KIDNEY DISEASE BIOMARKERS FOR DIAGNOSIS, PROGNOSIS OR CLINICAL TRIALS MONITORING

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T-016375

Technology Description

Researchers in Prof. Ying "Maggie" Chen's laboratory have identified three sensitive, urine-based biomarkers of kidney disease that could be used for non-invasive, early detection and clinical trials monitoring. In particular, these mechanistic biomarkers are associated with the endoplasmic reticulum (ER) stress which plays a pathogenic role in a range of renal disorders (e.g., focal segmental glomerulosclerosis, Alport syndrome, acute kidney injury and diabetic nephropathy).

ER stress activates the unfolded protein response (UPR) which results kidney cell (podocyte) injury and progresses to end stage renal failure. Therefore, it is imperative to detect ER stress in the early stage of disease to enable early intervention, prevent kidney damage and enable precision therapy. This technology provides three different protein biomarkers that can be found in patient urine prior to clinical manifestation of the disorder or significant proteinuria. These biomarkers could enable early diagnosis/prognosis to quickly identify patients at high risk for disease progression thereby expediting clinical decision making and early treatment. In addition, these biomarkers could be used in clinical trials to monitor treatment or guide development of ER stress-modulating drugs, dramatically reducing the amount of follow-up time to determine treatment efficacy.

Stage of Research

The inventors have validated three different mechanistic biomarkers in animal models and samples from human patients. Each of the markers is excreted in urine and identifies ER stress before clinical manifestations of the corresponding kidney disease. The inventors have also shown the relationship between biomarker concentration and severity of ER stress-related kidney injury.

Associated Technologies

- **WUSTL Technology T-014414:** MANF biomarker (mesencephalic astrocyte-derived neurotrophic factor; also known as ARMET – arginine-rich, mutated in early stage tumor)
- **WUSTL Technology T-016375**: BiP biomarker (binding immunoglobulin protein; also known as GRP-78, HSPA5, or Byun1)
- **WUSTL Technology T-016376**: CRELD2 biomarker (Cysteine-rich with EGF-like domains 2)
- **WUSTL Technology T-018591**: Related invention for small molecule drug candidates to treat ER stress-related kidney diseases

Applications

- **Biomarkers for kidney disease –** mechanistic markers for ER stress-related diseases - such as focal segmental glomerulosclerosis (FSGS), Alport syndrome, membranous nephropathy, acute

kidney injury (AKI), congenital nephrotic syndrome (CNS) and diabetic nephropathy (DN) – with end user applications in:

- **diagnostics/prognostics** – predict high risk patients, monitor disease progression, identify patients for targeted therapy/precision medicine
- **clinical trials –** patient stratification, surrogate marker and treatment monitoring

Key Advantages

- **Early detection -** biomarkers detect ER stress which occurs before significant proteinuria and prior to loss of kidney function
- **Non-invasive –** urine-based biomarkers avoid blood draw or kidney biopsy
- **Sensitive, mechanistic markers:**
  - biomarkers are associated with the central underlying pathogenesis of the disorder
  - biomarkers effectively discriminate between patients with ER stress-related kidney diseases and controls
  - higher concentrations of the biomarkers indicate worse disease

Publications

- Kim, Yeawon, et al. "Elevated urinary CRELD2 is associated with endoplasmic reticulum stress–mediated kidney disease." *JCI insight* 2.23 (2017).
- Kim, Yeawon, Sun-Ji Park, and Ying Maggie Chen. "Mesencephalic astrocyte-derived neurotrophic factor (MANF), a new player in endoplasmic reticulum diseases: structure, biology, and therapeutic roles." *Translational Research* 188 (2017): 1-9.
- Kim, Yeawon, et al. "Mesencephalic Astrocyte–Derived Neurotrophic Factor as a Urine Biomarker for Endoplasmic Reticulum Stress–Related Kidney Diseases." *Journal of the american society of nephrology* 27.10 (2016): 2974-2982.

Patents

- Methods of detecting biomarkers of endoplasmic reticulum (ER) stress-associated kidney diseases (U.S. Patent No. 10,156,564)
- Additional patent application pending

Website

- Chen Lab