PREDICTION OF PROGRESSION OF DIABETIC NEPHROPATHY IN A SMALL SET OF PATIENTS BY ARTIFICIAL NEURAL NETWORKS AND PROTEOMIC ANALYSIS

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Diabetes is the leading cause of renal failure in the US. Although urine albumin has been used for many years as the major prognostic marker to predict progression of diabetic nephropathy, it is neither sensitive nor specific. New markers are necessary to guide therapy and predict progression of nephropathy in patients with diabetes. We hypothesize that changes within the glomerular permeability barrier occur in a predictable pattern and occur early in the progression to diabetic nephropathy which result in different characteristics of proteinuria. In order to test our hypothesis that changes in the size and charge permeability of the glomerular permeability barrier precede and can predict progression of diabetic nephropathy, we used seven patients with whom we had follow up data about progression to dialysis. Urine proteins were separated and matched across 2D gels and the abundance of all visible proteins was determined. The duration between the collection of urine and initiation of dialysis was used as the outcome measure. Ranked protein abundances were used to train an Artificial Neural Network (ANN). For each patient the ANN predicted the number of months until the patient would require dialysis. The predicted duration was plotted against the observed duration ($R^2 = 0.88$). This demonstrates that in this relatively small dataset, there is a good correlation between the pattern of protein abundances and the length of time until the patient started dialysis. This correlation was found in spite of differences in medications and blood pressure that are also associated with changes in glomerular permeability in diabetic nephropathy. Ten proteins contributed the greatest amount of sensitivity to the assay. We identified six of the ten proteins using mass spectrometry. All six are plasma proteins that appear in the urine, are filtered at the glomerulus, and most are known to be glycosylated in the plasma. This further supports our hypothesis that differential filtration of glomerular proteins can be used to predict the renal outcome of patients with diabetic nephropathy. This observation demonstrates the potential of proteomics and ANNs to discern relationships between glomerular permeability and renal disease. Validation of the findings will require a larger group of patients.