd	59	68	nd	59	nd	nd	nd
nCohort 2	9	nd	6	9	nd	6	nd	nd	nd
Cutoff 1	1.61	nd	1.51	1.61	nd	1.51	nd	nd	nd
Sens 1	78%	nd	83%	78%	nd	83%	nd	nd	nd
Spec 1	60%	nd	59%	60%	nd	59%	nd	nd	nd
Cutoff 2	1.56	nd	1.51	1.56	nd	1.51	nd	nd	nd
Sens 2	89%	nd	83%	89%	nd	83%	nd	nd	nd
Spec 2	60%	nd	59%	60%	nd	59%	nd	nd	nd
Cutoff 3	0.466	nd	0.494	0.466	nd	0.494	nd	nd	nd
Sens 3	100%	nd	100%	100%	nd	100%	nd	nd	nd
Spec 3	19%	nd	19%	19%	nd	19%	nd	nd	nd
Cutoff 4	1.99	nd	2.08	1.99	nd	2.08	nd	nd	nd
Sens 4	67%	nd	50%	67%	nd	50%	nd	nd	nd
Spec 4	71%	nd	71%	71%	nd	71%	nd	nd	nd
Cutoff 5	2.24	nd	2.54	2.24	nd	2.54	nd	nd	nd
Sens 5	56%	nd	17%	56%	nd	17%	nd	nd	nd
Spec 5	81%	nd	81%	81%	nd	81%	nd	nd	nd
Cutoff 6	3.17	nd	3.77	3.17	nd	3.77	nd	nd	nd
Sens 6	22%	nd	17%	22%	nd	17%	nd	nd	nd
Spec 6	91%	nd	92%	91%	nd	92%	nd	nd	nd
OR Quart 2	0	nd	0	0	nd	0	nd	nd	nd
p Value	na	nd	na	na	nd	na	nd	nd	nd
95% CI of	na	nd	na	na	nd	na	nd	nd	nd
OR Quart2	na	nd	na	na	nd	na	nd	nd	nd
OR Quart 3	3.4	nd	3.5	3.4	nd	3.5	nd	nd	nd
p Value	0.31	nd	0.31	0.31	nd	0.31	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
95% CI of	0.32	nd	0.32	0.32	nd	0.32	nd	nd	nd
OR Quart3	36	nd	37	36	nd	37	nd	nd	nd
OR Quart 4	6.0	nd	2.0	6.0	nd	2.0	nd	nd	nd
p Value	0.12	nd	0.59	0.12	nd	0.59	nd	nd	nd
95% CI of	0.63	nd	0.16	0.63	nd	0.16	nd	nd	nd
OR Quart4	57	nd	24	57	nd	24	nd	nd	nd

Tumor necrosis factor receptor superfamily member 10B

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.141	0.904	0.141	0.904	nd	nd
Average	0.957	1.95	0.957	1.95	nd	nd
Stdev	1.61	2.64	1.61	2.64	nd	nd
p(t-test)		0.16		0.16	nd	nd
Min	0.00360	0.104	0.00360	0.104	nd	nd
Max	6.71	7.54	6.71	7.54	nd	nd
n (Samp)	41	8	41	8	nd	nd
n (Patient)	41	8	41	8	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.69	nd	nd	0.69	nd	nd	nd	nd	nd
SE	0.11	nd	nd	0.11	nd	nd	nd	nd	nd
p	0.092	nd	nd	0.092	nd	nd	nd	nd	nd
nCohort 1	41	nd	nd	41	nd	nd	nd	nd	nd
nCohort 2	8	nd	nd	8	nd	nd	nd	nd	nd
Cutoff 1	0.141	nd	nd	0.141	nd	nd	nd	nd	nd
Sens 1	75%	nd	nd	75%	nd	nd	nd	nd	nd
Spec 1	51%	nd	nd	51%	nd	nd	nd	nd	nd
Cutoff 2	0.107	nd	nd	0.107	nd	nd	nd	nd	nd
Sens 2	88%	nd	nd	88%	nd	nd	nd	nd	nd
Spec 2	49%	nd	nd	49%	nd	nd	nd	nd	nd
Cutoff 3	0.0796	nd	nd	0.0796	nd	nd	nd	nd	nd
Sens 3	100%	nd	nd	100%	nd	nd	nd	nd	nd
Spec 3	41%	nd	nd	41%	nd	nd	nd	nd	nd
Cutoff 4	0.693	nd	nd	0.693	nd	nd	nd	nd	nd
Sens 4	50%	nd	nd	50%	nd	nd	nd	nd	nd
Spec 4	71%	nd	nd	71%	nd	nd	nd	nd	nd
Cutoff 5	1.56	nd	nd	1.56	nd	nd	nd	nd	nd
Sens 5	38%	nd	nd	38%	nd	nd	nd	nd	nd
Spec 5	80%	nd	nd	80%	nd	nd	nd	nd	nd
Cutoff 6	3.31	nd	nd	3.31	nd	nd	nd	nd	nd
Sens 6	25%	nd	nd	25%	nd	nd	nd	nd	nd
Spec 6	90%	nd	nd	90%	nd	nd	nd	nd	nd
OR Quart 2	>4.0	nd	nd	>4.0	nd	nd	nd	nd	nd
p Value	<0.26	nd	nd	<0.26	nd	nd	nd	nd	nd
95% CI of	>0.35	nd	nd	>0.35	nd	nd	nd	nd	nd
OR Quart2	na	nd	nd	na	nd	nd	nd	nd	nd
OR Quart 3	>1.1	nd	nd	>1.1	nd	nd	nd	nd	nd
p Value	<0.95	nd	nd	<0.95	nd	nd	nd	nd	nd
95% CI of	>0.061	nd	nd	>0.061	nd	nd	nd	nd	nd
OR Quart3	na	nd	nd	na	nd	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
OR Quart 4	>5.3	nd	nd	>5.3	nd	nd	nd	nd	nd
p Value	<0.16	nd	nd	<0.16	nd	nd	nd	nd	nd
95% CI of	>0.51	nd	nd	>0.51	nd	nd	nd	nd	nd
OR Quart4	na	nd	nd	na	nd	nd	nd	nd	nd

[0159] Table 5: Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage R, I or F in Cohort 2.

Apolipoprotein A-II

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	50600	49600	50600	44300	50600	54300
Average	51700	52000	51700	50700	51700	57500
Stdev	22200	21100	22200	36000	22200	32700
p(t-test)		0.94		0.83		0.29
Min	5450	7970	5450	7680	5450	8560
Max	105000	97000	105000	253000	105000	152000
n (Samp)	105	45	105	50	105	24
n (Patient)	97	45	97	50	97	24

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	49500	59900	49500	50300	49500	57100
Average	51700	60100	51700	64100	51700	67500
Stdev	26400	18100	26400	55400	26400	44100
p(t-test)		0.26		0.097		0.062
Min	1810	34500	1810	12100	1810	10900
Max	253000	95300	253000	251000	253000	176000
n (Samp)	246	13	246	16	246	11
n (Patient)	160	13	160	16	160	11

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	50200	49600	50200	43800	50200	51400
Average	52500	51300	52500	51600	52500	58800
Stdev	20200	21600	20200	38000	20200	32900
p(t-test)		0.76		0.86		0.25
Min	8680	7970	8680	7680	8680	8560
Max	123000	97000	123000	253000	123000	152000
n (Samp)	96	40	96	44	96	21
n (Patient)	84	40	84	44	84	21

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.51	0.63	0.48	0.45	0.55	0.44	0.55	0.60	0.55
SE	0.052	0.085	0.055	0.050	0.076	0.053	0.066	0.092	0.071
p	0.89	0.12	0.75	0.35	0.55	0.24	0.50	0.27	0.49

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
nCohort 1	105	246	96	105	246	96	105	246	96
nCohort 2	45	13	40	50	16	44	24	11	21
Cutoff 1	39500	43000	39500	35500	37700	35000	40700	46100	40900
Sens 1	71%	77%	70%	70%	75%	70%	71%	73%	71%
Spec 1	33%	40%	28%	24%	31%	19%	35%	46%	31%
Cutoff 2	33000	42600	32500	29600	35500	25400	29600	37000	35000
Sens 2	80%	85%	80%	80%	81%	82%	83%	82%	81%
Spec 2	22%	39%	16%	19%	24%	6%	19%	29%	19%
Cutoff 3	23400	37000	23400	20800	14000	20800	14000	36200	21600
Sens 3	91%	92%	90%	90%	94%	91%	92%	91%	90%
Spec 3	10%	29%	5%	6%	5%	3%	4%	27%	4%
Cutoff 4	61300	61500	61500	61300	61500	61500	61300	61500	61500
Sens 4	33%	46%	30%	32%	44%	34%	46%	36%	48%
Spec 4	70%	70%	71%	70%	70%	71%	70%	70%	71%
Cutoff 5	69000	69400	67400	69000	69400	67400	69000	69400	67400
Sens 5	24%	38%	22%	18%	38%	16%	33%	36%	43%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	82000	82800	77900	82000	82800	77900	82000	82800	77900
Sens 6	9%	8%	12%	8%	12%	11%	21%	36%	19%
Spec 6	90%	90%	91%	90%	90%	91%	90%	90%	91%
OR Quart 2	1.6	4.1	0.74	0.60	0.98	0.76	0.80	4.2	0.61
p Value	0.36	0.21	0.58	0.32	0.98	0.60	0.74	0.21	0.49
95% CI of	0.59	0.45	0.25	0.22	0.24	0.27	0.22	0.46	0.15
OR Quart2	4.2	38	2.2	1.6	4.1	2.1	3.0	39	2.5
OR Quart 3	0.87	3.0	1.1	1.1	0.48	0.65	0.62	2.0	0.28
p Value	0.79	0.34	0.79	0.81	0.41	0.42	0.49	0.57	0.15
95% CI of	0.31	0.31	0.41	0.44	0.086	0.22	0.16	0.18	0.052
OR Quart3	2.5	30	3.2	2.8	2.7	1.9	2.4	23	1.5
OR Quart 4	1.2	5.2	1.1	1.2	1.5	1.8	1.6	4.1	1.6
p Value	0.67	0.14	0.79	0.75	0.53	0.22	0.42	0.21	0.41
95% CI of	0.46	0.60	0.41	0.46	0.41	0.69	0.50	0.45	0.50
OR Quart4	3.4	46	3.2	3.0	5.7	4.9	5.2	38	5.4

Bcl2 antagonist of cell death

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.432	0.221	nd	nd	nd	nd
Average	0.590	0.255	nd	nd	nd	nd
Stdev	0.478	0.204	nd	nd	nd	nd
p(t-test)		0.10	nd	nd	nd	nd
Min	0.0873	0.0786	nd	nd	nd	nd
Max	2.49	0.651	nd	nd	nd	nd
n (Samp)	32	6	nd	nd	nd	nd
n (Patient)	20	6	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.596	0.213	nd	nd	nd	nd
Average	0.643	0.243	nd	nd	nd	nd
Stdev	0.503	0.174	nd	nd	nd	nd
p(t-test)		0.035	nd	nd	nd	nd
Min	0.0873	0.0786	nd	nd	nd	nd
Max	2.49	0.651	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
n (Samp)	27	8	nd	nd	nd	nd
n (Patient)	17	8	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.21	nd	0.19	nd	nd	nd	nd	nd	nd
SE	0.12	nd	0.098	nd	nd	nd	nd	nd	nd
p	0.012	nd	0.0013	nd	nd	nd	nd	nd	nd
nCohort 1	32	nd	27	nd	nd	nd	nd	nd	nd
nCohort 2	6	nd	8	nd	nd	nd	nd	nd	nd
Cutoff 1	0.114	nd	0.181	nd	nd	nd	nd	nd	nd
Sens 1	83%	nd	75%	nd	nd	nd	nd	nd	nd
Spec 1	6%	nd	15%	nd	nd	nd	nd	nd	nd
Cutoff 2	0.114	nd	0.114	nd	nd	nd	nd	nd	nd
Sens 2	83%	nd	88%	nd	nd	nd	nd	nd	nd
Spec 2	6%	nd	7%	nd	nd	nd	nd	nd	nd
Cutoff 3	0	nd	0	nd	nd	nd	nd	nd	nd
Sens 3	100%	nd	100%	nd	nd	nd	nd	nd	nd
Spec 3	0%	nd	0%	nd	nd	nd	nd	nd	nd
Cutoff 4	0.703	nd	0.771	nd	nd	nd	nd	nd	nd
Sens 4	0%	nd	0%	nd	nd	nd	nd	nd	nd
Spec 4	72%	nd	70%	nd	nd	nd	nd	nd	nd
Cutoff 5	0.991	nd	1.01	nd	nd	nd	nd	nd	nd
Sens 5	0%	nd	0%	nd	nd	nd	nd	nd	nd
Spec 5	81%	nd	81%	nd	nd	nd	nd	nd	nd
Cutoff 6	1.05	nd	1.13	nd	nd	nd	nd	nd	nd
Sens 6	0%	nd	0%	nd	nd	nd	nd	nd	nd
Spec 6	91%	nd	93%	nd	nd	nd	nd	nd	nd
OR Quart 2	>1.2	nd	>1.1	nd	nd	nd	nd	nd	nd
p Value	<0.88	nd	<0.94	nd	nd	nd	nd	nd	nd
95% CI of	>0.067	nd	>0.060	nd	nd	nd	nd	nd	nd
OR Quart2	na	nd	na	nd	nd	nd	nd	nd	nd
OR Quart 3	>2.5	nd	>4.5	nd	nd	nd	nd	nd	nd
p Value	<0.49	nd	<0.24	nd	nd	nd	nd	nd	nd
95% CI of	>0.19	nd	>0.37	nd	nd	nd	nd	nd	nd
OR Quart3	na	nd	na	nd	nd	nd	nd	nd	nd
OR Quart 4	>5.0	nd	>9.0	nd	nd	nd	nd	nd	nd
p Value	<0.20	nd	<0.083	nd	nd	nd	nd	nd	nd
95% CI of	>0.42	nd	>0.75	nd	nd	nd	nd	nd	nd
OR Quart4	na	nd	na	nd	nd	nd	nd	nd	nd

Caspase-9

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	25.5	14.8	nd	nd	nd	nd
Average	44.5	24.6	nd	nd	nd	nd
Stdev	60.6	24.9	nd	nd	nd	nd
p(t-test)		0.27	nd	nd	nd	nd
Min	0.400	4.59	nd	nd	nd	nd
Max	366	78.6	nd	nd	nd	nd
n (Samp)	57	12	nd	nd	nd	nd
n (Patient)	37	12	nd	nd	nd	nd

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	22.8	13.2	nd	nd	nd	nd
Average	42.5	12.5	nd	nd	nd	nd
Stdev	58.2	7.24	nd	nd	nd	nd
p(t-test)		0.21	nd	nd	nd	nd
Min	0.400	4.32	nd	nd	nd	nd
Max	366	21.7	nd	nd	nd	nd
n (Samp)	89	6	nd	nd	nd	nd
n (Patient)	61	6	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	30.1	9.06	nd	nd	nd	nd
Average	50.3	20.6	nd	nd	nd	nd
Stdev	67.6	24.4	nd	nd	nd	nd
p(t-test)		0.12	nd	nd	nd	nd
Min	6.05	3.79	nd	nd	nd	nd
Max	366	78.6	nd	nd	nd	nd
n (Samp)	42	14	nd	nd	nd	nd
n (Patient)	27	14	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.39	0.28	0.26	nd	nd	nd	nd	nd	nd
SE	0.094	0.12	0.083	nd	nd	nd	nd	nd	nd
p	0.25	0.077	0.0038	nd	nd	nd	nd	nd	nd
nCohort 1	57	89	42	nd	nd	nd	nd	nd	nd
nCohort 2	12	6	14	nd	nd	nd	nd	nd	nd
Cutoff 1	8.91	3.65	6.05	nd	nd	nd	nd	nd	nd
Sens 1	75%	100%	71%	nd	nd	nd	nd	nd	nd
Spec 1	21%	7%	2%	nd	nd	nd	nd	nd	nd
Cutoff 2	8.22	3.65	4.59	nd	nd	nd	nd	nd	nd
Sens 2	83%	100%	86%	nd	nd	nd	nd	nd	nd
Spec 2	19%	7%	0%	nd	nd	nd	nd	nd	nd
Cutoff 3	4.59	3.65	3.79	nd	nd	nd	nd	nd	nd
Sens 3	92%	100%	93%	nd	nd	nd	nd	nd	nd
Spec 3	9%	7%	0%	nd	nd	nd	nd	nd	nd
Cutoff 4	46.1	45.3	49.3	nd	nd	nd	nd	nd	nd
Sens 4	17%	0%	14%	nd	nd	nd	nd	nd	nd
Spec 4	70%	71%	71%	nd	nd	nd	nd	nd	nd
Cutoff 5	54.5	57.5	54.5	nd	nd	nd	nd	nd	nd
Sens 5	17%	0%	14%	nd	nd	nd	nd	nd	nd
Spec 5	81%	81%	81%	nd	nd	nd	nd	nd	nd
Cutoff 6	90.6	94.1	106	nd	nd	nd	nd	nd	nd
Sens 6	0%	0%	0%	nd	nd	nd	nd	nd	nd
Spec 6	91%	91%	90%	nd	nd	nd	nd	nd	nd
OR Quart 2	1.1	>1.0	1.0	nd	nd	nd	nd	nd	nd
p Value	0.95	<0.98	1.0	nd	nd	nd	nd	nd	nd
95% CI of	0.13	>0.062	0.12	nd	nd	nd	nd	nd	nd
OR Quart2	8.6	na	8.3	nd	nd	nd	nd	nd	nd
OR Quart 3	1.7	>3.4	1.0	nd	nd	nd	nd	nd	nd
p Value	0.58	<0.30	1.0	nd	nd	nd	nd	nd	nd
95% CI of	0.25	>0.33	0.12	nd	nd	nd	nd	nd	nd
OR Quart3	12	na	8.3	nd	nd	nd	nd	nd	nd
OR Quart 4	3.3	>2.3	8.0	nd	nd	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
p Value	0.19	<0.51	0.026	nd	nd	nd	nd	nd	nd
95% CI of	0.55	>0.19	1.3	nd	nd	nd	nd	nd	nd
OR Quart4	20	na	50	nd	nd	nd	nd	nd	nd

Cadherin-1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	72700	88200	72700	92800	72700	98500
Average	102000	129000	102000	127000	102000	134000
Stdev	106000	88400	106000	90200	106000	91700
p(t-test)		0.26		0.28		0.28
Min	14500	34900	14500	3320	14500	25800
Max	621000	334000	621000	340000	621000	283000
n (Samp)	52	28	52	31	52	16
n (Patient)	50	28	50	31	50	16

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	86800	130000	86800	73000	86800	109000
Average	116000	145000	116000	120000	116000	116000
Stdev	94600	90700	94600	94900	94600	73700
p(t-test)		0.35		0.87		0.99
Min	3320	34900	3320	30700	3320	56100
Max	621000	334000	621000	340000	621000	283000
n (Samp)	123	10	123	16	123	8
n (Patient)	96	10	96	16	96	8

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	81200	88200	81200	103000	81200	89400
Average	119000	122000	119000	122000	119000	139000
Stdev	114000	85000	114000	78600	114000	94300
p(t-test)		0.89		0.89		0.59
Min	39700	38100	39700	3320	39700	25800
Max	621000	314000	621000	300000	621000	277000
n (Samp)	51	22	51	27	51	11
n (Patient)	44	22	44	27	44	11

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.62	0.63	0.54	0.59	0.47	0.57	0.62	0.56	0.59
SE	0.067	0.098	0.075	0.065	0.078	0.069	0.083	0.11	0.098
p	0.066	0.18	0.57	0.15	0.72	0.32	0.13	0.57	0.38
nCohort 1	52	123	51	52	123	51	52	123	51
nCohort 2	28	10	22	31	16	27	16	8	11
Cutoff 1	78500	79100	75400	62800	40700	67700	61700	61700	79100
Sens 1	71%	70%	73%	71%	75%	70%	75%	75%	73%
Spec 1	56%	46%	41%	42%	9%	37%	40%	31%	49%
Cutoff 2	52700	78500	52700	47600	39700	54300	57000	57000	70100
Sens 2	82%	80%	82%	81%	81%	81%	81%	88%	82%
Spec 2	21%	46%	12%	17%	8%	14%	29%	26%	39%

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Cutoff 3	40700	72100	47600	39700	31800	39700	48100	54700	47600
Sens 3	93%	90%	91%	90%	94%	93%	94%	100%	91%
Spec 3	10%	41%	10%	8%	6%	2%	19%	23%	10%
Cutoff 4	97000	131000	100000	97000	131000	100000	97000	131000	100000
Sens 4	46%	50%	32%	48%	38%	52%	50%	25%	45%
Spec 4	71%	71%	71%	71%	71%	71%	71%	71%	71%
Cutoff 5	114000	165000	138000	114000	165000	138000	114000	165000	138000
Sens 5	36%	40%	27%	42%	38%	33%	38%	12%	36%
Spec 5	81%	80%	80%	81%	80%	80%	81%	80%	80%
Cutoff 6	153000	243000	242000	153000	243000	242000	153000	243000	242000
Sens 6	32%	20%	18%	39%	6%	11%	31%	12%	27%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	0.78	3.2	0.74	0.47	0.14	0.54	1.0	2.0	0.93
p Value	0.72	0.33	0.70	0.27	0.079	0.41	1.0	0.58	0.94
95% CI of	0.19	0.32	0.16	0.12	0.016	0.13	0.17	0.17	0.11
OR Quart2	3.1	32	3.4	1.8	1.3	2.3	5.8	23	7.6
OR Quart 3	1.3	2.1	1.7	0.60	0.62	1.6	1.4	4.3	1.6
p Value	0.74	0.56	0.48	0.44	0.50	0.50	0.67	0.21	0.63
95% CI of	0.33	0.18	0.41	0.16	0.16	0.42	0.27	0.45	0.23
OR Quart3	4.7	24	6.7	2.2	2.4	5.9	7.7	41	11
OR Quart 4	2.3	4.3	1.2	2.0	0.83	1.8	2.5	0.97	2.2
p Value	0.20	0.21	0.80	0.27	0.78	0.39	0.25	0.98	0.42
95% CI of	0.64	0.45	0.29	0.58	0.23	0.48	0.52	0.058	0.33
OR Quart4	8.5	40	4.9	6.9	3.0	6.6	13	16	14

Cadherin-5

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	20.4	21.2	nd	nd	nd	nd
Average	20.5	23.9	nd	nd	nd	nd
Stdev	5.01	5.05	nd	nd	nd	nd
p(t-test)		0.065	nd	nd	nd	nd
Min	12.4	18.0	nd	nd	nd	nd
Max	35.9	32.1	nd	nd	nd	nd
n (Samp)	48	9	nd	nd	nd	nd
n (Patient)	30	9	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	20.5	21.2	nd	nd	nd	nd
Average	20.7	23.3	nd	nd	nd	nd
Stdev	4.09	5.02	nd	nd	nd	nd
p(t-test)		0.080	nd	nd	nd	nd
Min	12.4	17.0	nd	nd	nd	nd
Max	29.3	32.1	nd	nd	nd	nd
n (Samp)	34	11	nd	nd	nd	nd
n (Patient)	20	11	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.69	nd	0.64	nd	nd	nd	nd	nd	nd
SE	0.10	nd	0.10	nd	nd	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
p	0.077	nd	0.16	nd	nd	nd	nd	nd	nd
nCohort 1	48	nd	34	nd	nd	nd	nd	nd	nd
nCohort 2	9	nd	11	nd	nd	nd	nd	nd	nd
Cutoff 1	20.6	nd	19.5	nd	nd	nd	nd	nd	nd
Sens 1	78%	nd	73%	nd	nd	nd	nd	nd	nd
Spec 1	54%	nd	44%	nd	nd	nd	nd	nd	nd
Cutoff 2	18.9	nd	18.9	nd	nd	nd	nd	nd	nd
Sens 2	89%	nd	82%	nd	nd	nd	nd	nd	nd
Spec 2	42%	nd	38%	nd	nd	nd	nd	nd	nd
Cutoff 3	17.1	nd	17.1	nd	nd	nd	nd	nd	nd
Sens 3	100%	nd	91%	nd	nd	nd	nd	nd	nd
Spec 3	33%	nd	26%	nd	nd	nd	nd	nd	nd
Cutoff 4	22.6	nd	22.7	nd	nd	nd	nd	nd	nd
Sens 4	44%	nd	45%	nd	nd	nd	nd	nd	nd
Spec 4	71%	nd	71%	nd	nd	nd	nd	nd	nd
Cutoff 5	24.0	nd	24.0	nd	nd	nd	nd	nd	nd
Sens 5	44%	nd	45%	nd	nd	nd	nd	nd	nd
Spec 5	81%	nd	82%	nd	nd	nd	nd	nd	nd
Cutoff 6	26.5	nd	26.2	nd	nd	nd	nd	nd	nd
Sens 6	33%	nd	27%	nd	nd	nd	nd	nd	nd
Spec 6	92%	nd	91%	nd	nd	nd	nd	nd	nd
OR Quart 2	>2.3	nd	3.8	nd	nd	nd	nd	nd	nd
p Value	<0.51	nd	0.29	nd	nd	nd	nd	nd	nd
95% CI of	>0.19	nd	0.32	nd	nd	nd	nd	nd	nd
OR Quart2	na	nd	43	nd	nd	nd	nd	nd	nd
OR Quart 3	>3.8	nd	2.2	nd	nd	nd	nd	nd	nd
p Value	<0.27	nd	0.54	nd	nd	nd	nd	nd	nd
95% CI of	>0.35	nd	0.17	nd	nd	nd	nd	nd	nd
OR Quart3	na	nd	29	nd	nd	nd	nd	nd	nd
OR Quart 4	>5.1	nd	7.1	nd	nd	nd	nd	nd	nd
p Value	<0.17	nd	0.10	nd	nd	nd	nd	nd	nd
95% CI of	>0.50	nd	0.68	nd	nd	nd	nd	nd	nd
OR Quart4	na	nd	75	nd	nd	nd	nd	nd	nd

Cyclin-dependent kinase inhibitor 1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	208	138	nd	nd	nd	nd
Average	1230	1120	nd	nd	nd	nd
Stdev	2090	1790	nd	nd	nd	nd
p(t-test)		0.87	nd	nd	nd	nd
Min	0.116	28.5	nd	nd	nd	nd
Max	6840	5430	nd	nd	nd	nd
n (Samp)	56	12	nd	nd	nd	nd
n (Patient)	37	12	nd	nd	nd	nd

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	197	171	nd	nd	nd	nd
Average	1140	463	nd	nd	nd	nd
Stdev	1940	716	nd	nd	nd	nd
p(t-test)		0.40	nd	nd	nd	nd
Min	0.116	73.9	nd	nd	nd	nd

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Max	6840	1910	nd	nd	nd	nd
n (Samp)	88	6	nd	nd	nd	nd
n (Patient)	61	6	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	381	151	nd	nd	nd	nd
Average	1460	1310	nd	nd	nd	nd
Stdev	2310	2210	nd	nd	nd	nd
p(t-test)		0.84	nd	nd	nd	nd
Min	0.116	28.5	nd	nd	nd	nd
Max	6840	6400	nd	nd	nd	nd
n (Samp)	41	14	nd	nd	nd	nd
n (Patient)	27	14	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.49	0.46	0.44	nd	nd	nd	nd	nd	nd
SE	0.093	0.12	0.091	nd	nd	nd	nd	nd	nd
p	0.91	0.78	0.52	nd	nd	nd	nd	nd	nd
nCohort 1	56	88	41	nd	nd	nd	nd	nd	nd
nCohort 2	12	6	14	nd	nd	nd	nd	nd	nd
Cutoff 1	116	123	108	nd	nd	nd	nd	nd	nd
Sens 1	75%	83%	71%	nd	nd	nd	nd	nd	nd
Spec 1	32%	33%	27%	nd	nd	nd	nd	nd	nd
Cutoff 2	96.8	123	73.1	nd	nd	nd	nd	nd	nd
Sens 2	83%	83%	86%	nd	nd	nd	nd	nd	nd
Spec 2	30%	33%	17%	nd	nd	nd	nd	nd	nd
Cutoff 3	47.1	73.1	42.3	nd	nd	nd	nd	nd	nd
Sens 3	92%	100%	93%	nd	nd	nd	nd	nd	nd
Spec 3	12%	17%	12%	nd	nd	nd	nd	nd	nd
Cutoff 4	715	715	902	nd	nd	nd	nd	nd	nd
Sens 4	33%	17%	21%	nd	nd	nd	nd	nd	nd
Spec 4	71%	70%	71%	nd	nd	nd	nd	nd	nd
Cutoff 5	1430	1430	1760	nd	nd	nd	nd	nd	nd
Sens 5	25%	17%	21%	nd	nd	nd	nd	nd	nd
Spec 5	80%	82%	80%	nd	nd	nd	nd	nd	nd
Cutoff 6	5560	5160	6560	nd	nd	nd	nd	nd	nd
Sens 6	0%	0%	0%	nd	nd	nd	nd	nd	nd
Spec 6	91%	91%	90%	nd	nd	nd	nd	nd	nd
OR Quart 2	0.62	2.2	1.0	nd	nd	nd	nd	nd	nd
p Value	0.63	0.53	1.0	nd	nd	nd	nd	nd	nd
95% CI of	0.090	0.18	0.16	nd	nd	nd	nd	nd	nd
OR Quart2	4.3	26	6.1	nd	nd	nd	nd	nd	nd
OR Quart 3	1.9	2.1	2.0	nd	nd	nd	nd	nd	nd
p Value	0.42	0.56	0.41	nd	nd	nd	nd	nd	nd
95% CI of	0.38	0.18	0.38	nd	nd	nd	nd	nd	nd
OR Quart3	9.9	25	11	nd	nd	nd	nd	nd	nd
OR Quart 4	0.62	1.0	1.1	nd	nd	nd	nd	nd	nd
p Value	0.63	0.98	0.92	nd	nd	nd	nd	nd	nd
95% CI of	0.090	0.062	0.18	nd	nd	nd	nd	nd	nd
OR Quart4	4.3	18	6.8	nd	nd	nd	nd	nd	nd

Carcinoembryonic antigen-related cell adhesion molecule 5

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.66	2.13	1.66	2.36	1.66	2.26
Average	2.32	3.66	2.32	3.88	2.32	3.00
Stdev	2.32	4.90	2.32	5.35	2.32	2.72
p(t-test)		0.0028		6.3E-4		0.17
Min	0.183	0.453	0.183	0.562	0.183	0.363
Max	20.8	30.1	20.8	33.6	20.8	12.5
n (Samp)	260	51	260	56	260	25
n (Patient)	110	51	110	56	110	25

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.77	1.68	1.77	2.00	1.77	1.91
Average	2.76	3.12	2.76	3.22	2.76	1.68
Stdev	3.35	4.09	3.35	3.30	3.35	0.833
p(t-test)		0.66		0.54		0.25
Min	0.183	0.245	0.183	0.355	0.183	0.363
Max	33.6	17.1	33.6	14.5	33.6	2.69
n (Samp)	466	18	466	21	466	13
n (Patient)	180	18	180	21	180	13

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.62	2.22	1.62	2.36	1.62	2.26
Average	2.47	3.81	2.47	3.82	2.47	3.39
Stdev	2.58	4.85	2.58	5.27	2.58	2.98
p(t-test)		0.0067		0.0083		0.11
Min	0.183	0.622	0.183	0.562	0.183	0.591
Max	20.8	30.1	20.8	33.6	20.8	12.5
n (Samp)	213	51	213	53	213	23
n (Patient)	89	51	89	53	89	23

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.60	0.48	0.63	0.63	0.54	0.62	0.60	0.43	0.62
SE	0.045	0.070	0.046	0.043	0.066	0.045	0.062	0.084	0.065
p	0.026	0.73	0.0052	0.0029	0.51	0.0056	0.12	0.44	0.073
nCohort 1	260	466	213	260	466	213	260	466	213
nCohort 2	51	18	51	56	21	53	25	13	23
Cutoff 1	1.35	1.17	1.52	1.70	1.22	1.77	1.43	1.05	1.57
Sens 1	71%	72%	71%	71%	71%	72%	72%	77%	74%
Spec 1	40%	31%	47%	53%	32%	58%	43%	26%	49%
Cutoff 2	1.10	0.591	1.11	1.02	1.01	1.02	0.855	0.971	0.855
Sens 2	80%	83%	80%	80%	81%	81%	80%	85%	83%
Spec 2	32%	8%	32%	30%	25%	30%	23%	23%	22%
Cutoff 3	0.893	0.448	0.919	0.787	0.731	0.787	0.679	0.417	0.699
Sens 3	90%	94%	90%	91%	90%	91%	92%	92%	91%
Spec 3	25%	4%	23%	20%	13%	18%	16%	3%	15%
Cutoff 4	2.42	2.71	2.52	2.42	2.71	2.52	2.42	2.71	2.52
Sens 4	39%	28%	45%	45%	43%	42%	48%	0%	48%
Spec 4	70%	70%	71%	70%	70%	71%	70%	70%	71%
Cutoff 5	3.34	3.88	3.74	3.34	3.88	3.74	3.34	3.88	3.74
Sens 5	31%	22%	31%	32%	29%	28%	32%	0%	30%

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	4.93	5.28	5.88	4.93	5.28	5.88	4.93	5.28	5.88
Sens 6	20%	17%	12%	18%	14%	11%	12%	0%	17%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	2.0	0.59	1.1	0.67	0.99	0.45	0.48	>7.4	0.79
p Value	0.17	0.48	0.80	0.44	0.99	0.17	0.31	<0.063	0.73
95% CI of	0.75	0.14	0.41	0.24	0.28	0.15	0.11	>0.90	0.20
OR Quart2	5.3	2.5	3.2	1.9	3.5	1.4	2.0	na	3.1
OR Quart 3	2.2	1.0	2.5	2.3	0.58	2.4	1.2	>3.1	1.0
p Value	0.11	1.0	0.050	0.046	0.47	0.041	0.77	<0.33	1.0
95% CI of	0.83	0.28	1.0	1.0	0.14	1.0	0.38	>0.32	0.27
OR Quart3	5.8	3.5	6.3	5.4	2.5	5.7	3.7	na	3.7
OR Quart 4	2.8	1.0	2.5	2.2	1.6	2.1	1.5	>3.1	1.9
p Value	0.033	1.0	0.050	0.068	0.40	0.10	0.43	<0.33	0.26
95% CI of	1.1	0.28	1.0	0.94	0.52	0.87	0.52	>0.32	0.61
OR Quart4	7.2	3.5	6.3	5.1	5.1	4.9	4.6	na	6.2

Myoglobin

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	26.8	36.2	26.8	41.7	26.8	54.3
Average	66.0	106	66.0	168	66.0	113
Stdev	145	166	145	301	145	194
p(t-test)		0.078		1.8E-4		0.13
Min	4.60	6.86	4.60	4.40	4.60	7.57
Max	1720	737	1720	1470	1720	988
n (Samp)	260	51	260	56	260	25
n (Patient)	110	51	110	56	110	25

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	33.0	62.6	33.0	64.7	33.0	69.7
Average	83.7	266	83.7	272	83.7	94.9
Stdev	191	465	191	433	191	93.0
p(t-test)		2.8E-4		5.2E-5		0.83
Min	3.68	8.01	3.68	4.40	3.68	7.57
Max	2130	1880	2130	1470	2130	308
n (Samp)	466	18	466	21	466	13
n (Patient)	180	18	180	21	180	13

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	27.4	37.3	27.4	41.0	27.4	62.1
Average	72.4	102	72.4	147	72.4	165
Stdev	153	158	153	260	153	320
p(t-test)		0.22		0.0071		0.017
Min	4.60	6.86	4.60	8.81	4.60	8.40
Max	1720	737	1720	1410	1720	1310
n (Samp)	213	51	213	53	213	23
n (Patient)	89	51	89	53	89	23

	0hr prior to AKI stage	24hr prior to AKI stage	48hr prior to AKI stage

	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.60	0.65	0.59	0.65	0.61	0.64	0.63	0.62	0.63
SE	0.045	0.072	0.046	0.043	0.067	0.045	0.062	0.084	0.065
p	0.034	0.041	0.039	7.0E-4	0.086	0.0019	0.036	0.15	0.051
nCohort 1	260	466	213	260	466	213	260	466	213
nCohort 2	51	18	51	56	21	53	25	13	23
Cutoff 1	21.3	26.6	20.9	27.5	24.5	27.5	20.6	25.6	20.4
Sens 1	71%	72%	71%	71%	71%	72%	72%	77%	74%
Spec 1	40%	43%	40%	52%	38%	50%	39%	41%	40%
Cutoff 2	18.6	25.4	18.6	18.6	19.2	18.9	17.4	17.4	16.3
Sens 2	80%	83%	80%	80%	81%	81%	80%	85%	83%
Spec 2	33%	41%	34%	33%	31%	35%	30%	25%	29%
Cutoff 3	12.5	8.56	14.8	12.3	12.9	13.2	9.64	8.39	10.6
Sens 3	90%	94%	90%	91%	90%	91%	92%	92%	91%
Spec 3	18%	8%	26%	18%	17%	21%	13%	8%	15%
Cutoff 4	50.2	60.4	56.0	50.2	60.4	56.0	50.2	60.4	56.0
Sens 4	43%	50%	41%	46%	52%	45%	52%	54%	52%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	74.3	93.4	84.8	74.3	93.4	84.8	74.3	93.4	84.8
Sens 5	35%	39%	35%	43%	38%	42%	44%	31%	43%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	138	171	174	138	171	174	138	171	174
Sens 6	22%	33%	16%	29%	29%	26%	20%	15%	13%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	1.6	2.6	2.9	0.88	0.99	2.0	1.0	0.99	0.74
p Value	0.36	0.27	0.038	0.80	0.99	0.16	1.0	0.99	0.70
95% CI of	0.60	0.49	1.1	0.32	0.24	0.75	0.24	0.14	0.16
OR Quart2	4.1	13	8.1	2.4	4.1	5.5	4.2	7.2	3.4
OR Quart 3	1.7	1.5	2.0	1.8	0.99	1.7	1.5	1.5	1.3
p Value	0.26	0.65	0.20	0.19	0.99	0.31	0.51	0.66	0.73
95% CI of	0.67	0.25	0.69	0.75	0.24	0.61	0.42	0.25	0.32
OR Quart3	4.4	9.2	5.8	4.5	4.1	4.7	5.7	9.1	5.0
OR Quart 4	2.6	4.2	4.0	3.4	2.3	4.1	3.0	3.1	3.2
p Value	0.039	0.073	0.0059	0.0045	0.17	0.0030	0.070	0.17	0.063
95% CI of	1.1	0.88	1.5	1.5	0.70	1.6	0.91	0.61	0.94
OR Quart4	6.4	20	11	7.9	7.8	10	10.0	16	11

Mucin-16

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.11	1.51	1.11	2.02	1.11	1.59
Average	3.53	10.4	3.53	13.9	3.53	3.72
Stdev	14.4	41.9	14.4	46.3	14.4	6.27
p(t-test)		0.19		0.063		0.95
Min	0.117	0.204	0.117	0.122	0.117	0.122
Max	131	253	131	248	131	31.2
n (Samp)	82	36	82	45	82	26
n (Patient)	75	36	75	45	75	26

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.41	1.27	1.41	1.83	1.41	1.24
Average	8.87	1.81	8.87	5.69	8.87	1.52
Stdev	35.3	1.57	35.3	9.55	35.3	1.06
p(t-test)		0.49		0.74		0.53

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Min	0.117	0.481	0.117	0.631	0.117	0.631
Max	263	5.56	263	37.0	263	4.16
n (Samp)	197	12	197	14	197	9
n (Patient)	131	12	131	14	131	9

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.24	1.60	1.24	2.52	1.24	2.44
Average	3.82	12.7	3.82	14.8	3.82	4.48
Stdev	15.1	46.6	15.1	47.3	15.1	6.81
p(t-test)		0.14		0.067		0.84
Min	0.122	0.204	0.122	0.122	0.122	0.122
Max	131	253	131	248	131	31.2
n (Samp)	75	29	75	43	75	21
n (Patient)	62	29	62	43	62	21

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.62	0.47	0.61	0.65	0.61	0.64	0.62	0.45	0.66
SE	0.058	0.087	0.064	0.052	0.082	0.054	0.066	0.10	0.071
p	0.036	0.72	0.084	0.0055	0.18	0.0073	0.068	0.64	0.024
nCohort 1	82	197	75	82	197	75	82	197	75
nCohort 2	36	12	29	45	14	43	26	9	21
Cutoff 1	1.06	1.09	0.999	1.06	1.33	1.12	1.06	1.01	1.25
Sens 1	72%	75%	72%	71%	71%	72%	73%	78%	71%
Spec 1	50%	41%	44%	50%	47%	47%	50%	38%	52%
Cutoff 2	0.803	0.821	0.761	0.821	1.02	0.803	0.999	0.754	1.06
Sens 2	81%	83%	83%	80%	86%	81%	85%	89%	81%
Spec 2	46%	36%	33%	46%	38%	43%	48%	29%	47%
Cutoff 3	0.464	0.481	0.379	0.334	1.01	0.334	0.630	0.630	0.999
Sens 3	92%	92%	93%	91%	93%	91%	92%	100%	90%
Spec 3	16%	16%	11%	10%	38%	8%	24%	22%	44%
Cutoff 4	2.09	3.28	1.96	2.09	3.28	1.96	2.09	3.28	1.96
Sens 4	39%	17%	45%	49%	43%	56%	38%	11%	52%
Spec 4	72%	70%	71%	72%	70%	71%	72%	70%	71%
Cutoff 5	2.78	5.21	2.98	2.78	5.21	2.98	2.78	5.21	2.98
Sens 5	36%	8%	41%	44%	29%	47%	27%	0%	38%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	4.88	8.80	5.21	4.88	8.80	5.21	4.88	8.80	5.21
Sens 6	28%	0%	31%	29%	14%	28%	12%	0%	14%
Spec 6	90%	90%	91%	90%	90%	91%	90%	90%	91%
OR Quart 2	2.4	1.0	1.5	2.9	5.3	2.2	3.4	1.0	2.9
p Value	0.16	0.98	0.51	0.071	0.13	0.18	0.10	0.99	0.23
95% CI of	0.70	0.14	0.42	0.91	0.60	0.69	0.78	0.062	0.50
OR Quart2	8.2	7.5	5.7	8.9	47	7.1	14	17	17
OR Quart 3	1.8	3.3	1.0	1.2	3.1	1.7	2.3	6.7	3.7
p Value	0.35	0.15	1.0	0.80	0.34	0.37	0.28	0.085	0.14
95% CI of	0.52	0.64	0.25	0.34	0.31	0.52	0.51	0.77	0.66
OR Quart3	6.5	17	4.0	4.0	30	5.7	10	57	20
OR Quart 4	3.7	1.0	3.6	6.1	5.3	5.0	4.0	1.0	5.5
p Value	0.034	0.98	0.043	0.0018	0.13	0.0061	0.060	0.99	0.046
95% CI of	1.1	0.14	1.0	2.0	0.60	1.6	0.95	0.062	1.0
OR Quart4	12	7.5	12	19	47	16	17	17	29

Tumor necrosis factor receptor superfamily member 10B

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	1.00E-9	1.00E-9	0.00240	1.00E-9	1.00E-9
Average	0.00715	0.0102	0.00715	0.0133	0.00715	0.0150
Stdev	0.0203	0.0434	0.0203	0.0446	0.0203	0.0622
p(t-test)		0.60		0.30		0.34
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	0.114	0.262	0.114	0.286	0.114	0.300
n (Samp)	79	36	79	41	79	23
n (Patient)	72	36	72	41	72	23

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	1.00E-9	1.00E-9	0.00507	1.00E-9	1.00E-9
Average	0.00582	0.0263	0.00582	0.0316	0.00582	0.0334
Stdev	0.0146	0.0783	0.0146	0.0849	0.0146	0.0938
p(t-test)		0.0040		6.0E-4		7.1E-4
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	0.114	0.262	0.114	0.286	0.114	0.300
n (Samp)	187	11	187	11	187	10
n (Patient)	127	11	127	11	127	10

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	0.00131	1.00E-9	0.00131	0.00202	0.00131	1.00E-9
Average	0.00817	0.00387	0.00817	0.0104	0.00817	0.00218
Stdev	0.0213	0.00693	0.0213	0.0213	0.0213	0.00328
p(t-test)		0.28		0.60		0.25
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	0.114	0.0300	0.114	0.108	0.114	0.00903
n (Samp)	70	30	70	40	70	17
n (Patient)	56	30	56	40	56	17

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.47	0.44	0.45	0.61	0.62	0.57	0.47	0.51	0.43
SE	0.059	0.092	0.064	0.055	0.093	0.058	0.069	0.094	0.080
p	0.65	0.52	0.43	0.038	0.21	0.22	0.72	0.91	0.35
nCohort 1	79	187	70	79	187	70	79	187	70
nCohort 2	36	11	30	41	11	40	23	10	17
Cutoff 1	0	0	0	0	0	0	0	0	0
Sens 1	100%	100%	100%	100%	100%	100%	100%	100%	100%
Spec 1	0%	0%	0%	0%	0%	0%	0%	0%	0%
Cutoff 2	0	0	0	0	0	0	0	0	0
Sens 2	100%	100%	100%	100%	100%	100%	100%	100%	100%
Spec 2	0%	0%	0%	0%	0%	0%	0%	0%	0%
Cutoff 3	0	0	0	0	0	0	0	0	0
Sens 3	100%	100%	100%	100%	100%	100%	100%	100%	100%
Spec 3	0%	0%	0%	0%	0%	0%	0%	0%	0%
Cutoff 4	0.00274	0.00377	0.00377	0.00274	0.00377	0.00377	0.00274	0.00377	0.00377
Sens 4	33%	27%	33%	49%	64%	42%	30%	40%	24%
Spec 4	71%	71%	71%	71%	71%	71%	71%	71%	71%
Cutoff 5	0.00507	0.00819	0.00813	0.00507	0.00819	0.00813	0.00507	0.00819	0.00813
Sens 5	28%	27%	17%	37%	27%	35%	26%	30%	12%

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Spec 5	81%	82%	80%	81%	82%	80%	81%	82%	80%
Cutoff 6	0.0166	0.0136	0.0165	0.0166	0.0136	0.0165	0.0166	0.0136	0.0165
Sens 6	6%	18%	7%	17%	18%	18%	4%	20%	0%
Spec 6	91%	90%	90%	91%	90%	90%	91%	90%	90%
OR Quart 2	0.12	0	0.24	6.0	0	1.1	1.1	0.48	0.71
p Value	0.011	na	0.057	0.012	na	0.84	0.94	0.41	0.68
95% CI of	0.024	na	0.056	1.5	na	0.36	0.29	0.084	0.14
OR Quart2	0.61	na	1.0	24	na	3.5	3.8	2.7	3.6
OR Quart 3	2.0	1.4	1.2	5.2	1.0	1.2	2.4	0	1.7
p Value	0.19	0.70	0.77	0.021	1.0	0.77	0.14	na	0.47
95% CI of	0.71	0.29	0.38	1.3	0.24	0.38	0.74	na	0.40
OR Quart3	5.7	6.4	3.7	21	4.2	3.8	8.1	na	7.1
OR Quart 4	0.55	1.4	0.84	9.0	0.72	2.4	0	0.98	1.1
p Value	0.30	0.68	0.77	0.0020	0.68	0.13	na	0.98	0.94
95% CI of	0.17	0.30	0.26	2.2	0.15	0.78	na	0.23	0.23
OR Quart4	1.7	6.6	2.7	36	3.4	7.2	na	4.2	4.9

[0160] Table 6: Comparison of marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0 or R) and in EDTA samples collected from subjects at 0, 24 hours, and 48 hours prior to reaching stage I or F in Cohort 2.

Apolipoprotein A-II

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	54100	49700	54100	45500	54100	43300
Average	55400	59300	55400	51900	55400	46600
Stdev	29200	19900	29200	32000	29200	33800
p(t-test)		0.57		0.57		0.26
Min	5450	32800	5450	10700	5450	1810
Max	253000	97000	253000	176000	253000	152000
n (Samp)	230	19	230	26	230	15
n (Patient)	158	19	158	26	158	15

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	52600	51800	52600	45500	52600	43200
Average	54900	58300	54900	51000	54900	47000
Stdev	29800	21200	29800	31800	29800	35000
p(t-test)		0.62		0.54		0.35
Min	7680	23300	7680	10700	7680	1810
Max	253000	97000	253000	176000	253000	152000
n (Samp)	201	19	201	26	201	14
n (Patient)	133	19	133	26	133	14

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.56	nd	0.56	0.44	nd	0.43	0.36	nd	0.37
SE	0.071	nd	0.071	0.061	nd	0.062	0.079	nd	0.082
p	0.38	nd	0.40	0.30	nd	0.24	0.069	nd	0.11

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
nCohort 1	230	nd	201	230	nd	201	230	nd	201
nCohort 2	19	nd	19	26	nd	26	15	nd	14
Cutoff 1	43600	nd	43600	35400	nd	35000	36000	nd	36000
Sens 1	74%	nd	74%	73%	nd	73%	73%	nd	71%
Spec 1	35%	nd	36%	21%	nd	21%	21%	nd	21%
Cutoff 2	43000	nd	40500	30600	nd	30600	35900	nd	31700
Sens 2	84%	nd	84%	81%	nd	81%	80%	nd	86%
Spec 2	34%	nd	30%	17%	nd	18%	21%	nd	19%
Cutoff 3	40200	nd	32500	28300	nd	26600	7970	nd	7970
Sens 3	95%	nd	95%	92%	nd	92%	93%	nd	93%
Spec 3	30%	nd	20%	16%	nd	14%	1%	nd	1%
Cutoff 4	64400	nd	64800	64400	nd	64800	64400	nd	64800
Sens 4	42%	nd	42%	19%	nd	15%	13%	nd	14%
Spec 4	70%	nd	70%	70%	nd	70%	70%	nd	70%
Cutoff 5	72600	nd	72300	72600	nd	72300	72600	nd	72300
Sens 5	26%	nd	26%	12%	nd	12%	13%	nd	14%
Spec 5	80%	nd	80%	80%	nd	80%	80%	nd	80%
Cutoff 6	87100	nd	83600	87100	nd	83600	87100	nd	83600
Sens 6	16%	nd	16%	8%	nd	8%	7%	nd	7%
Spec 6	90%	nd	90%	90%	nd	90%	90%	nd	90%
OR Quart 2	12	nd	5.2	1.2	nd	1.9	0	nd	0
p Value	0.021	nd	0.041	0.75	nd	0.35	na	nd	na
95% CI of	1.5	nd	1.1	0.35	nd	0.51	na	nd	na
OR Quart2	95	nd	25	4.2	nd	6.7	na	nd	na
OR Quart 3	1.0	nd	0.49	1.2	nd	1.6	3.9	nd	3.9
p Value	1.0	nd	0.57	0.75	nd	0.51	0.099	nd	0.10
95% CI of	0.061	nd	0.043	0.35	nd	0.42	0.77	nd	0.77
OR Quart3	16	nd	5.6	4.2	nd	5.8	20	nd	20
OR Quart 4	7.6	nd	3.9	1.9	nd	2.5	3.3	nd	2.7
p Value	0.061	nd	0.10	0.26	nd	0.14	0.16	nd	0.25
95% CI of	0.91	nd	0.77	0.61	nd	0.73	0.63	nd	0.50
OR Quart4	64	nd	20	6.1	nd	8.8	17	nd	15

Caspase-1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	70.5	58.2	nd	nd	nd	nd
Average	90.5	69.4	nd	nd	nd	nd
Stdev	59.1	45.7	nd	nd	nd	nd
p(t-test)		0.31	nd	nd	nd	nd
Min	20.6	36.3	nd	nd	nd	nd
Max	326	188	nd	nd	nd	nd
n (Samp)	60	9	nd	nd	nd	nd
n (Patient)	37	9	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	72.3	58.2	nd	nd	nd	nd
Average	91.4	69.4	nd	nd	nd	nd
Stdev	54.9	45.7	nd	nd	nd	nd
p(t-test)		0.27	nd	nd	nd	nd
Min	33.8	36.3	nd	nd	nd	nd
Max	271	188	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
n (Samp)	45	9	nd	nd	nd	nd
n (Patient)	26	9	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.32	nd	0.31	nd	nd	nd	nd	nd	nd
SE	0.10	nd	0.10	nd	nd	nd	nd	nd	nd
p	0.089	nd	0.066	nd	nd	nd	nd	nd	nd
nCohort 1	60	nd	45	nd	nd	nd	nd	nd	nd
nCohort 2	9	nd	9	nd	nd	nd	nd	nd	nd
Cutoff 1	45.8	nd	45.8	nd	nd	nd	nd	nd	nd
Sens 1	78%	nd	78%	nd	nd	nd	nd	nd	nd
Spec 1	15%	nd	11%	nd	nd	nd	nd	nd	nd
Cutoff 2	42.1	nd	42.0	nd	nd	nd	nd	nd	nd
Sens 2	89%	nd	89%	nd	nd	nd	nd	nd	nd
Spec 2	13%	nd	9%	nd	nd	nd	nd	nd	nd
Cutoff 3	35.1	nd	33.8	nd	nd	nd	nd	nd	nd
Sens 3	100%	nd	100%	nd	nd	nd	nd	nd	nd
Spec 3	5%	nd	2%	nd	nd	nd	nd	nd	nd
Cutoff 4	95.6	nd	95.9	nd	nd	nd	nd	nd	nd
Sens 4	11%	nd	11%	nd	nd	nd	nd	nd	nd
Spec 4	70%	nd	73%	nd	nd	nd	nd	nd	nd
Cutoff 5	110	nd	103	nd	nd	nd	nd	nd	nd
Sens 5	11%	nd	11%	nd	nd	nd	nd	nd	nd
Spec 5	80%	nd	80%	nd	nd	nd	nd	nd	nd
Cutoff 6	147	nd	186	nd	nd	nd	nd	nd	nd
Sens 6	11%	nd	11%	nd	nd	nd	nd	nd	nd
Spec 6	90%	nd	91%	nd	nd	nd	nd	nd	nd
OR Quart 2	1.1	nd	1.1	nd	nd	nd	nd	nd	nd
p Value	0.97	nd	0.96	nd	nd	nd	nd	nd	nd
95% CI of	0.061	nd	0.061	nd	nd	nd	nd	nd	nd
OR Quart2	18	nd	19	nd	nd	nd	nd	nd	nd
OR Quart 3	5.2	nd	5.2	nd	nd	nd	nd	nd	nd
p Value	0.16	nd	0.17	nd	nd	nd	nd	nd	nd
95% CI of	0.52	nd	0.50	nd	nd	nd	nd	nd	nd
OR Quart3	53	nd	54	nd	nd	nd	nd	nd	nd
OR Quart 4	3.6	nd	3.9	nd	nd	nd	nd	nd	nd
p Value	0.29	nd	0.27	nd	nd	nd	nd	nd	nd
95% CI of	0.34	nd	0.35	nd	nd	nd	nd	nd	nd
OR Quart4	39	nd	43	nd	nd	nd	nd	nd	nd

Caspase-9

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	21.3	7.75	nd	nd	nd	nd
Average	42.0	23.4	nd	nd	nd	nd
Stdev	59.4	35.2	nd	nd	nd	nd
p(t-test)		0.36	nd	nd	nd	nd
Min	0.400	3.79	nd	nd	nd	nd
Max	366	114	nd	nd	nd	nd
n (Samp)	82	9	nd	nd	nd	nd
n (Patient)	59	9	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	23.9	7.75	nd	nd	nd	nd
Average	46.6	23.4	nd	nd	nd	nd
Stdev	65.1	35.2	nd	nd	nd	nd
p(t-test)		0.30	nd	nd	nd	nd
Min	0.400	3.79	nd	nd	nd	nd
Max	366	114	nd	nd	nd	nd
n (Samp)	64	9	nd	nd	nd	nd
n (Patient)	46	9	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.32	nd	0.28	nd	nd	nd	nd	nd	nd
SE	0.10	nd	0.10	nd	nd	nd	nd	nd	nd
p	0.085	nd	0.032	nd	nd	nd	nd	nd	nd
nCohort 1	82	nd	64	nd	nd	nd	nd	nd	nd
nCohort 2	9	nd	9	nd	nd	nd	nd	nd	nd
Cutoff 1	4.69	nd	4.69	nd	nd	nd	nd	nd	nd
Sens 1	78%	nd	78%	nd	nd	nd	nd	nd	nd
Spec 1	9%	nd	3%	nd	nd	nd	nd	nd	nd
Cutoff 2	4.59	nd	4.59	nd	nd	nd	nd	nd	nd
Sens 2	89%	nd	89%	nd	nd	nd	nd	nd	nd
Spec 2	9%	nd	3%	nd	nd	nd	nd	nd	nd
Cutoff 3	3.65	nd	0.400	nd	nd	nd	nd	nd	nd
Sens 3	100%	nd	100%	nd	nd	nd	nd	nd	nd
Spec 3	6%	nd	2%	nd	nd	nd	nd	nd	nd
Cutoff 4	43.6	nd	45.3	nd	nd	nd	nd	nd	nd
Sens 4	11%	nd	11%	nd	nd	nd	nd	nd	nd
Spec 4	71%	nd	70%	nd	nd	nd	nd	nd	nd
Cutoff 5	52.2	nd	54.5	nd	nd	nd	nd	nd	nd
Sens 5	11%	nd	11%	nd	nd	nd	nd	nd	nd
Spec 5	80%	nd	81%	nd	nd	nd	nd	nd	nd
Cutoff 6	87.8	nd	106	nd	nd	nd	nd	nd	nd
Sens 6	11%	nd	11%	nd	nd	nd	nd	nd	nd
Spec 6	90%	nd	91%	nd	nd	nd	nd	nd	nd
OR Quart 2	2.1	nd	2.2	nd	nd	nd	nd	nd	nd
p Value	0.56	nd	0.52	nd	nd	nd	nd	nd	nd
95% CI of	0.18	nd	0.19	nd	nd	nd	nd	nd	nd
OR Quart2	25	nd	27	nd	nd	nd	nd	nd	nd
OR Quart 3	1.0	nd	1.1	nd	nd	nd	nd	nd	nd
p Value	1.0	nd	0.97	nd	nd	nd	nd	nd	nd
95% CI of	0.059	nd	0.061	nd	nd	nd	nd	nd	nd
OR Quart3	17	nd	18	nd	nd	nd	nd	nd	nd
OR Quart 4	6.5	nd	6.9	nd	nd	nd	nd	nd	nd
p Value	0.10	nd	0.094	nd	nd	nd	nd	nd	nd
95% CI of	0.69	nd	0.72	nd	nd	nd	nd	nd	nd
OR Quart4	61	nd	67	nd	nd	nd	nd	nd	nd

Cadherin-1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	77700	123000	77700	103000	77700	117000
Average	113000	130000	113000	122000	113000	146000
Stdev	97300	57100	97300	77800	97300	81700

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
p(t-test)		0.64		0.70		0.26
Min	14500	51600	14500	3320	14500	50500
Max	621000	231000	621000	340000	621000	285000
n (Samp)	123	7	123	20	123	12
n (Patient)	97	7	97	20	97	12

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	86600	95800	86600	105000
Average	nd	nd	123000	105000	123000	128000
Stdev	nd	nd	101000	52100	101000	80100
p(t-test)	nd	nd		0.44		0.88
Min	nd	nd	25800	3320	25800	50500
Max	nd	nd	621000	209000	621000	277000
n (Samp)	nd	nd	104	20	104	10
n (Patient)	nd	nd	81	20	81	10

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.67	nd	nd	0.60	nd	0.54	0.69	nd	0.57
SE	0.12	nd	nd	0.071	nd	0.072	0.088	nd	0.098
p	0.14	nd	nd	0.16	nd	0.54	0.031	nd	0.47
nCohort 1	123	nd	nd	123	nd	104	123	nd	104
nCohort 2	7	nd	nd	20	nd	20	12	nd	10
Cutoff 1	108000	nd	nd	81200	nd	85700	100000	nd	79100
Sens 1	71%	nd	nd	70%	nd	70%	75%	nd	70%
Spec 1	70%	nd	nd	53%	nd	50%	67%	nd	45%
Cutoff 2	91400	nd	nd	69300	nd	70100	79100	nd	75400
Sens 2	86%	nd	nd	80%	nd	80%	83%	nd	80%
Spec 2	63%	nd	nd	45%	nd	38%	52%	nd	40%
Cutoff 3	51000	nd	nd	54100	nd	63600	75400	nd	54100
Sens 3	100%	nd	nd	90%	nd	90%	92%	nd	90%
Spec 3	20%	nd	nd	24%	nd	33%	48%	nd	18%
Cutoff 4	110000	nd	nd	110000	nd	114000	110000	nd	114000
Sens 4	57%	nd	nd	40%	nd	30%	50%	nd	40%
Spec 4	71%	nd	nd	71%	nd	70%	71%	nd	70%
Cutoff 5	165000	nd	nd	165000	nd	184000	165000	nd	184000
Sens 5	29%	nd	nd	25%	nd	10%	25%	nd	20%
Spec 5	80%	nd	nd	80%	nd	81%	80%	nd	81%
Cutoff 6	248000	nd	nd	248000	nd	257000	248000	nd	257000
Sens 6	0%	nd	nd	5%	nd	0%	25%	nd	20%
Spec 6	90%	nd	nd	90%	nd	90%	90%	nd	90%
OR Quart 2	0	nd	nd	0.97	nd	3.5	2.0	nd	0.96
p Value	na	nd	nd	0.97	nd	0.15	0.58	nd	0.97
95% CI of	na	nd	nd	0.18	nd	0.64	0.17	nd	0.13
OR Quart2	na	nd	nd	5.2	nd	19	23	nd	7.4
OR Quart 3	4.4	nd	nd	3.0	nd	5.0	6.9	nd	2.2
p Value	0.19	nd	nd	0.12	nd	0.054	0.083	nd	0.40
95% CI of	0.47	nd	nd	0.74	nd	0.98	0.78	nd	0.36
OR Quart3	42	nd	nd	13	nd	26	60	nd	13
OR Quart 4	2.0	nd	nd	2.1	nd	2.1	3.1	nd	0.96
p Value	0.58	nd	nd	0.31	nd	0.40	0.34	nd	0.97
95% CI of	0.17	nd	nd	0.49	nd	0.36	0.31	nd	0.13
OR Quart4	23	nd	nd	9.3	nd	13	31	nd	7.4

Cyclin-dependent kinase inhibitor 1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	178	415	nd	nd	nd	nd
Average	989	2040	nd	nd	nd	nd
Stdev	1850	2760	nd	nd	nd	nd
p(t-test)		0.13	nd	nd	nd	nd
Min	0.116	55.2	nd	nd	nd	nd
Max	6840	6400	nd	nd	nd	nd
n (Samp)	80	9	nd	nd	nd	nd
n (Patient)	58	9	nd	nd	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	182	415	nd	nd	nd	nd
Average	1090	2040	nd	nd	nd	nd
Stdev	2000	2760	nd	nd	nd	nd
p(t-test)		0.21	nd	nd	nd	nd
Min	0.116	55.2	nd	nd	nd	nd
Max	6840	6400	nd	nd	nd	nd
n (Samp)	62	9	nd	nd	nd	nd
n (Patient)	45	9	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.58	nd	0.56	nd	nd	nd	nd	nd	nd
SE	0.10	nd	0.11	nd	nd	nd	nd	nd	nd
p	0.44	nd	0.55	nd	nd	nd	nd	nd	nd
nCohort 1	80	nd	62	nd	nd	nd	nd	nd	nd
nCohort 2	9	nd	9	nd	nd	nd	nd	nd	nd
Cutoff 1	82.7	nd	82.7	nd	nd	nd	nd	nd	nd
Sens 1	78%	nd	78%	nd	nd	nd	nd	nd	nd
Spec 1	20%	nd	19%	nd	nd	nd	nd	nd	nd
Cutoff 2	61.7	nd	55.2	nd	nd	nd	nd	nd	nd
Sens 2	89%	nd	89%	nd	nd	nd	nd	nd	nd
Spec 2	18%	nd	16%	nd	nd	nd	nd	nd	nd
Cutoff 3	53.6	nd	52.0	nd	nd	nd	nd	nd	nd
Sens 3	100%	nd	100%	nd	nd	nd	nd	nd	nd
Spec 3	15%	nd	15%	nd	nd	nd	nd	nd	nd
Cutoff 4	429	nd	470	nd	nd	nd	nd	nd	nd
Sens 4	44%	nd	44%	nd	nd	nd	nd	nd	nd
Spec 4	70%	nd	71%	nd	nd	nd	nd	nd	nd
Cutoff 5	1300	nd	1410	nd	nd	nd	nd	nd	nd
Sens 5	33%	nd	33%	nd	nd	nd	nd	nd	nd
Spec 5	80%	nd	81%	nd	nd	nd	nd	nd	nd
Cutoff 6	3790	nd	5160	nd	nd	nd	nd	nd	nd
Sens 6	33%	nd	22%	nd	nd	nd	nd	nd	nd
Spec 6	90%	nd	90%	nd	nd	nd	nd	nd	nd
OR Quart 2	0.30	nd	0.27	nd	nd	nd	nd	nd	nd
p Value	0.32	nd	0.29	nd	nd	nd	nd	nd	nd
95% CI of	0.029	nd	0.026	nd	nd	nd	nd	nd	nd
OR Quart2	3.2	nd	2.9	nd	nd	nd	nd	nd	nd
OR Quart 3	0.30	nd	0.58	nd	nd	nd	nd	nd	nd
p Value	0.32	nd	0.58	nd	nd	nd	nd	nd	nd
95% CI of	0.029	nd	0.085	nd	nd	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
OR Quart3	3.2	nd	4.0	nd	nd	nd	nd	nd	nd
OR Quart 4	1.3	nd	0.93	nd	nd	nd	nd	nd	nd
p Value	0.73	nd	0.94	nd	nd	nd	nd	nd	nd
95% CI of	0.26	nd	0.16	nd	nd	nd	nd	nd	nd
OR Quart4	6.8	nd	5.4	nd	nd	nd	nd	nd	nd

Carcinoembryonic antigen-related cell adhesion molecule 5

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.71	2.13	1.71	2.32	1.71	2.36
Average	2.73	2.72	2.73	2.84	2.73	2.41
Stdev	3.35	2.76	3.35	2.87	3.35	1.73
p(t-test)		0.99		0.86		0.69
Min	0.183	0.324	0.183	0.245	0.183	0.355
Max	33.6	14.1	33.6	16.6	33.6	7.86
n (Samp)	434	27	434	34	434	17
n (Patient)	173	27	173	34	173	17

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.74	2.90	1.74	3.41	1.74	2.55
Average	2.76	4.92	2.76	2.99	2.76	3.08
Stdev	3.28	6.27	3.28	1.97	3.28	1.69
p(t-test)		0.11		0.84		0.80
Min	0.183	0.324	0.183	0.245	0.183	0.355
Max	33.6	17.1	33.6	5.37	33.6	5.44
n (Samp)	535	6	535	9	535	7
n (Patient)	207	6	207	9	207	7

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.77	2.36	1.77	2.32	1.77	1.93
Average	2.89	2.85	2.89	2.92	2.89	2.26
Stdev	3.55	2.71	3.55	2.91	3.55	1.79
p(t-test)		0.95		0.97		0.47
Min	0.183	0.491	0.183	0.710	0.183	0.324
Max	33.6	14.1	33.6	16.6	33.6	7.86
n (Samp)	359	27	359	32	359	17
n (Patient)	139	27	139	32	139	17

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.53	0.57	0.55	0.55	0.58	0.55	0.55	0.65	0.48
SE	0.058	0.12	0.059	0.053	0.10	0.054	0.073	0.11	0.072
p	0.56	0.57	0.43	0.35	0.42	0.37	0.54	0.20	0.81
nCohort 1	434	535	359	434	535	359	434	535	359
nCohort 2	27	6	27	34	9	32	17	7	17
Cutoff 1	1.26	0.825	1.49	1.23	1.22	1.27	1.68	2.44	1.62
Sens 1	70%	83%	70%	71%	78%	72%	71%	71%	71%
Spec 1	35%	16%	41%	34%	32%	34%	48%	66%	45%
Cutoff 2	1.04	0.825	1.09	0.971	0.562	1.06	1.04	2.28	0.679

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Sens 2	81%	83%	81%	82%	89%	81%	82%	86%	82%
Spec 2	28%	16%	28%	25%	7%	27%	28%	63%	10%
Cutoff 3	0.768	0.314	0.883	0.795	0.241	0.872	0.611	0.314	0.562
Sens 3	93%	100%	93%	91%	100%	91%	94%	100%	94%
Spec 3	15%	2%	18%	17%	1%	18%	10%	2%	6%
Cutoff 4	2.71	2.71	3.17	2.71	2.71	3.17	2.71	2.71	3.17
Sens 4	26%	50%	22%	38%	56%	34%	29%	43%	12%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	3.99	3.88	4.22	3.99	3.88	4.22	3.99	3.88	4.22
Sens 5	11%	33%	11%	18%	33%	16%	12%	29%	12%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	5.44	5.46	5.97	5.44	5.46	5.97	5.44	5.46	5.97
Sens 6	7%	17%	7%	12%	0%	3%	6%	0%	6%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	1.2	0	1.5	0.85	0.50	0.99	0.99	0	4.3
p Value	0.76	na	0.53	0.78	0.57	0.99	0.99	na	0.071
95% CI of	0.36	na	0.41	0.28	0.044	0.31	0.20	na	0.88
OR Quart2	4.1	na	5.6	2.6	5.5	3.2	5.0	na	21
OR Quart 3	2.1	0.50	3.0	1.8	0.50	2.3	3.1	3.0	1.5
p Value	0.19	0.57	0.070	0.24	0.57	0.10	0.092	0.34	0.65
95% CI of	0.69	0.044	0.91	0.68	0.044	0.84	0.83	0.31	0.25
OR Quart3	6.3	5.5	9.7	4.7	5.5	6.4	12	30	9.3
OR Quart 4	1.2	1.5	1.5	1.3	2.6	1.2	0.65	3.0	2.0
p Value	0.77	0.66	0.53	0.61	0.27	0.79	0.65	0.34	0.42
95% CI of	0.36	0.25	0.41	0.47	0.49	0.38	0.11	0.31	0.37
OR Quart4	4.0	9.1	5.6	3.6	13	3.6	4.0	29	11

Myoglobin

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	28.5	65.8	28.5	80.9	28.5	82.0
Average	82.5	171	82.5	252	82.5	221
Stdev	182	372	182	471	182	396
p(t-test)		0.024		1.2E-5		0.0040
Min	3.55	4.22	3.55	3.96	3.55	5.12
Max	2130	1880	2130	1880	2130	1310
n (Samp)	434	27	434	34	434	17
n (Patient)	173	27	173	34	173	17

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	32.7	142	32.7	125	32.7	151
Average	87.4	640	87.4	653	87.4	396
Stdev	195	849	195	793	195	429
p(t-test)		3.2E-10		3.3E-14		5.1E-5
Min	3.55	35.2	3.55	13.0	3.55	17.5
Max	2130	1880	2130	1880	2130	1180
n (Samp)	535	6	535	9	535	7
n (Patient)	207	6	207	9	207	7

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	30.3	56.9	30.3	86.9	30.3	79.1

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Average	83.3	103	83.3	171	83.3	261
Stdev	185	149	185	306	185	518
p(t-test)		0.59		0.016		7.1E-4
Min	4.60	4.22	4.60	3.96	4.60	5.12
Max	2130	646	2130	1410	2130	1880
n (Samp)	359	27	359	32	359	17
n (Patient)	139	27	139	32	139	17

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.66	0.83	0.64	0.66	0.70	0.67	0.64	0.81	0.65
SE	0.059	0.10	0.059	0.053	0.098	0.054	0.074	0.099	0.074
p	0.0056	0.0015	0.015	0.0030	0.041	0.0022	0.050	0.0018	0.040
nCohort 1	434	535	359	434	535	359	434	535	359
nCohort 2	27	6	27	34	9	32	17	7	17
Cutoff 1	42.7	66.9	42.7	34.8	31.4	38.6	34.8	101	34.8
Sens 1	70%	83%	70%	71%	78%	72%	71%	71%	71%
Spec 1	64%	73%	63%	57%	50%	59%	57%	82%	55%
Cutoff 2	22.9	66.9	22.9	16.2	19.2	18.9	17.5	87.6	18.7
Sens 2	81%	83%	81%	82%	89%	81%	82%	86%	82%
Spec 2	40%	73%	39%	25%	30%	31%	27%	78%	30%
Cutoff 3	18.3	34.8	18.3	12.9	12.9	12.9	11.1	17.4	11.1
Sens 3	93%	100%	93%	91%	100%	91%	94%	100%	94%
Spec 3	30%	53%	30%	18%	17%	18%	13%	25%	12%
Cutoff 4	56.0	60.1	57.8	56.0	60.1	57.8	56.0	60.1	57.8
Sens 4	52%	83%	48%	62%	56%	69%	65%	86%	65%
Spec 4	70%	70%	70%	70%	70%	70%	70%	70%	70%
Cutoff 5	93.4	95.1	95.1	93.4	95.1	95.1	93.4	95.1	95.1
Sens 5	33%	67%	22%	44%	56%	47%	35%	71%	35%
Spec 5	80%	80%	80%	80%	80%	80%	80%	80%	80%
Cutoff 6	182	180	188	182	180	188	182	180	188
Sens 6	15%	33%	7%	24%	44%	19%	18%	43%	18%
Spec 6	90%	90%	90%	90%	90%	90%	90%	90%	90%
OR Quart 2	2.6	>0	2.6	0.27	2.0	0.32	1.5	0	1.0
p Value	0.27	<na	0.27	0.11	0.57	0.16	0.66	na	1.0
95% CI of	0.49	>na	0.48	0.056	0.18	0.062	0.25	na	0.14
OR Quart2	14	na	13	1.3	22	1.6	9.2	na	7.3
OR Quart 3	4.8	>2.0	4.9	1.0	1.0	1.2	0.99	0	2.0
p Value	0.048	<0.57	0.047	1.0	1.0	0.79	0.99	na	0.42
95% CI of	1.0	>0.18	1.0	0.34	0.062	0.38	0.14	na	0.37
OR Quart3	23	na	23	2.9	16	3.6	7.2	na	11
OR Quart 4	5.9	>4.1	6.0	2.9	5.2	3.2	5.3	6.2	4.9
p Value	0.023	<0.21	0.022	0.024	0.14	0.020	0.033	0.094	0.047
95% CI of	1.3	>0.45	1.3	1.1	0.59	1.2	1.1	0.73	1.0
OR Quart4	27	na	28	7.1	45	8.5	25	52	23

Mucin-16

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.34	1.72	1.34	1.78	1.34	2.02
Average	4.05	40.6	4.05	23.6	4.05	19.4
Stdev	10.9	98.2	10.9	66.0	10.9	61.0
p(t-test)		4.2E-6		2.0E-4		0.0027

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Min	0.117	1.12	0.117	0.191	0.117	0.549
Max	131	263	131	253	131	248
n (Samp)	196	7	196	22	196	16
n (Patient)	130	7	130	22	130	16

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	1.46	2.02	1.46	3.28
Average	nd	nd	4.51	27.2	4.51	23.4
Stdev	nd	nd	11.7	70.6	11.7	67.5
p(t-test)	nd	nd		1.8E-4		0.0018
Min	nd	nd	0.122	0.191	0.122	0.549
Max	nd	nd	131	253	131	248
n (Samp)	nd	nd	170	19	170	13
n (Patient)	nd	nd	108	19	108	13

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.66	nd	nd	0.60	nd	0.59	0.64	nd	0.66
SE	0.11	nd	nd	0.067	nd	0.072	0.077	nd	0.085
p	0.16	nd	nd	0.12	nd	0.23	0.078	nd	0.059
nCohort 1	196	nd	nd	196	nd	170	196	nd	170
nCohort 2	7	nd	nd	22	nd	19	16	nd	13
Cutoff 1	1.33	nd	nd	1.09	nd	1.12	1.23	nd	1.28
Sens 1	71%	nd	nd	73%	nd	74%	75%	nd	77%
Spec 1	50%	nd	nd	41%	nd	39%	46%	nd	44%
Cutoff 2	1.23	nd	nd	1.01	nd	0.633	1.01	nd	1.01
Sens 2	86%	nd	nd	82%	nd	84%	81%	nd	85%
Spec 2	46%	nd	nd	38%	nd	22%	38%	nd	35%
Cutoff 3	1.09	nd	nd	0.464	nd	0.424	0.761	nd	0.821
Sens 3	100%	nd	nd	91%	nd	95%	94%	nd	92%
Spec 3	41%	nd	nd	14%	nd	12%	29%	nd	32%
Cutoff 4	2.77	nd	nd	2.77	nd	3.55	2.77	nd	3.55
Sens 4	43%	nd	nd	41%	nd	37%	44%	nd	46%
Spec 4	70%	nd	nd	70%	nd	70%	70%	nd	70%
Cutoff 5	4.41	nd	nd	4.41	nd	4.88	4.41	nd	4.88
Sens 5	29%	nd	nd	32%	nd	32%	38%	nd	38%
Spec 5	80%	nd	nd	80%	nd	80%	80%	nd	80%
Cutoff 6	6.95	nd	nd	6.95	nd	7.65	6.95	nd	7.65
Sens 6	29%	nd	nd	27%	nd	32%	31%	nd	38%
Spec 6	90%	nd	nd	90%	nd	90%	90%	nd	90%
OR Quart 2	>2.0	nd	nd	0.98	nd	1.0	6.6	nd	3.1
p Value	<0.57	nd	nd	0.98	nd	1.0	0.085	nd	0.34
95% CI of	>0.18	nd	nd	0.23	nd	0.23	0.77	nd	0.31
OR Quart2	na	nd	nd	4.1	nd	4.3	57	nd	31
OR Quart 3	>3.1	nd	nd	1.6	nd	1.0	3.1	nd	3.1
p Value	<0.33	nd	nd	0.51	nd	1.0	0.33	nd	0.34
95% CI of	>0.31	nd	nd	0.42	nd	0.23	0.31	nd	0.31
OR Quart3	na	nd	nd	5.9	nd	4.3	31	nd	31
OR Quart 4	>2.0	nd	nd	2.1	nd	1.8	6.6	nd	6.6
p Value	<0.57	nd	nd	0.24	nd	0.36	0.085	nd	0.087
95% CI of	>0.18	nd	nd	0.60	nd	0.50	0.77	nd	0.76
OR Quart4	na	nd	nd	7.5	nd	6.7	57	nd	57

Tumor necrosis factor receptor superfamily member 10B

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	0.00692	1.00E-9	0.00181	1.00E-9	0.00572
Average	0.00543	0.0417	0.00543	0.0242	0.00543	0.0256
Stdev	0.0150	0.0972	0.0150	0.0668	0.0150	0.0736
p(t-test)		4.5E-5		0.0018		0.0020
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	0.114	0.262	0.114	0.286	0.114	0.300
n (Samp)	189	7	189	18	189	16
n (Patient)	125	7	125	18	125	16

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	0.000420	0.00142	0.000420	0.00220
Average	nd	nd	0.00637	0.0151	0.00637	0.00604
Stdev	nd	nd	0.0161	0.0277	0.0161	0.00762
p(t-test)	nd	nd		0.053		0.94
Min	nd	nd	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	nd	nd	0.114	0.108	0.114	0.0222
n (Samp)	nd	nd	162	17	162	13
n (Patient)	nd	nd	101	17	101	13

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.63	nd	nd	0.61	nd	0.59	0.65	nd	0.57
SE	0.12	nd	nd	0.073	nd	0.076	0.077	nd	0.086
p	0.25	nd	nd	0.12	nd	0.25	0.060	nd	0.38
nCohort 1	189	nd	nd	189	nd	162	189	nd	162
nCohort 2	7	nd	nd	18	nd	17	16	nd	13
Cutoff 1	0	nd	nd	0	nd	0	0	nd	0
Sens 1	100%	nd	nd	100%	nd	100%	100%	nd	100%
Spec 1	0%	nd	nd	0%	nd	0%	0%	nd	0%
Cutoff 2	0	nd	nd	0	nd	0	0	nd	0
Sens 2	100%	nd	nd	100%	nd	100%	100%	nd	100%
Spec 2	0%	nd	nd	0%	nd	0%	0%	nd	0%
Cutoff 3	0	nd	nd	0	nd	0	0	nd	0
Sens 3	100%	nd	nd	100%	nd	100%	100%	nd	100%
Spec 3	0%	nd	nd	0%	nd	0%	0%	nd	0%
Cutoff 4	0.00367	nd	nd	0.00367	nd	0.00444	0.00367	nd	0.00444
Sens 4	57%	nd	nd	44%	nd	47%	50%	nd	38%
Spec 4	70%	nd	nd	70%	nd	70%	70%	nd	70%
Cutoff 5	0.00692	nd	nd	0.00692	nd	0.00819	0.00692	nd	0.00819
Sens 5	43%	nd	nd	39%	nd	35%	50%	nd	31%
Spec 5	81%	nd	nd	81%	nd	82%	81%	nd	82%
Cutoff 6	0.0124	nd	nd	0.0124	nd	0.0136	0.0124	nd	0.0136
Sens 6	29%	nd	nd	28%	nd	29%	31%	nd	23%
Spec 6	91%	nd	nd	91%	nd	90%	91%	nd	90%
OR Quart 2	>3.2	nd	nd	>7.9	nd	1.3	>5.5	nd	4.2
p Value	<0.32	nd	nd	<0.057	nd	0.72	<0.12	nd	0.21
95% CI of	>0.32	nd	nd	>0.94	nd	0.28	>0.62	nd	0.45
OR Quart2	na	nd	nd	na	nd	6.3	na	nd	39
OR Quart 3	>0	nd	nd	>4.2	nd	0.98	>3.2	nd	3.1
p Value	<na	nd	nd	<0.20	nd	0.98	<0.32	nd	0.34
95% CI of	>na	nd	nd	>0.46	nd	0.19	>0.32	nd	0.31
OR Quart3	na	nd	nd	na	nd	5.1	na	nd	31

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
OR Quart 4	>4.4	nd	nd	>7.9	nd	2.5	>9.3	nd	5.4
p Value	<0.20	nd	nd	<0.057	nd	0.20	<0.039	nd	0.13
95% CI of	>0.47	nd	nd	>0.94	nd	0.61	>1.1	nd	0.60
OR Quart4	na	nd	nd	na	nd	10	na	nd	48

Cellular tumor antigen p53

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Average	0.0690	0.289	0.0690	0.143	0.0690	0.172
Stdev	0.419	0.698	0.419	0.551	0.419	0.595
p(t-test)		0.19		0.49		0.36
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	3.70	1.87	3.70	2.35	3.70	2.39
n (Samp)	189	7	189	18	189	16
n (Patient)	125	7	125	18	125	16

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	nd	nd	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Average	nd	nd	0.0804	0.0131	0.0804	0.0283
Stdev	nd	nd	0.452	0.0316	0.452	0.0790
p(t-test)	nd	nd		0.54		0.68
Min	nd	nd	1.00E-9	1.00E-9	1.00E-9	1.00E-9
Max	nd	nd	3.70	0.117	3.70	0.285
n (Samp)	nd	nd	162	17	162	13
n (Patient)	nd	nd	101	17	101	13

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.64	nd	nd	0.62	nd	0.59	0.54	nd	0.52
SE	0.11	nd	nd	0.073	nd	0.076	0.077	nd	0.084
p	0.21	nd	nd	0.091	nd	0.23	0.57	nd	0.80
nCohort 1	189	nd	nd	189	nd	162	189	nd	162
nCohort 2	7	nd	nd	18	nd	17	16	nd	13
Cutoff 1	0	nd	nd	0	nd	0	0	nd	0
Sens 1	100%	nd	nd	100%	nd	100%	100%	nd	100%
Spec 1	0%	nd	nd	0%	nd	0%	0%	nd	0%
Cutoff 2	0	nd	nd	0	nd	0	0	nd	0
Sens 2	100%	nd	nd	100%	nd	100%	100%	nd	100%
Spec 2	0%	nd	nd	0%	nd	0%	0%	nd	0%
Cutoff 3	0	nd	nd	0	nd	0	0	nd	0
Sens 3	100%	nd	nd	100%	nd	100%	100%	nd	100%
Spec 3	0%	nd	nd	0%	nd	0%	0%	nd	0%
Cutoff 4	1.00E-9	nd	nd	1.00E-9	nd	1.00E-9	1.00E-9	nd	1.00E-9
Sens 4	43%	nd	nd	44%	nd	41%	25%	nd	23%
Spec 4	81%	nd	nd	81%	nd	80%	81%	nd	80%
Cutoff 5	1.00E-9	nd	nd	1.00E-9	nd	0.000790	1.00E-9	nd	0.000790
Sens 5	43%	nd	nd	44%	nd	35%	25%	nd	23%
Spec 5	81%	nd	nd	81%	nd	81%	81%	nd	81%
Cutoff 6	0.0225	nd	nd	0.0225	nd	0.0267	0.0225	nd	0.0267
Sens 6	43%	nd	nd	17%	nd	12%	25%	nd	15%
Spec 6	90%	nd	nd	90%	nd	90%	90%	nd	90%

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
OR Quart 2	3.1	nd	nd	10	nd	>13	>16	nd	>13
p Value	0.33	nd	nd	0.029	nd	<0.018	<0.0096	nd	<0.018
95% CI of	0.31	nd	nd	1.3	nd	>1.5	>2.0	nd	>1.5
OR Quart2	31	nd	nd	86	nd	na	na	nd	na
OR Quart 3	0	nd	nd	0	nd	>0	>0	nd	>0
p Value	na	nd	nd	na	nd	<na	<na	nd	<na
95% CI of	na	nd	nd	na	nd	>na	>na	nd	>na
OR Quart3	na	nd	nd	na	nd	na	na	nd	na
OR Quart 4	3.1	nd	nd	9.1	nd	>8.1	>4.2	nd	>3.1
p Value	0.33	nd	nd	0.041	nd	<0.055	<0.20	nd	<0.33
95% CI of	0.31	nd	nd	1.1	nd	>0.95	>0.46	nd	>0.31
OR Quart4	31	nd	nd	76	nd	na	na	nd	na

[0161] Table 7: Comparison of marker levels in EDTA samples collected within 12 hours of reaching stage R from Cohort 1 (patients that reached, but did not progress beyond, RIFLE stage R) and from Cohort 2 (patients that reached RIFLE stage I or F).

Apolipoprotein A-II

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	57100	48800	nd	nd	57100	45400
Average	57200	51600	nd	nd	57000	46300
Stdev	36400	24300	nd	nd	39000	21400
p(t-test)		0.53	nd	nd		0.34
Min	7970	1810	nd	nd	7970	1810
Max	251000	100000	nd	nd	251000	75500
n (Samp)	50	19	nd	nd	41	14
n (Patient)	50	19	nd	nd	41	14

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.47	nd	0.44
SE	0.079	nd	0.091
p	0.69	nd	0.49
nCohort 1	50	nd	41
nCohort 2	19	nd	14
Cutoff 1	37400	nd	32500
Sens 1	74%	nd	71%
Spec 1	26%	nd	24%
Cutoff 2	28800	nd	27600
Sens 2	84%	nd	86%
Spec 2	18%	nd	22%
Cutoff 3	23900	nd	23900
Sens 3	95%	nd	93%
Spec 3	16%	nd	20%
Cutoff 4	64400	nd	66800
Sens 4	26%	nd	21%
Spec 4	70%	nd	71%
Cutoff 5	72300	nd	72300
Sens 5	21%	nd	14%
Spec 5	80%	nd	80%
Cutoff 6	83600	nd	85700

	At Enrollment		
	sCr or UO	sCr only	UO only
Sens 6	11%	nd	0%
Spec 6	90%	nd	90%
OR Quart 2	0.80	nd	1.0
p Value	0.77	nd	1.0
95% CI of	0.17	nd	0.16
OR Quart2	3.7	nd	6.1
OR Quart 3	1.1	nd	1.5
p Value	0.91	nd	0.66
95% CI of	0.25	nd	0.26
OR Quart3	4.7	nd	8.2
OR Quart 4	1.1	nd	1.6
p Value	0.91	nd	0.58
95% CI of	0.25	nd	0.29
OR Quart4	4.7	nd	9.3

Myoglobin

	sCr or UO		sCr only		UO only	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	40.1	64.7	nd	nd	35.8	79.1
Average	139	182	nd	nd	132	88.9
Stdev	314	344	nd	nd	329	98.2
p(t-test)		0.60	nd	nd		0.60
Min	7.19	4.16	nd	nd	7.19	4.16
Max	2130	1310	nd	nd	2130	397
n (Samp)	54	23	nd	nd	46	17
n (Patient)	54	23	nd	nd	46	17

	At Enrollment		
	sCr or UO	sCr only	UO only
AUC	0.55	nd	0.54
SE	0.073	nd	0.083
p	0.48	nd	0.66
nCohort 1	54	nd	46
nCohort 2	23	nd	17
Cutoff 1	30.3	nd	34.2
Sens 1	74%	nd	71%
Spec 1	43%	nd	50%
Cutoff 2	17.8	nd	15.3
Sens 2	83%	nd	82%
Spec 2	19%	nd	13%
Cutoff 3	12.9	nd	4.16
Sens 3	91%	nd	94%
Spec 3	13%	nd	0%
Cutoff 4	91.7	nd	90.0
Sens 4	35%	nd	41%
Spec 4	70%	nd	72%
Cutoff 5	189	nd	141
Sens 5	17%	nd	18%
Spec 5	81%	nd	80%
Cutoff 6	328	nd	315
Sens 6	13%	nd	6%
Spec 6	91%	nd	91%
OR Quart 2	0.41	nd	0.29
p Value	0.26	nd	0.18

	At Enrollment		
	sCr or UO	sCr only	UO only
95% CI of	0.085	nd	0.046
OR Quart2	1.9	nd	1.8
OR Quart 3	1.6	nd	0.91
p Value	0.50	nd	0.90
95% CI of	0.42	nd	0.20
OR Quart3	5.9	nd	4.1
OR Quart 4	0.93	nd	0.91
p Value	0.91	nd	0.90
95% CI of	0.24	nd	0.20
OR Quart4	3.6	nd	4.1

[0162] Table 8: Comparison of the maximum marker levels in EDTA samples collected from Cohort 1 (patients that did not progress beyond RIFLE stage 0) and the maximum values in EDTA samples collected from subjects between enrollment and 0, 24 hours, and 48 hours prior to reaching stage F in Cohort 2.

Apolipoprotein A-II

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	52600	43600	52600	41100	52600	57700
Average	52700	57800	52700	57100	52700	72600
Stdev	22500	48900	22500	51100	22500	58900
p(t-test)		0.55		0.62		0.068
Min	5450	10700	5450	10700	5450	9430
Max	105000	176000	105000	176000	105000	176000
n (Samp)	97	11	97	10	97	6
n (Patient)	97	11	97	10	97	6

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	53400	57800	53400	52600	53400	57700
Average	53900	66500	53900	64700	53900	72600
Stdev	20600	54800	20600	54700	20600	58900
p(t-test)		0.18		0.25		0.073
Min	8680	10700	8680	10700	8680	9430
Max	123000	176000	123000	176000	123000	176000
n (Samp)	84	8	84	8	84	6
n (Patient)	84	8	84	8	84	6

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.46	nd	0.53	0.45	nd	0.51	0.57	nd	0.56
SE	0.094	nd	0.11	0.098	nd	0.11	0.13	nd	0.13
p	0.69	nd	0.78	0.61	nd	0.94	0.59	nd	0.66
nCohort 1	97	nd	84	97	nd	84	97	nd	84
nCohort 2	11	nd	8	10	nd	8	6	nd	6
Cutoff 1	37600	nd	37600	37600	nd	37600	37600	nd	37600
Sens 1	73%	nd	75%	70%	nd	75%	83%	nd	83%
Spec 1	27%	nd	19%	27%	nd	19%	27%	nd	19%
Cutoff 2	14000	nd	10700	14000	nd	10700	37600	nd	37600

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Sens 2	82%	nd	88%	80%	nd	88%	83%	nd	83%
Spec 2	4%	nd	1%	4%	nd	1%	27%	nd	19%
Cutoff 3	10700	nd	8680	10700	nd	8680	8680	nd	8680
Sens 3	91%	nd	100%	90%	nd	100%	100%	nd	100%
Spec 3	2%	nd	1%	2%	nd	1%	2%	nd	1%
Cutoff 4	61600	nd	61700	61600	nd	61700	61600	nd	61700
Sens 4	36%	nd	50%	40%	nd	50%	50%	nd	50%
Spec 4	70%	nd	70%	70%	nd	70%	70%	nd	70%
Cutoff 5	70000	nd	69100	70000	nd	69100	70000	nd	69100
Sens 5	36%	nd	50%	30%	nd	38%	50%	nd	50%
Spec 5	80%	nd	81%	80%	nd	81%	80%	nd	81%
Cutoff 6	82900	nd	77900	82900	nd	77900	82900	nd	77900
Sens 6	18%	nd	25%	20%	nd	25%	33%	nd	33%
Spec 6	91%	nd	90%	91%	nd	90%	91%	nd	90%
OR Quart 2	0	nd	0.30	0.31	nd	0.30	2.0	nd	0.45
p Value	na	nd	0.32	0.32	nd	0.32	0.58	nd	0.53
95% CI of	na	nd	0.029	0.030	nd	0.029	0.17	nd	0.038
OR Quart2	na	nd	3.2	3.2	nd	3.2	24	nd	5.4
OR Quart 3	1.0	nd	0	1.0	nd	0.30	0	nd	0
p Value	1.0	nd	na	1.0	nd	0.32	na	nd	na
95% CI of	0.22	nd	na	0.18	nd	0.029	na	nd	na
OR Quart3	4.5	nd	na	5.5	nd	3.2	na	nd	na
OR Quart 4	0.72	nd	1.4	1.0	nd	1.0	3.1	nd	1.5
p Value	0.69	nd	0.68	0.96	nd	1.0	0.34	nd	0.67
95% CI of	0.14	nd	0.28	0.19	nd	0.18	0.30	nd	0.23
OR Quart4	3.6	nd	7.1	5.7	nd	5.6	32	nd	10.0

Caspase-1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	91.6	138	91.6	90.7	91.6	83.0
Average	108	154	108	121	108	101
Stdev	74.7	96.4	74.7	71.9	74.7	53.3
p(t-test)		0.17		0.69		0.83
Min	33.8	44.7	33.8	44.7	33.8	44.7
Max	326	328	326	241	326	192
n (Samp)	26	8	26	7	26	6
n (Patient)	26	8	26	7	26	6

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.67	nd	nd	0.56	nd	nd	0.51	nd	nd
SE	0.12	nd	nd	0.13	nd	nd	0.13	nd	nd
p	0.15	nd	nd	0.62	nd	nd	0.94	nd	nd
nCohort 1	26	nd	nd	26	nd	nd	26	nd	nd
nCohort 2	8	nd	nd	7	nd	nd	6	nd	nd
Cutoff 1	71.0	nd	nd	70.7	nd	nd	66.1	nd	nd
Sens 1	75%	nd	nd	71%	nd	nd	83%	nd	nd
Spec 1	38%	nd	nd	38%	nd	nd	31%	nd	nd
Cutoff 2	70.7	nd	nd	66.1	nd	nd	66.1	nd	nd
Sens 2	88%	nd	nd	86%	nd	nd	83%	nd	nd
Spec 2	38%	nd	nd	31%	nd	nd	31%	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Cutoff 3	42.1	nd	nd	42.1	nd	nd	42.1	nd	nd
Sens 3	100%	nd	nd	100%	nd	nd	100%	nd	nd
Spec 3	15%	nd	nd	15%	nd	nd	15%	nd	nd
Cutoff 4	103	nd	nd	103	nd	nd	103	nd	nd
Sens 4	62%	nd	nd	43%	nd	nd	33%	nd	nd
Spec 4	73%	nd	nd	73%	nd	nd	73%	nd	nd
Cutoff 5	121	nd	nd	121	nd	nd	121	nd	nd
Sens 5	62%	nd	nd	43%	nd	nd	33%	nd	nd
Spec 5	81%	nd	nd	81%	nd	nd	81%	nd	nd
Cutoff 6	254	nd	nd	254	nd	nd	254	nd	nd
Sens 6	12%	nd	nd	0%	nd	nd	0%	nd	nd
Spec 6	92%	nd	nd	92%	nd	nd	92%	nd	nd
OR Quart 2	2.0	nd	nd	2.3	nd	nd	2.3	nd	nd
p Value	0.60	nd	nd	0.53	nd	nd	0.53	nd	nd
95% CI of	0.15	nd	nd	0.17	nd	nd	0.17	nd	nd
OR Quart2	27	nd	nd	33	nd	nd	33	nd	nd
OR Quart 3	0	nd	nd	1.0	nd	nd	1.0	nd	nd
p Value	na	nd	nd	1.0	nd	nd	1.0	nd	nd
95% CI of	na	nd	nd	0.052	nd	nd	0.052	nd	nd
OR Quart3	na	nd	nd	19	nd	nd	19	nd	nd
OR Quart 4	8.8	nd	nd	3.5	nd	nd	2.3	nd	nd
p Value	0.086	nd	nd	0.33	nd	nd	0.53	nd	nd
95% CI of	0.74	nd	nd	0.28	nd	nd	0.17	nd	nd
OR Quart4	100	nd	nd	43	nd	nd	33	nd	nd

Caspase-9

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	28.7	12.2	28.7	6.83	28.7	7.20
Average	50.0	16.5	50.0	13.7	50.0	14.2
Stdev	69.0	14.3	69.0	15.0	69.0	16.2
p(t-test)		0.16		0.18		0.22
Min	2.58	4.32	2.58	3.79	2.58	3.79
Max	366	46.4	366	46.4	366	46.4
n (Samp)	37	9	37	7	37	6
n (Patient)	37	9	37	7	37	6

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.29	nd	nd	0.22	nd	nd	0.23	nd	nd
SE	0.10	nd	nd	0.11	nd	nd	0.12	nd	nd
p	0.040	nd	nd	0.012	nd	nd	0.024	nd	nd
nCohort 1	37	nd	nd	37	nd	nd	37	nd	nd
nCohort 2	9	nd	nd	7	nd	nd	6	nd	nd
Cutoff 1	6.05	nd	nd	6.05	nd	nd	4.34	nd	nd
Sens 1	78%	nd	nd	71%	nd	nd	83%	nd	nd
Spec 1	11%	nd	nd	11%	nd	nd	8%	nd	nd
Cutoff 2	4.34	nd	nd	4.34	nd	nd	4.34	nd	nd
Sens 2	89%	nd	nd	86%	nd	nd	83%	nd	nd
Spec 2	8%	nd	nd	8%	nd	nd	8%	nd	nd
Cutoff 3	3.30	nd	nd	3.30	nd	nd	3.30	nd	nd
Sens 3	100%	nd	nd	100%	nd	nd	100%	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Spec 3	5%	nd	nd	5%	nd	nd	5%	nd	nd
Cutoff 4	50.7	nd	nd	50.7	nd	nd	50.7	nd	nd
Sens 4	0%	nd	nd	0%	nd	nd	0%	nd	nd
Spec 4	70%	nd	nd	70%	nd	nd	70%	nd	nd
Cutoff 5	71.4	nd	nd	71.4	nd	nd	71.4	nd	nd
Sens 5	0%	nd	nd	0%	nd	nd	0%	nd	nd
Spec 5	81%	nd	nd	81%	nd	nd	81%	nd	nd
Cutoff 6	106	nd	nd	106	nd	nd	106	nd	nd
Sens 6	0%	nd	nd	0%	nd	nd	0%	nd	nd
Spec 6	92%	nd	nd	92%	nd	nd	92%	nd	nd
OR Quart 2	>4.5	nd	nd	>1.1	nd	nd	>1.1	nd	nd
p Value	<0.23	nd	nd	<0.95	nd	nd	<0.95	nd	nd
95% CI of	>0.39	nd	nd	>0.060	nd	nd	>0.060	nd	nd
OR Quart2	na	nd	nd	na	nd	nd	na	nd	nd
OR Quart 3	>2.4	nd	nd	>2.4	nd	nd	>1.1	nd	nd
p Value	<0.50	nd	nd	<0.49	nd	nd	<0.95	nd	nd
95% CI of	>0.19	nd	nd	>0.19	nd	nd	>0.060	nd	nd
OR Quart3	na	nd	nd	na	nd	nd	na	nd	nd
OR Quart 4	>6.9	nd	nd	>6.3	nd	nd	>7.3	nd	nd
p Value	<0.11	nd	nd	<0.13	nd	nd	<0.10	nd	nd
95% CI of	>0.63	nd	nd	>0.58	nd	nd	>0.66	nd	nd
OR Quart4	na	nd	nd	na	nd	nd	na	nd	nd

Cadherin-1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	72700	112000	72700	112000	72700	162000
Average	103000	157000	103000	154000	103000	174000
Stdev	108000	103000	108000	105000	108000	96900
p(t-test)		0.13		0.15		0.13
Min	14500	38300	14500	38300	14500	50500
Max	621000	340000	621000	340000	621000	285000
n (Samp)	50	12	50	12	50	6
n (Patient)	50	12	50	12	50	6

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	77600	151000	77600	132000	nd	nd
Average	110000	170000	110000	163000	nd	nd
Stdev	96000	127000	96000	132000	nd	nd
p(t-test)		0.15		0.20	nd	nd
Min	14500	38300	14500	38300	nd	nd
Max	621000	340000	621000	340000	nd	nd
n (Samp)	96	6	96	6	nd	nd
n (Patient)	96	6	96	6	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	80200	162000	80200	162000	80200	162000
Average	114000	170000	114000	170000	114000	174000
Stdev	117000	86300	117000	86300	117000	96900
p(t-test)		0.21		0.21		0.24
Min	39700	64400	39700	64400	39700	50500

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Max	621000	285000	621000	285000	621000	285000
n (Samp)	44	8	44	8	44	6
n (Patient)	44	8	44	8	44	6

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.69	0.62	0.77	0.66	0.56	0.77	0.77	nd	0.74
SE	0.092	0.13	0.10	0.093	0.13	0.10	0.12	nd	0.12
p	0.038	0.35	0.0087	0.094	0.65	0.0087	0.021	nd	0.050
nCohort 1	50	96	44	50	96	44	50	nd	44
nCohort 2	12	6	8	12	6	8	6	nd	6
Cutoff 1	88900	53300	105000	62800	53300	105000	105000	nd	105000
Sens 1	75%	83%	75%	75%	83%	75%	83%	nd	83%
Spec 1	62%	22%	75%	42%	22%	75%	76%	nd	75%
Cutoff 2	62800	53300	88900	54100	53300	88900	105000	nd	105000
Sens 2	83%	83%	88%	83%	83%	88%	83%	nd	83%
Spec 2	42%	22%	59%	24%	22%	59%	76%	nd	75%
Cutoff 3	52600	38100	62800	52600	38100	62800	48100	nd	47600
Sens 3	92%	100%	100%	92%	100%	100%	100%	nd	100%
Spec 3	22%	6%	34%	22%	6%	34%	20%	nd	11%
Cutoff 4	97000	108000	97500	97000	108000	97500	97000	nd	97500
Sens 4	58%	50%	75%	58%	50%	75%	83%	nd	83%
Spec 4	70%	71%	70%	70%	71%	70%	70%	nd	70%
Cutoff 5	114000	151000	131000	114000	151000	131000	114000	nd	131000
Sens 5	50%	50%	50%	50%	50%	50%	67%	nd	50%
Spec 5	80%	80%	82%	80%	80%	82%	80%	nd	82%
Cutoff 6	153000	242000	153000	153000	242000	153000	153000	nd	153000
Sens 6	42%	33%	50%	42%	33%	50%	50%	nd	50%
Spec 6	90%	91%	91%	90%	91%	91%	90%	nd	91%
OR Quart 2	0.43	0	>1.1	0.27	0	>1.1	0	nd	0
p Value	0.51	na	<0.96	0.28	na	<0.96	na	nd	na
95% CI of	0.035	na	>0.061	0.025	na	>0.061	na	nd	na
OR Quart2	5.3	na	na	2.9	na	na	na	nd	na
OR Quart 3	1.6	0.48	>3.9	0.62	0	>3.9	1.0	nd	1.0
p Value	0.63	0.56	<0.27	0.63	na	<0.27	1.0	nd	1.0
95% CI of	0.23	0.041	>0.35	0.087	na	>0.35	0.056	nd	0.055
OR Quart3	11	5.7	na	4.3	na	na	18	nd	18
OR Quart 4	3.9	1.5	>5.8	2.4	0.96	>5.8	5.2	nd	4.9
p Value	0.14	0.67	<0.14	0.29	0.96	<0.14	0.17	nd	0.19
95% CI of	0.64	0.23	>0.55	0.47	0.17	>0.55	0.50	nd	0.46
OR Quart4	24	9.8	na	12	5.3	na	54	nd	52

Cyclin-dependent kinase inhibitor 1

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	212	243	212	255	212	299
Average	1210	333	1210	363	1210	402
Stdev	1930	337	1930	383	1930	405
p(t-test)		0.19		0.26		0.32
Min	42.3	73.9	42.3	68.7	42.3	68.7
Max	6840	1190	6840	1190	6840	1190
n (Samp)	37	9	37	7	37	6
n (Patient)	37	9	37	7	37	6

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.46	nd	nd	0.45	nd	nd	0.47	nd	nd
SE	0.11	nd	nd	0.12	nd	nd	0.13	nd	nd
p	0.71	nd	nd	0.68	nd	nd	0.81	nd	nd
nCohort 1	37	nd	nd	37	nd	nd	37	nd	nd
nCohort 2	9	nd	nd	7	nd	nd	6	nd	nd
Cutoff 1	138	nd	nd	138	nd	nd	138	nd	nd
Sens 1	78%	nd	nd	71%	nd	nd	83%	nd	nd
Spec 1	38%	nd	nd	38%	nd	nd	38%	nd	nd
Cutoff 2	125	nd	nd	125	nd	nd	138	nd	nd
Sens 2	89%	nd	nd	86%	nd	nd	83%	nd	nd
Spec 2	32%	nd	nd	32%	nd	nd	38%	nd	nd
Cutoff 3	73.1	nd	nd	61.7	nd	nd	61.7	nd	nd
Sens 3	100%	nd	nd	100%	nd	nd	100%	nd	nd
Spec 3	14%	nd	nd	11%	nd	nd	11%	nd	nd
Cutoff 4	866	nd	nd	866	nd	nd	866	nd	nd
Sens 4	11%	nd	nd	14%	nd	nd	17%	nd	nd
Spec 4	70%	nd	nd	70%	nd	nd	70%	nd	nd
Cutoff 5	1760	nd	nd	1760	nd	nd	1760	nd	nd
Sens 5	0%	nd	nd	0%	nd	nd	0%	nd	nd
Spec 5	81%	nd	nd	81%	nd	nd	81%	nd	nd
Cutoff 6	5160	nd	nd	5160	nd	nd	5160	nd	nd
Sens 6	0%	nd	nd	0%	nd	nd	0%	nd	nd
Spec 6	92%	nd	nd	92%	nd	nd	92%	nd	nd
OR Quart 2	6.3	nd	nd	3.8	nd	nd	3.8	nd	nd
p Value	0.13	nd	nd	0.29	nd	nd	0.29	nd	nd
95% CI of	0.58	nd	nd	0.32	nd	nd	0.32	nd	nd
OR Quart2	68	nd	nd	43	nd	nd	43	nd	nd
OR Quart 3	3.7	nd	nd	2.2	nd	nd	1.0	nd	nd
p Value	0.29	nd	nd	0.54	nd	nd	1.0	nd	nd
95% CI of	0.32	nd	nd	0.17	nd	nd	0.055	nd	nd
OR Quart3	42	nd	nd	29	nd	nd	18	nd	nd
OR Quart 4	1.1	nd	nd	1.0	nd	nd	1.1	nd	nd
p Value	0.95	nd	nd	1.0	nd	nd	0.94	nd	nd
95% CI of	0.060	nd	nd	0.055	nd	nd	0.060	nd	nd
OR Quart4	20	nd	nd	18	nd	nd	20	nd	nd

Carcinoembryonic antigen-related cell adhesion molecule 5

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.72	3.47	1.72	3.47	1.72	2.26
Average	2.52	4.00	2.52	3.11	2.52	2.81
Stdev	2.90	3.87	2.90	1.92	2.90	1.94
p(t-test)		0.065		0.42		0.77
Min	0.183	0.726	0.183	0.563	0.183	0.726
Max	20.8	17.1	20.8	5.94	20.8	5.94
n (Samp)	110	17	110	17	110	9
n (Patient)	110	17	110	17	110	9

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.88	2.35	1.88	2.35	nd	nd
Average	3.12	2.81	3.12	2.75	nd	nd
Stdev	4.09	2.17	4.09	2.23	nd	nd

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
p(t-test)		0.83		0.80	nd	nd
Min	0.183	0.726	0.183	0.563	nd	nd
Max	33.6	5.44	33.6	5.44	nd	nd
n (Samp)	180	8	180	8	nd	nd
n (Patient)	180	8	180	8	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.71	5.01	1.71	3.72	1.71	3.47
Average	2.73	5.08	2.73	3.75	2.73	3.38
Stdev	3.23	4.31	3.23	1.66	3.23	1.82
p(t-test)		0.030		0.30		0.60
Min	0.183	1.30	0.183	1.30	0.183	1.30
Max	20.8	17.1	20.8	5.94	20.8	5.94
n (Samp)	89	11	89	11	89	7
n (Patient)	89	11	89	11	89	7

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.66	0.50	0.78	0.63	0.48	0.75	0.60	nd	0.70
SE	0.076	0.10	0.086	0.077	0.11	0.088	0.10	nd	0.11
p	0.033	1.00	0.0012	0.086	0.83	0.0047	0.34	nd	0.085
nCohort 1	110	180	89	110	180	89	110	nd	89
nCohort 2	17	8	11	17	8	11	9	nd	7
Cutoff 1	1.44	0.826	2.71	1.44	0.710	2.52	1.28	nd	2.23
Sens 1	71%	75%	73%	71%	75%	73%	78%	nd	71%
Spec 1	45%	16%	73%	45%	12%	72%	40%	nd	64%
Cutoff 2	0.886	0.825	2.52	0.886	0.649	2.23	0.886	nd	1.49
Sens 2	82%	88%	82%	82%	88%	82%	89%	nd	86%
Spec 2	25%	16%	72%	25%	8%	64%	25%	nd	46%
Cutoff 3	0.825	0.710	1.49	0.649	0.504	1.49	0.710	nd	1.28
Sens 3	94%	100%	91%	94%	100%	91%	100%	nd	100%
Spec 3	23%	12%	46%	14%	6%	46%	17%	nd	40%
Cutoff 4	2.42	2.71	2.52	2.42	2.71	2.52	2.42	nd	2.52
Sens 4	65%	50%	82%	59%	50%	73%	44%	nd	57%
Spec 4	70%	70%	72%	70%	70%	72%	70%	nd	72%
Cutoff 5	3.25	3.88	3.74	3.25	3.88	3.74	3.25	nd	3.74
Sens 5	53%	38%	55%	53%	38%	45%	44%	nd	29%
Spec 5	80%	80%	81%	80%	80%	81%	80%	nd	81%
Cutoff 6	5.56	6.28	6.77	5.56	6.28	6.77	5.56	nd	6.77
Sens 6	12%	0%	9%	6%	0%	0%	11%	nd	0%
Spec 6	90%	90%	91%	90%	90%	91%	90%	nd	91%
OR Quart 2	0.97	0	>2.2	0.97	0	>2.2	3.1	nd	>2.2
p Value	0.97	na	<0.54	0.97	na	<0.54	0.34	nd	<0.54
95% CI of	0.18	na	>0.18	0.18	na	>0.18	0.30	nd	>0.18
OR Quart2	5.2	na	na	5.2	na	na	32	nd	na
OR Quart 3	0.62	0	>2.2	0.62	0	>2.2	0.97	nd	>1.0
p Value	0.62	na	<0.54	0.62	na	<0.54	0.98	nd	<0.98
95% CI of	0.097	na	>0.18	0.097	na	>0.18	0.058	nd	>0.062
OR Quart3	4.0	na	na	4.0	na	na	16	nd	na
OR Quart 4	3.7	1.0	>9.7	3.7	1.0	>9.7	4.3	nd	>4.8
p Value	0.073	1.0	<0.041	0.073	1.0	<0.041	0.20	nd	<0.18
95% CI of	0.88	0.23	>1.1	0.88	0.23	>1.1	0.45	nd	>0.50
OR Quart4	15	4.3	na	15	4.3	na	41	nd	na

Myoglobin

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	48.8	222	48.8	145	48.8	122
Average	109	574	109	498	109	407
Stdev	211	653	211	658	211	480
p(t-test)		4.0E-8		3.3E-6		4.7E-4
Min	5.55	16.2	5.55	16.2	5.55	16.2
Max	1720	1880	1720	1880	1720	1180
n (Samp)	110	17	110	17	110	9
n (Patient)	110	17	110	17	110	9

sCr only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	56.7	475	56.7	475	nd	nd
Average	143	694	143	683	nd	nd
Stdev	283	718	283	729	nd	nd
p(t-test)		2.1E-6		3.5E-6	nd	nd
Min	5.55	16.2	5.55	16.2	nd	nd
Max	2130	1880	2130	1880	nd	nd
n (Samp)	180	8	180	8	nd	nd
n (Patient)	180	8	180	8	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	46.2	222	46.2	145	46.2	122
Average	120	547	120	438	120	352
Stdev	223	581	223	574	223	423
p(t-test)		6.9E-6		5.8E-4		0.016
Min	5.55	86.7	5.55	69.7	5.55	69.7
Max	1720	1660	1720	1660	1720	1160
n (Samp)	89	11	89	11	89	7
n (Patient)	89	11	89	11	89	7

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.82	0.75	0.86	0.76	0.68	0.82	0.76	nd	0.79
SE	0.064	0.10	0.072	0.071	0.11	0.080	0.095	nd	0.10
p	5.2E-7	0.016	3.9E-7	3.1E-4	0.096	8.3E-5	0.0061	nd	0.0048
nCohort 1	110	180	89	110	180	89	110	nd	89
nCohort 2	17	8	11	17	8	11	9	nd	7
Cutoff 1	124	101	138	101	30.6	105	79.5	nd	87.6
Sens 1	71%	75%	73%	71%	75%	73%	78%	nd	71%
Spec 1	82%	69%	80%	77%	32%	75%	71%	nd	69%
Cutoff 2	101	34.3	124	66.9	19.2	101	66.9	nd	79.5
Sens 2	82%	88%	82%	82%	88%	82%	89%	nd	86%
Spec 2	77%	35%	78%	62%	19%	74%	62%	nd	67%
Cutoff 3	33.6	15.7	108	19.2	15.7	87.6	15.0	nd	66.9
Sens 3	94%	100%	91%	94%	100%	91%	100%	nd	100%
Spec 3	38%	12%	76%	21%	12%	69%	14%	nd	61%
Cutoff 4	78.9	105	97.8	78.9	105	97.8	78.9	nd	97.8
Sens 4	88%	62%	91%	76%	62%	82%	78%	nd	57%
Spec 4	70%	70%	71%	70%	70%	71%	70%	nd	71%

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Cutoff 5	112	150	146	112	150	146	112	nd	146
Sens 5	71%	62%	64%	59%	62%	45%	56%	nd	43%
Spec 5	80%	80%	81%	80%	80%	81%	80%	nd	81%
Cutoff 6	212	315	323	212	315	323	212	nd	323
Sens 6	53%	50%	36%	41%	50%	27%	44%	nd	29%
Spec 6	90%	90%	91%	90%	90%	91%	90%	nd	91%
OR Quart 2	0.97	1.0	>0	0.47	0.49	>0	0	nd	>0
p Value	0.98	1.0	<na	0.54	0.56	<na	na	nd	<na
95% CI of	0.058	0.061	>na	0.040	0.043	>na	na	nd	>na
OR Quart2	16	16	na	5.4	5.6	na	na	nd	na
OR Quart 3	3.1	1.0	>4.8	2.1	0	>6.2	3.1	nd	>4.8
p Value	0.34	1.0	<0.18	0.42	na	<0.11	0.34	nd	<0.18
95% CI of	0.30	0.061	>0.49	0.35	na	>0.67	0.30	nd	>0.50
OR Quart3	32	16	na	12	na	na	32	nd	na
OR Quart 4	18	5.5	>9.7	6.6	2.7	>7.9	5.6	nd	>3.4
p Value	0.0075	0.13	<0.041	0.022	0.25	<0.066	0.13	nd	<0.30
95% CI of	2.2	0.61	>1.1	1.3	0.49	>0.88	0.61	nd	>0.33
OR Quart4	150	49	na	33	15	na	51	nd	na

Mucin-16

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.17	8.40	1.17	7.52	nd	nd
Average	3.77	31.2	3.77	30.6	nd	nd
Stdev	15.1	67.4	15.1	67.6	nd	nd
p(t-test)		0.0035		0.0043	nd	nd
Min	0.117	2.02	0.117	2.02	nd	nd
Max	131	198	131	198	nd	nd
n (Samp)	75	8	75	8	nd	nd
n (Patient)	75	8	75	8	nd	nd

UO only	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.36	7.47	1.36	7.47	nd	nd
Average	4.38	38.3	4.38	38.3	nd	nd
Stdev	16.6	78.2	16.6	78.2	nd	nd
p(t-test)		0.0042		0.0042	nd	nd
Min	0.122	2.02	0.122	2.02	nd	nd
Max	131	198	131	198	nd	nd
n (Samp)	62	6	62	6	nd	nd
n (Patient)	62	6	62	6	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.89	nd	0.85	0.88	nd	0.85	nd	nd	nd
SE	0.079	nd	0.100	0.080	nd	0.100	nd	nd	nd
p	9.8E-7	nd	3.7E-4	1.6E-6	nd	3.7E-4	nd	nd	nd
nCohort 1	75	nd	62	75	nd	62	nd	nd	nd
nCohort 2	8	nd	6	8	nd	6	nd	nd	nd
Cutoff 1	4.24	nd	2.09	4.24	nd	2.09	nd	nd	nd
Sens 1	75%	nd	83%	75%	nd	83%	nd	nd	nd
Spec 1	88%	nd	68%	88%	nd	68%	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Cutoff 2	2.09	nd	2.09	2.09	nd	2.09	nd	nd	nd
Sens 2	88%	nd	83%	88%	nd	83%	nd	nd	nd
Spec 2	69%	nd	68%	69%	nd	68%	nd	nd	nd
Cutoff 3	1.96	nd	1.96	1.96	nd	1.96	nd	nd	nd
Sens 3	100%	nd	100%	100%	nd	100%	nd	nd	nd
Spec 3	67%	nd	66%	67%	nd	66%	nd	nd	nd
Cutoff 4	2.20	nd	2.56	2.20	nd	2.56	nd	nd	nd
Sens 4	75%	nd	67%	75%	nd	67%	nd	nd	nd
Spec 4	72%	nd	71%	72%	nd	71%	nd	nd	nd
Cutoff 5	2.98	nd	3.41	2.98	nd	3.41	nd	nd	nd
Sens 5	75%	nd	67%	75%	nd	67%	nd	nd	nd
Spec 5	80%	nd	81%	80%	nd	81%	nd	nd	nd
Cutoff 6	5.21	nd	6.93	5.21	nd	6.93	nd	nd	nd
Sens 6	62%	nd	50%	62%	nd	50%	nd	nd	nd
Spec 6	91%	nd	90%	91%	nd	90%	nd	nd	nd
OR Quart 2	>0	nd	>0	>0	nd	>0	nd	nd	nd
p Value	<na	nd	<na	<na	nd	<na	nd	nd	nd
95% CI of	>na	nd	>na	>na	nd	>na	nd	nd	nd
OR Quart2	na	nd	na	na	nd	na	nd	nd	nd
OR Quart 3	>2.1	nd	>2.3	>2.1	nd	>2.3	nd	nd	nd
p Value	<0.56	nd	<0.52	<0.56	nd	<0.52	nd	nd	nd
95% CI of	>0.18	nd	>0.19	>0.18	nd	>0.19	nd	nd	nd
OR Quart3	na	nd	na	na	nd	na	nd	nd	nd
OR Quart 4	>8.0	nd	>5.2	>8.0	nd	>5.2	nd	nd	nd
p Value	<0.066	nd	<0.16	<0.066	nd	<0.16	nd	nd	nd
95% CI of	>0.87	nd	>0.52	>0.87	nd	>0.52	nd	nd	nd
OR Quart4	na	nd	na	na	nd	na	nd	nd	nd

Tumor necrosis factor receptor superfamily member 10B

sCr or UO	0hr prior to AKI stage		24hr prior to AKI stage		48hr prior to AKI stage	
	Cohort 1	Cohort 2	Cohort 1	Cohort 2	Cohort 1	Cohort 2
Median	1.00E-9	0.0138	1.00E-9	0.0129	nd	nd
Average	0.00697	0.0265	0.00697	0.0259	nd	nd
Stdev	0.0202	0.0355	0.0202	0.0359	nd	nd
p(t-test)		0.020		0.024	nd	nd
Min	1.00E-9	1.00E-9	1.00E-9	1.00E-9	nd	nd
Max	0.114	0.108	0.114	0.108	nd	nd
n (Samp)	72	8	72	8	nd	nd
n (Patient)	72	8	72	8	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
AUC	0.81	nd	nd	0.79	nd	nd	nd	nd	nd
SE	0.095	nd	nd	0.098	nd	nd	nd	nd	nd
p	0.0012	nd	nd	0.0031	nd	nd	nd	nd	nd
nCohort 1	72	nd	nd	72	nd	nd	nd	nd	nd
nCohort 2	8	nd	nd	8	nd	nd	nd	nd	nd
Cutoff 1	0.00462	nd	nd	0.00438	nd	nd	nd	nd	nd
Sens 1	75%	nd	nd	75%	nd	nd	nd	nd	nd
Spec 1	79%	nd	nd	79%	nd	nd	nd	nd	nd
Cutoff 2	0.00438	nd	nd	0.00207	nd	nd	nd	nd	nd
Sens 2	88%	nd	nd	88%	nd	nd	nd	nd	nd

	0hr prior to AKI stage			24hr prior to AKI stage			48hr prior to AKI stage		
	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only	sCr or UO	sCr only	UO only
Spec 2	79%	nd	nd	65%	nd	nd	nd	nd	nd
Cutoff 3	0	nd	nd	0	nd	nd	nd	nd	nd
Sens 3	100%	nd	nd	100%	nd	nd	nd	nd	nd
Spec 3	0%	nd	nd	0%	nd	nd	nd	nd	nd
Cutoff 4	0.00274	nd	nd	0.00274	nd	nd	nd	nd	nd
Sens 4	88%	nd	nd	75%	nd	nd	nd	nd	nd
Spec 4	71%	nd	nd	71%	nd	nd	nd	nd	nd
Cutoff 5	0.00507	nd	nd	0.00507	nd	nd	nd	nd	nd
Sens 5	62%	nd	nd	50%	nd	nd	nd	nd	nd
Spec 5	81%	nd	nd	81%	nd	nd	nd	nd	nd
Cutoff 6	0.0124	nd	nd	0.0124	nd	nd	nd	nd	nd
Sens 6	50%	nd	nd	50%	nd	nd	nd	nd	nd
Spec 6	90%	nd	nd	90%	nd	nd	nd	nd	nd
OR Quart 2	>1.1	nd	nd	>1.1	nd	nd	nd	nd	nd
p Value	<0.97	nd	nd	<0.97	nd	nd	nd	nd	nd
95% CI of	>0.061	nd	nd	>0.061	nd	nd	nd	nd	nd
OR Quart2	na	nd	nd	na	nd	nd	nd	nd	nd
OR Quart 3	>2.2	nd	nd	>2.2	nd	nd	nd	nd	nd
p Value	<0.53	nd	nd	<0.53	nd	nd	nd	nd	nd
95% CI of	>0.19	nd	nd	>0.19	nd	nd	nd	nd	nd
OR Quart3	na	nd	nd	na	nd	nd	nd	nd	nd
OR Quart 4	>6.7	nd	nd	>6.7	nd	nd	nd	nd	nd
p Value	<0.098	nd	nd	<0.098	nd	nd	nd	nd	nd
95% CI of	>0.70	nd	nd	>0.70	nd	nd	nd	nd	nd
OR Quart4	na	nd	nd	na	nd	nd	nd	nd	nd

[0163] While the invention has been described and exemplified in sufficient detail for those skilled in this art to make and use it, various alternatives, modifications, and improvements should be apparent without departing from the spirit and scope of the invention. The examples provided herein are representative of preferred embodiments, are exemplary, and are not intended as limitations on the scope of the invention. Modifications therein and other uses will occur to those skilled in the art. These modifications are encompassed within the spirit of the invention and are defined by the scope of the claims.

[0164] It will be readily apparent to a person skilled in the art that varying substitutions and modifications may be made to the invention disclosed herein without departing from the scope and spirit of the invention.

[0165] All patents and publications mentioned in the specification are indicative of the levels of those of ordinary skill in the art to which the invention pertains. All patents and publications are herein incorporated by reference to the same extent as if each individual publication was specifically and individually indicated to be incorporated by reference.

[0166] The invention illustratively described herein suitably may be practiced in the absence of any element or elements, limitation or limitations which is not specifically disclosed herein. Thus, for example, in each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms. The terms and expressions which have been employed are used as terms of description and not of limitation, and there is no intention that in the use of such terms and expressions of excluding any equivalents of the features shown and described or portions thereof, but it is recognized that various modifications are possible within the scope of the invention claimed. Thus, it should be understood that although the present invention has been specifically disclosed by preferred embodiments and optional features, modification and variation of the concepts herein disclosed may be resorted to by those skilled in the art, and that such modifications and variations are considered to be within the scope of this invention as defined by the appended claims.

[0167] Other embodiments are set forth within the following claims.

We claim:

1. A method for evaluating renal status in a subject, comprising:

performing one or more assaysconfigured to detect one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, Carcinoembryonic antigen-related cell adhesion molecule 5, and Cellular tumor antigen p53 on a body fluid sample obtained from the subject to provide an assay result; and

correlating the assay result(s) to the renal status of the subject.

2. A method according to claim 1, wherein said correlation step comprises correlating the assay result(s) to one or more of risk stratification, diagnosis, staging, classifying and monitoring of the renal status of the subject.

3. A method according to claim 1, wherein said correlating step comprises assigning a likelihood of one or more future changes in renal status to the subject based on the assay result(s).

4. A method according to claim 1, wherein said one or more future changes in renal status comprise one or more of a future injury to renal function, future reduced renal function, future improvement in renal function, and future acute renal failure (ARF).

5. A method according to claim 1, wherein the subject is not in acute renal failure.

6. A method according to claim 1, wherein the subject has not experienced a 1.5-fold or greater increase in serum creatinine over a baseline value determined prior to the time at which the body fluid sample is obtained.

7. A method according to claim 1, wherein the subject has a urine output of at least 0.5 ml/kg/hr over the 12 hours preceding the time at which the body fluid sample is obtained.

8. A method according to claim 1, wherein the subject has not experienced an increase of 0.3 mg/dL or greater in serum creatinine over a baseline value determined prior to the time at which the body fluid sample is obtained.

9. A method according to claim 1, wherein the subject (i) has not experienced a 1.5-fold or greater increase in serum creatinine over a baseline value determined prior to the time at which the body fluid sample is obtained, (ii) has a urine output of at least 0.5 ml/kg/hr over the 12 hours preceding the time at which the body fluid sample is obtained, and (iii) has not experienced an increase of 0.3 mg/dL or greater in serum creatinine over a baseline value determined prior to the time at which the body fluid sample is obtained.

10. A method according to claim 1, wherein the subject is in RIFLE stage 0 or R.

11. A method according to claim 10, wherein the subject is in RIFLE stage 0, and said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage R, I or F within 72 hours.

12. A method according to claim 10, wherein the subject is in RIFLE stage 0 or R, and said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage I or F within 72 hours.

13. A method according to claim 12, wherein the subject is in RIFLE stage 0, and said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage F within 72 hours.

14. A method according to claim 12, wherein the subject is in RIFLE stage R, and said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage I or F within 72 hours.

15. A method according to claim 1, wherein the subject is in RIFLE stage 0, R, or I, and said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage F within 72 hours.

16. A method according to claim 15, wherein the subject is in RIFLE stage I, and said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage F within 72 hours.

17. A method according to claim 11, wherein said correlating step comprises assigning likelihood that the subject will reach RIFLE stage R, I or F within 48 hours.

18. A method according to claim 12, wherein said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage I or F within 48 hours.

19. A method according to claim 13, wherein said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage I or F within 48 hours.

20. A method according to claim 17, wherein said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage F within 48 hours.

21. A method according to claim 18, wherein said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage F within 48 hours.

22. A method according to claim 19, wherein said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage F within 48 hours.

23. A method according to claim 17, wherein said correlating step comprises assigning likelihood that the subject will reach RIFLE stage R, I or F within 24 hours.

24. A method according to claim 18, wherein said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage I or F within 24 hours.

25. A method according to claim 19, wherein said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage I or F within 24 hours.

26. A method according to claim 20, wherein said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage F within 24 hours.

27. A method according to claim 21, wherein said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage F within 24 hours.

28. A method according to claim 22, wherein said correlating step comprises assigning a likelihood that the subject will reach RIFLE stage F within 24 hours.

29. A method according to claim 1, wherein said assay result(s) comprise one or more of:

a measured urine or plasma concentration of Tumor necrosis factor receptor superfamily member 10B,

a measured urine or plasma concentration of Cadherin-16,

a measured urine or plasma concentration of Caspase-9,

a measured urine or plasma concentration of Bcl2 antagonist of cell death,

a measured urine or plasma concentration of Caspase-1,

a measured urine or plasma concentration of Cadherin-1,

a measured urine or plasma concentration of Poly [ADP-ribose] polymerase 1,

a measured urine or plasma concentration of Cyclin-dependent kinase inhibitor 1,

a measured urine or plasma concentration of Cadherin-5,

a measured urine or plasma concentration of Myoglobin,

a measured urine or plasma concentration of Apolipoprotein A-II,

a measured urine or plasma concentration of Mucin-16,

a measured urine or plasma concentration of Carcinoembryonic antigen-related cell adhesion molecule 5, or

a measured urine or plasma concentration of Cellular tumor antigen p53

and said correlation step comprises comparing each measured concentration to a corresponding threshold concentration, and

for a positive going marker, assigning an increased likelihood of progression to a worsening RIFLE stage to the subject, relative to the subject's current RIFLE stage, when the measured concentration is above the threshold, or assigning a decreased likelihood of progressing to a worsening RIFLE stage to the subject, relative to the subject's current RIFLE stage, when the measured concentration is below the threshold, or

for a negative going marker, assigning a decreased likelihood of progression to a worsening RIFLE stage to the subject, relative to the subject's current RIFLE stage, when the measured concentration is above the threshold, or assigning an increased likelihood of progressing to a worsening RIFLE stage to the subject, relative to the subject's current RIFLE stage, when the measured concentration is below the threshold.

30. A method according to claim 1, wherein said assay result(s) comprise one or more of:

a measured urine or plasma concentration of Tumor necrosis factor receptor superfamily member 10B,

a measured urine or plasma concentration of Cadherin-16,

a measured urine or plasma concentration of Caspase-9,

a measured urine or plasma concentration of Bcl2 antagonist of cell death,

a measured urine or plasma concentration of Caspase-1,

a measured urine or plasma concentration of Cadherin-1,

a measured urine or plasma concentration of Poly [ADP-ribose] polymerase 1,

a measured urine or plasma concentration of Cyclin-dependent kinase inhibitor 1,

a measured urine or plasma concentration of Cadherin-5,

a measured urine or plasma concentration of Myoglobin,

a measured urine or plasma concentration of Apolipoprotein A-II,

a measured urine or plasma concentration of Mucin-16,

a measured urine or plasma concentration of Carcinoembryonic antigen-related cell adhesion molecule 5, or

a measured urine or plasma concentration of Cellular tumor antigen p53

and said correlation step comprises comparing each measured concentration to a corresponding threshold concentration, and

for a positive going marker, assigning an increased likelihood of progressing to a need for renal replacement therapy to the subject when the measured concentration is above the threshold, or assigning a decreased likelihood of progressing to a need for renal replacement therapy when the measured concentration is below the threshold, or

for a negative going marker, assigning a decreased likelihood of progressing to a need for renal replacement therapy to the subject when the measured concentration is above the threshold, or assigning an increased likelihood of progressing to a need for renal replacement therapy when the measured concentration is below the threshold.

31. A method according to claim 5, wherein said assay result(s) comprise one or more of:

a measured urine or plasma concentration of Tumor necrosis factor receptor superfamily member 10B,

a measured urine or plasma concentration of Cadherin-16,

a measured urine or plasma concentration of Caspase-9,

a measured urine or plasma concentration of Bcl2 antagonist of cell death,

a measured urine or plasma concentration of Caspase-1,

a measured urine or plasma concentration of Cadherin-1,

a measured urine or plasma concentration of Poly [ADP-ribose] polymerase 1,

a measured urine or plasma concentration of Cyclin-dependent kinase inhibitor 1,

a measured urine or plasma concentration of Cadherin-5,

a measured urine or plasma concentration of Myoglobin,

a measured urine or plasma concentration of Apolipoprotein A-II,

a measured urine or plasma concentration of Mucin-16,

a measured urine or plasma concentration of Carcinoembryonic antigen-related cell adhesion molecule 5, or

a measured urine or plasma concentration of Cellular tumor antigen p53

and said correlation step comprises comparing each measured concentration to a corresponding threshold concentration, and

for a positive going marker, assigning an increased likelihood of progressing to acute renal failure when the measured concentration is above the threshold, or assigning a decreased likelihood of progressing to acute renal failure to the subject when the measured concentration is below the threshold, or

for a negative going marker, assigning a decreased likelihood of progressing to acute renal failure when the measured concentration is above the threshold, or assigning an increased likelihood of progressing to acute renal failure to the subject when the measured concentration is below the threshold.

32. A method according to claim 11, wherein said assay result(s) comprise one or more of:

a measured urine or plasma concentration of Tumor necrosis factor receptor superfamily member 10B,

a measured urine or plasma concentration of Cadherin-16,

a measured urine or plasma concentration of Caspase-9,

a measured urine or plasma concentration of Bcl2 antagonist of cell death,

a measured urine or plasma concentration of Caspase-1,

a measured urine or plasma concentration of Cadherin-1,

a measured urine or plasma concentration of Poly [ADP-ribose] polymerase 1,

a measured urine or plasma concentration of Cyclin-dependent kinase inhibitor 1,

a measured urine or plasma concentration of Cadherin-5,

a measured urine or plasma concentration of Myoglobin,

a measured urine or plasma concentration of Apolipoprotein A-II,

a measured urine or plasma concentration of Mucin-16,

a measured urine or plasma concentration of Carcinoembryonic antigen-related cell adhesion molecule 5, or

a measured urine or plasma concentration of Cellular tumor antigen p53

and said correlation step comprises comparing each measured concentration to a corresponding threshold concentration, and

for a positive going marker, assigning an increased likelihood of progressing to RIFLE stage R, I or F to the subject, when the measured concentration is above the threshold, or assigning a decreased likelihood of progressing to RIFLE stage R, I or F to the subject when the measured concentration is below the threshold, or

for a negative going marker, assigning a decreased likelihood of progressing to RIFLE stage R, I or F to the subject, when the measured concentration is above the threshold, or assigning an increased likelihood of progressing to RIFLE stage R, I or F to the subject when the measured concentration is below the threshold.

33. A method according to claim 12, wherein said assay result(s) comprise one or more of:

a measured urine or plasma concentration of Tumor necrosis factor receptor superfamily member 10B,

a measured urine or plasma concentration of Cadherin-16,

a measured urine or plasma concentration of Caspase-9,

a measured urine or plasma concentration of Bcl2 antagonist of cell death,

a measured urine or plasma concentration of Caspase-1,

a measured urine or plasma concentration of Cadherin-1,

a measured urine or plasma concentration of Poly [ADP-ribose] polymerase 1,

a measured urine or plasma concentration of Cyclin-dependent kinase inhibitor 1,

a measured urine or plasma concentration of Cadherin-5,

a measured urine or plasma concentration of Myoglobin,

a measured urine or plasma concentration of Apolipoprotein A-II,

a measured urine or plasma concentration of Mucin-16,

a measured urine or plasma concentration of Carcinoembryonic antigen-related cell adhesion molecule 5, or

a measured urine or plasma concentration of Cellular tumor antigen p53

and said correlation step comprises comparing each measured concentration to a corresponding threshold concentration, and

for a positive going marker, assigning an increased likelihood of progressing to RIFLE stage I or F to the subject, when the measured concentration is above the threshold, or assigning a decreased likelihood of progressing to RIFLE stage I or F to the subject when the measured concentration is below the threshold, or

for a negative going marker, assigning a decreased likelihood of progressing to RIFLE stage I or F to the subject, when the measured concentration is above the threshold, or assigning an increased likelihood of progressing to RIFLE stage I or F to the subject when the measured concentration is below the threshold.

34. A method according to claim 13, wherein said assay result(s) comprise one or more of:

a measured urine or plasma concentration of Tumor necrosis factor receptor superfamily member 10B,

a measured urine or plasma concentration of Cadherin-16,

a measured urine or plasma concentration of Caspase-9,

a measured urine or plasma concentration of Bcl2 antagonist of cell death,

a measured urine or plasma concentration of Caspase-1,

a measured urine or plasma concentration of Cadherin-1,

a measured urine or plasma concentration of Poly [ADP-ribose] polymerase 1,

a measured urine or plasma concentration of Cyclin-dependent kinase inhibitor 1,

a measured urine or plasma concentration of Cadherin-5,

a measured urine or plasma concentration of Myoglobin,

a measured urine or plasma concentration of Apolipoprotein A-II,

a measured urine or plasma concentration of Mucin-16,

a measured urine or plasma concentration of Carcinoembryonic antigen-related cell adhesion molecule 5, or

a measured urine or plasma concentration of Cellular tumor antigen p53

and said correlation step comprises comparing each measured concentration to a corresponding threshold concentration, and

for a positive going marker, assigning an increased likelihood of progressing to RIFLE stage F to the subject, when the measured concentration is above the threshold, or assigning a decreased likelihood of progressing to RIFLE stage I or F to the subject when the measured concentration is below the threshold, or

for a negative going marker, assigning a decreased likelihood of progressing to RIFLE stage F to the subject, when the measured concentration is above the threshold, or assigning an increased likelihood of progressing to RIFLE stage I or F to the subject when the measured concentration is below the threshold.

35. A method according to claim 14, wherein said assay result(s) comprise one or more of:

a measured urine or plasma concentration of Tumor necrosis factor receptor superfamily member 10B,

a measured urine or plasma concentration of Cadherin-16,

a measured urine or plasma concentration of Caspase-9,

a measured urine or plasma concentration of Bcl2 antagonist of cell death,

a measured urine or plasma concentration of Caspase-1,

a measured urine or plasma concentration of Cadherin-1,

a measured urine or plasma concentration of Poly [ADP-ribose] polymerase 1,

a measured urine or plasma concentration of Cyclin-dependent kinase inhibitor 1,

a measured urine or plasma concentration of Cadherin-5,

a measured urine or plasma concentration of Myoglobin,

a measured urine or plasma concentration of Apolipoprotein A-II,

a measured urine or plasma concentration of Mucin-16,

a measured urine or plasma concentration of Carcinoembryonic antigen-related cell adhesion molecule 5, or

a measured urine or plasma concentration of Cellular tumor antigen p53

and said correlation step comprises comparing each measured concentration to a corresponding threshold concentration, and

for a positive going marker, assigning an increased likelihood of progressing to RIFLE stage F to the subject, when the measured concentration is above the threshold, or assigning a decreased likelihood of progressing to RIFLE stage I or F to the subject when the measured concentration is below the threshold, or

for a negative going marker, assigning a decreased likelihood of progressing to RIFLE stage F to the subject, when the measured concentration is above the threshold, or assigning an increased likelihood of progressing to RIFLE stage I or F to the subject when the measured concentration is below the threshold.

36. A method according to claim 15, wherein said assay result(s) comprise one or more of:

a measured urine or plasma concentration of Tumor necrosis factor receptor superfamily member 10B,

a measured urine or plasma concentration of Cadherin-16,

a measured urine or plasma concentration of Caspase-9,

a measured urine or plasma concentration of Bcl2 antagonist of cell death,

a measured urine or plasma concentration of Caspase-1,

a measured urine or plasma concentration of Cadherin-1,

a measured urine or plasma concentration of Poly [ADP-ribose] polymerase 1,

a measured urine or plasma concentration of Cyclin-dependent kinase inhibitor 1,

a measured urine or plasma concentration of Cadherin-5,

a measured urine or plasma concentration of Myoglobin,

a measured urine or plasma concentration of Apolipoprotein A-II,

a measured urine or plasma concentration of Mucin-16,

a measured urine or plasma concentration of Carcinoembryonic antigen-related cell adhesion molecule 5, or

a measured urine or plasma concentration of Cellular tumor antigen p53

and said correlation step comprises comparing each measured concentration to a corresponding threshold concentration, and

for a positive going marker, assigning an increased likelihood of progressing to RIFLE stage F to the subject, when the measured concentration is above the threshold, or assigning a decreased likelihood of progressing to RIFLE stage F to the subject when the measured concentration is below the threshold, or

for a negative going marker, assigning a decreased likelihood of progressing to RIFLE stage F to the subject, when the measured concentration is above the threshold, or assigning an increased likelihood of progressing to RIFLE stage F to the subject when the measured concentration is below the threshold.

37. A method according to claim 16, wherein said assay result(s) comprise one or more of:

a measured urine or plasma concentration of Tumor necrosis factor receptor superfamily member 10B,

a measured urine or plasma concentration of Cadherin-16,

a measured urine or plasma concentration of Caspase-9,

a measured urine or plasma concentration of Bcl2 antagonist of cell death,

a measured urine or plasma concentration of Caspase-1,

a measured urine or plasma concentration of Cadherin-1,

a measured urine or plasma concentration of Poly [ADP-ribose] polymerase 1,

a measured urine or plasma concentration of Cyclin-dependent kinase inhibitor 1,

a measured urine or plasma concentration of Cadherin-5,

a measured urine or plasma concentration of Myoglobin,

a measured urine or plasma concentration of Apolipoprotein A-II,

a measured urine or plasma concentration of Mucin-16,

a measured urine or plasma concentration of Carcinoembryonic antigen-related cell adhesion molecule 5, or

a measured urine or plasma concentration of Cellular tumor antigen p53

and said correlation step comprises comparing each measured concentration to a corresponding threshold concentration, and

for a positive going marker, assigning an increased likelihood of progressing to RIFLE stage F to the subject, when the measured concentration is above the threshold, or assigning a decreased likelihood of progressing to RIFLE stage F to the subject when the measured concentration is below the threshold, or

for a negative going marker, assigning a decreased likelihood of progressing to RIFLE stage F to the subject, when the measured concentration is above the threshold, or assigning an increased likelihood of progressing to RIFLE stage F to the subject when the measured concentration is below the threshold.

38. A method according to claim 1, wherein the subject is selected for evaluation of renal status based on the pre-existence in the subject of one or more known risk factors for prerenal, intrinsic renal, or postrenal ARF.

39. A method according to claim 1, wherein the subject is selected for evaluation of renal status based on an existing diagnosis of one or more of congestive heart failure, preeclampsia, eclampsia, diabetes mellitus, hypertension, coronary artery disease, proteinuria, renal insufficiency, glomerular filtration below the normal range, cirrhosis, serum creatinine above the normal range, sepsis, injury to renal function, reduced renal function, or ARF, or based on undergoing or having undergone major vascular surgery, coronary artery bypass, or other cardiac surgery, or based on exposure to NSAIDs, cyclosporines, tacrolimus, aminoglycosides, foscarnet, ethylene glycol, hemoglobin,

myoglobin, ifosfamide, heavy metals, methotrexate, radiopaque contrast agents, or streptozotocin.

40. Measurement of IGFBP7 for the diagnosis, risk stratification, prognosis, classifying and monitoring of renal status of a subject not receiving renal replacement therapy.

41. Measurement of one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, Carcinoembryonic antigen-related cell adhesion molecule 5, and Cellular tumor antigen p53 for the diagnosis, risk stratification, prognosis, classifying and monitoring of renal status of a subject not in acute renal failure.

42. Measurement of one or more biomarkers selected from the group consisting of Tumor necrosis factor receptor superfamily member 10B, Cadherin-16, Caspase-9, Bcl2 antagonist of cell death, Caspase-1, Cadherin-1, Poly [ADP-ribose] polymerase 1, Cyclin-dependent kinase inhibitor 1, Cadherin-5, Myoglobin, Apolipoprotein A-II, Mucin-16, Carcinoembryonic antigen-related cell adhesion molecule 5, and Cellular tumor antigen p53 for assigning an increased likelihood of progressing to a worsening RIFLE stage to a subject, relative to the subject's current RIFLE stage.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 10/46910

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - G01N 33/53 (2010.01)
USPC - 435/7.1
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
USPC: 435/7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 424/145.1; 435/6, 7.1; 514/2, 12 (see search terms below)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Electronic data bases searched: PubWEST (EPAB, PGPB, USPT, JPAB); Google Scholar; Search terms: Kidney, renal, acute kidney injury (AKI) (also known as acute renal failure (ARF)), biomarker, RIFLE, status, diagnosis, staging, monitoring; TNFSFR10B, caspase 1 or 9 (CASP1 or CASP9), cadherin 1,5 or 16 (CDH1, CDH5, CDH16), APOA2, Bcl2, MUC16, CEACAM5,

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---- Y ----- A	US 7,141,382 B1 (PARIKH et al.) 28 November 2006 (28.11.2006) especially col 2 ln 40-44; col 4, ln 45-50; col 8, ln 36-41, ln 45-56; col 17, ln 14-26; col 19, ln 23-29, ln 45-47; col 20 ln 40-43	1-9, 30-31, 38, 41 ---------- 39 ---------- 10-29, 32-37, 42
X	TAULAN et al. Comprehensive analysis of the renal transcriptional response to acute uranyl nitrate exposure. BMC Genomics [online] 11 January 2006 [retrieved 29 September 2010] Vol 7, No 2, pp 1-14; especially pg 9 right col para 2; Available on the internet: <URL: http://www.biomedcentral.com/1471-2164/7/2> especially pg 9 right col para 2	40
Y	PARIKH et al. Urinary IL-18 is an early predictive biomarker of acute kidney injury after cardiac surgery. Kidney Internat, 2006, Vol 70, No 1, pp 199-203; especially abstract	39
A	KELLUM. Acute Kidney Injury. Crit Care Med, 2008, Vol 36, No 4, Suppl PP S141-S145; especially pg S143 fig 1, S144 center col para 2.	10-29, 32-37, 42

☒ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 September 2010 (21.09.2010)	18 NOV 2010
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (July 2009)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 10/46910

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P/A	WO 2010/048347 A2 (ANDERBERG et al.) 29 April 2010 (29.04.2010) especially para [0035]	10-29, 32-37, 42
A	COCA et al. Biomarkers for the diagnosis and risk stratification of acute kidney injury: A systematic review. Kidney Internat, 2008, Vol 73, No 9, pp 1008-16	1-42
A	MELNIKOV et al. Impaired IL-18 processing protects caspase-1-deficient mice from ischemic acute renal failure. J Clin Invest, 2001 Vol 107, No 9, pp 1145-1152	1-9, 30-31, 38, 41