Early Biomarkers of Nephropathy in Type 2 Diabetes

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Abstract

Identification of chronic disease biomarkers is difficult in heterogeneous human populations and animal models are unlikely to yield biomarkers that readily translate into the clinic. Accordingly, human disease biomarker investigations should begin with well-defined and well-characterized human populations that are predisposed to diseases for which early detection would be beneficial. One such population is the Pima Indians of the Gila River Indian Community. This group of American Indians has very high rates of type 2 diabetes mellitus (T2DM) and diabetic nephropathy (DN). These diseases have been exceptionally well characterized in a longitudinal study over the past 43 years. Banked blood and urine specimens are available for thousands of subjects from serial examinations throughout the study, making it possible to select specimens for assay that pre-date the onset of clinically recognized disease. Such feasibility and proof of principle studies may yield the foundation for the metabolomic investigation of other diseases, including cancer. Early biomarkers of DN using urine samples collected from the well-characterized and well-defined Pima Indian population, in which T2DM and DN are common. Using cutting-edge ultra-performance liquid chromatography (UPLC) coupled with time-of-flight mass spectrometry (TOFMS) and sophisticated chemometric and multivariate data analysis, endogenous urinary biomarkers are now being identified, characterized, and validated in retrospective and prospective studies. Ultimately, urinary biomarkers will be correlated with urinary albumin excretion as well as other indicators of DN such as blood pressure serum creatinine concentration, and estimated glomerular filtration rate.

Figure 3. DN biomarker mining using Volcano plots. Threshold values were as follows: p-value<0.01, FC>2. Red circles indicate potentially informative variables.