L-FABP and TGF-β1 as Biomarkers of Lupus Nephritis

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Introduction: The pathogenesis of systemic lupus erythematosus (SLE) is poorly understood, with lupus nephritis (LN) continuing to lead to significant morbidity and mortality. Current treatments could be used more effectively and with less toxicity if LN activity, flare severity, response to treatment, and prognosis were able to be predicted with greater accuracy. Hence, there is a dire need for high-quality LN biomarkers, i.e. laboratory measures that are easy to measure, of high sensitivity plus specificity, and anticipate the course of LN and its responsiveness to therapy early. L-FABP (liver fatty-acid-binding protein) and TGF-β1 (transforming growth factor – beta 1) have been identified as potential urinary biomarkers of LN. We investigated concerns of the clinical efficacy of these biomarkers by examining their concentrations in patients with various stages of LN as well as their resilience when placed in frozen storage.

Methods: Urine samples were collected at Cincinnati Children's Hospital from juvenile SLE patients with no history of LN, inactive LN, alnd active LN and separated into three aliquots. Fresh urine sample aliquots were tested within 24 hours of collection to determine concentrations of L-FABP and TGF-β1. Aliquots undergoing one freeze-thaw cycle and two freeze-thaw cycles were tested at a later date to determine concentrations of L-FABP and TGF-β1. CMIC Human L-FABP Assay Kits were used for testing L-FABP concentrations. R&D Systems Quantikine® Human TGF-β1 ELISA kits were used for testing TGF-β1 concentrations.

Results: L-FABP and TGF-β1 concentrations failed to indicate any statistical associations between samples collected from patients with no history of LN, inactive LN, and active LN ($p=.495$, $p=.451$). Both L-FABP and TGF-β1 concentrations displayed high variance within these sample populations. L-FABP and TGF-β1 concentrations exhibited high resiliency between fresh samples, samples undergoing one freeze-thaw cycle, and samples undergoing two freeze-thaw cycles ($p=.995$, $p=.876$). Both L-FABP and TGF-β1 concentrations exhibited low average coefficient of variation between storage modalities (CV=9.68%, CV=21.85%).

Conclusions: Initial evidence was obtained about the clinical efficacy of L-FABP and TGF-β1 as urinary biomarkers of LN. Both L-FABP and TGF-β1 concentrations displayed high variability and little statistical association between patient pathologies, indicating questionable clinical efficacy in regards to early diagnosis and comparison between patients. However, both L-FABP and TGF-β1 concentrations exhibited remarkable resiliency in frozen storage. This resistance to degradation paves the way for the usage of considerable databases of frozen urine samples in future studies, circumventing the need for the collection of fresh urine samples. Future studies would be wise to elucidate the potential of L-FABP and TGF-β1 in terms of tracking LN patient disease progression over time.

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